Comparison of Comorbid Conditions between Open-Angle Glaucoma Patients and a Control Cohort

A Case-Control Study

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Objective: To determine the prevalence of selected comorbidities in patients with open-angle glaucoma (OAG) and whether these comorbidities are more prevalent among individuals with OAG than those without OAG.

Design: A retrospective, nationwide, case-control study using an administrative database.

Participants: The study group comprised 76 673 OAG patients. The comparison group comprised 230 019 subjects matched to the study cohort.

Methods: Data were collected retrospectively from the Taiwan National Health Insurance Research Database. The study cohort comprised all patients with a diagnosis of OAG (International Classification of Diseases, 9th Revision, Clinical Modification codes 365.1–365.11) in 2005 (n = 76 673). The comparison cohort comprised randomly selected patients (3 for every 1 OAG patient; n = 230 019) matched with the study group in terms of age, gender, urbanization level, and monthly income. In total, 31 medical comorbidities were selected based mainly on the Elixhauser Comorbidity Index. Separate conditional logistic regression analyses were used to estimate the adjusted odds ratio for each of the medical comorbidities between patients with and without OAG.

Main Outcome Measures: The prevalences of selected comorbidities.

Results: More than half (50.5%) of the OAG patients had hypertension, and more than 30% had hyperlipidemia or diabetes (30.5% and 30.2%, respectively). The prevalences of 28 of 31 comorbidities were significantly higher for OAG patients than subjects without glaucoma after adjusting for age, gender, urbanization level, and monthly income. The adjusted odds ratio was more than 1.50 for hypertension, hyperlipidemia, systemic lupus erythematosus, diabetes, hypothyroidism, fluid and electrolyte disorders, depression, and psychosis. Among the studied comorbidities, the prevalence difference of the OAG group minus the control group was 3% or higher for hypertension, hyperlipidemia, stroke, diabetes, liver disease, and peptic ulcer.

Conclusions: Open-angle glaucoma patients are significantly more likely to have comorbidities, many of which can be life threatening or can affect the quality of life appreciably.

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Glaucoma is one of the leading causes of blindness worldwide,[1,2] and one of the most prevalent forms of glaucoma is open-angle glaucoma (OAG).[3] The burden of the disease is increasing because the population is aging.[4] It is estimated that there will be 60.5 million people with glaucoma in 2010, increasing to 79.6 million by 2020, and of these, 74% will have OAG.[5] Bilateral blindness will be present in 4.5 million people with OAG in 2010, rising to 5.9 million people in 2020. However, patients with even mild visual impairment secondary to glaucoma may have difficulties with mobility, driving, and social interactions.[6]

In addition to the burden imposed by impaired visual function, glaucoma patients, as a function of their age, are at increased risk for chronic conditions and comorbidities that also negatively affect their health and quality of life. A large number of studies demonstrated that OAG is associated with some cardiovascular, metabolic, immunologic, neuro-degenerative, and psychological diseases, although the literature also revealed some conflicting information.[7–37] When compared with patients without glaucoma, glaucoma patients more likely died of cardiovascular disease, diabetes, chronic obstructive pulmonary disease, asthma, Alzheimer's disease, Parkinson's disease, and accidents.[38] Using a nationwide data set from Taiwan, this case-control study investigated the prevalences of selected comorbidities in the OAG population. In particular, the prevalences of selected comorbidities in those with OAG were compared with those in persons without glaucoma.

Patients and Methods

Database

The data used in this study were sourced from the National Health Insurance Research Database. Taiwan launched a single-payer

National Health Insurance Program in 1995. As of 2007, 22.60 million (approximately 98.5% of the entire population of Taiwan) of Taiwan's population were enrolled in this program. The National Health Insurance Research Database contains registration files and original claims data for reimbursement of all enrollees. Therefore, this nationwide data set provides a unique opportunity to explore the prevalence and risk of various comorbidities among patients with OAG.

Because the data set used in this study consisted of de-identified secondary data released to the public for research purposes, the study was exempt from full review by the Institutional Review Board as determined after consulting with the Director of the Institutional Review Board of the authors' institution.

Study Sample

This study featured a study group and a comparison group. First, all patients who sought ambulatory care for treatment of OAG (International Classification of Diseases, 9th Revision, Clinical Modification codes 365.1–365.11) in 2005 were identified. Because the diagnostic validity of administrative data sets often is questioned, only patients who had at least 3 consensus OAG diagnoses were included in the study sample to assure the validity and reliability of the diagnoses (n = 97 177). Those younger than 40 years (n = 12 988) were excluded. (Because glaucoma at a young age is sometimes associated with additional birth defects of other parts of the body, including those cases might have biased the analysis toward more frequent comorbidities in the OAG group.) In addition, patients who were not prescribed topical antiglaucoma medication and were not operated on for glaucoma during the study period (n = 494) were excluded. Patients who had ever undergone laser iridotomy or had never undergone a visual field examination in the previous 5 years (n = 7022) also were excluded. Ultimately, 76 673 patients with OAG were included in the study group.

The patients in the comparison group were extracted from the remaining patients who were 40 years or older and were not diagnosed as having any type of glaucoma in the database. To reduce the possibility of selecting patients who may have undetected glaucoma, only those who had ever visited any ophthalmology clinic or department of ophthalmology of any hospital during the period of 2004 through 2006 were included. Ultimately, 230 019 enrollees (3 for every patient with glaucoma) were included in the comparison group matched with the study subjects in terms of gender, age (40–49, 50–59, 60–69, and ≥70 years), monthly income (< New Taiwan Dollar [NT$]15 000, NT$15 000–30 000, NT$30 001–50 000, and ≥NT$50 001), and level of urbanization of the community in which the patient resided (urbanization levels in Taiwan are divided into 5 strata, with 1 referring to the most urbanized communities and 5 referring to least urbanized communities). The method of urbanization level stratification was based on criteria used in prior studies in Taiwan.[39]

Comorbidities

Medical comorbidities for analysis in this study were selected based on the Elixhauser Comorbidity Index.[40] There are 30 comorbidity measures included in the Elixhauser Comorbidity Index, but only 19 comorbidities were selected because some conditions such as obesity, weight loss, coagulopathy, and alcohol abuse have very low prevalences in Taiwan. Furthermore, 12 additional comorbid conditions (stroke, ischemic heart disease, hyperlipidemia, headaches, migraine, epilepsy, dementia, systemic lupus erythematosus, hepatitis B, tuberculosis, asthma, and chronic obstructive pulmonary disease) that have high prevalences in the general adult population in Taiwan were selected. Stroke was defined in this

study as having an International Classification of Diseases, 9th Revision, Clinical Modification code of 430 through 438. These diagnosis codes include ischemic infarction, intracerebral hemorrhage, subarachnoid hemorrhage, and transient ischemic attack. In the analysis, selected medical comorbidities were counted only if the condition occurred either in an inpatient setting or in more than 2 ambulatory care claims coded during the study period.

Statistical Analysis

The SAS statistical package (SAS System for Windows version 8.2; SAS Inc., Cary, NC) was used for all analyses in this study. Pearson chi-square tests were conducted to explore the difference in the prevalences of each of the 31 comorbidities among patients with and without OAG. In addition, separate conditional logistic regression analyses conditioned on gender, age, monthly income, and level of urbanization of the community in which the patient resided were carried out to estimate the odds ratio and 95% confidence interval (CI) for each of the 31 medical comorbidities among patients with and without OAG. In the analyses, discrete combinations of gender, age, monthly income, and urbanization level were treated as separate strata. That is, there were 160 (= 2×4×4×5) different strata for the 4 variables. A 2-sided P value of <0.05 was used to determine the significance of the predictors in the models.

Results

Table 1 presents the distribution of sociodemographic characteristics of patients in the study and comparison groups. Overall, the mean age of the sampled patients was 62.7 years, with a standard deviation of 13.1 years. More than one third of patients (36.0%) were older than 70 years, and most patients had a monthly income of NT$15 000 to NT$30 000.

Table 2 shows the prevalence of each of the 31 medical comorbidities by patient group. Interestingly, more than half

Table 1. Sociodemographic Characteristics of Open-Angle Glaucoma Patients Compared with Patients in the Comparison Group (n = 306 692)

Variable	Glaucoma Patients (n = 76 673), n (%)	Comparison Group (n = 230 019), n (%)
Age (yrs)		
40–49	14951 (19.5)	44853 (19.5)
50–59	17788 (23.2)	53364 (23.2)
60–69	16332 (21.3)	48996 (21.3)
≥70	27602 (36.0)	82806 (36.0)
Gender		
Male	40023 (52.2)	120069 (52.2)
Female	36650 (47.8)	109950 (47.8)
Urbanization level		
1 (most urbanized)	21622 (28.2)	64866 (28.2)
2	20932 (27.3)	62796 (27.3)
3	11731 (15.3)	35193 (15.3)
4	11654 (15.2)	34962 (15.2)
5 (least urbanized)	10734 (14.0)	32202 (14.0)
Monthly income		
<NT$15 000	12728 (16.6)	38184 (16.6)
NT$15 000–30 000	31283 (40.8)	93849 (40.8)
NT$30 001–50 000	6977 (9.1)	20931 (9.1)
>NT$50 000	25685 (33.5)	77055 (33.5)

NT$ = New Taiwan Dollar.