Åstrand test: a comparison between patients with Parkinson's Disease and healthy controls

E.S. Horst
Studentnummer: 3331253
Eindscriptie: 10 Augustus 2011
Utrecht University, School of Clinical Health Sciences; Program Physiotherapy Science

MSc A.D. Speelman
Radboud University Nijmegen Medical Centre (RUNMC); Nijmegen Centre of Evidence Based Practice (NCEBP); Nijmegen, The Netherlands

“ONDERGETEKENDE

E.S.Horst

bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld.”

ACKNOWLEDGMENTS

The author gives warm thanks for all the subjects participated in this study. Special thanks are given to AD Speelman for her time and her coaching.

The author give thanks to GF Borm for supervising the statistical analysis, and to M Munneke and T Takken for reviewing the manuscript.

SAMENVATTING

Achtergrond: De Ziekte van Parkinson (ZvP) is een neurodegeneratieve aandoening die gekenmerkt wordt door motorische en niet-motorische symptomen. De voornaamste doodsoorzaken in de ZvP zijn respiratoire complicaties en cardiovasculaire aandoeningen. De mate van fysieke activiteit neemt bij patiënten met ZvP meer af dan bij gezonde gelijken. Daarom wordt lichaamsbeweging aanbevolen. Het is belangrijk de aerobe capaciteit te meten voordat er gestart wordt met lichaamsbeweging. Een recente studie, ParkFit studie, laat zien dat 50% van inactieve patiënten met de ZvP niet in staat was om een submaximaal test (de zogenoemde Åstrand test) te volbrengen. Het is onduidelijk of dit wordt veroorzaakt door de ziekte of door de inactieve leefstijl.

Methode: In totaal hebben 453 patiënten met de ZvP en 29 gezonde gelijken een vragenlijst over fysieke activiteit ingevuld en de Åstrand test uitgevoerd. Beide groepen werden vergeleken door middel van een onafhankelijke T-Test. Univariate analyses werden uitgevoerd om variabelen te identificeren die geassocieerd waren met een goed uitgevoerde Åstrand test.

Resultaten: Drieënvijftig procent van de patiënten met ZvP was niet in staat een goede Åstrand test uit te voeren. Bij de gezonde deelnemers was dit 14%. De gezonde deelnemers waren significant minder fysiek actief dan de patiënten met de ZvP. De regressie analyse liet zien dat body mass index, systolische bloeddruk, geslacht, leeftijd, rust hartfrequentie en de maxiamale weerstand geassocieerd waren met een goed uitgevoerde Åstrand test.

Conclusie: De mate van uitvoerbaarheid van de Åstrand test is laag bij patiënten met de ZvP. Een inactieve leefstijl is niet de belangrijkste reden voor een niet goed uitgevoerde Åstrand test. Verklarende factoren zijn niet gevonden.

Trefwoorden: Ziekte van Parkinson; Inspanningstest; Åstrand test; Inactieve leefstijl

ABSTRACT

Background: Parkinson's disease (PD) is a chronic progressive neurological disease characterized by motor and non-motor symptoms. In patients with PD the leading causes of death are respiratory complications and cardiovascular diseases. Physical activity levels decline more in patients with PD than their healthy peers. Therefore exercise has been recommended. Before starting exercise therapy measuring aerobic capacity is important. A recent study, the ParkFit study, showed that 50% of sedentary patients with PD did not accomplish a submaximal exercise test (the so called Åstrand test). It is unclear whether this is caused by the disease or by the sedentary lifestyle.

Methods: A total of 453 sedentary patients with PD and 29 age-, gender and sedentary lifestyle matched healthy subjects completed a questionnaire regarding physical activity and performed the Åstrand test. Comparisons between two groups were performed by using the Independent-Samples T-Test. Univariate analyses were performed to identify variables significantly associated with a well-performed Åstrand test.

Results: Fifty-three percent of the patients with PD failed the Åstrand test and 14% of healthy subject failed the test. Healthy subjects were significantly less active than patients with PD. The regression analysis showed that body mass index, systolic blood pressure, gender, age, resting heart rate and maximum workload were associated with a well-performed Åstrand test.

Conclusion: The feasibility of the Åstrand test is low in patients with PD. Sedentary lifestyle is not the mayor reason for not well-performing the Åstrand test. No explanatory factor for not well-performing the Åstrand test could be identified.

Key words: Parkinson's Disease; Exercise testing; Åstrand test; Sedentary lifestyle

INTRODUCTION AND RATIONALE

Parkinson's disease (PD) is a chronic progressive neurological disease characterized by motor symptoms (MS) and non-motor symptoms (NMS)(1). Although these MS and NMS cause a loss of functional abilities and a loss of independence, the leading causes of death in patients with PD are respiratory complications, such as pneumonia, and cardiovascular diseases(2,3).

Regular physical activity, fitness and exercise are important for the health of people of all ages(4). It is known that physical activity levels decline with advancing age(5,6). In patients with PD physical activity levels decline more quickly than their healthy peers(7). Physical inactivity results in a reduced exercise capacity and cardio respiratory fitness, leading to a higher risk for developing cardiovascular diseases(4,8). Therefore, in patients with PD exercise has been recommended to improve functional performance and decrease cardiovascular and respiratory complications(2,9).

Due to the reduced levels of physical activity in patients with PD, measuring aerobic capacity before starting exercise therapy is important. The individual's aerobic capacity or cardio respiratory endurance depends on the supply of oxygen to the working muscles(10). The maximal oxygen consumption (VO2max) one utilizes during a maximal exercise test is an objective measure of the maximal capacity of the circulatory system to deliver oxygen. Direct measurement of VO2max is only practical in a laboratory setting(2). Current maximal cycle ergometer tests to estimate VO2max are difficult for inactive adults because most of these tests are lengthy and require a high initial exercise rate(11). A short submaximal exercise test avoids these problems.

During standardized graded exercise tests heart rate (HR) and blood pressure (BP) increase as exercise intensity increases(12). Some studies report that during exercise the HR en BP in patients with PD does not always respond similarly as in healthy controls(2,13). In these studies maximal exercise tests are used. During submaximal exercise no differences are found between patients with PD and healthy controls for increase in HR and BP(13,14). Although, in a recent study (15) we observed that fifty percent of the 453 sedentary patients with PD, did not accomplish a submaximal exercise test (the so called Åstrand test)(10). Patients with PD in this study did not accomplish the test because they did not met the standardized criteria of the Åstrand test, which means the minimal required exercise heart rate was not reached, or the difference in HR between the fifth and sixth minute was greater than 5 beats per minute (BPM).

It is unclear whether this is caused by the disease or by the sedentary lifestyle of the patients. Normative data for the Åstrand test based on healthy subjects with exactly the same characteristics as the patients with PD (e.g. sedentary older subjects) are not yet available. Therefore an age-, gender and sedentary lifestyle matched healthy control group is necessary.

The aim of the current study is therefore to perform the Åstrand test in sedentary healthy subjects and compare the feasibility of the Åstrand test with our recent cohort of patients with PD from the Parkfit study.

METHODS

Subjects

From 2007 to 2009, patients diagnosed with PD were asked by their neurologist, to participate in the Parkfit study. The protocol of this study has been published elsewhere (van Nimwegen M, Speelman AD, Smulders K, Overeem S, Borm GF, Backx FJ, Bloem BR, Munneke M; ParkFit Study Group.Design and baseline characteristics of the ParkFit study, a randomized controlled trial evaluating the effectiveness of a multifaceted behavioral program to increase physical activity in Parkinson patients. BMC Neurol. 2010 Aug 19;10:70).

Eligibility criteria were: (a) PD, according to the UK Brain Bank Criteria(16); (b) age between 40 and 75 years; (c) sedentary lifestyle according to the guidelines of the American College of Sports Medicine (ACSM)(6). The ACSM recommends a moderate-intensity aerobic physical activity for a minimum of 30 minutes on five days a week or vigorous-intensity aerobic activity for a minimum of 20 minutes on three days a week(6); (d) Hoehn and Yahr (HY) ≤ 3. HY is a disability scale, range from stage I to stage V. Stage I: unilateral involvement only, usually with minimal or no functional impairment. Stage V: confinement to bed or wheelchair unless aided (17).

Exclusion criteria were: (a) unclear diagnosis (no gratifying and sustained response to dopaminergic therapy); (b) MMSE < 24; (c) unable to complete Dutch questionnaires; (d) severe co-morbidity: neurological or orthopaedic disorder severely affects daily functioning; (e) pulmonary diseases; (f) high risk of cardiovascular complications: hypertension (systole >190 and diastole > 120), Diabetes Mellitus, hyperlipaemia, Body Mass Index (BMI) >30; (g) use of ß-blockers; (h) daily institutionalized care; and (i) deep brain surgery. A total of 453 patients with PD agreed to participate.

Thirty-eight age-, gender and sedentary lifestyle matched healthy subjects were recruited from societies of chess and bridge clubs in the surrounding of Nijmegen and Zutphen, the Netherlands. The same eligibility criteria used in the Parkfit study were used for the healthy subjects. Twenty-nine subjects participated in the study. The reasons for nonparticipation (n=9) were not meeting criteria (n=5), not willing to participate (n=1), sudden illness (n=1) and unknown (n=2).

A power analysis was performed to determine the required sample size. On the basis of the results from our previous study with people with PD, we expect to find 30% of the control group that does not reach the required heart rate. To yield a minimum 0.80 power with an alpha level set at 0.05 would require enrolling at least 30 controls.

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

Measurements

Demographic data and subjects characteristics.

Before the test started the subjects had to fill in a questionnaire containing the demographic data and questions about the use of medication. Weight was measured using an electronic scale. Height was measured with the participants in standing position using a wall mounted centimetre scale. BMI was derived from weight and height (kg/m^2). Blood pressure (BP) was measured using an automatic arm sphygmomanometer. BP was taken from the left arm only.

Physical activity

Physical activity was measured with an interview based physical activity questionnaire (LAPAQ)(18). The LAPAQ is a face-to-face questionnaire that covers the frequency and duration of walking outside, bicycling, gardening, light household activities, heavy household activities, and a maximum of two sport activities during the previous two weeks(18)(19). The LAPAQ appears to be a valid and reliable instrument for classifying physical activity in older people(19).

Perceived exertion

The perceived exertion at the end of the test was recorded by the Borg's 6–20 rating of perceived exertion (RPE)-scale. The scale is constructed to increase linearly with the exercise intensity; a score of 6 indicates 'light exertion' and 20 indicates 'extreme exertion'(20,21). This scale is well validated for bicycle ergometry(22).

The Åstrand test

The Åstrand test is a submaximal exercise test for estimating the VO2max. VO2max was calculated based on heart rate (HR) response to a given submaximal workload on a bicycle ergometer using the Astrand-Rhyming nomogram(10). The Åstrand test is a safe and valid submaximal exercise test(11).

Physiotherapy students who were trained in the testing procedure carried out the tests. A Monark bicycle ergometer, model 939E (Monark, Vansbro, Sweden) was used. The HR was recorded by a Polar Pacer Tester (Polar, Favor, Kempele, Finland). Bicycle seat height was adjusted so that the knee was almost fully extended at the lowest pedal position.

The duration of the test was 6-7 minutes with a pedaling rate of 70 rounds per minute (RPM). During the first three minutes of the test the resistance was adjusted for men between 50-100 watt and for women between 50-75 Watt. The adjusted workload depended on individual's physical activities. During the last three minutes the workload was not be adjusted anymore so a steady-state HR could be reached. If the HR difference between the

end of the fifth minute and sixth minute was greater than five beats per minute (BPM) the test was prolonged with 1 minute because a steady-state was not reached. The mean HR was calculated in the last two minutes of the test. The minimum HR in the steady state should be 120 BPM. 120 BPM was based on 70-75% of the maximum HR ([220 minus age]x0.85). The test was ended with a cooling down of three minutes.

The VO2max was estimated from the Astrand-nomogram using the mean steady-state HR with a correction in age and gender (11).

The test was ended immediately by symptoms of cardio respiratory problems (Angina Pectoris, serious dyspnea, dizziness, extreme paleness, getting blue, abnormal course of HR).

The test was failed when the subject was not able to complete the 6 minutes or when the minimum heart rate of 120 BPM was not reached or when the HR varied more than 5 BPM during the last minute of the steady-state phase.

Statistical Analysis

For all variables the mean and SD were calculated. Comparisons between two groups (patients with PD and healthy subjects) were performed by using the Independent-Samples T-Test with a two-sided alpha of 0.05 and a normal distribution of the data. In case of non-normal distribution of the data, the Mann-Whitney test was used. For normative data χ^2 tests were used.

Univariate analyses were performed to identify variables significantly associated with a well-performed Åstrand test. Variables in univariate analysis with $P<0.05$ were included in binary logistic regression analysis with forward stepwise regression. All statistical analysis were performed with SPSS software, version 16.0.

RESULTS

Demographic data and subjects characteristics.

Data for the patients with PD and the healthy subjects are presented in table 1. Except for resting diastolic blood pressure and the level of physical activity ($P<0.05$) there were no statistically significant differences between patients with PD and healthy subjects. The scores of the LAPAQ showed that healthy subjects were less physical active than patients with PD.

Drop-outs

Four hundred fifty-three patients with PD performed the Åstrand test, 241 (53%) of them failed the Åstrand test because they prematurely stopped (n=53) or they did not reach the minimum heart rate (n=131) or the difference in HR between the fifth and sixth minute was greater than 5 BPM (n=57).

Twenty-nine healthy subjects performed the Åstrand test. Four of them did not complete the test, one subject because of not reaching the minimum heart rate and three subjects prematurely stopped (table 2).

The Åstrand test

The mean estimated VO_2max in healthy subjects was 33.5 (SD 8.6) mL/kg/min. The VO_2max in patients with PD was calculated for 212 patients. These 212 patients met the criteria for a well-performed Åstrand test. The mean VO_2max in these patients with PD was 21.9 (SD 5.4) mL/kg /min. In healthy subjects the VO_2max was significantly higher than in the patients with PD. The mean workload at the end of the Åstrand test did not significantly differ between the groups. For healthy subjects the mean workload was 94 Watt and for patients with PD the mean workload was 84 Watt. The mean HR calculated in the last two minutes of the test was 125 BPM in patients with PD and 138 BPM in healthy subjects ($P<0.05$).

Patients with PD reported a significantly higher perceived exertion compared with the healthy subjects. The median score in patients with PD was 15 points with an interquartile range (IQR) of 14-17. The median score in healthy subjects was 14 points with an IQR of 13-15. The scores in patients with PD ranged from 8-20 and in healthy subjects from 11-20.

Variables associate with a well-performed Åstrand test

Because 53.2% of the patients with PD did not complete the test, the baseline characteristics were compared to those patients with PD who successfully completed the Åstrand test (table 3). The people who did not complete the Åstrand test because the minimum heart rate was not reached were significantly older, the BMI was significantly higher and the resting HR and BP were significantly lower. There was also a significantly difference in disease duration and

the UPDRS motor section did also significantly differ between the groups. Patients with PD who did not complete the Åstrand test had a higher disease duration and the UPDRS was also higher. Height, level of physical activity and HY did not significantly differ between the groups.

In the PD group univariate analyses were performed to identify variables significantly associated with a well-performed Åstrand test. Variables in univariate analysis with $P<0.05$ were included in binary logistic regression analysis with forward stepwise regression

In univariate analysis, HR>120 was used as dependent variable and age, gender, BMI, resting HR, resting BP, disease duration, UPDRS motor section, HY, level of physical activity and maximum workload were used as independent variables. All independent variables were significantly associated with HR>120 except HY (table 4). The significant variables were used for performing a binary logistic regression. The binary logistic regression showed that BMI, systolic BP, gender, age, resting HR and maximum workload were associated with a well-performed Åstrand test.

DISCUSSION

The aim of the current study is therefore to perform the Åstrand test in sedentary healthy subjects and compare the feasibility of the Åstrand test with our recent cohort of patients with PD from the Parkfit study.

We observed a significant difference in the performance of the Åstrand test between PD patients compared to control subjects. In patients with PD a larger proportion of non well-performed (53.2%) Åstrand tests was observed compared to healthy controls (13.8%). This is a clinically higher percentage, suggesting that submaximal exercise testing is not feasible in almost 50% of the patients with PD and that that a sedentary lifestyle is not the mayor reason for not well-performing the Åstrand test. This is supported by the fact that the healthy subjects were significantly less physical active compared to the patients with PD.

From the patients with PD 131 did not complete the test because the minimum heart rate was not reached. In contrast with this Reuter et al.(14) tested patients with PD also on a cycle ergometer. In this study there was no statistically significant difference in heart rate increase between patients with PD and healthy controls. A difference between the study of Reuter et al. and our study is that the patients with PD used in the study of Reuter et al. were exercising for at least 2 hours/ week. Which might have resulted in a selection bias. Our results suggest that patients with PD might have a chronotropic incompetence. The origin of the chronotropic incompetence is unknown, however it might be cause by a disturbed cardiovascular regulation in patients with PD (see below).

In the current study, statistically significant differences were found between patients with PD, who did and did not well-perform the Åstrand test, for age, resting HR, BP, weight, disease duration and UPDRS. The study of Kallio et al.(23), evaluating the cardiovascular responses in patients with untreated PD, showed the presence of disturbed cardiovascular regulation. Hypokinesia/ rigidity as the first manifest of PD was associated with the most pronounced involvement of the cardiovascular responses. A possible reason for more advanced cardiovascular autonomic nervous system (ANS) dysfunction in patients with hypokinesia/ rigidity onset might be due to more advanced neuronal damage, affecting more autonomic centres or peripheral ANS structures. In that study disturbed cardiovascular regulation was not due to age. Considering above mentioned, hypokinesia/ rigidity might be due to the differences between patients with PD who did and did not well-perform the Åstrand test.

Another study evaluated the role of anti-Parkinson medication on ANS. In this study the use of anti-Parkinson medication was related to poorer autonomic responsiveness(24).

According to Werner et al.(13) there is evidence that patients with PD have a diminished HR response and abnormal cardiac reflexes(25-27). Although other studies are in discrepancy

with the finding of a decreased HR response(2,14). Reuter et al.(14) found that HR responded similarly in patients with PD and healthy controls during submaximal and maximal exercise testing.

Another important factor is the mode of an exercise test, cycle ergometer versus treadmill. In patients with PD a cycle ergometer has been the recommended mode for exercise testing due to gait and balance abnormalities(28). However, a recent study showed that exercise treatmill testing is possible for patients with PD with moderate PD (HY 1.5 to 3)(29).

A maximal exercise test in healthy subjects is preferably not performed on a cycle ergometer, as it has been demonstrated that muscular fatigue is generally achieved before maximal cardiorespiratory levels are attained (30). On the treadmill maximum oxygen uptake is 20% higher and peak HR is 5% to 20% higher than on the cycle ergometer (30).

In patients with chronic obstructive pulmonary disease (COPD) skeletal muscle dysfunction, particularly of the quadriceps, is well recognized. Man et al.(31) demonstrated in their study Quadriceps fatigue after cycling and such fatigue was infrequent after walking. Controversy exists as to whether muscle weakness is present in patients with PD. A recent literature review have provided evidence that muscle strength was decreased in patients with PD and that muscle weakness was not specially related to tremor or rigidity(32). Other studies showed reduced muscle strength in patients with PD compared with age-matched controls. Reuter et al.(14) suggested in their study that muscle metabolism may not be a limitation of physical performance. In this study patients with PD were exercising for at least 2 hours/ week. It is reasonable that in sedentary patients with PD muscle metabolism may be a limitation for physical performance. Therefore exercise treadmill testing might be a better option for patients with moderate PD.

Anti-Parkinson medication is related to poorer autonomic responsiveness(24). In our study we did not examine the role of medication. Another weakness in our study is that we did not examine muscle metabolism. It is reasonable that in sedentary patients with PD muscle metabolism may be a limitation for physical performance.

In summary, our results demonstrate that the feasibility of the Åstrand test is low in patients with PD. Fifty-three percent of the sedentary patients with PD did not well-perform the Åstrand test compared to 13.8% of the sedentary healthy subjects. One reason for not well-performing the test was because the minimum heart rate was not reached. The literature is contradictory about the HR response in patients with PD during submaximal en maximal exercise testing. The reason for not reaching the minimum required exercise HR is still unclear. Muscle metabolism and anti-Parkinson medication may play a role. It is also convincing that a disturbed cardiovascular regulation might be a reason for not reaching the minimal required exercise HR.

To get more insight in HR response during exercise analyzing individuals both on and off anti-Parkinson medication may help determine differences. Also determine hypokinesia/ rigidity may help to find differences in HR response. A detailed study about the course of HR and BP during exercise might give understanding in cardiovascular regulation.

LITERATURE

(1) Politis M, Wu K, Molloy S, G Bain P, Chaudhuri KR, Piccini P. Parkinson's disease symptoms: the patient's perspective. Mov Disord 2010 Aug 15;25(11):1646-1651.

(2) Stanley RK, Protas EJ, Jankovic J. Exercise performance in those having Parkinson's disease and healthy normals. Med Sci Sports Exerc 1999 Jun;31(6):761-766.

(3) Pennington S, Snell K, Lee M, Walker R. The cause of death in idiopathic Parkinson's disease. Parkinsonism Relat Disord 2010 Aug;16(7):434-437.

(4) Prasad DS, Das BC. Physical inactivity: a cardiovascular risk factor. Indian J Med Sci 2009 Jan;63(1):33-42.

(5) Verweij LM, van Schoor NM, Dekker J, Visser M. Distinguishing four components underlying physical activity: a new approach to using physical activity questionnaire data in old age. BMC Geriatr 2010 May 3;10(1):20.

(6) Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc 2007 Aug;39(8):1435-1445.

(7) Fertl E, Doppelbauer A, Auff E. Physical activity and sports in patients suffering from Parkinson's disease in comparison with healthy seniors. J Neural Transm Park Dis Dement Sect 1993;5(2):157-161.

(8) Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. Annu Rev Public Health 1987;8:253-287.

(9) Baatile J, Langbein WE, Weaver F, Maloney C, Jost MB. Effect of exercise on perceived quality of life of individuals with Parkinson's disease. J Rehabil Res Dev 2000 Sep-Oct;37(5):529-534.

(10) ASTRAND PO, RYHMING I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work. J Appl Physiol 1954 Sep;7(2):218-221.

(11) Siconolfi SF, Cullinane EM, Carleton RA, Thompson PD. Assessing VO2max in epidemiologic studies: modification of the Astrand-Rhyming test. Med Sci Sports Exerc 1982;14(5):335-338.

(12) Roitman JL HM. ACSM's recource manual for guidelines for exercise testing and prescription, 4th ed. .

(13) Werner WG, DiFrancisco-Donoghue J, Lamberg EM. Cardiovascular response to treadmill testing in Parkinson disease. J Neurol Phys Ther 2006 Jun;30(2):68-73.

(14) Reuter I, Engelhardt M, Freiwaldt J, Baas H. Exercise test in Parkinson's disease. Clin Auton Res 1999 Jun;9(3):129-134.

(15) van Nimwegen M, Speelman AD, Smulders K, Overeem S, Borm GF, Backx FJ, et al. Design and baseline characteristics of the ParkFit study, a randomized controlled trial

evaluating the effectiveness of a multifaceted behavioral program to increase physical activity in Parkinson patients. BMC Neurol 2010 Aug 19;10:70.

(16) Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Arch Neurol 1999 Jan;56(1):33-39.

(17) Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967 May;17(5):427-442.

(18) Visser M, Pluijm SM, Stel VS, Bosscher RJ, Deeg DJ, Longitudinal Aging Study Amsterdam. Physical activity as a determinant of change in mobility performance: the Longitudinal Aging Study Amsterdam. J Am Geriatr Soc 2002 Nov;50(11):1774-1781.

(19) Stel VS, Smit JH, Pluijm SM, Visser M, Deeg DJ, Lips P. Comparison of the LASA Physical Activity Questionnaire with a 7-day diary and pedometer. J Clin Epidemiol 2004 Mar;57(3):252-258.

(20) Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377-381.

(21) Borg G. Psychophysical scaling with applications in physical work and the perception of exertion. Scand J Work Environ Health 1990;16 Suppl 1:55-58.

(22) Dunbar CC, Robertson RJ, Baun R, Blandin MF, Metz K, Burdett R, et al. The validity of regulating exercise intensity by ratings of perceived exertion. Med Sci Sports Exerc 1992 Jan;24(1):94-99.

(23) Kallio M, Haapaniemi T, Turkka J, Suominen K, Tolonen U, Sotaniemi K, et al. Heart rate variability in patients with untreated Parkinson's disease. Eur J Neurol 2000 Nov;7(6):667-672.

(24) van Dijk JG, Haan J, Zwinderman K, Kremer B, van Hilten BJ, Roos RA. Autonomic nervous system dysfunction in Parkinson's disease: relationships with age, medication, duration, and severity. J Neurol Neurosurg Psychiatry 1993 Oct;56(10):1090-1095.

(25) Ludin SM, Steiger UH, Ludin HP. Autonomic disturbances and cardiovascular reflexes in idiopathic Parkinson's disease. J Neurol 1987 Oct;235(1):10-15.

(26) Turkka JT, Tolonen U, Myllyla VV. Cardiovascular reflexes in Parkinson's disease. Eur Neurol 1987;26(2):104-112.

(27) Mesec A, Sega S, Trost M, Pogacnik T. The deterioration of cardiovascular reflexes in Parkinson's disease. Acta Neurol Scand 1999 Nov;100(5):296-299.

(28) American College of Sports Medicine editor. Acsm's Exercise Management for Persons with Chronic Diseases and Disebilities. ; 2nd ed. Champain, Ill: Human Kinetics; 2003.

(29) Katzel LI, Sorkin JD, Macko RF, Smith B, Ivey FM, Shulman LM. Repeatability of Aerobic Capacity Measurements in Parkinson Disease. Med Sci Sports Exerc 2011 May 20.

(30) Kaminsky I.A e editor. ACSM's Recource Manual for Guidlines for Exercise Testing and Prescription. 5th ed. ; Philadelphia, Pa: Lippincott Williams & Wilkins; 2006.

(31) Man WD, Soliman MG, Gearing J, Radford SG, Rafferty GF, Gray BJ, et al. Symptoms and quadriceps fatigability after walking and cycling in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2003 Sep 1;168(5):562-567.

(32) Cano-de-la-Cuerda R, Perez-de-Heredia M, Miangolarra-Page JC, Munoz-Hellin E, Fernandez-de-Las-Penas C. Is there muscular weakness in Parkinson's disease? Am J Phys Med Rehabil 2010 Jan;89(1):70-76.

Table 1- Subjects Characteristics

	Patients with PD (N=453)	**Healthy Control (N=29)**
Age (yr)	63.7 (7.7)	61.5 (10.8)
Gender (%male)	65.6	69.0
Height (m)	1.72 (0.1)	1.71 (8.7)
Weight (kg)	81.0 (13.9)	80.1 (10.0)
BMI	27.4 (4.1)	27 (3.7)
Resting HR (bpm)	76.4 (12.8)	79.7 (11.3)
Resting systolic BP	141.5 (19.2)	152.1 (21.9)
Resting diastolic BP*	83.0 (10.9)	91.2 (13.9)
Level of physical activity (hours/week)*	15.6 (10.1)	9.3 (4.8)
Disease duration (years)	5.2 (4.5)	-
HY 1 1.5 2 2.5 3	 7 (1.5%) 16 (3.5%) 339 (74.8%) 68 (15%) 23 (5.1%)	-
UPDRS motor section	32.7 (10.4)	-

Values are mean ± SD or percentage

BMI= body mass index; HR=heart rate; Bpm = beats per minute; BP= blood pressure; UPDRS = Unified Parkinson's Disease Rating Scale; *P<0.05

Table 2- Overview and reason for drop-outs

	Patients with PD (N=453)	**Healthy control (N=29)**
N started, not finished	53	3
HR<120 BPM	131	1
ΔHR 5-6 minute > 5 BPM	57	-
non well-performed Åstrand test	241 (53.2%)	4 (13.8%)
well-performed Åstrand test	212	25

HR=heart rate; BPM=beats per minute; Δ= difference

Table 3 – Differences between people with PD who successfully completed the test and those who did not.

	Patients with PD with HR < 120 (N=131)	**People with PD with HR > 120 (N=212)**
Age (yr) *	66.1 (6.8)	61.8 (7.7)
Gender (%male) *	73.3%	62.7%
Height (m)	1.73 (9.7)	1.73 (10.1)
Weight (kg)	84.5 (15.2)	80.1 (12.9)
BMI*	28.1 (3.9)	26.9 (4.1)
Resting HR (BPM) *	70.7 (11.2)	80.8 (13.2)
Resting BP (systole) *	138.3 (19.9)	142.7 (18.6)
Resting BP (diastole) *	80.6 (10.2)	84.9 (10.7)
Level of physical activity (hours/week)	14.7 (10.5)	16.2 (9.8)
Disease duration (yr) *	5.7 (4.8)	4.7 (4.2)
HY		
1	2 (1.5%)	3 (1.4%)
1,5	4 (3.1%)	11 (5.2%)
2	98 (74.8%)	164 (77.4%)
2.5	20 (15.3%)	28 (13.2%)
3	7 (5.3%)	6 (2.8%)
UPDRS motor section*	33.8 (9.5)	31.0 (10.3)

Values are mean ± SD or percentages

BMI= body mass index; HR= heart rate; BPM= beats per minute; BP: blood pressure, HY= Hoehn and Yahr; UPDRS= Unified Parkinson's Disease Rating scale; *$p<0.05$

Table 4 – Univariate regression analysis for HR>120 as dependent variable and age, gender, BMI, resting HR, resting BP, disease duration, UPDRS motor section, HY, Level of physical activity and maximum workload as independent variables.

Variabele	**B**	**P**
Disease duration (years)	-0.053	0.032*
HY	-0.483	0.187
UPDRS	-0.028	0.013*
BMI	-0.070	0.012*
Gender	0.488	0.045*
Age	-0.082	0.000*
Level of physical activity LOG (hours/ week)	36%	0.040*
Resting HR	0.070	0.000*
Maximum workload	0.015	0.001*
BP_diastole	0.040	0.000*
BP_systole	0.012	0.038*

HY= Hoehn and Yahr; UPDRS: Unified Parkinson's Disease Rating Scale; BMI= body mass index; HR= heart rate; BP= blood pressure; *p<0.05