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Increased risk of stroke in patients with osteoarthritis: a population-based cohort study

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SUMMARY

Objectives: Osteoarthritis (OA) is related to carotid atherosclerosis. Few studies have investigated the incidence of cerebrovascular diseases in patients with OA. Therefore, we conducted a population-based cohort study to determine the incidence and risk of stroke in patients with OA.
Methods: We used data from Taiwan's Longitudinal Health Insurance Database 2000 (LHID2000) to investigate the incidence of stroke in 43,635 patients with OA newly diagnosed between 2002 and 2003. The non-osteoarthritis (non-OA) cohort comprised 43,635 people from the general population. The follow-up period was from the index date of OA to the date of censoring date or stroke diagnosis, or to the end of 2010.
Results: The overall incidence of stroke was 36% higher in the OA cohort than in the non-OA cohort, with an adjusted hazard ratio (aHR) of 1.10 (95% confidence interval [CI] = 1.06–1.14) after adjustment for covariates. Men, age, comorbidity, non-selective nonsteroidal anti-inflammatory drugs (NSAIDs), and Cox-2 selective NSAIDs are independent risk factors of stroke. The OA adults with mild to moderate OA (aHR = 1.97, 95% CI = 1.70–2.28 for young adults; aHR = 1.33, 95% CI = 1.25–1.42 for middle-aged adults; aHR = 1.16, 95% CI = 1.12–1.21 for older adults) and severe OA (aHR = 3.78, 95% CI = 2.50–5.70 for young adults; aHR = 1.34, 95% CI = 1.16–1.56 for middle-aged adults; and aHR = 1.01, 95% CI = 0.92–1.10 for older adults) exhibited increased risks of stroke compared with their counterparts without OA.
Conclusion: OA may be associated with a slightly increased risk of stroke.

Introduction

Osteoarthritis (OA), a chronic degenerative disorder, involves the cartilage and its surrounding tissues. It typically affects joints in the hands, knees, hips, and spine, causing joint pain, stiffness, and limited movement. Nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, reduced body weight, and lubricant injections remain the treatment options for mild to moderate OA. No effective therapy exists for managing severe knee and hip OA; therefore, total joint replacement is the final solution to relieve pain and disability. In developed countries, the prevalence of OA is rapidly escalating, which is associated with a briskly aging population and increasing obesity rate[1,2]. In addition to causing physical and psychological effects, OA may cause social and economic burden[3,4].

Previous studies have reported the correlation between OA and an increased mortality rate[5–7]. This epiphenomenon of increased mortality in patients with OA exists because of advanced age, poor physical activity, and increased cardiovascular risks[8,9]. The US National Health and Nutrition Examination Survey III reported an association between OA and an increased prevalence of metabolic syndrome[10]. Recent studies have indicated increased carotid intimal–medial thickness and carotid plaque in patients with OA[11–13].

Stroke, a cerebrovascular disease, can be classified into hemorrhagic and ischemic stroke. Stroke is a devastating disease with high

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rates of morbidity and mortality despite of advanced treatment worldwide. In Taiwan, stroke is the main cause of disability in adults and the third leading cause of death[14,15]. A Canadian community health survey revealed an increased prevalence of heart diseases, namely coronary artery disease (CAD) and heart failure (HF), in patients with OA. Stroke is not significantly different in participants with and without OA[16]. However, the diseases in the Canadian study were assessed using a self-reported and cross-sectional study that lacked a longitudinal follow-up to evaluate the possible causal relationship between cerebrovascular diseases and OA. Therefore, we conducted a population-based cohort study to investigate whether patients with OA are at an increased risk of stroke.

Methods

Data source

The Taiwan government established the National Health Insurance (NHI) program in 1995. According to the National Health Insurance Administration (NHIA), the NHI program covers approximately 99% of residents and is contracted with more than 97% of health care institutions in Taiwan (http://www.nhi.gov.tw/english/index.aspx). In 2000, the National Health Research Institutes established the Longitudinal Health Insurance Database 2000 (LHID2000), which contains the claims data and prescribed drugs of patients who received outpatient, inpatient, emergency, or dental care. The NHIA encrypted the patient identities in the LHID before releasing it to researchers. We used the LHID2000, which comprises data of 1 million randomly selected beneficiaries of the NHI program. No statistically significant differences existed in the distribution of age, sex, or health care expenses between the LHID2000 and all NHI beneficiaries (http://nhird.nhri.org.tw/en/Data_Subsets.html#S3). The patients in the LHID2000 were diagnosed according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. This database has been reliably used in our previous studies[17,18]. This cohort study was approved by the Institutional Review Board of Tsaotun Psychiatric Center.

Study design

In this retrospective cohort study, we enrolled patients aged 20–90 years who were newly diagnosed with OA between 2002 and 2003 in the OA cohort, with the date of the diagnosis being the index date. Each patient from the OA cohort was frequency-matched with one participant without OA from the general population according to sex, age, and index year. We excluded patients younger than 20 years or older than 90 years; those with incomplete information regarding sex or the birth date; and those with a history of OA or stroke before 2002. We followed up each participant from the index date until the diagnosis of stroke, withdrawal from the NHI program, death, or the end of 2010 (Fig. 1).

Definition of outcome variables

The diagnoses of stroke (ICD-9-CM 430-438), including hemorrhagic and thrombotic stroke, listed in the LHID2000 were made on the basis of clinical neurology, brain computed tomography, or brain magnetic resonance imaging.

Definition of exposure variables

Patients aged 20–90 years and diagnosed with OA (ICD-9-CM 715 and 721) for more than three visits to health care institutions between 2002 and 2003 were identified as the OA cohort.

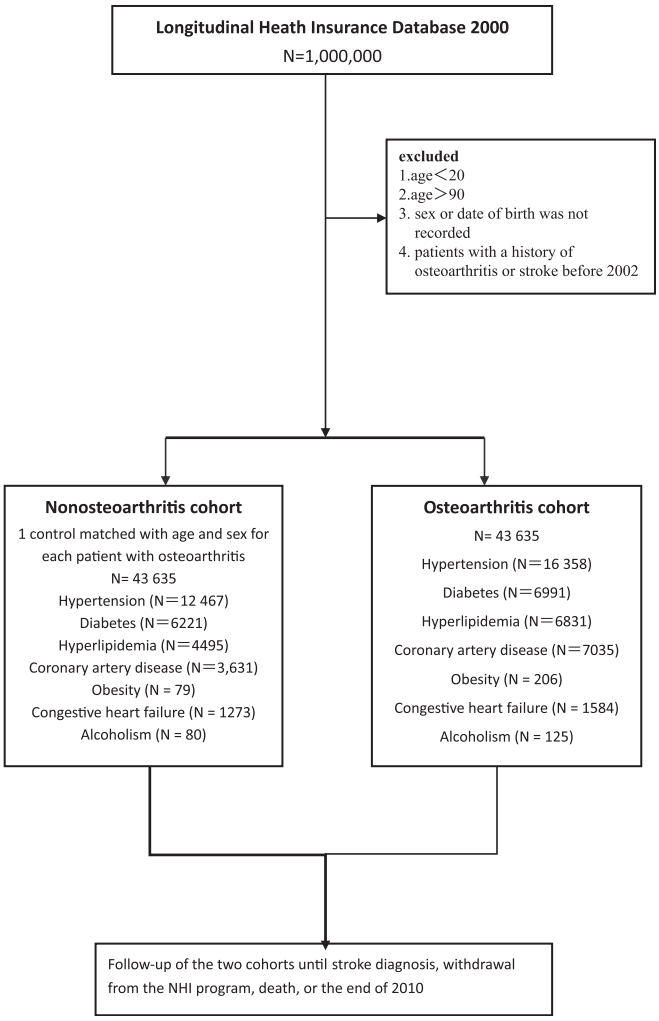

Fig. 1. Flow scheme of the study participants.

Definition of OA severity

Severe OA was defined as OA requiring the application of orthopedics for a total knee or hip joint replacement (procedure codes, 64,164 B and 64,162 B for total knee and hip replacements, respectively). The NHIA audits applications for total knee and hip replacements by conducting peer reviews of the medical records before surgical interventions; patients must exhibit great pain and discomfort when walking or moving the joint in addition to considerable joint space narrowing, large osteophytes, sclerosis, and definite bony deformity on X-ray images. Patients diagnosed with OA but who did not require surgery were defined as having mild to moderate OA.

Covariates

We stratified age into three groups: young adults (20–49 years), middle-aged adults (50–64 years), and older adults (≥65 years). Baseline comorbidities included hypertension (ICD-9-CM 410-415), diabetes (ICD-9-CM 250), hyperlipidemia (ICD-9-CM 272), CAD (ICD-9-CM 410-414), obesity (ICD-9-CM 278), congestive HF (CHF, ICD-9-CM 428), and alcoholism (ICD-9-CM 291, 303, 305.00, 305.01, 305.02, 305.03, 790.3, and V11.3). Eleven oral non-selective NSAIDs commercially available in Taiwan, including indomethacin, sulindac, diclofenac, aceclofenac, piroxicam, ibuprofen,