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Physical Assessment as a Predictor of Mortality in People with Parkinson's Disease: A Study over 7 Years

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Abstract: The primary aim of this study was to ascertain whether a battery of physical function measures in a Parkinson's disease (PD) patient cohort predicted mortality status at 7-year follow-up. Secondary aims were establishing which specific tests were the most useful, and whether PD phenotype was a predictor. A retrospective correlation design was used in this study. A cohort of 109 PD patients underwent baseline physiotherapy assessment of gait, balance, posture, muscle strength, and ability to change postural set. We compared mortality status at 7-year follow-up and baseline physical assessment tests. Tinetti gait and balance scores, UPDRS score, 10-m walk test (time, velocity, and number of strides), posture in standing, lying to sitting, sitting to standing, getting up from floor assessments, and time to ascend and descend four steps were found to be statistically significant physical predictors of mortality at 7-year follow-up. In addition, age, sex, and mini-mental state examination were significant nonphysical predictors of mortality. Using Cox regression, a survival model was constructed with age, sex, and Tinetti gait score as independent predictors of mortality. The results of this study suggest that there is a link between reduced physical function and an increased mortality risk in PD populations. © 2009 Movement Disorder Society

Key words: Parkinson's disease; physiotherapy; mortality; predictors; physical assessment; Tinetti gait assessment

A number of primary studies and reviews have looked at predictors of disease progression in Parkinson's disease (PD).[1–5] These studies found strong evidence that a rapid disease course could be predicted by higher age at onset, but there was limited evidence for dementia, higher bradykinesia score, nontremor dominant phenotype, gait disturbance, symmetrical disease at baseline, and depression as predictors of rapid decline. A study over 20 years by Hely et al.[6–8] has indicated that mortality rates are significantly higher than those seen in the general population and that nondrug responsive symptoms predominate late in the disease cycle.

PD is predominantly a movement disorder, and physical assessment is a key component in diagnosis of individuals presenting with PD.[9] There is however a lack of information on physical ability as a predictor of mortality in PD patients. Within the general population, a number of studies have attempted to consider whether physical assessment can be used to predict mortality. Notable among these is a study from 1994.[10] The study looked at whether mortality risk in community dwelling elderly persons was predicted by three lower limb physical function tests and self-reported capability with activities of daily living (ADLs) requiring the use of lower limbs. The study of 5,174 individuals found that self-reported disabilities in ADLs and walking half a mile were significant predictors of death. Other researchers have suggested that reduced physical fitness and loss of upper limb muscle bulk and grip strength may also predict an increased mortality risk in the general population.[11,12]

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The primary aim of this study was to understand whether physical assessment of individuals diagnosed with PD is a useful tool in predicting mortality rates at 7-year follow-up.

PATIENTS AND METHODS

The NHS trust involved in this study runs a comprehensive PD service for people with PD in their catchment area. A prevalence study determined that more than 85% of persons with idiopathic PD in the local catchment area are under the care of the service so these patients are thought to be representative of community dwelling PD patients.[13] All 141 patients registered with this service in January 2000 with idiopathic PD according to the UK brain bank criteria were considered for inclusion in a prospective study of falls.[14] The only exclusion criteria were being totally bedfast or major cognitive impairment. Thirty two patients declined to take part in the study.

A cohort of 109 (77%) individuals was eligible and consented, and was assessed using reliable and validated measures of physical function and ability from January to March 2000. Mortality status after 7 years (end of 2006) was then obtained, with retrospective assessment of the correlation between initial assessment and status at follow-up as the key aim of the study. National Research Ethics Service approval was granted for the use of both data sets used in this study.

Follow-up data on date of death and cause and place of death for individuals within the 2000 cohort who had died by 31st of December 2006 were obtained from the Office of National Statistics (ONS). Progression has been considered over 7 years, allowing a sufficiently long period of time for outcomes to be monitored. Because no patients are discharged from the service, ONS data on all those who were ever registered with the service were requested, including all persons who had moved away from the catchment area during the intervening 7 years. Thus, data from all 109 participants were included in this study, with no patients lost to follow-up.

The data collected in January 2000 can be divided into five main categories; general information and social history (e.g., sex, age, and domicile), previous medical history (e.g., blackouts, falls, and malignancies), medication and drug history, autonomic function, and physical function. Data within all these categories were collected using standard measuring devices, quality of life, and physical function rating scales, medical records or patient responses, as appropriate.

PD patients are known to present with widely varying physical signs and symptoms depending on which stage in their daily medication cycle they are at. A patient's physical ability when in an "on" state is often markedly better than when they are in an "off" state.[15,16] All patients were assessed in the morning after having taken their medication and, thus, were in the "on" state.

Data relating to physical function and ability were collected during a 30 minute objective and subjective assessment by a single senior physiotherapist with a special interest in PD at North Tyneside General Hospital. The specific tests carried out during the objective assessment are detailed in Table 1, included the 10-m walk test,[17] Tinetti balance and gait assessment,[18] Hoehn and Yahr rating,[19] and the Unified Parkinson's Disease Rating Scale (UPDRS) assessment.[20]

Statistics

The data were quantitative in nature and collected at a nominal, ordinal, and interval/ratio level. They were analyzed using standard statistical software, *SPSS-16 for Windows* (SPSS, Chicago, IL). With the exception of age, all predictor variables were found to be nonnormally distributed (Kolmogorov-Smirnov test) and so did not meet parametric assumptions.[21] Therefore, Spearman's correlation test was used to assess whether scores from one predictor were associated with scores from other predictors (multicollinearity) as part of a preliminary screening of the data. Because the outcome (mortality) was a dichotomy, a point biserial correlation test was used to assess correlation between predictor variables and mortality.[21] Finally, Cox proportional hazards regression analysis does not require data to be parametric and so was used to identify independent predictors of outcome and to obtain survival ratios. Time to event (death) was entered in months, with 1st January 2000 taken as baseline. A large value for the Wald statistic generally indicates that the predictor variable is a significant predictor of outcome and therefore makes a contribution to the predictive power of the model. Calculating Exp(B) from B, allows the relative change in the odds of the outcome occurring for a unit change in the predictor to be calculated.

RESULTS

Means, standard deviations, and spread of results for the baseline physiotherapy assessment data in January–March 2000 for all 109 individuals in the study are shown in Table 1. Of the 109 individuals in the original study, 46 (42.2%) were no longer alive by 31st December 2006. Table 2 shows demographic information

TABLE 1. *Baseline physiotherapy assessment data*

	Mean	Minimum	Maximum	Range	Standard deviation
Age at January 2000*	74.71	54	92	38	7.933
Years since diagnosis in 2000	5.42	0	31	31	5.563
Years since symptom onset in 2000	6.93	1	37	36	6.099
Total UPDRS score*	34.10	8	64	56	11.184
Hoehn and Yahr rating	2.023	1	4	3.0	0.7372
Total MMSE score*	26.33	15	30	15	3.594
Posture when standing rating (1–4)[a]*	3.11	2	4	2	0.637
Sitting to standing time (s)	3.03	1	16	15	2.282
Sitting to standing rating (0–3)[b]*	2.19	0	3	3	0.477
Lying to sitting time (s)	6.30	1	26	25	4.694
Lying to sitting rating (0–3)[c]*	2.08	1	3	2	0.367
Climb 4 stairs up time (s)*	7.11	3	62	59	6.774
Climb 4 stairs up rating (0–3)[c]	1.90	0	3	3	0.729
Climb 4 stairs down time (s)*	7.76	2	89	87	9.604
Climb 4 stairs down rating (0–3)[c]*	1.88	0	3	3	0.739
Getting up from floor time (s)	14.17	4	47	43	9.356
Getting up from floor rating (0–3)[b]*	1.24	0	3	3	0.956
Festination present in gait (0–1)[d]	0.14	0	1	1	0.350
Initiation difficulty (0–2)[e]	1.73	1	2	1	0.444
Gait description (0–3)[f]	2.55	1	3	2	0.573
Arm swing (0–4)[g]	1.88	0	4	4	1.305
10 m walk time (s)*	18.58	7	96	89	14.828
10 m walk number of strides*	26.05	13	82	69	13.801
10 m walk velocity (m/s)*	0.7362	0.10	1.43	1.33	0.32458
10 m walk seconds per stride	0.6691	0.16	1.82	1.66	0.21500
10 m walk stride length (m)	0.4666	0.01	1.64	1.63	0.22194
Tinetti Gait score (9–18)*	13.04	9	18	9	2.514
Tinetti Balance score (13–39)*	23.82	13	37	24	6.167
Total Tinetti Balance + Gait (22–57)*	36.86	22	54	32	8.220

*Correlation between mortality and predictors at $P \leq 0.05$ significance level.

[a]1, fully stooped posture; 2, significant flexion at hips, knees, trunk and shoulders; 2, some flexion at hips, knees, trunk and shoulders; 4, fully upright posture.

[b]0, unable to assess; 1, unable to do; 2, able with use of an aid; 3, able without use of any aid.

[c]0, unable to assess; 1, unable to do; 2, able with use of rail or stick; 3, able without use of rail or stick.

[d]0, not present; 1, present.

[e]0, unable to assess; 1, no initiation difficulty; 2, present.

[f]0, unable to assess; 1, toe strike then heel; 2, flat footed; 3, heel then toe.

[g]0, unable to assess; 1, bilateral loss; 2, unilateral loss; 3, unilateral reduction; 4, full bilateral.

on the data set with participants split into deceased or alive. The average age at death was 80.8 years (79.8 years for men and 82.4 years for women), with average years since onset of symptoms at death of almost 10 years.

Furthermore, of the 52 men in the study, 28 (53.8%) had died during the 7 year follow-up period, compared with only 18 (39.1%) of the 57 women. The ages in January 2000 for men and women were 74.0 and 75.3 years, respectively. The difference in mortality rates between

TABLE 2. *Demographic data split into deceased or alive*

Mortality status Dec. 2006	Mean	Minimum	Maximum	Range	Std. Deviation
Alive					
Age at January 2000	72.70	54	92	38	7.655
Years since diagnosis in 2000	5.08	0	27	27	5.629
Years since symptom onset in 2000	6.94	1	27	26	6.247
Deceased					
Age at January 2000	77.46	60	92	32	7.545
Years since diagnosis in 2000	5.89	1	31	30	5.498
Years since symptom onset in 2000	6.91	1	37	36	5.958
Age at death	80.80	63	99	36	7.398
Years from diagnosis to death	8.91	2.0	34.4	32.4	5.965
Years from symptom onset to death	9.93	3.3	40.4	37.1	6.446

TABLE 3. *Correlations between selected predictor variables*

	Sex	Age at start	Total UPDRS	10 m walk time	10 m walk time per stride	Tinetti Gait score	Tinetti Balance score
Sex							
Correlation Coefficient	1.000	0.052	−0.057	0.281[a]	0.136	0.036	0.214[b]
Sig. (2-tailed)	–	0.591	0.558	0.003	0.157	0.714	0.028
Age at start							
Correlation Coefficient	0.052	1.000	0.035	0.443[a]	0.293[a]	0.318[a]	0.328[a]
Sig. (2-tailed)	0.591	–	0.720	0.000	0.002	0.001	0.001
Total UPDRS							
Correlation Coefficient	−0.057	0.035	1.000	0.484[a]	0.216[b]	0.567[a]	0.646[a]
Sig. (2-tailed)	0.558	0.720	–	0.000	0.024	0.000	0.000
10 m walk time							
Correlation Coefficient	0.281[a]	0.443[a]	0.484[a]	1.000	0.729[a]	0.786[a]	0.777[a]
Sig. (2-tailed)	0.003	0.000	0.000	–	0.000	0.000	0.000
10 m walk time per stride							
Correlation Coefficient	0.136	0.293[a]	0.216[b]	0.729[a]	1.000	0.439[a]	0.479[a]
Sig. (2-tailed)	0.157	0.002	0.024	0.000	–	0.000	0.000
Tinetti Gait score							
Correlation Coefficient	0.036	0.318[a]	0.567[a]	0.786[a]	0.439[a]	1.000	0.750[a]
Sig. (2-tailed)	0.714	0.001	0.000	0.000	0.000	–	0.000
Tinetti Balance score							
Correlation Coefficient	0.214[b]	0.328[a]	0.646[a]	0.777[a]	0.479[a]	0.750[a]	1.000
Sig. (2-tailed)	0.028	0.001	0.000	0.000	0.000	0.000	–

[a]Correlation is significant at the 0.01 level (2-tailed).
[b]Correlation is significant at the 0.05 level (2-tailed).

men and women was significant ($\chi^2 = 5.528$, $P = 0.019$). There was no significant difference between women and men when years since diagnosis (5.00 years for women, 5.88 years for men) or years since onset of symptoms (6.81 for women and 7.06 for men) were compared.

Correlation between selected predictor variables is shown in Table 3. Tinetti gait and balance scores and all five measures of walking were correlated to various degrees with one another in all combinations ($r = -0.324$–0.924, $P = 0.001$–0.000). UPDRS score was highly correlated with Hoehn and Yahr score ($r = 0.555$, $P = 0.000$), 10 m walk test time ($r = 0.484$, $P = 0.000$), Tinetti balance score ($r = 0.567$, $P = 0.000$), and Tinetti gait score ($r = 0.646$, $P = 0.000$). Correlation coefficients between age and sex and physical predictors, although statistically significant in some cases, are relatively small.

All variables were screened to discover whether any variables had a statistically significant association with mortality status. The 16 predictors marked with an asterisk in Table 1, together with sex, showed significant correlations at the $P \leq 0.05$ level of statistical significance.

Given that many of the apparent predictor variables correlate highly with each other, and can therefore be said to be measuring the same phenomenon (i.e., physical ability, muscle strength etc.), a Cox regression model was constructed in an attempt to adjust for interactions. The differences in sex and age between outcome groups can be partially explained by demographics within the general population. The different life expectancies of men and women and increased mortality rates with increasing age, mean that these two factors are likely to be significant predictors of outcome, hence their inclusion in the model.

The key outputs from this model are shown in Table 4. The value of Exp(B) indicates that a change of one unit in the Tinetti gait score (score, 9–18) results in an increase of 1.3 in the odds of death occur-

TABLE 4. *Cox regression model*

							95.0% CI for Exp(B)	
	B	SE	Wald	Df	Sig.	Exp(B)	Lower	Upper
Sex	1.052	0.324	10.505	1	0.001	2.863	1.515	5.407
Age at January 2000	0.064	0.024	7.129	1	0.008	1.066	1.017	1.117
Tinetti gait score	0.263	0.068	14.975	1	0.000	1.301	1.139	1.486

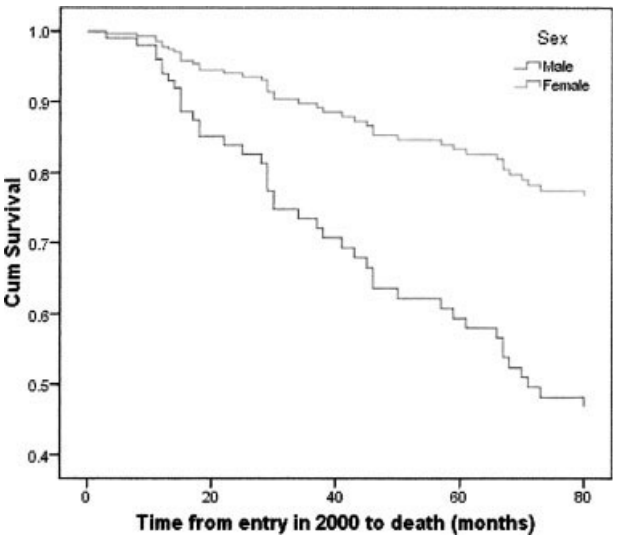

FIG. 1. Cumulative survival plot, for a hypothetical individual, at the mean of the covariates for men and women.

ring. The cumulative survival plot based on the Cox regression model is shown in Figure 1, with patients split into men or women, the hazard for male patients is 2.86 that of female patients.

UPDRS Phenotype Analysis

The UPDRS was developed in 1987[20] as an overall rating tool designed to follow the longitudinal course of PD. It is used to assess all aspects of disability and functional limitation resulting from PD.[22,23] Using the method described by Jankovic et al.,[24] it is possible to place patients into either a tremor predominant subgroup or a PIGD predominant subgroup. In total, 77 individuals (70.6%) were categorized as PIGD predominant, 12 (11.0%) fell into the tremor predominant subgroup, and 20 (18.4%) fell between the two cut-off scores for categorization and were thus of an indeterminate subgroup. In the study of 800 patients by Jankovic et al.,[24] 233 (29.1%) fell into the tremor phenotype, 441 (55.1%) into the PIGD phenotype, and 126 patients (15.8%) into the indeterminate group.

Of the 89 individuals categorized as either PIGD or tremor predominant, a total of 50 patients (56%) were still alive in December 2006. Sixty-seven percent (n = 8) of patients in the tremor predominant phenotype were still alive versus 55% (n = 42) in the PIGD group, $P = 0.43$. There was evidence of a small association between mortality status and mean UPDRS tremor subscore ($r^2 = 0.04$, $P = 0.038$).

DISCUSSION

For the most part, the cohort used in this study is significantly older and has a significantly higher percentage of women than those studied by other authors. In a study of disease prevalence in the North Tyneside general hospital catchment area, Porter et al.[13] observed the mean age of individuals with PD to be 74.1 years. Given this, and the broad inclusion criteria of this study, it is felt that the demographics of the population described here is more representative of the general population of PD patients than that used in similar studies.[24–31]

The average age at death was 79.8 years for men and 82.4 years for women, with an overall average of almost 81 years; the average years since onset of symptoms at death was almost 10 years. In comparison, Hoehn and Yahr's[19] study found an average age at death of 67.0 years and a mean disease duration at death of 9.4 years amongst 340 idiopathic PD patients. More recently, a community-based study in Sweden in 2003 found an average age at death of 81.9 years (83.2 years for women and 81.0 years for men) in 121 cases.[32] The relatively younger age at death in the 1967 study may be attributable to a number of factors such as increasing life expectancy within the general population, greater diagnostic accuracy, earlier diagnosis and treatment and improvements in therapy for PD patients since the mid-1960s.[33] The similarities in age at death between the Swedish study and this study may, in part, be due to broad inclusion criteria used in both studies.

A total of 17 predictors showed significant correlations with mortality and, of these, 13 are measures of either muscle strength or gait or balance or posture. Furthermore, sections II and III of the UPDRS score measure physical ability and ability with ADLs and so can be thought of as measuring the same phenomenon. Age at January 2000, sex, and total mini-mental state examination (MMSE) score were the only predictor variables that correlated highly with mortality status at 7 years follow-up that were not directly measuring physical function. The fact that MMSE score was a significant predictor of mortality suggests that cognitive decline, and other nonmotor factors, may also be important predictors of disease progression and mortality in PD, as noted by other authors.[6,8,34,35]

Tinetti gait score, age, and sex appear to be independent predictors of mortality. More explicitly, the low multicollinearity between scores for these three variables suggests that they predict different parts of the variance within the survival model and therefore

all contribute to its overall predictive power. The link between age, sex, and mortality is well established, but the influence of poor gait on mortality in PD has not previously been reported. Nevertheless, other variables may also be useful predictors of mortality, but do not appear in the model because they are measuring the same fundamental characteristic or phenomenon (i.e., physical ability). The strong association between Tinetti gait and Tinetti balance scores is of particular interest and emphasizes the link between poor balance and impaired walking ability.

Mortality status was not significantly correlated with PD phenotype, although the weak association between UPDRS tremor subscore and mortality status merits further investigation. Those alive in December 2006 had had higher mean tremor scores, indicating a greater degree of tremor or a more global bilateral tremor. Jankovic and Kapadia[28] have suggested that the slower rate of decline to disability in individuals with greater tremor may be due to a distinct biochemical or degenerative pathway of the disease not seen in PIGD predominant subjects. Strong evidence for a more rapid rate of progression to disability within the PIGD phenotype was also noted in a recent systematic review.[2]

Gait and balance impairment, together with a more flexed and stooped posture in standing, are the strongest physical predictors of mortality and are manifestations of the complex neurological changes associated with PD.[36] It may be that, ultimately, it is the rate of these neurological changes that predict mortality. If this is the case, then improving gait and balance may have little or no overall impact on mortality.

In contrast, it may also be suggested that improving gait and balance would reduce falls risk and therefore improve mobility, ability to perform ADLs, and social interaction. This would lead to an improved quality of life and reduced risk from conditions, which can be exacerbated by being house bound or immobile for long periods of time, such as depression and chest infection.[19] Indeed, pneumonia has long been recognized as a major cause of death in PD patients and of the 46 patients in this study who were deceased by December 2006, 21 (46%) had pneumonia or chest infection listed as the primary cause of death on their death certificate.[32,37]

Physiotherapy aimed at improving gait, balance, and posture is recommended by a number of clinical guidelines.[38,39] Recent systematic reviews concluded that therapy aimed at improving balance, physical capacity, and gait can be beneficial, although a lack of high quality evidence to support specific treatment approaches was noted.[40,41] Nevertheless, there is evidence to suggest that improving physical fitness can be beneficial in preventing immobility in PD populations, and that patients who exercise have a lower mortality rate.[42]

In conclusion, this study suggests a link between diminished performances in commonly used tests of physical function, in particular, measures of gait, balance, posture, ability to climb and descend stairs and ability to change postural set, and an increased risk of mortality amongst PD patients. Furthermore, age, sex, and Tinetti gait score are independent predictors of mortality.

Having indicated which tests of physical function may be the most useful predictors of an increased mortality risk, it would be useful for future studies to consider the rate at which these scores decline and whether such measures can be useful in predicting the rate of decline of physical function and impending terminal decline. Interestingly, an association between a decreased mortality risk and higher scores in the tremor items of the UPDRS was observed.

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