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Association between instrumental activities of daily living and incidence of Parkinson's disease: a nationwide population-based cohort study

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Several studies have investigated the prodromal factors for early diagnosis of Parkinson's disease (PD). Instrumental activities of daily living (IADL) involve both motor and non-motor functions, and has been used as a screening tool for dementia. This study aimed to examine the association between IADL dependency and PD incidence and identify specific IADL items linked to an increased likelihood of developing PD. This population-based cohort study used data from the Korean National Health Insurance Service database, that contains information on long-term care services. Individuals who underwent at least one health screening and completed the geriatric assessment sheet between 2009 and 2021 were included in this study. Information on IADL was extracted from the geriatric assessment sheet. The Fine-Gray subdistribution hazard model was used to assess the association between IADL dependency and PD incidence. During a mean follow-up period of 3.78 ± 3.34 years, 308 of the 21,662 participants developed PD. The highest IADL dependency was significantly associated with an increased incidence of PD (adjusted hazard ratio [aHR] = 1.458, 95% confidence interval [CI] 1.037–2.050), particularly among women or ≥75 years. Among the 10 IADL items, dependency in financial management (aHR 1.420, 95% CI 1.057–1.909, $p = 0.0201$) or telephone use was significantly associated with an increased incidence of PD (aHR 1.536, 95% CI 1.204–1.961, $p = 0.0006$). Our results suggests that IADL dependency is a potential prodromal indicator of PD. Further research on other ethnicities that considers sociocultural differences is required to confirm this association.

Parkinson's disease (PD), the second most common neurodegenerative disease, is characterized by four cardinal motor features and is diagnosed after the appearance of these motor symptoms[1]. Various non-motor symptoms manifest not only in the advanced stages of disease but also several years before diagnosis. These prodromal non-motor symptoms can have important implications for the early diagnosis of PD[2,3]. The motor symptoms of PD appear when ~40–60% of dopamine cells in the brain are lost[4,5]. Considering the overall course of disease, diagnosis of PD seems to be considerably delayed. As a result, several efforts have been made to identify the risk factors or prodromal factors for the early diagnosis of PD[2,6–9].

Instrumental activities of daily living (IADL) encompass complex daily activities that includes food preparation, financial management, and shopping[10]. Proper motor and cognitive functions are required for IADL performance[10]. Although activities of daily living (ADL) are generally well-preserved on PD, IADL impairment can occur even in the early stages of cognitive decline in patients with PD[11]. Following the PD diagnosis, the ability to perform IADL progressively deteriorates[12]. Previous studies have identified related risk factors, such as old age, male sex, and more severe and progressive motor dysfunction[13]. However, only a few studies have reported IADL status prior PD diagnosis, primarily focusing on motor and non-motor functions before and after onset of PD thorough serial follow-up[2,14].

Performing complex IADLs is related to the cognitive domains of attention, executive function, memory, and visuospatial abilities[11]. Recently, some studies have reported a decline in cognitive functions, including

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executive function, at the time of PD diagnosis or during the prodromal stage[14]. In individuals with dementia, several studies have suggested that IADL decreases before the diagnosis of the disease[15–17]. While various screening tools have been suggested for the early diagnosis of dementia[10,16–18], screening tools for PD have not been well defined. We hypothesized that IADL could serve as a potential screening tool for PD. Therefore, this study aimed to investigate whether IADL dependency is associated with the occurrence of PD using long-term care (LTC) service data from Korea. Additionally, we conducted subgroup analyzes by age and sex and examined which IADL items were associated with PD incidence.

Results

Baseline characteristics of the study population

The baseline characteristics of the study population stratified by IADL quartiles are presented in Table 1. The analysis included 21,662 participants with a mean age of 77.70 years (±6.68). Participants in the highest quartile (Q4) were older than their counterparts, and the proportion of men increased as IADL dependency increased, reaching 47.69% in Q4. Individuals in Q1 were associated with low-income levels and lower proportions of urban residence. The percentage of participants covered by medical aid was highest in Q1 (4.47%), as was the proportion of those living alone (55.90%). The prevalence of comorbidities, such as diabetes, chronic kidney disease, and myocardial infarction, was highest in Q4. Lifestyle factors also varied across quartiles, and the higher IADL quartiles had a greater percentage of smokers, drinkers, and individuals who engaged in physical activity.

The demographic and clinical characteristics of the study population according to PD occurrence are shown in Supplementary Table 1.

Association between IADL and the incidence of PD

Over a mean follow-up period of 3.78 ± 3.34 years, 308 participants developed PD. Table 2 presents the hazard ratios (HRs) for PD incidence across the IADL quartiles. The incidence rates of PD were 2.94 per 1000 person-years in Q1 and 6.12 per 1000 person-years in Q4. A significant trend across the IADL quartiles was observed (p for trend = 0.0370), indicating an increased incidence of PD with higher IADL scores. In the fully adjusted model (Model 3), participants in the highest IADL quartile (Q4) had a 45.8% higher risk of developing PD compared with those in the lowest quartile (Q1) (adjusted HR [aHR] 1.458, 95% CI 1.037–2.050, $p = 0.0300$), independent of demographic characteristics, socioeconomic status, lifestyle factors, and comorbidities. The HRs for the association between all covariables included in the analyzes and PD incidence are provided in Supplementary Table 2. The overall pattern of the association between higher IADL dependency and PD risk was generally preserved across time-lag sensitivity analyzes (Supplementary Table 3). The cumulative incidence of PD according to IADL quartiles is shown in Fig. 1.

The associations between IADL and PD stratified by sex and age group are shown in Fig. 2. The analysis indicated that participants in Q4 had a significantly higher incidence of PD than those in Q1, particularly among women or those aged 75 years and older. Supplementary Fig. 2 shows the associations between IADL quartiles and PD incidence stratified by 5-year age group. In the subgroup analysis of participants aged 75–79 years, the aHR for PD was significantly higher in Q3 than in Q1. Among participants aged 80–84 years, the aHR for PD was significantly higher in IADL Q4 than in Q1. No statistically significant associations were observed between the IADL quartiles and PD incidence in the other age groups.

Associations between specific IADL items and PD

Table 3 presents the association between each IADL item and the incidence of PD. Across all 10 IADL items, participants who were dependent on these activities had higher PD incidence rates per 1000 person-years than those who were independent. The Fine-Gray subdistribution hazard model showed that dependency on financial management (aHR 1.420, 95% CI 1.057–1.909, $p = 0.0201$) or telephone use (aHR 1.536, 95% CI 1.204–1.961, $p = 0.0006$) was significantly associated with an increased incidence of PD.

The associations between IADL items and PD stratified by sex and age are shown in Supplementary Fig. 3. In the subgroup analysis according to sex, no significant associations were found between any IADL items and PD incidence in men. However, dependency on financial management or telephone use was significantly associated with an increased incidence of PD in women. A subgroup analysis by age showed that dependency on telephone use was significantly associated with PD incidence in both participants under 75 years of age and those aged 75 years and older.

Discussion

In this study, we investigated the incidence of PD according to IADL dependency in 21,662 individuals who received geriatric assessment sheets for LTC services. Overall, 308 individuals were diagnosed with PD, and the incidence rate was 45.8% higher in the group with the highest IADL dependency than that in the group with the most independent IADL. Particularly, this correlation was significant only in women or those aged ≥ 75 years. Among the IADL items, dependency on financial management or telephone use was significantly associated with increased PD incidence. Our findings suggest that functional dependency captured by IADL is a prodromal feature of PD, and IADL can be used for the early diagnosis of PD.

As there is no cure for PD yet, the treatment focuses on symptom management[19]. Therefore, the initiation of early treatment through early detection is crucial for the course of the disease[2]. There have been several studies on risk factors or prodromal markers for detecting individuals at risk of PD. In addition to the typical prodromal symptoms of PD, such as constipation, depression, and impaired olfaction, cognitive impairment[3], and functional decline, including ADL or IADL, have been suggested to be associated with PD risk[2,14]. A population-based study in France suggested that while global cognition was preserved, psychomotor speed and ADL have declined since 2 years before PD diagnosis[14]. Executive function has been reported to decline 15 years before PD diagnosis, leading to a decrease in IADLs in patients with PD[20]. There has also been a report that IADL decline started ~7 years before the diagnosis of PD[2]. For the methodological aspects, previous studies primarily followed-up several symptoms, including IALD, serially before and after the diagnosis of PD. As IADL dependency is strongly related to mortality[21], a confounding effect may occur, which should be considered in the analysis and interpretation of results. Therefore, our study applied the Fine-Gray model with death as a competing risk to provide a more in-depth examination of the association between IADL dependency and PD occurrence. This study used LTC service data from Korea and included a relatively large number of PD participants ($n = 308$) compared with previous studies. Additionally, we focused on the association between IADL and PD occurrence and performed subgroup analyzes according to age and sex.

In our study, individuals with the highest IADL dependency showed an ~46% higher incidence of PD. The presence or absence of cognitive decline at the time of PD diagnosis varies according to the literature[14,20]; however, some studies have reported a decline in executive function at the time of diagnosis. In addition, depression has been reported in several patients at the time of PD diagnosis[3,22]. These factors seem to influence IADL function even before the diagnosis of PD[14]. IADL has been suggested to play a role as a screening tool for dementia, including Alzheimer's disease, because it reflects subtle cognitive and functional decline[16–18]. Although a previous study investigated IADL in relation to cognitive decline in patients with PD[23], our findings extend this concept by suggesting that IADL dependency may also capture early functional changes associated with prodromal PD. Several screening tools for PD have been proposed in previous studies, usually incorporating PD-specific symptoms or formal physical examination[24]. In contrast, IADL assessments are already routinely performed in geriatric and LTC settings. To our knowledge, this is the first study to highlight IADL as a prodromal feature of PD, which could be widely and easily applicable to elderly populations in clinical practice. In this context, IADL dependency may serve as a functional marker of prodromal PD, with potential utility for risk stratification in large populations and for

Table 1 | Demographic and medical characteristics of participants

Variables	Total (*N* = 21,662)	Instrumental activities of daily living				*p*-value
		Q1 (*N* = 5435)	Q2 (*N* = 7180)	Q3 (*N* = 4495)	Q4 (*N* = 4552)	
Age (years)	77.7 ± 6.68	77.05 ± 6.26	77.72 ± 6.51	77.83 ± 6.89	78.33 ± 7.17	<0.0001
Sex						<0.0001
Male	7,678 (35.44%)	1841 (33.87%)	2013 (28.04%)	1653 (36.77%)	2171 (47.69%)	
Female	13,984 (64.56%)	3594 (66.13%)	5167 (71.96%)	2842 (63.23%)	2381 (52.31%)	
Low income level (lower 25%)	4189 (19.34%)	1235 (22.72%)	1366 (19.03%)	811 (18.04%)	777 (17.07%)	<0.0001
Residential area (urban)	7124 (32.89%)	1534 (28.22%)	2294 (31.95%)	1598 (35.55%)	1698 (37.30%)	<0.0001
Insurance type						<0.0001
National health insurance	21,167 (97.71%)	5192 (95.53%)	7041 (98.06%)	4426 (98.46%)	4508 (99.03%)	
Medical aid	495 (2.29%)	243 (4.47%)	139 (1.94%)	69 (1.54%)	44 (0.97%)	
Living alone	6974 (32.19%)	3038 (55.90%)	2575 (35.86%)	857 (19.07%)	504 (11.07%)	<0.0001
Comorbidities						
Hypertension (I10-I13, I15)	13,193 (60.9%)	3298 (60.68%)	4568 (63.62%)	2700 (60.07%)	2627 (57.71%)	<0.0001
Diabetes mellitus (E08-E13)	6058 (27.97%)	1450 (26.68%)	2008 (27.97%)	1276 (28.39%)	1324 (29.09%)	0.0526
Chronic kidney disease (N18)	837 (3.86%)	158 (2.91%)	268 (3.73%)	194 (4.32%)	217 (4.77%)	<0.0001
Dyslipidemia (E780-E785)	4374 (20.19%)	1117 (20.55%)	1438 (20.03%)	872 (19.40%)	947 (20.80%)	0.3383
Myocardial infarction (I21-I23)	320 (1.48%)	63 (1.16%)	99 (1.38%)	80 (1.78%)	78 (1.71%)	0.0317
Depression (F32)	1768 (8.16%)	442 (8.13%)	590 (8.22%)	348 (7.74%)	388 (8.52%)	0.5959
Smoking status						<0.0001
Never	16,868 (77.87%)	4251 (78.22%)	5851 (81.49%)	3506 (78.00%)	3260 (71.62%)	
Former	2847 (13.14%)	666 (12.25%)	756 (10.53%)	606 (13.48%)	819 (17.99%)	
Current	1947 (8.99%)	518 (9.53%)	573 (7.98%)	383 (8.52%)	473 (10.39%)	
Alcohol consumption						<0.0001
None	18,088 (83.50%)	4463 (82.12%)	6144 (85.57%)	3783 (84.16%)	3698 (81.24%)	
Mild r (1–3 days per week)	2348 (10.84%)	636 (11.70%)	695 (9.68%)	463 (10.30%)	554 (12.17%)	
Heavy r (4–7 days per week)	1226 (5.66%)	336 (6.18%)	341 (4.75%)	249 (5.54%)	300 (6.59%)	
Physically active subjects						<0.0001
Non	16,285 (75.18%)	4005 (73.69%)	5509 (76.73%)	3415 (75.97%)	3356 (73.73%)	
Mild (1–3 days per week)	3429 (15.83%)	917 (16.87%)	1110 (15.46%)	683 (15.19%)	719 (15.80%)	
Heavy (4–7 days per week)	1948 (8.99%)	513 (9.44%)	561 (7.81%)	397 (8.83%)	477 (10.48%)	
Body mass index (kg/m^2)	23.58 ± 3.76	23.84 ± 3.68	23.76 ± 3.76	23.42 ± 3.81	23.16 ± 3.78	<0.0001
Systolic blood pressure (mmHg)	130.42 ± 16.80	130.43 ± 16.32	130.86 ± 16.63	130.52 ± 17.21	129.63 ± 17.22	0.0017
Diastolic blood pressure (mmHg)	77.60 ± 10.29	77.64 ± 10.04	77.93 ± 10.26	77.61 ± 10.51	77.00 ± 10.39	<0.0001
Laboratory findings						
Total cholesterol (mg/dL)	190.44 ± 46.21	191.32 ± 41.80	192.44 ± 45.80	191.08 ± 54.51	185.59 ± 42.49	<0.0001
Triglyceride (mg/dL)	136.73 ± 85.23	139.11 ± 84.12	138.70 ± 86.45	136.71 ± 81.62	130.81 ± 87.81	<0.0001
HDL-C (mg/dL)	52.93 ± 20.41	53.35 ± 17.88	53.48 ± 21.51	52.90 ± 25.20	51.56 ± 15.51	<0.0001
LDL-C (mg/dL)	110.17 ± 45.07	110.14 ± 38.72	111.23 ± 45.90	110.84 ± 55.45	107.86 ± 38.87	0.0008
Hemoglobin	12.77 ± 1.67	12.90 ± 1.58	12.67 ± 1.65	12.75 ± 1.70	12.81 ± 1.77	<0.0001
Fasting glucose	108.58 ± 34.91	107.79 ± 33.23	108.43 ± 34.74	109.33 ± 37.83	109.00 ± 34.10	0.1284

HDL-C high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol.
Values are presented as mean ± SD or number (%).

complementing existing approaches to early identification of individuals at higher risk for PD. In our analysis, the association between IADL dependency and PD incidence became significant in Model 3 after adjusting comorbidities and lifestyle factors. The observed difference between Models 2 and 3 appeared to be driven primarily by the inclusion of comorbidity-related variables rather than by lifestyle factors (data not shown). Given that the elderly population typically presents with multiple chronic conditions, our findings underscore the importance of adequately accounting for overall morbidity burden to reduce residual confounding and to better estimate the association between IADL and PD risk.

In this study, items related to non-motor symptoms such as telephone use and financial management were found to be discriminative in the diagnosis of PD. Telephone use (smartphone use) and financial management require high-level cognitive abilities such as executive function, complex attention, and working memory. Previous studies have reported that executive function is impaired compared to other cognitive domains in patients with PD, even before diagnosis, which supports our results. In addition, telephone use requires not only executive function but also fine motor control, visuomotor coordination, and processing speed. Therefore, impairment in this domain may capture early motor symptoms such as

Table 2 | Associations between IADL and the incidence of PD

IADL	*N*	Event	Person-years	Incidence rate	Model 1	*p*-value	Model 2	*p*-value	Model 3	*p*-value	*p* for trend
Q1	5435	73	24,843.02	2.94	1.000		1.000		1.000		0.0370
Q2	7180	101	29,586.55	3.41	1.033 (0.765–1.397)	0.8310	1.021 (0.755–1.381)	0.8921	1.047 (0.775–1.416)	0.7647	
Q3	4495	66	16,449.21	4.01	1.063 (0.762–1.483)	0.7185	1.101 (0.788–1.537)	0.5731	1.156 (0.828–1.616)	0.3946	
Q4	4552	68	11,110.49	6.12	1.131 (0.813–1.573)	0.4662	1.287 (0.920–1.800)	0.1402	1.458 (1.037–2.050)	0.0300	

IADL instrumental activities of daily living, *PD* Parkinson's disease.
Model 1: unadjusted.
Model 2: adjusted for age, sex, income level and residential area.
IModel 3: adjusted for age, sex, income level, residential area, comorbidities, and lifestyle factors.

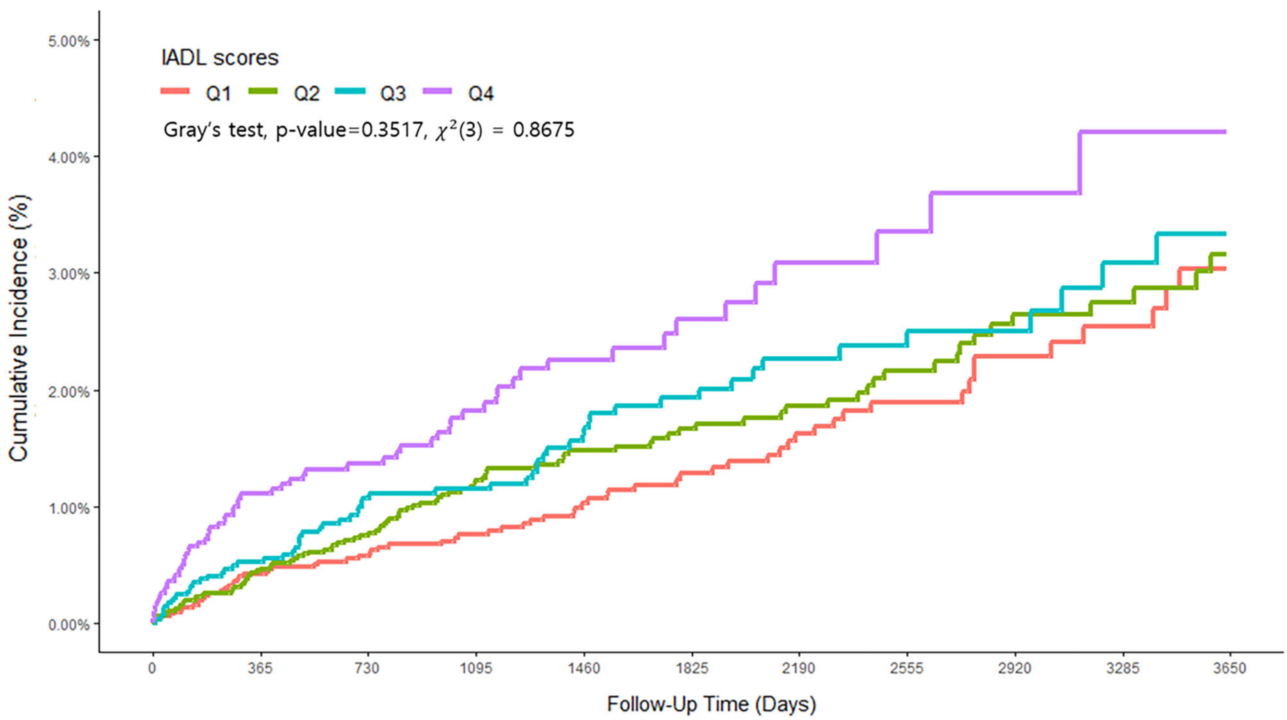

Fig. 1 | Comparison of cumulative incidence of Parkinson's disease (PD) according to instrumental activities of daily living (IADL).

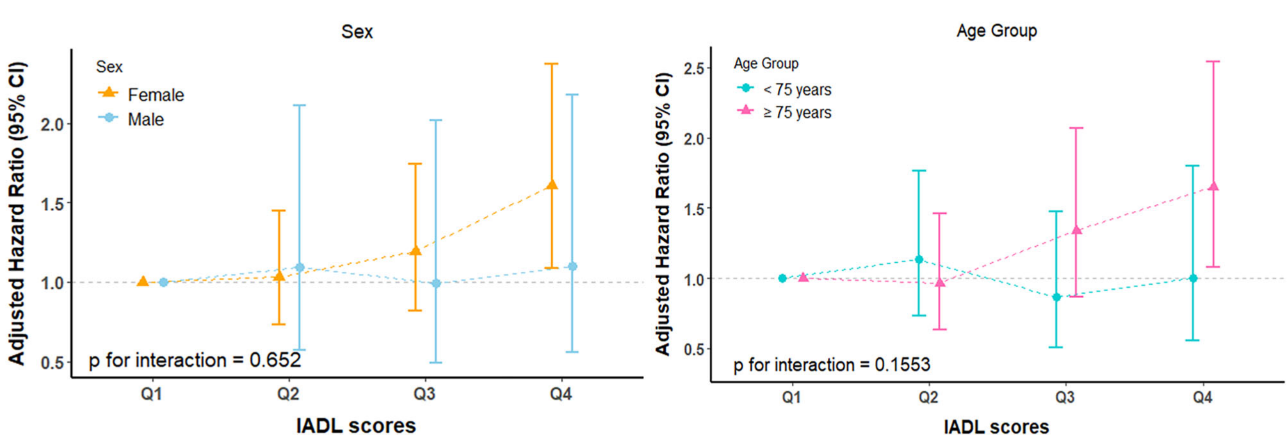

Fig. 2 | Associations between instrumental activities of daily living (IADL) and the incidence of Parkinson's disease (PD) stratified by sex and age group.

Table 3 | Associations between each item of IADL and the incidence of PD

		N	Event	Person-years	Incidence rate	aHR (95% CI)	*p*-value
Housekeeping	Independence	1994	23	9513.22	2.42	1.000	
	Dependence	19,618	285	72,479.00	3.93	1.383 (0.902–2.120)	0.1366
Food preparation	Independence	2622	36	12,975.22	2.77	1.000	
	Dependence	19,040	272	69,014.10	3.94	1.244 (0.878–1.763)	0.2190
Laundry	Independence	2657	35	12,420.58	2.82	1.000	
	Dependence	19,005	273	69,588.70	3.92	1.202 (0.844–1.710)	0.3074
Ability to handle finances	Independence	4737	54	22,049.02	2.45	1.000	
	Dependence	16,925	254	59,940.30	4.24	1.420 (1.057–1.909)	0.0201
Shopping	Independence	4474	61	20,333.67	3.00	1.000	
	Dependence	17,188	247	61,655.60	4.01	1.107 (0.836–1.466)	0.4781
Ability to use telephone	Independence	8032	94	35,691.50	2.63	1.000	
	Dependence	13,630	214	46,297.80	4.62	1.536 (1.204–1.961)	0.0006
Ability to use transportation	Independence	3173	34	13,890.43	2.45	1.000	
	Dependence	18,489	274	68,098.90	4.02	1.363 (0.952–1.952)	0.0908
Going out for short distance	Independence	6404	88	27,645.29	3.18	1.000	
	Dependence	15,258	220	54,344.00	4.05	1.070 (0.833–1.374)	0.5981
Grooming	Independence	7461	97	32,544.01	2.98	1.000	
	Dependence	14,201	211	49,445.30	4.27	1.229 (0.964–1.567)	0.0959
Responsibility for own medications	Independence	10,631	148	47,087.70	3.14	1.000	
	Dependence	11,031	160	34,903.60	4.58	1.195 (0.950–1.503)	0.1276

Adjusted for age, sex, income level, residential area, comorbidities, and lifestyle factors.

bradykinesia or reduced dexterity in addition to cognitive changes. Notably, 'telephone use' has been suggested as an item that was preserved until the late stages of dementia in a previous study[18]. This somewhat different result about telephone use may originate from the sociocultural differences in the use and access of smartphones. Since the late 2000s, smartphones have been widely used in Korea, which demand more complex functions, including unlocking the screen with a password and navigating through various apps to make call[25]. Considering our results, the definition and interpretation of IADL items need to be updated to reflect sociocultural changes[26,27]. In a previous study of patients with PD, the decline in executive functioning and attention associated with depression has shown a close association with impairment of financial management in patients with PD[22]. The prevalence of depression has been suggested as 40–50% at the time of diagnosis of PD[3], and prevalent depression at PD diagnosis could also be a possible reason for the association between impaired financial management and PD occurrence.

In the subgroup analysis by sex, the increased PD incidence in individuals with IADL dependency was only significant in women or those aged 75 years or older. Previous studies revealed that in women, executive function and functional status influencing IADL declined more rapidly than in men even before the diagnosis of PD, which is compatible with the results of this study[20]. Another possible reason is that depression, which can act as a predictor of IADL decline[28], generally shows a higher prevalence in women at the time of PD diagnosis[29,30]. In the analysis by age, the result was significant for those aged 75 years and above (considering the Supplement, it was significant between 75 and 85 years). The age group 75–85 years had the highest incidence of PD, increasing the clinical applicability for early diagnosis based on the association between IADL and PD in this age group. After the oldest age of 85 years, IADL function has been suggested to generally decline owing to factors such as frailty[31]; therefore, the association between IADL and PD appears to be indistinguishable in this age group.

This study has some limitations. First, because we used claims-based data from the Korean NHIS, we cannot rule out misclassification of PD. Second, the study population may have been subject to selection bias as it included only individuals who applied for LTC services and completed a geriatric assessment tool. Third, we were unable to include information related to PD occurrence, such as dietary habits and environmental factors, in the analysis. Fourth, cognitive functions affecting IADL were not included in the analysis. Instead, we adjusted for various comorbidities, including depression. Finally, the performance and interpretation of IADL should reflect differences in sociocultural environments. This study was conducted in a single ethnic group, highlighting the need for future research in diverse ethnic and sociocultural populations.

Methods

Data source

The National Health Insurance Service (NHIS) of Korea manages eligibility, insurance premiums, and reimbursements for healthcare and LTC services, maintaining comprehensive records of ~50 million residents. The NHIS database includes detailed demographic information, healthcare utilization data (diagnoses, treatments, and prescriptions), health screening data (checkups, lifestyle, and medical history surveys), and LTC assessments and claims.

The LTC database provides in-depth information on service applications, health assessments, and care grade determination. In Korea, LTC services are provided on an application basis. Individuals aged 65 years and older and persons under 65 years with age-related diseases who are deemed incapable of carrying out daily activities alone for 6 months or longer are eligible for LTC services, and final eligibility for LTC services is determined by the Long-Term Care Rating Board. Qualified NHIS employees used the geriatric assessment sheet, a comprehensive tool consisting of 90 items, during home visits to assess the physical and mental status of applicants. This assessment evaluates various functional capacities, including the ability to perform daily activities and cognitive functions. The results of this assessment, combined with a physician's opinion, form the basis for determining the required level of care.

Study population

This study used data from the NHIS Health Screening Database from 2009 to 2021. Individuals aged ≥40 years who had undergone at least one health screening during this period were included, yielding an initial sample size of 2,301,623 individuals. Of these, 133,103 individuals who underwent geriatric assessment were enrolled. The exclusion criteria were missing data on IADL (60 excluded), diagnosis of age-related diseases before the LTC eligibility assessment (89,315 excluded), lack of participation in regular health screenings within 2 years before and after the LTC eligibility assessment (20,545 excluded), and residency in LTC facilities (1521 excluded). After exclusion, the final study cohort comprised 21,662 participants (Supplementary Fig. 1). This study was approved by the Institutional Review Board of Yonsei University Severance Hospital, that waived the requirement for informed consent. This study was conducted in accordance with the Declaration of Helsinki.

IADL

The independent variable was IADL, a key component of the geriatric assessment sheet used to evaluate an individual's ability to perform daily items independently. These items included housekeeping, food preparation, laundry, financial management, shopping, telephone use, transportation, going out for short distances, grooming, and medication management. Each item is scored on a four-point scale (1 = very independent to 4 = very dependent). The total IADL score was calculated by summing the item scores and categorizing them into quartiles, representing varying levels of dependency. Quartile 1 (Q1) included the most independent individuals ($n = 5435$), whereas quartile 4 (Q4) included those with the highest dependency ($n = 4552$). Q2 and Q3 included 7180 and 4495 participants, respectively.

Other variables

The primary outcome was the incidence of PD, defined using the International Classification of Diseases, 10th Revision (ICD-10) code G20 and the rare intractable disease registration code V124. The rare intractable disease registration program introduced in South Korea in 2004 provides financial support to patients with rare intractable diseases, including PD. To be registered in the program with PD, the physician must confirm the patient meets strict criteria, which are almost the same as the those of the UK Parkinson's Disease Society Brain Bank. In addition, the NHIS program conducts regular cross-checking by reviewing medical records to prevent miscoding or inaccurate medical claims; therefore, the rare intractable diseases registry data are considered valid and reliable. To define incident PD, individuals with a diagnosis of PD (ICD-10 code G20 or V124) prior to the baseline LTC eligibility assessment were excluded, and PD was defined as a first-time diagnosis occurring after baseline.

Covariates were defined using demographic, clinical, and health-screening data collected at baseline (LTC eligibility assessment). The collected sociodemographic data included age, sex, income level, residential area, and living status. Comorbidities such as hypertension (ICD-10: I10-I13, I15), diabetes (ICD-10: E08-E13), chronic kidney disease (ICD-10: N18), dyslipidemia (ICD-10: E780-E785), and depression (ICD-10: F32) were identified using ICD-10 codes. Lifestyle factors (smoking status, alcohol consumption, and physical activity) were assessed using self-reported questionnaires during health screening. Other variables, such as body mass index, blood pressure, and laboratory findings (cholesterol, triglycerides, hemoglobin, and fasting glucose), were collected from the health screening data. These covariates were adjusted in the analysis to control confounding factors.

Statistical analysis

Participant characteristics across the four IADL quartiles were compared using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Continuous variables were reported as means with standard deviations, while categorical variables were presented as numbers and percentages. These tests assessed significant differences in baseline characteristics among the groups. As IADL has been suggested as an independent risk factor for mortality, death was considered a competing risk[21]. To assess the association between IADL and PD incidence, a competing risk survival analysis was performed using the Fine-Gray subdistribution hazard model, and hazard ratios (HRs) and 95% confidence intervals (CIs) were reported. Survival time was defined as the time from the LTC eligibility assessment to the first PD diagnosis or end of follow-up. The analysis was conducted using three models: model 1 was unadjusted; model 2 was adjusted for age, sex, income level, and residential area; and model 3 included additional adjustments for comorbidities and lifestyle factors. To evaluate effect modification, interaction terms between IADL quartiles and sex or age group were included in the Fine–Gray subdistribution hazard models. Statistical significance of interaction was assessed using Wald tests. To address potential reverse causality, time-lag sensitivity analyzes (1–3 years) were conducted. All analyzes were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$. Bonferroni correction was applied for post hoc analyzes, with the significance level set at $p < 0.0125$ (0.05/4 ANOVA models).

Data availability

The source NHIS data do not belong to the researchers, and we are not allowed to transfer the data file to a third party under Korean law. The data were used after obtaining approval from the Institutional Review Board and the Korean NHIS (https://nhiss.nhis.or.kr/) Big Data Operations Department (https://nhiss.nhis.or.kr/bd/ay/bdaya 001 iv.do).

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Author contributions

Y.H.P.: Statistical analysis (Design, Execution); Research project (Execution); H.J.L.: Writing of the first draft (Execution), Research project (Execution); Y.W.K.: Research project (Conception, Organization); S.C.L.: Research project (Conception, Organization), Review and critique; S.Y.Y.: Research project (Conception, Organization, Execution), Review and critique.

Competing interests

The authors declare no competing interests.

Additional information

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