Cardiovascular comorbidities in patients with rosacea: A nationwide case-control study from Taiwan

Tuan-Chun Hua, MD,[a,b,c] Pei-I Chung, MD,[b,d] Yi-Ju Chen, MD, PhD,[b,e] Lung-Chi Wu, MD,[b,d,f,g]
Yen-Da Chen, MD,[b,d] Chian-Yaw Hwang, MD,[b,c] Szu-Yin Chu, MD,[b,d] Chih-Chiang Chen, MD,[b,d]
Ding-Dar Lee, MD, PhD,[b,d] Yun-Ting Chang, MD, PhD,[b,d] and Han-Nan Liu, MD[b,d,g]
Hsinchu, Taipei, and Taichung, Taiwan

See related article on page 308

Background: Rosacea is a chronic inflammatory skin disease. Inflammation plays a prominent role in atherosclerosis and its complications.

Objective: We sought to investigate the associations of rosacea with cardiovascular disease risk factors and cardiovascular diseases from a nationwide population-based database.

Methods: A total of 33,553 patients with rosacea and 67,106 age- and gender-matched control subjects were identified from the National Health Insurance Research Database in Taiwan from 1997 to 2010. Multivariate logistic regressions were performed to compare the odds of comorbidities between the 2 groups.

Results: Dyslipidemia (odds ratio 1.41; 95% confidence interval 1.36-1.46), coronary artery disease (odds ratio 1.35, 95% confidence interval 1.29-1.41), and hypertension (odds ratio 1.17, 95% confidence interval 1.12-1.21) were significantly associated with rosacea. Coronary artery disease remained independently associated with rosacea after adjustment for hypertension, diabetes mellitus, and dyslipidemia. Male patients with rosacea had higher risks for all comorbidities than female patients with rosacea.

Limitations: The National Health Insurance Research Database does not contain information regarding rosacea subtypes or disease severity, or laboratory data.

Conclusion: Patients with rosacea are more likely to have dyslipidemia and hypertension. They are also at increased risk of coronary artery disease after adjustment for cardiovascular disease risk factors. (J Am Acad Dermatol 2015;73:249-54.)

Key words: atherosclerosis; cardiovascular disease; coronary artery disease; dyslipidemia; inflammation; psoriasis; rosacea.

Rosacea is a chronic skin disease characterized by transient or persistent central facial erythema, visible blood vessels, and often papules and pustules. The precise pathophysiology remains unclear, but rosacea is generally accepted as an inflammatory disease.

The chronic inflammatory nature of rosacea is similar to many other skin diseases such as psoriasis.[1]

Inflammation plays a prominent role in atherosclerosis,[2] and an association between psoriasis and cardiovascular diseases (CVDs) has been reported repeatedly.[3,4] However, to our knowledge, only 1 study with small sample size has shown that patients with rosacea may have a higher risk of CVDs.[5] The main objective of this nationwide population-based case−control study in Taiwan was to clarify the

associations of rosacea with CVD risk factors and various CVDs.

METHODS
Data sources
We analyzed published national data from the National Health Insurance Research Database (NHIRD) in Taiwan. The National Health Insurance program covered up to 99.6% of Taiwan's population and contracted with about 92% of all health providers.[6,7]

The database provides scrambled patient identification number along with date of birth, gender, diagnostic codes in the format of the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*, medical specialty, and dates of outpatient clinic visits.

Study sample
We identified all individuals with diagnoses of rosacea (*ICD-9-CM* code 695.3) between 1997 and 2010 from the NHIRD. To ensure diagnostic validity, we focused on patients with at least 2 diagnoses that were made by dermatologists. Because acne (*ICD-9-CM* code 706.1), seborrheic dermatitis (*ICD-9-CM* code 690.1), and cutaneous lupus erythematosus (*ICD-9-CM* code 695.4) are frequently confused with rosacea, patients with 2 diagnoses of any of these diseases were excluded from the study group.

To serve as the comparison group, we randomly selected 2 age- and gender-matched subjects without rosacea from the Longitudinal Health Insurance Database 2000 for each case in the study group. Longitudinal Health Insurance Database 2000 contains the entire original claims data from 1 million people randomly sampled from the NHIRD.

The study protocol was reviewed and approved by the institutional review board of Taipei Veterans General Hospital (2013-02-007AC).

Ascertainment of diseases associated with rosacea
Cardiovascular comorbidities were investigated by corresponding *ICD-9-CM* codes between 1997 and 2010. To be designated as having a certain disease, the patient had to have at least 2 diagnoses made by a physician with the corresponding specialty. The CVD risk factors included hypertension (*ICD-9-CM* codes 401-402), diabetes mellitus (DM) (*ICD-9-CM* code 250), and dyslipidemia (*ICD-9-CM* code 272). The comorbid CVDs included coronary artery disease (CAD) (*ICD-9-CM* codes 411-414), peripheral arterial occlusive disease (PAOD) (*ICD-9-CM* codes 440.2, 444.2), and cerebral infarction (*ICD-9-CM* codes 433-434, 436-437).

Statistical analysis
Microsoft SQL Server 2008 (Microsoft Corp, Redmond, WA) and SPSS Statistics 17.0 for Windows (IBM Corp, Armonk, NY) were used to analyze the data. Continuous data are presented as median ± interquartile range. For between-group comparisons, the Pearson χ^2 test was used for nominal data. Multivariate logistic regressions were performed to calculate the odds ratio (OR) and 95% confidence interval (CI), after adjusting for age, gender, and concomitant comorbidities to estimate the magnitude of associations between individual diseases and rosacea. The *P* values were corrected by the Bonferroni method by dividing the *P* value by the number of variates. A 2-tailed corrected *P* value of less than .008 was considered statistically significant.

We conducted sensitivity analyses to determine the associations if those with diagnoses of acne, seborrheic dermatitis, and cutaneous lupus erythematosus had not been excluded, and if the diagnoses were made either by a specialist or nonspecialist.

RESULTS
Characteristics of patients with rosacea and control subjects
A total of 33,553 patients with rosacea were identified. The median age of onset was 44 (interquartile range 33-53) years. There were 24,947 (74.4%) female and 8606 (25.6%) male patients. The prevalences of hypertension, dyslipidemia, CAD, PAOD, and cerebral infarction were higher in the study group (*P* < .05). The prevalence of DM did not differ statistically between the 2 groups (*P* = .559) (Table I).

Associations of rosacea and cardiovascular comorbidities
In the multivariate logistic regression analysis adjusted for age and gender, patients with rosacea

CAPSULE SUMMARY

- Rosacea is a chronic inflammatory disease. Inflammation plays a prominent role in atherosclerosis.

- Our study demonstrated that patients with rosacea tend to have an increased incidence of dyslipidemia, hypertension, and coronary artery disease.

- Coronary artery disease was independently associated with rosacea after adjustment for cardiovascular disease risk factors.