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Suicide Risk and Associated Factors in Parkinson Disease: A Nationwide Cohort Study

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ABSTRACT

Background: Although increased mortality in patients with Parkinson disease (PD) is well documented, studies on suicide-related mortality have yielded conflicting results. Moreover, the impact of comorbidities, socioeconomic factors and health behaviours as potential risk factors for suicide remains underinvestigated. This study aimed to investigate suicide mortality risk in patients with PD and comprehensively elucidate the association between comorbidities, socioeconomic factors, health behaviours and suicide in PD.

Methods: This nationwide population-based cohort study used Korean National Health Insurance Service data from 2009, with a longitudinal follow-up until 31 December 2021.

This study included 2,732,294 (PD, $n = 4132$; without PD, $n = 2{,}728{,}162$) individuals. PD was defined by ICD-10 code (G20) and registration code (V124). Comorbidities were identified using medical history, ICD-10 codes, laboratory data and prescribed medications. Health behaviours were obtained from a self-reported National Health Screening Program questionnaire. The primary outcome was suicide mortality, determined by ICD-10 codes for intentional self-harm (X60-X84).

Results: Suicide mortality in patients with PD increased by 2.71-fold. Males with PD had more than a sevenfold higher risk (HR = 7.34, 95% CI, 5.25–10.26). Low-income patients with PD had an approximately fivefold higher risk compared to high-income non-PD individuals (HR = 5.10, 95% CI, 3.07–8.46). Patients with PD concomitant with depression (HR = 5.00, 95% CI, 3.06–8.16) and alcohol consumption (HR = 3.54, 95% CI, 2.14–5.89) also showed increased suicide risk.

Conclusion: This study suggests that patients with PD have a higher risk of suicide, particularly males, those with lower income, depression or alcohol consumption.

1 | Introduction

Parkinson disease (PD) is the second most prevalent progressive neurodegenerative disorder after Alzheimer, increasing with age [1]. With the global population ageing, the number of individuals aged > 65 years is rapidly rising [2], leading to an unprecedented increase in PD cases [2]. PD is characterised by cardinal motor symptoms including bradykinesia, resting tremor, rigidity and

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postural instability, as well as nonmotor symptoms [3, 4] such as psychiatric disorders, gastrointestinal problems and autonomic dysfunction. These nonmotor symptoms significantly impact the functional ability and quality of life of individuals with PD. [5]

Many studies have shown increased mortality in PD. [6] However, research on suicide-related mortality in patients with PD has yielded conflicting results [7]. Several studies report high suicide rates in these patients [8, 9], while others do not [10, 11] and one study even indicates a significantly lower risk compared to the general population [12]. Depression and other psychiatric disorders (common throughout the course of PD) are significant suicide risk factors [13]. Approximately 40%–50% of people with PD experience depression, and 30%–40% experience anxiety disorders such as generalised anxiety, social phobia and panic attacks [4, 5, 14]. These prevalent psychiatric symptoms in PD may explain the positive association between PD and suicide.

Studies on the correlation between PD and suicide suggest mental disorders, male sex, younger age and urban residence as risk factors [7]. However, the association between suicide in patients with PD and other comorbid conditions is underresearched. PD typically affects older adults, who often have various comorbidities. Alcohol and smoking are known suicide risk factors and have a complex relationship with PD onset and progression [15, 16]. As comorbidities and lifestyle factors can be modified, it is crucial to investigate their association with comorbidities, lifestyle factors and suicide among patients with PD to enhance outcomes through lifestyle interventions. Therefore, this study aimed to investigate suicide mortality risk in patients with PD using the National Health Insurance Service (NHIS) database, focusing on socioeconomic factors, comorbidities, health behaviours and their association with suicide in these patients.

2 | Materials and Methods

2.1 | Data Source

We used the Korean NHIS database, an administrative database based on health insurance claims for the entire South Korean population. All individuals born in South Korea are given a unique resident registration number and are included in the NHIS system—the single insurer that provides medical coverage to over 97% of Korean citizens and medical aid to approximately 3% of the population. The NHIS contains information on demographic characteristics, healthcare use and diagnostic codes based on the ICD-10. In addition, the NHIS provides a national health screening programme (NHSP) without charging all insured individuals biannually. The NHSP comprises a self-report questionnaire on health behaviour, medical history, anthropometric measurements and laboratory tests. This study was approved by the Institutional Review Board (IRB) of the tertiary hospital, which waived the requirement for obtaining informed consent from patients.

2.2 | Study Population

This study included individuals who underwent a health screening examination provided by the NHIS in 2009. Those with incomplete data or those under 40 years of age were excluded. To minimise the possible effects of reverse causality on the association between PD and suicide, suicides within the first year of enrolment were excluded. The Korean government operates a registration programme for rare intractable diseases (RID), including PD, and offers copayment reductions. The diagnosis of PD eligibility for the RID programme is based on strict diagnostic criteria, similar to the UK Brain Bank criteria. In this study, PD was defined based on the ICD-10 code (G20) and registration code (V124) of the RID programme in 2009. Finally, 2,732,294 individuals (4132 with PD and 2,728,162 without PD) were included in the study population and followed up until their date of death or 31 December 2021, whichever occurred first (Figure S1).

2.3 | Other Variables

All-cause mortality was evaluated based on nationwide death certificate data from the Korea National Statistical Office, and suicide mortality was determined based on the cause of death pertaining to ICD-10 codes for intentional self-harm (X60-X84).

The NHI premium was used as a proxy measure of income, and an individual with a low-income level was considered as receiving medical aid or being in the lowest quartile of the NHI premium. Residential areas were categorised into urban and rural. Current smoking was defined as ever having smoked cigarettes in one's lifetime. Drinking was defined as any type of alcohol intake > 0 g/day. Regular exercise was defined as vigorous-intensity physical activity ≥ 3 days/week or moderate-intensity physical activity ≥ 5 days/week. Baseline comorbidities were identified based on a combination of medical history, ICD-10 codes, laboratory data and prescribed medications. Anthropometric data, including height, weight and blood pressure (systolic and diastolic), were assessed. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2), and obesity was defined as $\geq 25\,kg/^2m^2$. Venous blood samples were drawn after overnight fasting to determine fasting glucose and total cholesterol levels.

2.4 | Statistical Analyses

The basic characteristics of individuals are presented as mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. The variables in the two groups were compared using Student's t-test for continuous variables or the chi-square test for categorical variables. The incidence of suicide was calculated by dividing the number of events by 1000 person-years. Univariate and multivariate Cox proportional hazard regression models were used to estimate the HR and 95% CIs for the suicide risk depending on the presence of PD. Kaplan–Meier curves were plotted and compared using log-rank tests to determine the cumulative incidence probabilities of suicide in the two groups. We conducted several sensitivity analyses on the association between PD and suicide risk by considering the occurrence of PD during the follow-up period. Subgroup analyses were performed according to socioeconomic factors, health

behaviours and comorbidities to evaluate whether the association remained consistent and to account for the confounding effects of each variable and PD diagnosis on suicide risk. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA), with statistical significance defined as a two-tailed p-value < 0.05.

3 | Results

3.1 | Baseline Characteristics of Study Population

The baseline characteristics of the study population according to the presence or absence of PD are presented in Table 1. After a median follow-up duration of 11.31 (interquartile range, 11.08–11.58) years, 9701 (0.36%) suicides occurred [56 cases (1.36%) in individuals with PD and 9645 (0.35%) in individuals without PD]. The PD group had a lower proportion of men, a lower income level and urban residence, and the age of the PD group was higher than that of the control group. Individuals with PD were less likely to smoke, drink alcohol or engage in regular physical activity than those without PD. The PD group had a higher prevalence of hypertension, diabetes mellitus (DM), metabolic syndrome, dyslipidaemia, chronic kidney disease and depression than that of the control group.

3.2 | Suicide Risk in Parkinson Disease

Table 2 displays the HRs for suicide risk during the follow-up period using univariate and multivariate Cox proportional hazards regression models. Significantly increased suicide risk was observed in individuals with PD compared to those without PD in all models. After adjusting for confounding variables, the Cox proportional regression model showed an aHR of 2.71 (95% CI, 2.08–3.53) for suicide risk in the PD group. Kaplan–Meier survival curves and log-rank tests according to the presence of PD also revealed that PD was significantly associated with increased suicide risk ($p < 0.001$, Figure 1).

We conducted sensitivity analyses of the suicide risk in patients with PD by considering the occurrence of PD during the follow-up period, which showed similar results. When new-onset PD during the follow-up period was excluded from the analysis,

TABLE 1 | Demographic and medical characteristics of participants.

		Parkinson disease		
	Total ($n = 2{,}732{,}294$)	**No ($n = 2{,}728{,}162$)**	**Yes ($n = 4132$)**	***p***
Male	1,370,921 (50.17)	1,369,073 (50.18)	1848 (44.72)	< 0.0001
Age (years)	54.4 ± 10.52	54.38 ± 10.5	68.59 ± 8.66	< 0.0001
Low income level	553,116 (20.24)	552,461 (20.25)	655 (15.85)	< 0.0001
Residential area, urban	1,236,834 (45.27)	1,235,173 (45.27)	1661 (40.2)	< 0.0001
Current smoking	570,268 (20.87)	570,035 (20.89)	233 (5.64)	< 0.0001
Drinking	1,128,267 (41.29)	1,127,631 (41.33)	636 (15.39)	< 0.0001
Regular exercise	546,615 (20.01)	545,896 (20.01)	719 (17.4)	< 0.0001
Obesity	953,826 (34.91)	952,385 (34.91)	1441 (34.87)	0.9621
Hypertension	908,806 (33.26)	906,598 (33.23)	2208 (53.44)	< 0.0001
Diabetes mellitus	318,517 (11.66)	317,633 (11.64)	884 (21.39)	< 0.0001
Metabolic syndrome	838,919 (30.7)	836,976 (30.68)	1943 (47.02)	< 0.0001
Dyslipidaemia	596,407 (21.83)	595,147 (21.81)	1260 (30.49)	< 0.0001
Chronic kidney disease	226,605 (8.29)	225,736 (8.27)	869 (21.03)	< 0.0001
Depression	109,179 (4)	108,172 (3.97)	1007 (24.37)	< 0.0001
Height (cm)	61.65 ± 8.83	161.65 ± 8.83	157.25 ± 9.34	< 0.0001
Weight (kg)	62.83 ± 10.61	62.83 ± 10.61	59.08 ± 10.46	< 0.0001
Body mass index (kg/m^2)	23.97 ± 3.04	23.97 ± 3.04	23.81 ± 3.25	0.0013
Waist circumference (cm)	81.23 ± 8.59	81.23 ± 8.59	83.04 ± 8.81	< 0.0001
Systolic blood pressure (mmHg)	124.25 ± 15.53	124.25 ± 15.53	126.92 ± 16.31	< 0.0001
Diastolic blood pressure (mmHg)	77.2 ± 10.23	77.2 ± 10.23	77.19 ± 10.3	0.9605
Fasting glucose (mg/dL)	100.08 ± 25.92	100.08 ± 25.91	105 ± 30.64	< 0.0001
Total cholesterol (mg/dL)	199.04 ± 37.25	199.05 ± 37.25	192.26 ± 39.63	< 0.0001

Note: Values are presented as mean ± SD or number (%).

TABLE 2 | Cox proportional hazard regression analysis on the suicide risk in individuals with Parkinson disease compared to general populations.

PD	*N*	Suicide (*n*)	Person-years	Incidence rate	Model 1	Model 2	Model 3	Model 4
No	2,728,162	9645	29,884,150.77	0.32	1.00	1.00	1.00	1.00
Yes	4132	56	34,413.11	1.63	4.50 (3.84–6.49)	3.30 (2.54–4.30)	3.56 (2.73–4.63)	2.71 (2.08–3.53)
p-value					< 0.0001	< 0.0001	< 0.0001	< 0.0001

Note: Incidence rate is the incidence of suicide per 1000 person-year.
Model 1: unadjusted.
Model 2: adjusted for age and sex.
Model 3: adjusted for age, sex, income level, residential area, lifestyle factors (smoking, drinking and physical activity) and obesity.
Model 4: adjusted for age, sex, income level, residential area, lifestyle factors (smoking, drinking and physical activity), obesity and comorbidities (diabetes mellitus, hypertension, dyslipidaemia, chronic kidney disease and depression).

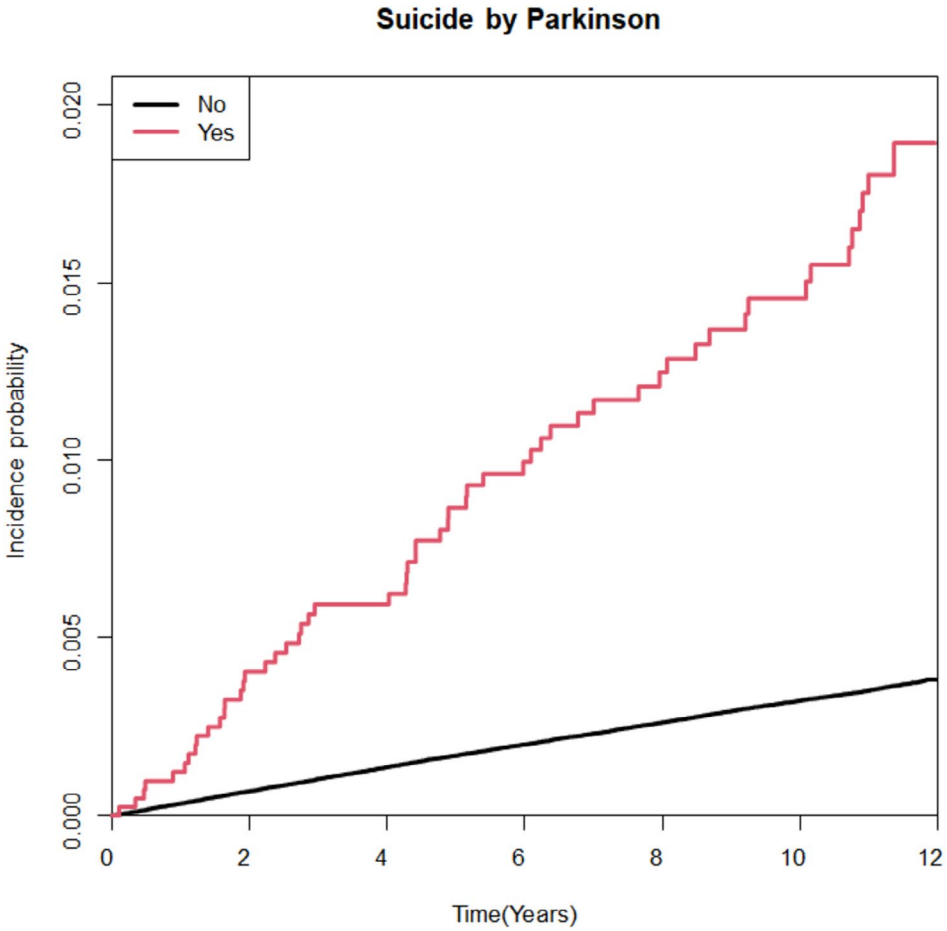

FIGURE 1 | Kaplan–Meier curves of suicide risk in Parkinson disease and comparison groups.

the aHR for suicide risk in PD was 2.62 (95% CI, 2.01–3.42) (Table S1). When new-onset PD during the follow-up period was included in the PD group, the aHR for suicide risk in PD was 2.71 (95% CI, 2.19–3.35) (Table S2).

The results of suicide risk according to the duration of PD are presented in Table S3. As the duration of PD increased, the suicide risk gradually increased (1 year, HR = 2.02, 95% CI, 1.19–3.41; 2–4 years, HR = 2.66, 95% CI, 1.76–4.00; and ≥ 5 years, HR = 3.75, 95% CI, 2.39–5.85).

3.3 | Subgroup Analysis

The results of the subgroup analyses based on socioeconomic factors (age, sex, income level and residential area), health behaviours (smoking, drinking and physical activity) and comorbidities (hypertension, DM, metabolic syndrome, dyslipidaemia, chronic kidney disease and depression) are shown in Figure 2. The interaction term for age showed a trend towards increased suicide mortality in the 40–64 years age group compared to that in the ≥ 65 years age group. The interaction terms for depression,

DM, dyslipidaemia and metabolic syndrome were significant. In individuals without these comorbidities, PD was associated with a more than threefold increased risk of suicide; however, when these comorbidities were present, there was no significant PD-related increase in suicide risk. The interaction terms for the other variables were not significant.

The confounding effects of PD and other variables on suicide risk are shown in Table 3. Compared to females without PD, those with PD showed approximately a threefold increased suicide risk (HR = 2.88, 95% CI, 1.87–4.42), whereas the risk of suicide increased more than sevenfold in males with PD (HR = 7.34, 95% CI, 5.25–10.26), revealing a synergistic effect between PD and male sex on suicide risk. Individuals with PD and low-income levels were found to have an approximately fivefold increased risk of suicide compared to those without PD and high-income levels (HR = 5.10, 95% CI, 3.07–8.46). Alcohol consumption in patients with PD increased the suicide risk approximately 3.5 times compared to those without PD who did not consume alcohol (HR = 3.54, 95% CI, 2.14–5.89). In individuals with PD and depression, the risk of suicide was approximately five times greater than in those without PD and depression (HR = 5.00, 95% CI, 3.06–8.16). Regarding other comorbidities, although PD-related suicide risk increased more than threefold in individuals without metabolic diseases such as DM, dyslipidaemia and metabolic syndrome, there was no significant association between PD and suicide risk in those with metabolic diseases.

4 | Discussion

This study investigated the association between PD and suicide mortality in a cohort of 4132 individuals with PD. Our results revealed a 2.71-fold increase in the suicide mortality rate among patients with PD. In the sensitivity analyses considering

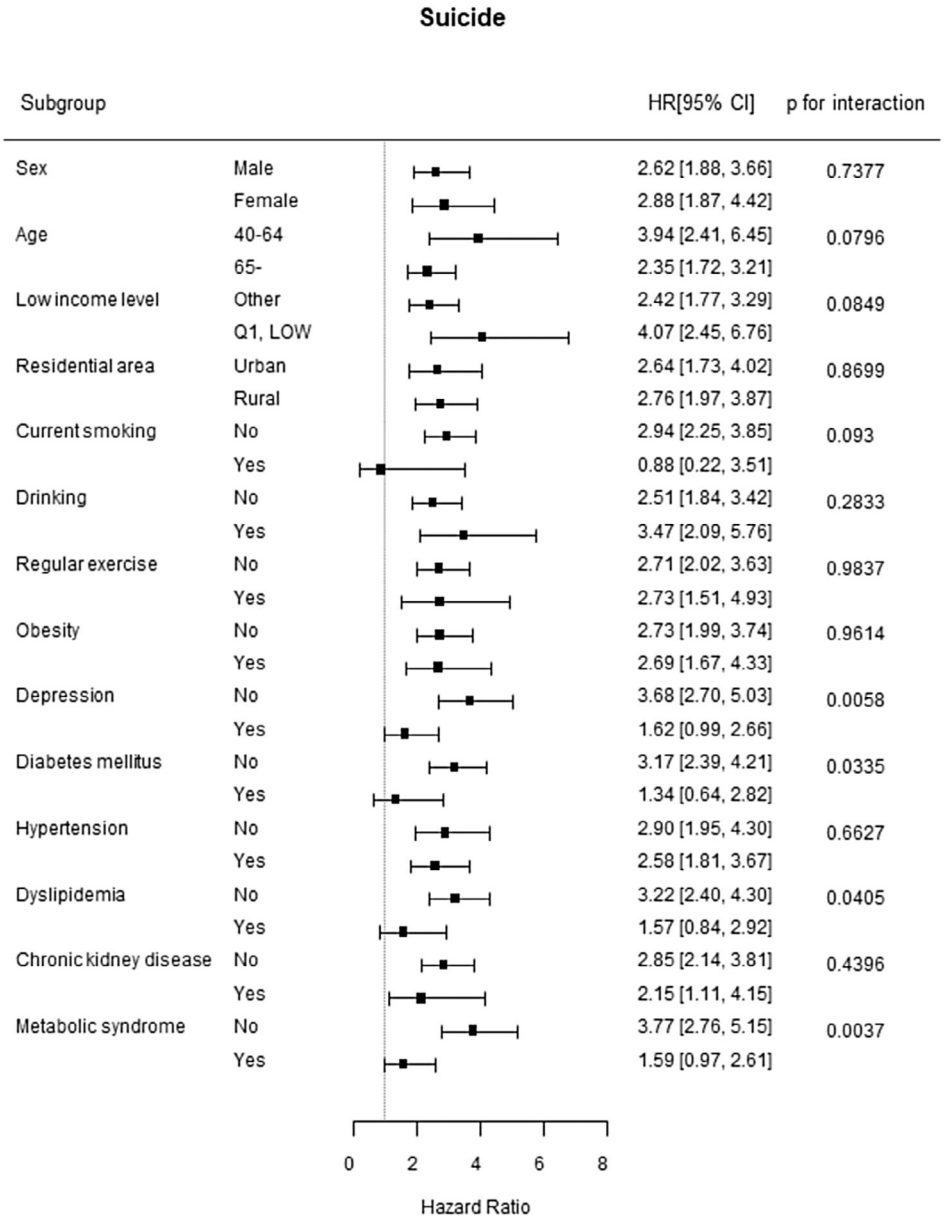

FIGURE 2 | Subgroup analysis of the suicide risk according to Parkinson disease by sociodemographic, lifestyle factors and comorbidities.

TABLE 3 | Adjusted Hazard Ratio (HR) of the suicide risk by Parkinson's disease and confounding variables.

Variables		PD	N	Suicide	Person-years	Incidence rate	Adjusted HR	*p* for trend
Sex	Male	No	1,369,073	7215	14,804,008.66	0.49	2.80 (2.66–2.96)	< .0001
		Yes	1848	35	14,123.61	2.48	7.34 (5.25–10.26)	
	Female	No	1,359,089	2430	15,080,142.1	0.16	1.00	
		Yes	2284	21	20,289.49	1.04	2.88 (1.87–4.42)	
Age	40–64	No	2,209,406	6435	24,696,952.93	0.26	1.00	< .0001
		Yes	1151	16	11,719.1	1.37	3.94 (2.41–6.45)	
	65—	No	518,756	3210	5,187,197.83	0.62	1.40 (1.30–1.51)	
		Yes	2981	40	22,694.01	1.76	3.29 (2.39–4.52)	
Low income level	No	No	2,175,701	7431	23,847,031.3	0.31	1.00	< .0001
		Yes	3477	41	28,933.39	1.42	2.42 (1.77–3.29)	
	Yes	No	552,461	2214	6,037,119.47	0.37	1.25 (1.20–1.32)	
		Yes	655	15	5,479.72	2.74	5.10 (3.07–8.46)	
Residential area	Urban	No	1,235,173	4124	13,600,532.68	0.30	1.00	< .0001
		Yes	1661	22	14,240.75	1.54	2.64 (1.73–4.02)	
	Rural	No	1,492,989	5521	16,283,618.09	0.34	1.08 (1.04–1.13)	
		Yes	2471	34	20,172.35	1.69	2.98 (2.13–4.19)	
Depression	No	No	2,619,990	8618	28,734,603.57	0.30	1.00	< .0001
		Yes	3125	40	26,295.07	1.52	3.68 (2.70–5.03)	
	Yes	No	108,172	1027	1,149,547.2	0.89	3.08 (2.88–3.29)	
		Yes	1007	16	8,118.04	1.97	5.00 (3.06–8.16)	
Current smoking	No	No	2,158,127	6149	23,726,402.19	0.26	1.00	< .0001
		Yes	3899	54	32,624.17	1.66	2.94 (2.25–3.85)	
	Yes	No	570,035	3496	6,157,748.58	0.57	1.65 (1.58–1.73)	
		Yes	233	2	1,788.94	1.12	1.45 (0.36–5.80)	
Drinking	No	No	1,600,531	4793	17,483,151.51	0.27	1.00	< .0001
		Yes	3496	41	28,816.16	1.42	2.51 (1.84–3.42)	
	Yes	No	1,127,631	4852	12,400,999.26	0.39	1.02 (0.98–1.07)	
		Yes	636	15	5,596.95	2.68	3.54 (2.14–5.89)	
Regular exercise	No	No	2,182,266	7616	23,870,553.92	0.32	1.00	< .0001
		Yes	3413	45	27,804.55	1.62	2.71 (2.02–3.64)	
	Yes	No	545,896	2029	6,013,596.85	0.34	0.98 (0.93–1.03)	
		Yes	719	11	6,608.56	1.66	2.67 (1.48–4.83)	
Obesity	No	No	1,775,777	6682	19,388,186.35	0.34	1.00	< .0001
		Yes	2691	39	21,461.15	1.82	2.73 (1.99–3.74)	
	Yes	No	952,385	2963	10,495,964.42	0.28	0.78 (0.75–0.82)	
		Yes	1441	17	12,951.96	1.31	2.10 (1.31–3.39)	

(Continues)

TABLE 3 | (Continued)

Variables		PD	N	Suicide	Person-years	Incidence rate	Adjusted HR	*p* for trend
Diabetes mellitus	No	No	2,410,529	8057	26,558,390.51	0.30	1.00	< .0001
		Yes	3248	49	27,533.98	1.78	3.18 (2.39–4.21)	
	Yes	No	317,633	1588	3,325,760.26	0.48	1.17 (1.11–1.24)	
		Yes	884	7	6,879.13	1.02	1.57 (0.75–3.31)	
Hypertension	No	No	1,821,564	5593	20,191,904.97	0.28	1.00	< .0001
		Yes	1924	25	16,526.46	1.51	2.90 (1.95–4.30)	
	Yes	No	906,598	4052	9,692,245.8	0.42	1.15 (1.10–1.20)	
		Yes	2208	31	17,886.65	1.73	2.953(2.07–4.21)	
Dyslipidemia	No	No	213,3015	7535	23,387,699.43	0.32	1.00	< .0001
		Yes	2872	46	23,333.64	1.97	3.22 (2.40–4.30)	
	Yes	No	595,147	2110	6,496,451.34	0.32	0.94 (0.90–0.99)	
		Yes	1260	10	11,079.47	0.90	1.48 (0.80–2.76)	
Chronic kidney disease	No	No	2,502,426	8759	27,522,755.3	0.32	1.00	< .0001
		Yes	3263	47	27,619.5	1.70	2.85 (2.14–3.81)	
	Yes	No	225,736	886	2,361,395.47	0.38	0.99 (0.93–1.07)	
		Yes	869	9	6,793.61	1.32	2.14 (1.11–4.12)	
Metabolic syndrome	No	No	1,891,186	6299	20,850,333.7	0.30	1.00	< .0001
		Yes	2189	40	18,070.85	2.21	3.77 (2.76–5.15)	
	Yes	No	836,976	3346	9,033,817.07	0.37	0.98 (0.93–1.03)	
		Yes	1943	16	16,342.25	0.98	1.56 (0.96–2.56)	

Note: Incidence rate is the incidence of suicide per 1000 person-year.
Adjusted for age, sex, income level, residential area, lifestyle factors, obesity and comorbidities.

new-onset PD during the follow-up period, a 2.71-fold increase in the suicide mortality rate among PD patients remained significant. As the duration of PD increased, the suicide risk gradually increased. Regarding the association between comorbidities and suicide mortality in PD, patients with both PD and metabolic diseases such as DM, dyslipidaemia and metabolic syndrome did not show an increased suicide mortality risk. Conversely, suicide mortality rates were higher in patients with PD who were male, younger, had lower income levels and experienced depression and alcohol consumption.

Studies exploring the correlation between PD and suicide have yielded inconsistent findings, with some reporting elevated suicide rates among patients with PD and others finding no such associations [11, 17]. Our results indicate a 2.7-fold increase in suicide mortality among PD patients, which is consistent with previous studies [7, 9, 17, 18]. Mechanisms for this positive association include the PD diagnosis itself, depression and functional decline leading to disability and social isolation [17]. Discrepancies regarding suicide risk in PD between the previous studies might originate from social and cultural differences across the countries. Korea has the highest suicide rate among Organisation for Economic Cooperation and Development (OECD) countries [19], and the reasons for the high suicide rate in Korea have been suggested to be psychiatric problems, economic difficulties and physical illness [20]. Economic burden and physical impairment after PD diagnosis might influence suicide rates among the Korean population already vulnerable to suicide risk. Previous studies have suggested that the suicide risk of PD is increased more than that of stroke [21, 22]. When considering this previous finding and our results according to PD duration, the progressive functional decline after PD diagnosis appears to be an important factor in the suicide risk of PD patients. On the other hand, previous studies conducted in welfare countries, such as Denmark, Finland and Canada, showed no difference in the suicide rate between PD and the comparison group [10, 11, 23]. Although the Korean RID registration programme offers copayment reduction for PD patients, the relative lack of a social welfare system in Korea could be related to an increased suicide rate in PD. Depression in PD has particularly been identified as a significant risk factor and has been extensively investigated in previous studies [9, 17]. Another reason for the elevated suicide rate in PD patients can be the negative perception of mental illness in Korea. Due to the strong societal stigma surrounding mental illness, only around 15% of those with depression are actively receiving medical treatment, leading to an increasing suicide rate in Korea [24].

Although numerous studies have focused on psychiatric risk factors for suicide in PD, the role of sociodemographic factors, health behaviours and comorbidities as potential risk factors for suicide in PD remains understudied. Therefore, to investigate the confounding effects of various factors such as comorbidities, socioeconomic factors and health behaviours on the association between PD and suicide, we conducted multidimensional analyses in this study.

When considering comorbidities, significant differences emerged based on the presence of depression, DM, dyslipidaemia and metabolic syndrome. Among patients without these comorbidities, the risk of PD-related suicide mortality rate increased, whereas among those with these comorbidities, the suicide mortality risk in patients with PD did not significantly rise. Depression is widely recognised as a major suicide risk factor in numerous studies [25]. Our findings suggest that a PD diagnosis in individuals with pre-existing depression did not appear to further heighten suicide mortality risk, aligning with previous studies indicating a strong association between depression and suicide. While numerous studies have explored the link between metabolic diseases and PD occurrence [26, 27], relatively few have investigated their association with PD prognosis, including suicide mortality [28]. In subgroup analyses by comorbidities, the presence of metabolic disease did not significantly increase suicide risk in PD. We speculate that mechanisms different from those linking depression to PD suicide mortality may influence these results. Metabolic diseases have been strongly associated with increased all-cause mortality [29, 30], yet the relationship with suicide mortality remains somewhat controversial [31, 32]. Similarly, in our analyses considering confounding effects of comorbidities and PD on suicide mortality, metabolic diseases did not exhibit clear associations with increased suicide mortality. Another possible mechanism is the impact of metabolic disease on PD progression, including all-cause mortality. Recent evidence suggests that DM and metabolic syndrome [33] may accelerate motor progression and cognitive decline in PD [33], potentially leading to disease-related death rather than suicide in individuals with PD and metabolic syndrome.

In this study, among the socioeconomic factors, male sex, younger age and lower income level were associated with increased suicide mortality among patients with PD. The role of sex as a risk factor for suicide has been extensively studied. The suicide rate among men is known to be approximately 3–4 times higher than that among women [34]. One possible explanation for why suicide occurs more often in men is the social construction of hegemonic masculinity and femininity. The emphasis on characteristics such as greater levels of strength, independence, risk-taking behaviour, economic status and individualism in males, as part of this gender role, is known to make it difficult for men to seek help for suicidal feelings and depression, thus increasing the suicide rate among them [35]. In this study, both male and female PD patients had an increased suicide rate compared to that of the general population, whereas suicide mortality was elevated up to approximately sevenfold higher in male patients. Older adults have a significant risk of suicide compared to any other age group in the general population [36]. In the subgroup analysis by age of 65 years, suicide mortality rates increased in PD in both age groups. However, the HR was 2.35 in the ≥65 years age group, whereas it was 3.94-fold higher in the 40–64 years age group. This finding may be related to the characteristics of early-onset PD (EOPD). Individuals with EOPD experience more frequent depression and a significantly higher prevalence of suicidal ideation than those with late-onset PD [37], which is consistent with the higher suicide mortality rate of the 40–64 years age group than the ≥65 years age group. Owing to the low number of suicides ($N = 16$) in patients with PD <65 years, subgroup analysis by age 40 or 50 years, which is a definition criterion for EOPD, could not be performed in this study. Further studies are required to determine the association between suicide mortalities and EOPD.

Suicide rates are reportedly higher in rural areas than in urban areas, attributing this trend to geographical and interpersonal isolation, as well as a lack of access to mental health services [38]. However, in the present study, there was no difference in suicide rates between urban and rural areas. Patients with PD commonly experience social withdrawal and isolation; therefore [39], it is likely that there would be minimal rural–urban differences, resulting in no significant regional variation in suicide rates. Income levels and suicide among patients with PD have scarcely been addressed in the existing literature. A previous study in the general population showed that Medicaid recipients had increased suicide risk (2.28; 95% CI, 1.87–2.77) [40]. Our results showed increased suicide mortality rates in PD regardless of income level; however, the aHR for suicide mortality was 5.10-fold higher in patients with a low income level. This finding may aid in establishing a policy for these patients with a low income level.

While smoking and alcohol consumption have long been recognised as significant risk factors for suicide [41, 42], research on the relationship between smoking, alcohol consumption and PD is controversial. Furthermore, studies on the impact of smoking and alcohol consumption on suicide among patients with PD are scarce. Smoking is known to decrease the risk of developing PD but does not seem to affect mortality rates [43, 44]. In the subgroup analysis by smoking, suicide mortality rates increased in patients with PD without smoking, while there was no significant association between PD and suicide in the smoking group. Although both PD and smoking are risk factors for suicide, we did not find an increase in suicide rates among patients with PD who smoked. In this study, there were only two suicides among the 233 patients with PD who were current smokers, which could not provide enough statistical power to draw clear conclusions and requires cautious interpretation. Alcohol consumption has yielded controversial results regarding both the development and progression of PD. [45] In this study, both drinkers and nondrinkers with PD showed an increase in suicide rates. However, mortality rates were 3.47-fold higher in these patients who consumed alcohol. Therefore, lifestyle modifications related to alcohol consumption are recommended to reduce suicide rates among patients with PD. Regarding physical activity, although higher physical activity levels have been associated with lower suicidal ideation and attempts [46], it was found that regular exercise did not have an impact on suicide rates among these patients.

Our study had several limitations. First, although we tried to adjust for many variables that could be related to suicide in patients with PD, clinical symptoms such as motor function could

not be included in this claims-based study. Progression of motor symptoms could result in disability, dependence and feelings of perceived burdensomeness, which are related to suicide risk [47]. Although we performed an additional analysis according to the duration of PD, future studies including clinical symptoms and PD severity for the association between PD and suicide mortality are required. Second, although we considered various factors, including diagnostic codes, laboratory values and medications, for the definition of PD and other comorbidities, misclassification cannot be excluded. Third, suicide attempts could not be accurately obtained from claims-based data; therefore, they could not be included in this study. Finally, this study's inclusion of only the Korean population presents a challenge in generalising our results to other ethnicities.

5 | Conclusion

Patients with PD have a higher suicide risk, particularly males and those with lower income, depression or alcohol consumption.

Author Contributions

Seo Yeon Yoon: conceptualization, methodology, investigation, supervision, visualization, project administration, writing – original draft, writing – review and editing, funding acquisition, software. **Jee Hyun Suh:** writing – original draft, conceptualization, data curation. **Jin Hyung Jung:** data curation, validation, formal analysis, resources, visualization. **Sang Chul Lee:** data curation, validation, formal analysis. **Kyungdo Han:** data curation, supervision, formal analysis, validation. **Yong Wook Kim:** data curation, writing – review and editing, project administration, conceptualization.

Ethics Statement

This article does not contain any studies with human participants or animals performed by any of the authors.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available in Institutional Review Board and the Korea NHIS Big Data Opera at https://nhiss.nhis.or.kr. These data were derived from the following resources available in the public domain: - https://nhiss.nhis.or.kr, https://nhiss.nhis.or.kr

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.