Assessment of the risk of cardiovascular disease in patients with rosacea

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Background: Recent studies have shown a higher prevalence of cardiovascular (CV) risk factors in patients with rosacea. However, it remains unknown whether rosacea represents an independent CV risk factor.

Objective: We evaluated the risk of myocardial infarction, stroke, CV death, major adverse CV events, and all-cause mortality, respectively.

Methods: Between January 1, 1997, and December 31, 2012, a total of 4948 patients with rosacea were identified and matched with 23,823 control subjects. We used Poisson regression to calculate incidence rate ratios.

Results: Adjusted incidence rate ratios were 0.75 (95% confidence intervals [CI] 0.57-1.00) for myocardial infarction, 1.08 (95% CI 0.86-1.35) for ischemic stroke, 1.01 (95% CI 0.61-1.67) for hemorrhagic stroke, 0.99 (95% CI 0.80-1.24) for CV death, 0.99 (95% CI 0.86-1.15) for major adverse CV events, and 0.95 (95% CI 0.85-1.06) for all-cause mortality.

Limitations: We were unable to distinguish between the different subtypes and severities of rosacea.

Conclusions: In this population-based study, rosacea was not associated with increased risk of adverse CV outcomes or death. (J Am Acad Dermatol 2016;75:336-9.)

Key words: cardiovascular disease; epidemiology; risk factors; rosacea.

Rosacea is a chronic facial skin condition that predominately affects women[1] and fair-skinned individuals.[2] Recent articles have suggested that rosacea may be associated with dyslipidemia, hypertension, alcohol consumption, tobacco smoking, and coronary artery disease.[3,4] However, it remains unclear whether rosacea is also associated with myocardial infarction (MI), stroke (ischemic or hemorrhagic), cardiovascular (CV) death, major adverse CV events (MACE) (ie, a composite of MI, stroke, and CV death), and all-cause mortality. We evaluated such possible relationship in Danish patients with rosacea.

Abbreviations used:

CI:	confidence interval
CV:	cardiovascular
MACE:	major adverse cardiovascular events
MI:	myocardial infarction

METHODS

The study was approved by the Danish Data Protection Agency, and ethical review is not required for Danish register studies. Health care is free for Danish citizens and information from the Civil

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Personal Register[5] can be linked at individual level with nationwide registers to obtain complete information on hospital admissions, procedures, diagnosis (according to the *International Classification of Diseases*),[6] and tax-reported income.[7]

We identified all patients between January 1, 1997, and December 31, 2012, with a first-time hospital (inpatient or outpatient) diagnosis of rosacea (*International Statistical Classification of Diseases, 10th Revision* code L71). We defined the index date as the time of the first diagnosis of rosacea for each individual patient, and patients were matched 1:5 (on age, sex, and calendar time) with healthy control subjects. The index date for the control subjects was defined as the date of first rosacea diagnosis for the corresponding case, and the cohort was followed up until migration, death from any cause, or the occurrence of an end point, whichever came first. We excluded patients with a history of MI or stroke (ischemic or hemorrhagic) before study start. The primary end points were a diagnosis of MI (ICD-10 codes I21–I22), ischemic stroke (ICD-10 codes I63–I64), hemorrhagic stroke (ICD-10 codes I60–I61), and CV death (ICD-10 codes I00–I99), respectively, and secondary end points were all-cause mortality and MACE, ie, a composite of MI, stroke (ischemic or hemorrhagic), and CV death, respectively. The identification of MI and stroke was previously validated.[8,9] Baseline treatment up to 6 months before study inclusion was defined for antimigraine drugs and cholesterol-lowering agents. Baseline comorbidity was assessed up to 5 years before study inclusion for alcohol abuse, cardiac dysrhythmia, diabetes, and hypertension. Hypertension was defined by use of 2 antihypertensive drugs, as previously described and validated with a positive predictive value of 80% and a specificity of 95%.[10] Diabetes was defined by either a hospital diagnosis or use of glucose-lowering drugs. Collection of data on smoking history and alcohol abuse has been described elsewhere.[11,12] Age-standardized socioeconomic status from 0 to 4 was calculated based on income during up to 5 years before study inclusion.

Statistical analysis

We summarized incidence rates per 1000 person-years, and used Poisson regression to estimate crude and fully adjusted (for age, sex, socioeconomic status, smoking, cholesterol-lowering drugs, and comorbidity) incidence rate ratios. Rosacea is significantly associated with migraine, and it is firmly established that certain forms of migraine are significantly associated with increased risk of ischemic stroke.[13,14] Therefore, we also adjusted for antimigraine drugs in fully adjusted analyses of ischemic stroke. *P* less than .05 was considered statistically significant and results were reported with 95% confidence intervals (CIs) where applicable. Analyses were performed using SAS, Version 9.4 (SAS Institute Inc, Cary, NC) and STATA, Version 11.2 (StataCorp, College Station, TX).

CAPSULE SUMMARY

- Rosacea has been associated with dyslipidemia, hypertension, alcohol consumption, tobacco smoking, and cardiovascular disease.
- Rosacea is not independently associated with increased cardiovascular risk or all-cause mortality.
- Focus on modifiable (lifestyle) risk factors in patients with rosacea may be warranted.

RESULTS

The final study population comprised a total of 4948 patients with rosacea and 23,023 control subjects matched on age, sex, and calendar time. The baseline characteristics are listed in Table I, and during the study there were a total of 387 MIs, 491 ischemic strokes, 101 hemorrhagic strokes, 492 CV deaths, 1199 MACE, and 1963 deaths of any cause. The incidence rates per 1000 person-years are shown in Table II. The fully adjusted analyses gave incidence rate ratios of 0.75 (95% CI 0.57-1.00) for MI, 1.08 (95% CI 0.86-1.35) for ischemic stroke, 1.01 (95% CI 0.61-1.67) for hemorrhagic stroke, 0.99 (95% CI 0.80-1.24) for CV death, 0.99 (95% CI 0.86-1.15) for MACE, and 0.95 (95% CI 0.85-1.06) for all-cause mortality, respectively (Table III).

DISCUSSION

After adjustment for confounding factors, the CV risk in Danish patients with rosacea was generally comparable with control subjects albeit with a slightly lower risk of MI. Rosacea was significantly associated with CV comorbidities including dyslipidemia, hypertension, and coronary artery disease, respectively, in a recent Taiwanese study although it lacked adjustment for important CV risk factors such as smoking and alcohol abuse.[3] Moreover, a small (n = 130) single-center study recently reported a rosacea disease severity–dependent risk of comorbidities including hyperlipidemia, hypertension, and CV disease.[4] In addition, a case-control study from Turkey reported that hypercholesterolemia, hyperlipidemia, increased C-reactive protein levels, family history of CV