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Gout is associated with organic and psychogenic erectile dysfunction

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ABSTRACT

Background: Gout is a deposition disease with an inflammatory response that can increase the risk of cardiovascular disease. Gout is stressful for affected individuals, and can cause erectile dysfunction (ED). The objective of this study was to identify the association between gout and psychogenic ED (PED) and organic ED (OED).
Method: We analyzed 35,265 patients from the National Health Insurance Research Database who had been diagnosed with gout between 2000 and 2011. A total of 70,529 matched controls were included in the study as a comparison. Patients with a history of PED and OED occurring before the index date, aged less than 20 years, or with incomplete demographic information were excluded. Control patients were selected from the population of people without a history of gout, PED, or OED. The following risk factors for PED and OED were included as covariates in the multivariable models: age, comorbidities of coronary artery disease (CAD), peripheral arterial disease, chronic kidney disease (CKD), hypertension, diabetes, hyperlipidemia, depression and anxiety.
Result: Men with gout were more likely to have an increased risk (1.21 times) of ED than were those without gout. Patients with gout were 1.52 times more likely to develop OED and 1.18 times more likely to develop PED than patients in the control group. The risk of developing ED was greater for patients with comorbidities of CKD, diabetes, hyperlipidemia, depression and anxiety.
Conclusion: Gout is associated with organic and psychogenic ED. Clinical physicians should consider this association when treating patients with gout.

1. Introduction

Gout is the common prevalently inflammatory arthritis, which is caused by the accumulation of urate crystals in the joints. The global prevalence of gout was 0.08% [1]. It affects at least 2.5% of the adult population in developed countries [2], and the incidence and prevalence of gout have been rising yearly [3,4]. Gout increased in Taiwan from 1993–1996 to 2005–2008 (4.7% vs 8.2% in men and 2.2% vs 2.3% in women, respectively) [5], males have a higher prevalence than females [6]. Taiwanese aborigines had the highest prevalence (11.7%) of gout compared with non-aborigines [7]. A recent study by an Italian primary care database revealed that the prevalence of gout increased from 6.7 to 9.1 per 1000 inhabitants in the last 10 years [8]. Smith et al. reported that the burden of gout as well as disability-adjusted life years is rising. With increasing aging populations, they considered that the treatment and management of gout are necessary [1].

Organic erectile dysfunction (OED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance [9], and OED can be caused by vasculogenic problems. Recent reports have reported the prevalence of ED were at a minimum of 40% [10,11], and the appearance of vasculogenic ED is an early sign of cardiovascular disease [12,13]. Psychogenic erectile dysfunction (PED) is defined as the inability to achieve sexual satisfaction or arousal in the appropriate situations because of mental or emotional challenges. The prevalence of PED has been reported as 15% [14].

Gout is an inflammatory response that can increase the risk of cardiovascular disease [15–17], and it is as a stressful factor for affected individuals, both reasons may cause development of ED [18]. Based on the findings of these studies, a relationship between gout and ED may exist [19]. The objective of this study is to identify the association between gout and OED and PED.

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2. Methods

2.1. Data source

The National Health Insurance (NHI) program was implemented in Taiwan in 1995; it has enrolled nearly 99% of Taiwan's population (N = 23.74 million) and has contracts with 97% of hospitals and clinics nationwide (http://www.nhi.gov.tw/english/index.aspx). The National Health Insurance Research Database (NHIRD) was developed and is managed by the National Health Research Institute (NHRI), and confidentiality is maintained according to the directives of the Bureau of NHI. This is a retrospective cohort study, data sourced from the Longitudinal Health Insurance Database 2000 (LHID2000), which comprises a random sampling of one million patients from the NHIRD from 1996 to 2011. In order to protect privacy, the NHRI encrypts personal information of patients with anonymous identification numbers that connect to relevant claim information, including the gender of patients, date of birth, record of medical services, and prescriptions. Diagnosis of disease was coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). This study was approved by the Institutional Review Board of China Medical University in Central Taiwan (CMU-REC-101-012).

2.2. Study population

We analyzed 35,265 patients who had been diagnosed with gout (ICD-9-CM code 274) between 2000 and 2011, and the date of gout diagnosis was defined as the index date. Patients with a history of PED or OED (ICD-9-CM codes 302.72 and 607.84) before the index date, aged less than 20-years, or with incomplete demographic information were excluded. Control group was selected from the population without a history of gout, PED or OED documented in the LHID2000. The control individuals were randomly assigned an index date as a patient with gout and were frequency-matched as the patients with gout according to age (in 5y bands) and index date in a ratio of 2:1. A total of 70,529 controls without gout were included in the study.

2.3. Outcome measurement and comorbidities

All participants were followed from the index date until the first PED or OED occurred, withdrawal from the NHI or the end of 2011. In this study, the baseline comorbidities were considered as cardiovascular disease (ICD-9-CM code 410–414, 428, 430–438, 440–448), chronic kidney disease (CKD) (ICD-9-CM codes 580-589), hypertension (ICD-9-CM codes 401–405), diabetes (ICD-9-CM code 250), hyperlipidemia (ICD-9-CM code 272), depression (ICD-9-CM codes 296.2, 296.3, 300.4, 311), and anxiety (ICD-9-CM code 300.00).

2.4. Statistical analysis

The SAS statistical package (Version 9.2 for Windows; SAS Institute Inc., Cary, NC, USA) was used to perform all statistical analysis. A *P* value < .05 was considered statistically significant. Baseline characteristics and comorbidities between the 2 cohorts were compared. A chi-square test and a *t*-test were used to examine the differences between categorical and continuous variables. The cumulative incidences of PED and OED were estimated. The survival curves were analyzed by using the Kaplan–Meier method, the differences between the 2 cohorts were examined by the log-rank test. Univariable and multivariable Cox proportional hazard regression analysis was performed to estimate the association between gout and the risk of developing PED and OED, expressed as hazard ratios (HR) and 95% confidence intervals (CI). The following risk factors for PED and OED were included as covariates in the multivariable models: age, comorbidities of CAD, PAD, CKD, hypertension, diabetes, hyperlipidemia, depression and anxiety.

3. Results

The baseline characteristics of patients in the 2 cohorts are listed in Table 1. The distribution of age was similar in both cohorts, and 54.3% of the participants in the gout cohort were ≤ 49 years of age. Mean age for the gout and non-gout cohorts were 49.6 (SD = 16.20) and 49.1 years (SD = 16.50), respectively. The patients with gout were more likely than the non-gout patients to have cardiovascular disease (CVD) (21.0% vs 13.3%), CKD (9.08% vs 3.94%), hypertension (38.70% vs 20.20%), diabetes (8.55% vs 5.76%), hyperlipidemia (29.10% vs 8.97%), depression (2.64% vs 2.09%) and anxiety (3.82% vs 2.50%), respectively (all *p*-value < .001). Fig. 1 shows the cumulative PED and OED incidence curve for the 2 cohorts; the gout incidence curve is significantly higher than that of the non-gout cohort (log-rank test $p < .001$). The mean follow-up time were 7.44 (SD = 3.20) and 7.68 years (SD = 3.09) for the gout cohort and the non-gout cohort, respectively.

Overall, we observed 1110 events of ED (PED and OED) over 805,985 person-years: 476 in the gout cohort and 634 in the non-gout cohort, with an incidence density of 17.6 per 10000 person-years for the gout cohort and 12.1 per 10,000 person-years for the non-gout cohort (crude HR = 1.46, 95% CI = 1.29–1.64) (Table 2). After adjusting for age and comorbidities of CAD, PAD, CKD, hypertension, diabetes, hyperlipidemia, depression and anxiety, and gout patients had a 1.21-fold risk of ED (95% CI = 1.07–1.37). The age-specific gout cohort to non-gout cohort adjusted HR of ED was significant in the 35–49 year-old group (adjusted HR = 1.39, 95% CI = 1.11–1.74). The comorbidity-specific gout cohort to non-gout cohort adjusted HR of ED was significant without comorbidities (adjusted HR = 1.48, 95% CI = 1.20–1.81). Stratified analysis by follow-up duration revealed that the incidence of ED decreased with the follow-up time. The adjusted HR of ED was significantly higher at ≦7 follow-up years (adjusted HR = 1.32, 95% CI = 1.15–1.52) than in later on (adjusted HR = 1.26, 95% CI = 0.95–1.67). The results of the univariable and multivariable Cox proportional hazard analyses for the association between ED and gout are shown in Table 3. The risk of developing ED was 1.01 times (95% CI = 1.01–1.02) greater for each year a patient's age increased. The risk of developing ED was greater for patients with comorbidities of CKD (adjusted HR = 1.47, 95% CI = 1.21–1.79), diabetes (adjusted HR = 1.31, 95% CI = 1.07–1.60), hyperlipidemia (adjusted HR = 1.50, 95% CI = 1.29–1.74), depression (adjusted HR = 2.01, 95% CI = 1.53–2.65) and anxiety (adjusted HR = 1.50, 95% CI = 1.15–1.97).

Table 4 shows the incidence rate and HR of the various outcomes between patients with and without gout. Patients with gout were 1.52 (95% CI = 1.03–2.22) times more likely to develop OED and 1.18 (95%

Table 1
Demographic characteristics and comorbidities in cohorts with and without gout.

Variable	Gout		*p*-Value
	No	Yes	
	N = 70,529	N = 35,265	
Age, year			0.99
≤34	14760(20.9)	7380(20.9)	
35–49	23546(33.4)	11773(33.4)	
50–64	17576(24.9)	8788(24.9)	
65+	14647(20.8)	7324(20.8)	
Mean ± SD†	49.1 ± 16.5	49.6 ± 16.2	<0.001
Comorbidity			
Cardiovascular disease	9362(13.3)	7410(21.0)	<0.001
CKD	2777(3.94)	3201(9.08)	<0.001
Hypertension	14223(20.16)	13631(38.65)	<0.001
Diabetes	4063(5.76)	3016(8.55)	<0.001
Hyperlipidemia	6329(8.97)	10249(29.06)	<0.001
Depression	1474(2.09)	931(2.64)	<0.001
Anxiety	1764(2.50)	1346(3.82)	<0.001

Chi-square test; †: T-test.
CKD denotes chronic kidney disease.