Movement Disorders
Vol. 22, No. 13, 2007, pp. 1892–1900

A Meta-Analysis of Six Prospective Studies of Falling in Parkinson's Disease

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Abstract: Recurrent falls are a disabling feature of Parkinson's disease (PD). We have estimated the incidence of falling over a prospective 3 month follow-up from a large sample size, identified predictors for falling for PD patients repeated this analysis for patients without prior falls, and examined the risk of falling with increasing disease severity. We pooled six prospective studies of falling in PD (n = 473), and examined the predictive power of variables that were common to most studies. The 3-month fall rate was 46% (95% confidence interval: 38–54%). Interestingly, even among subjects without prior falls, this fall rate was 21% (12–35%). The best predictor of falling was two or more falls in the previous year (sensitivity 68%; specificity 81%). The risk of falling rose as UPDRS increased, to about a 60% chance of falling for UPDRS values 25 to 35, but remained at this level thereafter with a tendency to taper off towards later disease stages. These results confirm the high frequency of falling in PD, as almost 50% of patients fell during a short period of only 3 months. The strongest predictor of falling was prior falls in the preceding year, but even subjects without any prior falls had a considerable risk of sustaining future falls. Disease severity was not a good predictor of falls, possibly due to the complex U-shaped relation with falls. Early identification of the very first fall therefore remains difficult, and new prediction methods must be developed. © 2007 Movement Disorder Society

Key words: falling; prediction; sensitivity; specificity; Parkinson's disease; meta-analysis; UPDRS.

Recurrent falls are an important and disabling feature of idiopathic Parkinson's disease (PD).[1-4] Fall-related injuries such as hip fractures or head traumas are among the most recognizable consequences of falls.[5,6] However, falls have many other sequelae that may be less obvious clinically, but which have a significant negative impact on the patients' quality of life. For example, PD patients who have sustained prior falls often develop a fear of renewed falls[7,8] and this may cause or aggravate a concurrent loss of mobility. In turn, this reduced mobility is associated with a host of negative consequences, including a loss of independence, development of weakness, promotion of osteoporosis, and, eventually, a deterioration of overall fitness, leading to cardiovascular disease and reduced survival.[9,10] Furthermore, postural instability and falls are associated with increased risk of admission to hospitals[11] or nursing homes.[12]

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Received 22 January 2007; Accepted 24 April 2007

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Published online 22 June 2007 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21598

In light of these consequences of falls, it would be helpful to identify which persons are most at risk of sustaining a fall in the near future. Postural instability and falls are generally difficult to treat pharmacologically, but a host of additional therapeutic measures may help to alleviate falls in individual patients.[13,14] Because asking about previous falls is often unreliable, falls are best studied using a prospective design where patients are asked to document the occurrence of falls shortly after they have occurred. In the past few years, six prospective studies have examined fall rates and consequences of falls in PD.[7,15-19] These studies emphasized the high incidence of falls in PD: depending on the duration of follow-up (which ranged from 3 to 12 months), the percentage of patients with at least one fall amounted to almost 70% for those who were followed for a full year.[19] However, they produced inconsistent findings in their search for a clinically useful risk factor for falls in PD. Ashburn et al.[15] concluded that a reported history of two or more falls in the previous year was the best predictor of future falls, and a previous review including all six studies indicated that the presence of prior falls was the only consistently present predictor of future falls.[20]

However, presence of prior falls as a predictor is suboptimal because ideally intervention should occur before the first fall has occurred. Indeed, no previous study has attempted to predict future falls in PD patients who are not currently falling. Moreover, previous studies were based on relatively small numbers, with no study including substantially more than 100 subjects. Here, we report a meta-analysis of individual data from 473 patients in all six previous prospective studies. Our specific aims were as follows: to estimate the incidence of falling from larger numbers; to examine predictors of falling, not only among the group as a whole, but also among patients who had not fallen in the previous year; and to examine the relationship between increasing severity of disease—as measured by the Unified Parkinson Disease Rating Scale motor examination (UPDRS)—and falling.

MATERIALS AND METHODS

The six studies were identified from a PubMed search using the following search terms: "Parkinson's disease" AND "accidental falls" AND ("prospective studies" OR "longitudinal studies"), and this yielded four studies that had been published as full papers.[7,15,17,19] This was supplemented with information available to the authors from international conferences, and this yielded two further studies that have thus far appeared only in abstract form.[18,21] The studies were performed among community-dwelling patients with PD living in Ottawa Canada,[17] Leiden the Netherlands,[7] Brisbane Australia,[18] and three centers in the United Kingdom: Southampton,[15] North Tyneside,[19] and London.[21] The London study was originally designed as a study focused on progressive supranuclear palsy, but this study was included because the PD patients, who served as controls in this study, were followed in the same way as in the other five PD studies.[21]

There was some heterogeneity across the six identified studies, but the methods were sufficiently similar to allow for a pooling of the data (Table 1). The duration of follow-up ranged from a minimum of 3 months to a maximum of 12 months. The prospective follow-up data were therefore recalculated for a comparable 3-month interval for all studies, which was possible because all studies included in this meta-analysis provided actual number of falls over the first 3 months, so ascertainment of falls was identical for all studies. Methods used to ascertain falls during the follow-up period also varied somewhat across studies, but were all deemed of sufficient quality to reliably ascertain faller status (single or recurrent faller). There was also a discrepancy in the time interval over which previous falls and near falls were reported (Table 1). To accommodate this, we only used the three studies with a time interval of 12 months in analyses incorporating prior faller status or number of falls. Some patients had large numbers of previous falls, the extreme being 500 falls. To reduce the impact of outliers, numbers of falls above 25 were replaced with the value 25, though sensitivity analyses with different numbers or using the original variable showed little difference.

Table 2 shows the number of patients with PD in each study, totalling 473 across all six studies. Whether or not a patient fell in a 3-month prospective follow-up period was available from all the studies. The following potentially predictive variables were common to all (or most) of the studies: age, gender, Hoehn and Yahr stage, UPDRS, previous falls, and fear of falling. The distribution of these variables was broadly similar across studies (Table 2).

The UPDRS motor examination score was not recorded using the same version in all studies. The majority recorded the full version in which key symptoms are rated specifically for different areas of the body, making 27 items in total.[22] Two studies (Southampton and North Tyneside) used a reduced version in which only an overall rating of symptoms across body areas was obtained from each patient, resulting in 14 items. To produce a score that was compatible across studies, we assumed that singly rated symptoms in the reduced version were the average of values that would have been

TABLE 1. *Characteristics of the six contributing studies*

	Ottawa[17]	Leiden[7]	Southampton[15]	North Tyneside[19]	London[21]	Brisbane[18]
Inclusion criteria	Idiopathic PD	UK Brain Bank criteria, clear response to medication	UK Brain Bank criteria, independently mobile, live in the community	UK Brain Bank criteria	UK Brain Bank criteria, clear response to medication	UK Brain Bank criteria, clear response to medication
Exclusion criteria	Unable to walk, other causes for falls	Unable to walk, other causes for falls	Other causes for falls, cognitive impairment	Totally bedfast, severe medical instability	Unable to walk, other causes for falls	Unable to walk, other causes for falls
Duration follow-up	3 mo	6 mo	3 mo	12 mo	3 mo	6 mo
Fall ascertainment	Fall diaries, returned at 1-, 4-, and 8-wk intervals; follow-up phone calls at 2- and 4-wk intervals; final study visit to review fall descriptions	Fall diaries, returned immediately after each fall; phone call every 2 wk	Telephone call at 3 mo using 10 question interview	Weekly postcards, followed by phone call when fall was reported	Fall diaries, returned immediately after each fall; phone call every 2 wk	Monthly falls calendar postcards with follow-up phone calls
Prior faller status	Previous 3 mo	Previous 12 mo	Previous 12 mo	Previous 12 mo	Since diagnosis	Previous 6 mo

obtained had symptoms been rated separately for specific body parts, and weighted the symptom by the number of parts rated in the full version of the UPDRS score. One could justly argue that this "scaling up" of these values to calculate the full UPDRS is a flawed assumption with subsequent overestimation of the full UPDRS scores. Therefore, in a separate approach, we also repeated our analyses when the available full scores were scaled down to the reduced version, using the single maximum score for each item instead. The results were very similar according to these alternative analyses. We prefer the first approach because the majority of cases came from studies where 27 UPDRS items were checked, so only the minority had to be scaled up to become consistent with the 27 item version. Hence only the analyses using the "scaled up" UPDRS scores will be reported here.

Confidence intervals (CIs) around risks of falling were obtained from logistic regression with study included as a random effect, fitted in Stata 9. We examined the potential of age, gender, Hoehn and Yahr stage, UPDRS and reported number of falls in the previous year, as predictors of falling in the 3-month follow-up period in uncontrolled logistic regression models, and models controlled for all the other variables. Because these models were based on only three studies (number of falls in the previous year only being available in Leiden, Southampton and North Tyneside), study was included as a fixed rather than random effect taking account of possible differences in falling between studies. The possibility of nonlinear dependency of risk of falling and UPDRS score was examined by additionally including as a regressor UPDRS squared: if the risk of falling were to decrease at higher values of UPDRS the squared term would be needed in the model. Estimated risks from the logistic models are reported as odds ratios with their associated 95% CIs, and likelihood ratio tests are reported. A similar set of logistic models examined the predictive power of items within the UPDRS in relation to risk of subsequent falling. For studies that reported the full version of the UPDRS, symptoms rated over different body parts were averaged and included as a single regressor in the model. Number of previous falls, UPDRS, and Hoehn and Yahr stage were also examined as predictors of falling in ROC curves; and the area under the curve (AUC) statistics are reported, along with sensitivity and specificity at selected cut points. Lowess smoothed curves of the relationship between increasing severity of disease (as measured by the UPDRS motor examination score) and risk of falling were produced in Stata. The default bandwidth of 80% was used.

RESULTS

Table 2 shows the baseline characteristics of all contributing studies, as well as the findings on prior and prospectively documented falls. The rate of falling in the 3-month follow-up period among all subjects was 213/461 (46%; CI: 38–54%). Among subjects who reported not having fallen in the previous year the rate was 21/99 (21%; CI: 12–35%), while among those reporting falling once or more the rate was 71/124 (57%; CI: 53–61%). Observations on injurious falls were only available for three studies (Table 2). Two of these studies reported the

TABLE 2. *Summary statistics and numbers missing in each study and combined. Figures are number (%) unless stated otherwise*

VARIABLE	Ottawa (n = 118)	Leiden (n = 59)	Southampton (n = 63)	North Tyneside (n = 109)	Brisbane (n = 56)	London (n = 68)	Overall (n = 473)
Subsequent faller in 3 mo							
Yes	70 (59%)	21 (36%)	22 (38%)	49 (46%)	23 (44%)	28 (41%)	213 (46%)
No	48 (41%)	38 (64%)	35 (61%)	58 (54%)	29 (56%)	40 (59%)	248 (54%)
Missing			6	2	4		12
Subsequent injurious faller in 3 mo							
Yes	(92 falls	14 (24%)				18 (27%)	
No	amongst	45 (76%)				50 (74%)	
Missing	the 118)		63	109	56		
Age in years							
Mean (SD)	71 (10)	61 (10)	71 (8)	75 (8)	65 (9)	64 (9)	69 (10)
Min to max	43 to 90	39 to 80	46 to 87	54 to 92	46 to 84	35 to 81	35 to 92
Missing	2						2
Sex							
Male	73 (62%)	38 (64%)	33 (52%)	52 (48%)	35 (63%)	42 (62%)	273 (58%)
Female	45 (38%)	21 (36%)	30 (48%)	57 (52%)	21 (38%)	26 (38%)	200 (42%)
Hoehn and Yahr stage							
Mean (median)	2.6 (2.5)	2.3 (2.5)	2.8 (3.0)	2.0 (2.0)	2.7 (3.0)	2.5 (2.5)	2.4 (2.5)
Min to max	1 to 4	1 to 4	1 to 4	1 to 4	1.5 to 4	1 to 5	1 to 5
Missing					12	1	13
UPDRS							
Mean (median)	33.3 (33.0)	31.9 (30.5)	38.4 (38.0)	29.3 (29.0)	20.1 (20.0)	23.8 (21.5)	30.1 (29.0)
Min to max	2.5 to 64	7 to 64	4 to 74	6 to 58	8 to 41.5	2 to 69	2 to 74
Missing	12	1	3		13	4	33
Reported number of falls in previous year							
Mean (median)		1.3 (0)	2.8 (1)	11.0 (1)			6.3 (1)
Min to max		0 to 20	0 to 20	0 to 500			0 to 500
Missing	118				56	68	231
Reported falls in the previous year							
Yes		23 (39%)	40 (64%)	68 (62%)			131 (57%)
No		36 (61%)	23 (36%)	41 (38%)			100 (43%)
Missing	118				56	68	242
Reported repeat falls in the previous year							
Yes		11 (19%)	29 (46%)	53 (49%)			93 (40%)
No		48 (81%)	34 (54%)	56 (51%)			138 (60%)
Missing	118				56	68	242
Reported near falls in the previous year							
Yes			47 (75%)			50 (74%)	97 (131%)
No			16 (25%)			18 (26%)	34 (26%)
Missing	118	59		109	56		342
Fear of falling							
Yes		27 (46%)	23 (36%)			39 (58%)	89 (47%)
No		32 (54%)	40 (64%)			28 (42%)	100 (53%)
Missing	118			109	56	1	284

proportions of subjects with injurious falls, and the findings were remarkably comparable (24% in the Leiden study, and 27% in the London study). The third study (Ottawa) merely reported the number of falls that were associated with injuries, and this proportion was very high (78%).

The single most important predictor of subsequent falling was the reported number of falls in the previous year (Table 3). Number of previous falls was also the only variable to provide independent predictive power ($P = 0.000$) that was not explained by the two disease severity measures (Hoehn and Yahr stage and UPDRS).

Of the two severity measures, the Hoehn and Yahr stage contributed most to predicting falling in the three-month follow-up. Hoehn and Yahr stage was associated with large increases in risk in the uncontrolled model which were reduced to borderline nonsignificance ($P =$

TABLE 3. *Odds ratios (OR) of falling in 3 mo for study, age, Hoehn and Yahr, UPDRS, and number of falls reported in the previous year (n = 219)*

VARIABLE	Uncontrolled		Controlled*	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Study				
Leiden	1.00	0.303	1.00	0.188
Southampton	1.12 (0.52, 2.42)		0.70 (0.25, 1.95)	
North Tyneside	1.61 (0.88, 3.11)		1.63 (0.63, 4.22)	
Age (years; per unit increase)	1.00 (0.98, 1.03)	0.781	0.98 (0.94, 1.01)	0.183
Sex				
Female/male	1.03 (0.60, 1.77)	0.921	0.78 (0.40, 1.51)	0.452
Hoehn and Yahr (per unit increase)	2.05 (1.41, 2.98)	0.000	1.72 (0.99, 2.97)	0.051
UPDRS27 (per unit increase)	1.10 (1.00, 1.21)	0.023[a]	1.05 (0.94, 1.17)	0.661[b]
UPDRS27[a]	1.00 (1.00, 1.00)	0.223[a]	1.00 (0.98, 1.00)	
Number of falls in the previous year (per unit increase)	1.54 (1.32, 1.81)	0.002	1.49 (1.25, 1.78)	0.000

*Controlled for the other predictor variables in the table.
[a]*P* values for uncontrolled UPDRS27 are based on likelihood ratio tests for the linear term on its own, and the quadratic term in the presence of the linear term.
[b]*P* value for controlled UPDRS27 is based on likelihood ratio test for the linear and quadratic terms removed together, df = 2.

0.051) in the presence of the other variables. The UPDRS was significant in the uncontrolled models, but its explanatory power was largely explained by the other variables. Age and gender had little predictive value, in controlled or uncontrolled models.

Figure 1a–c show the ROC curves for reported number of falls in the previous year, the UPDRS, and the Hoehn and Yahr stage. The curves agree with the results of the logistic regression in showing the superiority of number of previous falls in predicting future falls, both in terms of the area under the curve, and the closeness of the curve to the top left corner of the plot (indicating perfect prediction). The point closest to the top left corner of Figure 1a indicates a sensitivity of 68% and specificity of 81% from predicting future falling based on two or more previous reported falls. The point to the right with increased sensitivity of 77% was obtained by predicting patients to fall if they had one or more previous falls, but this was only achieved at the cost of increasing 1-specificity to 40%. Figure 1d shows the predictive power of a combined score, obtained from logistic regression including the three variables together. The combination was not superior to that from number of previous falls alone, the optimal cut point having sensitivity of 72% and specificity of 79%. Figure 1e shows the ROC curve for UPDRS in the subgroup of patients reporting no falls in the previous year. The curve was close to the diagonal line of equality (indicating no predictive power) and the AUC statistic was not much greater than 0.50. Finally, Figure 1f shows slightly better predictive power from the Hoehn and Yahr stage in this group.

Table 4 presents the sensitivity and specificity of various potential predictors of subsequent falling. The sensitivity and specificity of previous repeat falling was better in the Southampton study than the others. The accuracy of prediction is acceptable in the North Tyneside study, while in the Leiden study, the sensitivity of

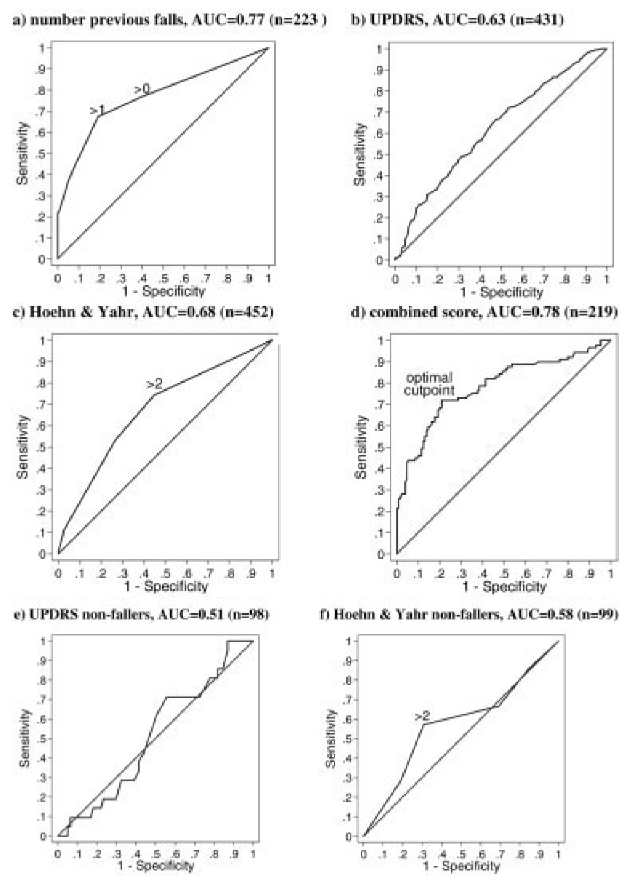

FIG. 1. ROC curves for possible predictors of falling in 3 months: (a–d) all patients; (e–f) patients reporting no falls in the previous year.

TABLE 4. *Performance of various predictors of falling at 3 mo in each study and overall. Figures are number (%)*

	Ottawa*		Leiden		Southampton		North Tyneside		Brisbane**		London		Overall	
Predictor	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
2 or more previous falls	39/70 (56%)	42/48 (88%)	8/21 (38%)	35/38 (92%)	19/22 (86%)	30/35 (86%)	35/49 (71%)	41/58 (72%)	Na	Na	Na	Na	62/92[a] (68%)	106/131[a] (81%)
1 or more previous falls	51/70 (73%)	36/48 (75%)	12/21 (57%)	27/38 (71%)	21/22 (95%)	22/35 (63%)	38/49 (78%)	29/58 (50%)	13/23 (57%)	26/29 (90%)	Na	Na	71/92[a] (77%)	78/131[a] (60%)
Hoehn and Yahr >2	54/70 (77%)	20/48 (42%)	16/21 (75%)	24/38 (63%)	20/22 (91%)	18/35 (57%)	26/49 (53%)	40/58 (69%)	13/16 (81%)	9/27 (33%)	24/28 (86%)	24/39 (62%)	86/120 (72%)	106/171 (62%)
Optimal cut point for combined score	Na	Na	11/20 (55%)	35/38 (92%)	17/20 (85%)	25/34 (74%)	36/49 (73%)	43/58 (74%)	Na	Na	Na	Na	64/89 (72%)	103/130 (79%)
Fear of falling	Na	Na	14/21 (67%)	25/38 (66%)	12/22 (54%)	28/35 (80%)	Na	Na	Na	Na	22/28 (79%)	22/39 (56%)	48/71 (68%)	75/112[b] (67%)

*Previous falls and near falls in the Ottawa study over 3 mo.
**Previous falls and near falls in the Brisbane study over 6 mo, only the presence of falls not the number was available.
[a]Combined over Leiden, Southampton, and North Tyneside.
[b]Combined over Leiden, Southampton, and London

previous repeat falling is lower. Figures combined over these three studies show only moderately high sensitivity (68%), although specificity was high (81%). Figures from the Ottawa study were based on falling in the previous 3 months, and higher sensitivity would be anticipated had falls over the previous year been reported. Specificity in the Ottawa study was high (88%), and this would be likely to drop were fall histories over a longer period to be used. A Hoehn and Yahr stage of more than two showed only moderately high sensitivity and specificity. Prediction from the combined score mirrored that from two or more previous falls in the studies separately and combined. Moderately high sensitivity and specificity for fear of falling is also shown.

For the subgroup reporting no falls in the previous year, a reported fear of falling showed only moderate sensitivity (50%) and higher specificity (71%), while sensitivity was somewhat higher (54%) for Hoehn and Yahr stage greater than 2.0, with a specificity of 69%.

Figure 2a shows the relationship between risk of subsequent falling and the UPDRS. The curve starts at low levels of risk for UPDRS close to zero, and then increases to a risk of about 60% chance of falling in 3 months for UPDRS values above 50. The curve shows a tendency for the risk of falling to drop with increasing UPDRS over values of 50, but the observed decrease is slight and is estimated from only few cases. In Table 3 including a quadratic term in UPDRS which would allow the risk of subsequent falling to decrease after an initial rise with UPDRS showed no additional predictive power over the linear term ($P = 0.223$), indicating that any decrease at high values of UPDRS is not important in explaining falling. Figure 2b shows the relation between risk of falling and UPDRS for the subgroup reporting no falls in the previous year. The risk of falls is much lower when compared to the entire group, and a tendency for risk of falling to decrease with increasing UPDRS over 35 to 40 can be detected.

We also calculated the odds ratios of individual items of the UPDRS as predictors of falling, for the group as a whole (data not shown). Except for resting tremor, all items were associated with risk of falling when controlled only for study. Speech, gait, and postural stability

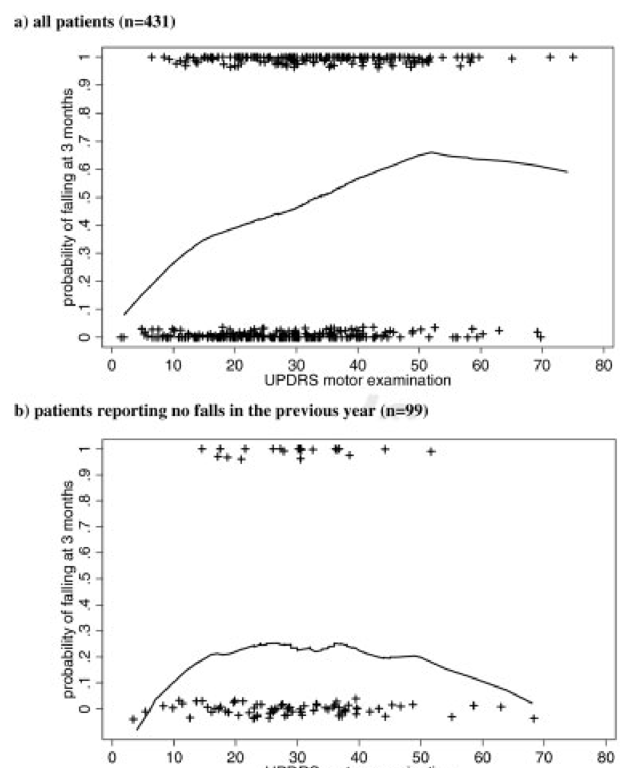

FIG. 2. Lowess smoothed curves of risk of falling in 3 months for increasing UPDRS: (a) all patients; (b) patients reporting no falls in the previous year. Points plotted with symbol (+) and subject to jittering.

were the most important predictors in this analysis, and were the only items that contained independent predictive power after controlling additionally for the other UPDRS items. Within the subgroup of patients reporting no falls in the previous year, none of the items showed significant predictive power (data not shown).

DISCUSSION

The main findings of this meta-analysis were as follows. First, among the total group of patients with PD, we observed a very high rate of falling (46% of subjects) during a relatively brief follow-up of only 3 months. Injuries were common and occurred in about a quarter of subjects. An interesting new finding was that even subjects reporting no falls in the previous year had a substantial risk of falling during this period (21%). Second, falling was best predicted by the presence of two or more prior falls during the previous year, but even the optimal combination of sensitivity (68%) and specificity (81%) remained less than perfect. Prediction was not improved by the addition of the severity measures UPDRS and Hoehn and Yahr stage. Finally, we identified fear of falling as possible predictors for falls, but this needs to be scrutinized further.

Incidence of Falls

Our meta-analysis represents the largest study of falls in PD to date. The observed high rate of falls in the total group confirms the impression gained previously from the contributing individual studies. Fall rates over 3 months were reasonably consistent across the six studies, despite some methodological differences and possible variation introduced by cultural differences. Injuries were common and occurred in about a quarter of subjects (available from two studies). A third study expressed this differently, and reported that 78% of all individual falls were associated with injuries. A likely explanation is that those persons with injurious falls apparently sustain recurrent injuries. A new and important observation is that even subjects who reported not having fallen in the previous year had a substantial risk of falling during the next 3 months (21%). Although this rate is lower than that of the group as a whole, it constitutes an unexpectedly high risk for people reporting not having fallen in the previous year.

Prediction of Falls

The best predictor of falls in the next 3 months was simply asking patients whether they had fallen in the past year. The importance of previous falls in predicting future falling is not unexpected, given earlier observations in elderly persons[23] and in one of the contributing studies in PD.[15] There are a number of issues concerning the practicalities of using reported histories of falls in predicting future falls. First, elderly people tend to forget prior falls,[24] or they may have difficulty remembering the timing of previous fall events. It is not unlikely that people demonstrate inaccuracy in remembering whether events occurred within the specified time window, particularly when these are longer periods of time. But despite these inaccuracies, self-report of prior falls still predicted future falls. We have not attempted to show the predictive power of the "true" number of previous falls, because the accuracy of the reported answer probably depends on how subjects were specifically interviewed. Indeed, methodological differences in ascertaining the fall history may explain some of the observed differences in predictive power across studies included in this meta-analysis.

A second issue is the choice for the cut point. In our meta-analysis, the combined sensitivity and specificity was better using the cut point of two or more falls (sensitivity 68% and specificity 81%) compared to one or more falls (sensitivity 82% and specificity 59%). As expected, when previous falls were ascertained over a shorter period (3 months in the Ottawa study[17]), the cut point of two or more falls achieved lower sensitivity. What is judged as the best combination depends on how a test is intended to be used. To prevent future falls and potential injuries (assuming there is an effective treatment program), a high sensitivity is required to optimally detect possible candidates for falls. However, this is inevitably achieved at the expense of lower specificity, resulting in higher immediate costs because more persons are falsely identified as fall candidates, so interventions are offered to people who may not fall.

A third important issue is that, by definition, prior falls are unable to predict the very first falls. We repeated the analysis for the subgroup of 100 subjects who reported no falls in the previous year. The results suggested that along with the Hoehn and Yahr stage, asking about fear of falling has some potential to identify these new fallers. Fear of falling had only moderate sensitivity and higher specificity in the reduced group in which the data was available. It may be that "asking is better than measuring", and this may also prove true for other potential predictors, given the lack of validated and reliable clinical tests of balance and gait in PD.[9] Fear of falling can be evaluated using the ABC scale, which has been validated for use in PD[8] and, more recently, also in abbreviated form.[25] One or two of the studies obtained information about prior near-falls, but more work is needed to develop clear definitions and a reliable way of ascertaining near-falls.

Relation With Disease Severity

Another objective of this meta-analysis was to examine the pattern of increasing risk of falling with disease severity, which, in a large retrospective study, was related to falls.[26] We addressed this question using the UPDRS motor examination score, because this continuous scale has more potential to show trends than the wider categories of the Hoehn and Yahr scale. In a previous paper[7] the risk was hypothesized to initially increase to a plateau, but to decline thereafter because of compensatory strategies adopted by patients and eventually become effectively zero as severely affected patients became immobilized and therefore no longer at risk of falling. This pattern was not observed as clearly as expected. The risk of falling did indeed increase to a plateau around the 60% chance of falling in 3 months (for UPDRS values of about 50), but there was only a slight decline in risk of falling observed among very few cases thereafter, and inclusion of a quadratic term allowing risk to decline at high severity did not produce significant improvement in the fit of the logistic risk model. The most likely explanation is that the constituent studies recruited patients from the community. Hence, many patients who were "beyond moving" could have moved to a nursing home or other institutional care and were effectively excluded. The drop in risk of falls anticipated at high disease severity might have been observed had institutionalized people been included, or within the context of a long term follow-up study.

We also analyzed the relation between falls and individual items of the UPDRS. Except for tremor, all items were related to falls, the strongest being the scores for gait and speech. In the multiple regression analysis, only speech, and to a marginal level gait and postural stability, had independent predictive power in the presence of the other items. The intuitively more logical items of posture, gait, balance, and rising from a chair were not independently associated with falls, possibly because they all act as markers of disease severity and being inter-related did not provide independent predictive power. Another explanation is that current clinical tests for balance and gait are imperfect predictors of falls in everyday life. For example, the retropulsion test is only poorly related to prospectively monitored falls in PD.[7] The relation with speech was unexpected and could well be coincidental, but might also reflect an interdependence between "axial" motor features of PD (which speech and falls both are). Such interdependence has been observed previously, for example in terms of resistance to dopaminergic medication.[27,28]

Shortcomings

This study was not without shortcomings. First, the contributing studies were somewhat heterogeneous in design. We partially accommodated this by restricting the analyses to time frames common to all studies, but this does not deal with differences in fall ascertainment. However, all studies used a reasonable approach to identify faller status. Differences in ascertainment are likely to have introduced a discrepancy in absolute numbers of reported previous falls, but we feel confident that all approaches reliably classified subjects as subsequent fallers or non-fallers, which was the main outcome measure in this study. Second, baseline assessment included only a limited number of balance tests common to all studies, and it is possible that certain combinations of different gait and balance tests, along with asking for prior falls, may yield a better prediction of future falls.[29] Third, it would have been interesting to look at the influence of polypharmacy. We had to drop this analysis because the methods of recording medications were not consistent across the studies. The issue is also compounded by potential differences in prescribing across countries. Future research should further focus on the effects of drugs, prescribed for either PD or co-morbid conditions, on the risk of falls in PD patients. Finally, it would have been interesting to correlate falls to mental decline (in particular frontal executive dysfunction), given the increasing evidence for links between cognition on the one hand, and gait, balance, and falls on the other.[30] However, this analysis was not possible because cognitive status was either not examined or studied using methods that were inconsistent across studies.

CONCLUSION

Our findings suggest that simple clinical measures are insufficient predictors of falling in PD. It proves particularly difficult to identify fallers before they have sustained their very first fall. For these prior nonfallers, asking about fear of falling may have some potential as an early predictor of falling. This will need to be clarified in future large-scale studies among prior nonfallers. Additional work is required to broaden our understanding of the etiology underlying falling, as this might offer new clues for early detection.

Acknowledgments: Dr. B.R. Bloem was supported by a research grant of the Prinses Beatrix Fonds and a ZonMw VIDI grant (number 016.076.352). The Brisbane study was supported by a research grant from Parkinson's Queensland and Queensland University of Technology.

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