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Increased Risk of Multimorbidity in Patients With Sarcoidosis: A Population-Based Cohort Study 1976 to 2013

Patompong Ungprasert, MD, MS; Eric L. Matteson, MD, MPH; and Cynthia S. Crowson, MS

Abstract

Objective: To evaluate the risk and pattern of multimorbidity in patients with sarcoidosis.

Patients and Methods: A cohort of all residents of Olmsted County, Minnesota, first diagnosed with sarcoidosis between January 1, 1976, and December 31, 2013, was identified through the medical record linkage system of the Rochester Epidemiology Project. Diagnosis was verified by individual medical record review. A cohort of sex- and age-matched comparators without sarcoidosis was assembled from the same population. Data on 18 chronic conditions recommended by the US Department of Health and Human Services for both cases and comparators were retrieved and compared.

Results: The prevalence of multimorbidity (ie, the presence of ≥2 chronic conditions) was similar between the 2 groups: 111 of 345 cases (32.2%) and 110 of 345 comparators (31.9%) (P=.99). After the index date, 156 cases (43.8%) and 142 comparators (41.2%) developed multimorbidity, corresponding to a hazard ratio of 1.60 (95% CI, 1.27-2.01; P<.001). The cumulative incidence of the presence of ≥3, 4, and 5 chronic conditions was also consistently significantly higher in cases than in comparators (P value=.01, .004 and .002, respectively). Analysis by specific type of chronic condition revealed a significantly higher cumulative incidence of coronary artery disease, congestive heart failure, arrhythmia, stroke or transient ischemic attack, arthritis, depression, diabetes, and major osteoporotic fracture.

Conclusion: In this population, patients with sarcoidosis had a significantly higher risk of developing multimorbidity than did sex- and age-matched individuals without sarcoidosis.

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Multimorbidity is defined as the coexistence of 2 or more chronic medical conditions in the same individual.[1] The concept of multimorbidity is slightly different from the concept of comorbidity. In the traditional comorbidity model, an index disease is defined and is generally considered as the most important entity and studies of comorbidity generally focus on the co-occurrence of any additional disease entities and their effect on the treatment/prognosis of the index disease. In contrast, the concept of multimorbidity is more patient-centric with all morbidities regarded as of equal importance. Studies of multimorbidity usually put more emphasis on function and well-being of patients as a result of all morbidities.[1,2]

Comorbidity has long been a focus of epidemiological studies of immune-mediated diseases. The incidence of several comorbidities, particularly cardiovascular diseases, is increased in different immune-mediated diseases such as rheumatoid arthritis, systemic lupus erythematosus, vasculitis, and psoriasis.[3-8] More recently, attention has also turned to multimorbidity in patients with immune-mediated diseases, especially rheumatoid arthritis.[2,9] There is more limited understanding of the extent and influence of multimorbidity in patients with other diseases, including sarcoidosis. The present study used a previously identified population-based cohort of patients with sarcoidosis to describe the occurrence of multimorbidity compared with persons without sarcoidosis randomly selected from the same underlying population.

From the Division of Rheumatology (P.U., E.L.M., C.S.C.), Division of Epidemiology (E.L.M.), and Division of Biomedical Statistics and Informatics (C.S.C.), Mayo Clinic, Rochester, MN; and Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (P.U.).

PATIENTS AND METHODS

This study used a previously identified cohort of 345 cases of incident sarcoidosis diagnosed

between January 1, 1976, and December 31, 2013, which was identified through the resources of the Rochester Epidemiology Project (REP).[10] The REP is a unique medical record linkage system that provides complete access to inpatient and outpatient medical records of all residents of Olmsted County, Minnesota, for more than 6 decades from all local health care providers, which include Mayo Clinic, the Olmsted Medical Center and its affiliated hospitals, local nursing homes, and the few private practitioners. The history and utility of the REP for epidemiological investigations have been described in detail elsewhere.[11]

This cohort of patients with sarcoidosis was initially identified from diagnostic codes related to sarcoidosis and noncaseating granuloma and was confirmed by individual medical record review, which required physician diagnosis of sarcoidosis supported by the presence of noncaseating granuloma on biopsy, radiographic evidence of intrathoracic sarcoidosis, and compatible clinical manifestations, after exclusion of other granulomatous diseases such as tuberculosis and fungal infection. The only exception for the histopathological requirement was stage I pulmonary sarcoidosis that required only the evidence of symmetric bilateral hilar adenopathy on imaging. Isolated extrathoracic sarcoidosis of a specific organ without intrathoracic sarcoidosis was included (except for isolated cutaneous disease) if there was no better alternative diagnosis for the presence of noncaseating granuloma.[12] Isolated cutaneous disease was not included as it could be mimicked by several conditions, including cutaneous foreign body reaction, resulting in over-ascertainment of cases in the face of diagnostic uncertainty. Patients diagnosed with sarcoidosis before residency in Olmsted County (ie, prevalent cases) were excluded.

A cohort of sex- and age (within 3 years)–matched comparators without sarcoidosis at the time of the patient's sarcoidosis diagnosis was randomly selected from the same underlying population in a 1:1 ratio. Data on 20 chronic conditions recommended by the US Department of Health and Human Services[13] for both cases and comparators were retrieved electronically from the diagnostic codes in the REP medical record linkage system. However, 2 chronic conditions recommended by the US Department of Health and Human Services (ie, human immunodeficiency virus infections and autism spectrum disorders) were excluded from the analysis because of their rarity in this population. Diagnosis of the remaining 18 chronic conditions was made on the basis of the presence of these diagnostic codes within a category at least twice (and separated by at least 30 days) except for selected conditions that were collected by manual medical record review. These included physician diagnoses of congestive heart failure (CHF), coronary artery disease (CAD), stroke, transient ischemic attack, osteoporotic fracture, and/or hepatitis occurring at any time, either before or after the index date, as well as hypertension, hyperlipidemia, and diabetes mellitus diagnosed before the index date.[14,15] Similarly, diagnosis of cancer was confirmed with Mayo Clinic's cancer registry, which continuously collects data on every type of malignancy except for nonmelanoma skin cancer.[16] Data on the use of glucocorticoids, disease-modifying antirheumatic agents, and biological agents after sarcoidosis diagnosis were collected from cases.

Approval for this study was obtained from the Mayo Clinic and the Olmsted Medical Center institutional review boards (Mayo Clinic Institutional Review Board 14-008651; Olmsted Medical Center Institutional Review Board 012-OMC-15). The need for informed consent was waived.

Descriptive statistics (percentage, mean, etc) were used to summarize the characteristics of cases and comparators as well as the prevalence of each chronic condition at the incidence/index date. Comparisons between the cohorts were performed using chi-square, Fisher exact, and rank-sum tests. The cumulative incidence of the each chronic condition adjusted for the competing risk of death was estimated.[17] These methods are similar to the Kaplan-Meier method with censoring of patients who are still alive at last follow-up. However, patients who die before experiencing a chronic condition are appropriately accounted for to avoid overestimation of the rate of occurrence of the chronic condition, which can occur if such individuals are simply censored at death. For each chronic condition, patients whose diagnosis was before the diagnosis of sarcoidosis, or for individuals in the comparison cohort, before the index date,