

## Increased risk of Parkinson's disease in cataract patients: A population-based cohort study



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### ABSTRACT

**Background:** The purpose of this study was to investigate whether there is an association between cataracts and Parkinson's disease in Taiwan.

**Methods:** A retrospective cohort study was conducted to analyze the database of the Taiwan National Health Insurance Program from 1999 to 2002. This study consisted of 26,031 individuals aged 40–84 years with newly diagnosed cataracts as the cataract group and 25,937 randomly selected individuals without cataracts as the non-cataract group. Both groups were matched for sex, age and index year of diagnosing cataracts. The incidence of Parkinson's disease by the end of 2011 and the association of Parkinson's disease with cataracts and other comorbidities were measured.

**Results:** The overall incidence of Parkinson's disease was 1.48-fold higher in the cataract group than the non-cataract group (3.18 vs. 2.15 per 1000 person-years, crude HR 1.48, 95% CI 1.32, 1.66). After adjusting for confounding factors, the adjusted HR of Parkinson's disease was 1.26 (95% CI 1.12, 1.42) for the cataract group, when compared with the non-cataract group. Dementia (HR 2.72, 95% CI 1.92, 3.84), depression (HR 2.09, 95% CI 1.63, 2.66), hypertension (HR 1.42, 95% CI 1.26, 1.61), cerebrovascular disease (HR 1.32, 95% CI 1.07, 1.63) and age (every one year, HR 1.08, 95% CI 1.07, 1.09) were other factors significantly related to Parkinson's disease.

**Conclusions:** Overall, this study discloses a 26% increased hazard of Parkinson's disease in cataract patients. Further studies are required to investigate whether cataracts are one of non-motor manifestations of Parkinson's disease.

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### 1. Introduction

Parkinson's disease is the second most common neurodegenerative disease associated with motor dysfunction, after Alzheimer's disease. Traditionally, the typical motor-related manifestations of Parkinson's disease are bradykinesia, rigidity and resting tremor, which result from progressive loss of dopaminergic neurons in the substantia nigra [1,2]. In addition to motor dysfunction, recently, there is growing evidence demonstrating

that numerous non-motor manifestations may exist in patients with Parkinson's disease and even may develop before the onset of motor-related manifestations. These non-motor manifestations mainly include anxiety, depression, sleep disorder, as well as gastrointestinal, cognitive and autonomic dysfunction [3–6], but cataracts have not been reported.

Cataracts are one of the leading causes of vision loss worldwide and are also a major public health problem. It is estimated that cataracts account for 39% of the world's 37 million blind individuals [7]. Although the real etiology of cataracts remains inconclusive, to date, many factors have been identified to be associated with the risk of cataracts [8,9]. Moreover, the sparsely available epidemiological studies using a nationwide database have not provided the information of an association between cataracts and Parkinson's disease. If cataracts are one of non-motor manifestations of

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Parkinson's disease, physicians can inform cataract patients about the possibility of developing Parkinson's disease. Therefore, we conducted a retrospective cohort study to study the risk of Parkinson's disease in cataract patients.

## 2. Materials and methods

### 2.1. Data sources

A retrospective cohort study was conducted to analyze the database of the Taiwan National Health Insurance Program. In a brief, The Taiwan National Health Insurance Program began in March 1995 and covered at least 99% of 23 million residents in Taiwan [10]. It provides outpatient, hospitalization and emergency services. The details of this insurance program can be found in previous studies [11–13]. This study was approved by the Institutional Review Board of China Medical University and Hospital, Taiwan (CMU-REC-101-012).

### 2.2. Participants

This study consisted of individuals aged 40–84 years with newly diagnosed cataracts in 1999–2002 (according to the International Classification of Diseases (ICD) 9th Revision, ICD-9 codes 366) as the cataract group. For each cataract individual included in this study, one individual without cataracts was randomly selected from the same database as the non-cataract group. Both groups were matched for sex, age (within 5 years) and index year of diagnosing cataracts. We defined the index date as the date of diagnosing cataracts. Both groups were followed up until individuals received a diagnosis of Parkinson's disease (ICD-9 codes 332.0), withdrawal from the insurance program, loss of follow-up, death or December 31, 2011.

### 2.3. Comorbidities assessment

To enhance unbiased results, individuals who had a diagnosis of Parkinson's disease, secondary Parkinsonism or congenital cataracts before the date of diagnosing cataracts were excluded from the study. Baseline comorbidities were included as follows: cerebrovascular disease, chronic kidney disease, dementia, depression, diabetes mellitus, head injury, hyperlipidemia and hypertension. In order to increase the diagnosis accuracy and to avoid individuals who were misdiagnosed or were mistakenly coded by similar manifestations with unconfirmed diagnosis, only those with at least 3 episodes of the same diagnosis for cataracts, Parkinson's disease and other comorbidities in the ambulatory care could be included in this study. Individuals with only 1–2 episodes of diagnosis of cataracts, Parkinson's disease or other comorbidities were excluded from this study. All disorders were diagnosed with ICD-9 codes. The validity of disease diagnosis, such as Parkinson's disease, cerebrovascular disease, chronic kidney diseases, dementia, depression, diabetes mellitus, head injury, hyperlipidemia and hypertension, was documented in previous studies [14–16].

### 2.4. Statistical analysis

We compared the differences in sex, age, and comorbidities between the cataract group and the non-cataract group by the Chi-square test. The incidence of Parkinson's disease was calculated as the number of Parkinson's disease patients

identified during follow-up period, divided by the total follow-up person-years for each group. Initially, all variables were included in a univariable Cox proportional hazards regression model. Next, the significant variables were further included in a multivariable Cox proportional hazards regression model to calculate the hazard ratio (HR) and 95% confidence interval (CI) of Parkinson's disease. To address the concern of constant proportionality, we have examined the proportional hazard assumption using a test of scaled Schoenfeld residuals. The test suggests the proportionality assumption is not violated ( $P = 0.13$ ). The statistical significance level was set at probability value of  $<0.05$  (SAS software version 9.1, SAS Institute Inc., Cary, North Carolina, USA).

## 3. Results

### 3.1. Baseline characteristics of the study population

In total, the study included 26,031 Individuals in the cataract group and 25,937 Individuals in the non-cataract group, with similar distributions in sex and age. Some characteristics of the study population are shown in Table 1. There were higher proportions of chronic kidney disease, depression, diabetes mellitus, head injury, hyperlipidemia and hypertension in the cataract group than those in the non-cataract group ( $P = 0.0004$  for head injury and  $P < 0.0001$  for others), but cerebrovascular disease and dementia were more prevalent in the non-cataract group ( $P < 0.0001$ ). The mean ages (standard deviation) were 65.64 (8.65) years in the cataract group and 65.22 (9.08) years in the non-cataract group.

### 3.2. Incidence of Parkinson's disease in both groups

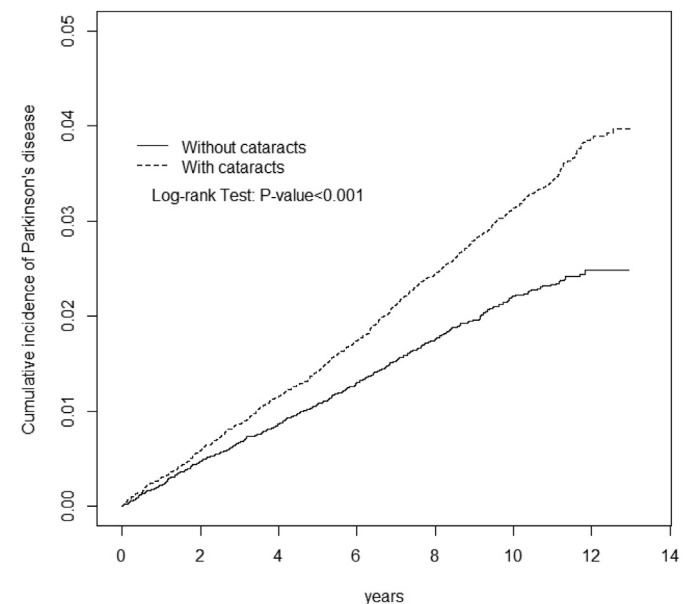
At the end of the cohort study, there were 792 Parkinson's disease patients and 249,182 person-years in the cataract group. There were 476 Parkinson's disease patients and 221,579 person-years in the non-cataract group. The overall incidence of Parkinson's disease was 3.18 per 1000 person-years in the cataract group and 2.15 per 1000 person-years in the non-cataract group (crude HR 1.48, 95% CI 1.32, 1.66). Fig. 1 shows that the cumulative incidence of Parkinson's disease was higher in the cataract group than that in the non-cataract group for 1.39% by the end of follow-up (3.87% vs. 2.48%;  $P < 0.001$ ).

**Table 1**  
Basic characteristics between cataract group and non-cataract group.

Characteristics	Cataracts N = 26,031		Non-cataracts N = 25,937		P value <sup>a</sup>
	n	%	n	%	
Sex					0.71
Male	11,798	45.32	11,798	45.49	
Female	14,223	54.68	14,139	54.51	
Age group (years)					0.71
40–64	11,834	45.46	11,834	45.63	
65–84	14,197	54.54	14,103	54.37	
Baseline comorbidities					
Cerebrovascular disease	1229	4.72	1599	6.16	<0.0001
Chronic kidney disease	700	2.69	412	1.59	<0.0001
Dementia	142	0.55	294	1.13	<0.0001
Depression	867	3.33	476	1.84	<0.0001
Diabetes mellitus	4885	18.77	1997	7.70	<0.0001
Head injury	715	2.75	586	2.26	0.0004
Hyperlipidemia	7333	28.17	3699	14.26	<0.0001
Hypertension	14,306	54.96	10,628	40.98	<0.0001

Data are presented as the number of subjects in each group, with percentages given in parentheses.

<sup>a</sup> Chi-square test comparing subjects with cataracts and non-cataracts.



**Fig. 1.** Cumulative incidence of Parkinson's disease was higher in individuals with cataracts than that in individuals without cataracts (3.87% vs. 2.48%;  $P < 0.001$ ).

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