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INTERSTITIAL LUNG DISEASE

Inpatient Prevalence, Expenditures, and Comorbidities of Sarcoidosis: Nationwide Inpatient Sample 2013–2014

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Abstract

Purpose To investigate inpatient prevalence, expenditures, and comorbidities of hospitalized patients with sarcoidosis in the USA.

Methods Patients with sarcoidosis were identified within the Nationwide Inpatient Sample (NIS) database for the years 2013 and 2014 using the respective ICD-9 diagnostic code. Data on patient and hospital characteristics, comorbidities, total hospital costs, and total hospitalization charges were collected. A propensity-matched cohort of patients without sarcoidosis from the same database was created and used as comparators for the analysis of comorbidities.

Results A cohort of 78,055 patients with sarcoidosis was identified within the database, corresponding to an inpatient prevalence of 2.21 cases per 1000 admissions. Analysis of comorbidities found that patients with sarcoidosis had significantly higher odds of atrial fibrillation [adjusted odds ratio (aOR): 1.41, 95% CI 1.13–1.76, $p < 0.01$], conduction abnormalities [aOR: 2.04, 95% CI 1.45–2.89, $p < 0.01$], aortic valvulopathy [aOR: 1.78, 95% CI 1.30–2.44, $p < 0.01$], congestive heart failure [aOR: 1.23, 95% CI 1.04–1.45, $p = 0.02$], cardiomyopathy [aOR: 1.25, 95% CI 1.08–1.44, $p < 0.01$], deep venous thrombosis (aOR: 1.58, $p < 0.01$), pulmonary embolism (aOR: 1.70, $p < 0.01$), and osteoporosis (aOR: 1.81, $p < 0.01$), compared with propensity-matched patients without sarcoidosis. After adjusting for confounders, patients with sarcoidosis displayed a mean additional $1,250 ($p = 0.24$) in total hospital costs and a mean additional $27,205 ($p < 0.01$) in total hospitalization charges when compared to hospitalized patients without sarcoidosis.

Conclusions The inpatient prevalence of sarcoidosis was relatively high compared with its overall incidence. Hospitalization of patients with sarcoidosis was associated with a significantly higher total hospitalization charges compared to hospitalized patients without sarcoidosis. Patients with sarcoidosis have a higher risk of several cardiac comorbidities.

Keywords Sarcoidosis · Hospitalization · Epidemiology · Prevalence

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Introduction

Sarcoidosis is a multi-systemic disease of unknown etiology characterized by the presence of non-caseating granulomas. Its clinical course is highly variable, with many patients being asymptomatic and having the disease discovered incidentally by radiographic investigations for other reasons. Others may have symptoms related to self-limited, acute inflammation, or may have chronic progressive disease that leads to organ failure [1–3]. The epidemiology and clinical characteristics of sarcoidosis are also variable across ethnic groups. For instance, the reported incidence rate of sarcoidosis among African Americans is as high as 35 new cases/100,000 persons per year, while the reported incidence rates among Caucasians and Asians

are only approximately 5–10/100,000 persons per year and 1–3/100,000 persons per year, respectively [1, 4–10].

Little is known about the inpatient burden and healthcare utilization in patients with sarcoidosis. Previous studies have focused on trends of hospitalization rates of patients with sarcoidosis over time, but none has investigated its inpatient prevalence, mortality, and expenditures [11–14]. The current study was conducted with the aims to explore those characteristics as well as to investigate the comorbidities in patients with sarcoidosis using data from a large national database.

Methods

Data Source

The Nationwide Inpatient Sample (NIS) is the largest publicly available inpatient database in the USA, which was developed and is maintained by the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality (AHRQ), which itself is a branch of the US Department of Health and Human Services. Data for more than seven million individual hospitalizations across all-payers in the USA are recorded annually in the NIS database. This is itself a 20% stratified sample of over 4000 non-federal acute care hospitals from more than 40 states of the USA and is representative of 95% of hospital discharges nationwide. A principal diagnosis, defined as the primary discharge diagnosis, is included in the dataset, as well as up to 29 other secondary diagnoses. The dataset also includes codes for up to 15 procedures performed during the hospital stay. Additionally, it allows determining length of hospital stay (LOS), total hospital costs, hospitalization charges, and desired outcome measures such as calculations of inpatient disease prevalence. Patients were identified within the NIS database. All analyzed data were extracted from the database for the year 2014 to design this retrospective cohort study.

Study Population

All patients older than or equal to 18 years of age with any International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) diagnosis code for sarcoidosis (135) were included in the study. Patients undergoing elective admission were excluded from statistical analysis because they are typically planned admissions for specialized testing or procedures. Therefore, the vast majority of elective admissions are considered to be patients who are not sick from the condition.

Variable Definition

Basic information was divided into patient and hospital characteristics. Patient characteristics included demographics such as age, gender, ethnicity, median income in zip code, and insurance type. Hospital characteristics included hospital region, hospital teaching status, number of hospital beds (hospitals are further categorized into small, medium, and large based on this number - definition provided as **online supplementary material**), and hospital location. The HCUP divides the USA into four geographical locations into census regions: Northeast, Midwest, South, and West. Hospital location refers to whether the hospital is located in an urban or rural area. Each patient's vital status at the conclusion of hospital stay, LOS, and total hospitalization charges were also abstracted from the database. To account for patient comorbidities, the Deyo adaptation of the Charlson Comorbidity Index was used, which is a validated tool for large database analysis [15].

Outcomes

The primary outcome was to determine the inpatient prevalence of sarcoidosis in the USA. The main analysis was based on patients with either primary or secondary diagnoses of sarcoidosis as described under the section Study Population. In addition, a sensitivity analysis was also conducted by using only patients with a primary diagnosis of sarcoidosis to determine the inpatient prevalence of sarcoidosis. This sensitivity analysis was conducted with the concern over inaccuracy of secondary diagnosis of sarcoidosis as diagnostic code of sarcoidosis often remains lifelong in the patient's medical record, even after the initial suspicion for sarcoidosis has been dismissed. Secondary outcomes included reasons for admission, inpatient mortality and associations with comorbidities, with the focus on cardiovascular comorbidities, including atrial fibrillation, conduction abnormalities, congestive heart failure (CHF), cardiomyopathy, coronary artery disease (CAD), and aortic valvulopathy. In addition, hospital length of stay and expenditures were abstracted from the dataset. Expenditures were sub-divided into total hospitalization charges and hospital costs. Total hospital charges represent the amount of money that each hospital billed for providing its service on each case, while hospital costs represent the amount of money invested by each institution in providing patient care. Hospital costs were calculated by multiplying the cost-to-charge (CCR) ratios for the respective institutions with the total hospitalization charges. Cost-to-charge ratios are provided by the HCUP as supplementary files that are merged in each dataset in order to enable this calculation.

Statistical Analysis

Discharge-level weights published by the HCUP were used to estimate the total number of patients with sarcoidosis. Propensity score matching was used to create two balanced cohorts: one consisted of patients with sarcoidosis and the other consisted of patients without sarcoidosis. These cohorts were matched using age, gender, and Charlson Comorbidity Index as covariates. Descriptive statistics were used to describe the characteristics of the cohort. Fisher's exact test was used to compare proportions, and Student's *t* test was utilized to compare means. A hybrid multivariate logistic regression model was built by first conducting a univariate regression analysis on variables that were identified from other studies as being relevant to our outcome. If these variables impacted the outcome in any direction with a p value of less than 0.1, they were included in the multivariate logistic regression model. On multivariate logistic regression, odds ratios (OR) and means were adjusted for the remainder of the variables that were not propensity-matched for, such as insurance, median income in the patient's zip code, hospital region, urban location, number of hospital beds, and teaching status. All statistical analyses were conducted using STATA, version 14 (StataCorp LP, College Station, TX, USA).

Results

Patients and Hospital Characteristics

A total of 35,351,351 admissions occurred during the study period. After propensity-matching for covariates, a cohort of 156,110 patients was obtained, consisting of patients with sarcoidosis ($n = 78{,}055$) and patients without sarcoidosis ($n = 78{,}055$). The mean age of patients was 58.6 years (standard deviation, 13.7 years) and 63.3% were female.

As the sarcoidosis and non-sarcoidosis cohorts were matched for age, gender, and Charlson Comorbidity Index, they had an equal distribution in these variables. The sarcoidosis cohort was composed of proportionately more African-American patients of lower socioeconomic status and with Medicare insurance when compared to non-sarcoidosis patients.

In terms of hospital characteristics, the two cohorts differed statistically in hospital region, urban location, teaching status, and number of hospital beds. Table 1 displays the values and significance levels between both cohorts.

Table 1 Baseline characteristics of patients in this study

	No sarcoidosis	Sarcoidosis	*p* value
Patient characteristics			
Mean age (years)	58.6	58.6	0.50
Female	63.3%	63.3%	0.80
Ethnicity			
Caucasian	76.5%	47.3%	
African-American	11.7%	46.1%	< 0.01
Hispanic	9.9%	3.8%	
Other	1.9%	2.8%	
Income in zip code			
$1–$37,999	21.7%	35.1%	
$38K–47,999	12.3%	24.4%	< 0.01
$48K–63,999	34.2%	21.9%	
> $64,000	31.8%	18.7%	
Charlson score			
0	20.0%	20.0%	
1–2	45.6%	45.6%	0.8
> 3	34.4%	34.4%	
Insurance			
Medicare	47.7%	52.3%	
Medicaid	21.6%	14.4%	< 0.01
Private	27.6%	28.1%	
Other	3.1%	5.2%	
Hospital characteristics			
Region			
Northeast	18.7	24.0	
Midwest	22.5	25.4	< 0.01
South	39.0	40.1	
West	19.8	10.5	
Urban location	98.1%	93.2%	< 0.01
Hospital bed size			
Small	22.0%	17.1%	
Medium	18.6%	27.4%	< 0.01
Large	59.4%	55.6%	
Teaching status	84.2%	71.8%	< 0.01

Primary Outcome

The inpatient prevalence of sarcoidosis in the USA was 2.21 cases per 1000 admissions, using both primary and secondary diagnoses to identify cases of sarcoidosis. The inpatient prevalence of sarcoidosis decreased to 0.16 cases per 1000 admissions when only primary diagnosis was used.

Secondary Outcomes

Reasons for Admission

The most common reasons for admission among patients with sarcoidosis in this cohort were as follows: pneumonia (34.3%), respiratory failure (26.1%), cardiomyopathy (10.9%), coronary artery disease (9.2%), acute kidney injury (8.5%), and atrial fibrillation (5.5%). In contrast, the most common reasons for admission in patients without

sarcoidosis were obstetric-related (12.1%), sepsis (3.2%), pneumonia (2.1%), osteoarthritis (1.4%), acute kidney injury (1.3%), and exacerbation of chronic obstructive pulmonary disease (1.2%).

Mortality

A total of 1,665 (2.13%) patients with sarcoidosis died during admission in the study period, compared to 1,850 (2.37%) of propensity-matched patients with no sarcoidosis, although there was no statistically significant difference between the cohorts ($p = 0.32$).

These findings were confirmed after adjusting for confounders in the multivariate model as, although the adjusted OR (aOR) pointed in the direction of more inpatient mortality in the sarcoidosis cohort (aOR: 1.05), it did not reach statistical significance (95% CI 0.80–1.36, $p = 0.74$) when compared to patients without sarcoidosis.

Association with Comorbidities

Proportionately, more patients with sarcoidosis had a coexisting diagnosis of atrial fibrillation compared to the patients without sarcoidosis (hereafter referred to as the "control group") (13.77% vs. 12.07%), although there was no statistically significant difference between the cohorts. However, after adjusting for confounders, patients with sarcoidosis did display statistically significantly higher odds compared to patients without sarcoidosis (aOR: 1.41, $p < 0.01$).

Rates of conduction abnormalities (blocks) were statistically significantly higher in the sarcoidosis cohort (3.77% vs. 2.27%). This was corroborated in the multivariate model, with conduction abnormality aOR of 2.04 in patients with sarcoidosis compared to controls ($p < 0.01$).

Higher rates of CAD in general were evident in the sarcoidosis cohort (18.45% vs. 17.85%), although it did not reach statistical significance. The lack of difference was confirmed in the multivariate model.

Patients with sarcoidosis had statistically significantly higher rates of CHF compared to controls (23.18% vs. 17.10%). After adjusting for confounders, these findings were corroborated with sarcoidosis patients having aOR of 1.23 of having associated CHF compared to controls.

Statistically significantly higher rates of cardiomyopathy were also observed in the sarcoidosis cohort (21.92% vs. 15.74%). These findings were also confirmed after adjusting for confounders, with cardiomyopathy aOR of 1.25 in patients with sarcoidosis compared to controls.

Aortic valvulopathy rates were higher in the sarcoidosis group, although this was not a statistically significant difference. However, in the multivariate model, patients with sarcoidosis did display markedly higher odds of aortic valvulopathy compared to controls (aOR: 1.78, $p < 0.01$).

Patients with sarcoidosis displayed higher odds of deep venous thrombosis (DVT) and pulmonary embolism (PE) (aOR: 1.58 and aOR: 1.70, respectively, both with $p < 0.01$). Although there was a significant association between sarcoidosis and osteoporosis (aOR: 1.81, $p < 0.01$), these patients did not display statistically significantly different odds of osteoporotic fractures.

All outcomes and respective 95% confidence intervals and p values are displayed in Table 2.

Hospital Length of Stay

Patients in the sarcoidosis cohort had an average LOS of 5.5 days compared to 5.4 days in the non-sarcoidosis cohort. The existence of a difference was confirmed on the multivariate model, with an average of 0.3 more days of length of stay in the sarcoidosis cohort, which did reach statistical significance ($p = 0.05$), although its clinical relevance is questionable.

Expenditures: Total Hospital Costs and Total Hospitalization Charges

The mean hospital costs for patients in the sarcoidosis cohort were $13,880 compared to $14,083 in the non-sarcoidosis cohort, difference which was not statistically significant. These differences also did not reach statistical significance in the multivariate model (additional adjusted mean: $1,250, $p = 0.24$) when comparing to the non-sarcoidosis cohort.

Mean total hospitalization charges were also greater in the sarcoidosis cohort ($52,768) compared to the non-sarcoidosis cohort ($37,631) at a statistically significant level ($p < 0.01$). This difference was confirmed after adjusting for confounders in the multivariate model, with the sarcoidosis

Table 2 Odds ratio comparing inpatient mortality and comorbidities between patients with sarcoidosis and patients without sarcoidosis

Variable	Adjusted odds ratio	95% confidence interval	p value
Mortality	1.05	0.80–1.36	0.74
Atrial fibrillation	1.41	1.13–1.76	< 0.01
Conduction abnormalities (blocks)	2.04	1.45–2.89	< 0.01
CAD	1.10	0.94–1.29	0.26
CHF	1.23	1.04–1.45	0.02
Cardiomyopathy	1.25	1.08–1.44	< 0.01
Aortic valvulopathy	1.78	1.30–2.44	< 0.01
Deep venous thrombosis	1.58	1.47–1.69	< 0.01
Pulmonary embolism	1.70	1.57–1.83	< 0.01
Osteoporosis	1.81	1.30–1.99	< 0.01
Osteoporotic fracture	0.92	0.62–1.38	0.71

cohort displaying an additional $27,205 when compared to the non-sarcoidosis cohort ($p < 0.01$).

Discussion

The current study is the first study to utilize a large national database to investigate the characteristics of hospitalized patients with sarcoidosis. Despite a relatively low incidence rate of sarcoidosis in the USA, the inpatient prevalence was over 2 per 1000 admission which is higher than what would be expected from the incidence alone. One explanation is that, due to the nature of the disease, patients with sarcoidosis may often require hospitalization for invasive procedures and hence be coded as the diagnosis that required these procedures [16]. About one-third of admissions were due to pneumonia, which could be predisposed by immunosuppression from glucocorticoids and disease-modifying anti-rheumatic drugs that are used in the treatment of sarcoidosis. Another explanation involves the increased risk of cardiac comorbidities among patients with sarcoidosis, as these comorbidities often require inpatient care for close monitoring, parenteral therapy, and procedures. This may also explain why adjusted mean hospital costs, hospitalization charges, and hospital LOS were higher among patients with sarcoidosis compared to non-sarcoidosis cohort.

The increased risk of cardiac comorbidities has been demonstrated by previous studies [17, 18] and is confirmed by this study. The higher risk is likely to be a result of two contributing factors. First, sarcoidosis can have cardiac involvement, causing granulomatous inflammation in the myocardium [19]. The damage caused by this inflammation could eventually lead to impairment of myocardial function, leading to cardiomyopathy and CHF. Similarly, the inflammation can cause the damage in the conductive tissue, leading to conduction defects and heart blocks. Second, although no specific studies have evaluated this in sarcoidosis, inflammation associated with immune-mediated disorders has been shown to cause deleterious effects on endothelial integrity and function. Studies have demonstrated that several inflammatory cytokines, such as C-reactive protein, interleukin-6, and tumor necrosis factor-alpha can accelerate the rate of atherogenesis through the activation of immune cells and smooth muscle cells in the sub-endothelial layer [20, 21]. The presence of excessive reactive oxygen species is associated with increased oxidation rates of low-density lipoproteins, which are taken up by scavenger receptors of macrophages and would eventually evolve to form foam cells [22]. In addition, circulating inflammatory cytokines can also cross-activate the coagulation pathway, leading to a hypercoagulable state, which is another predisposing factor for cardiovascular events, especially DVT and PE [23, 24].

The role of glucocorticoids, the most commonly prescribed medication for patients with symptomatic and/or progressive sarcoidosis, in the increased risk of atherosclerotic and cardiac comorbidities is a subject of debate. The use of glucocorticoids increases the risk of several traditional atherosclerotic risk factors, including diabetes mellitus, hypertension, and dyslipidemia [25]. However, they are potent anti-inflammatory drugs that may assist in reducing the inflammatory burden, which may offset their metabolic adverse effects.

In contrast to previous studies that observed a twofold increased risk of mortality in patients with sarcoidosis compared to individuals without sarcoidosis [7, 26], the current study found no significant difference in mortality between the groups. The difference in database and study design is a possible explanation for this discrepancy. This study utilized an inpatient database, and therefore, controls in this study were hospitalized patients, whereas controls in the previous studies were the general population. In addition, propensity-score matching was utilized in this study to ensure that baseline characteristics (namely comorbidities) of patients in both groups were as similar as possible, but only few of such parameters were adjusted for in prior studies [7, 26].

The major strength of this study is the unique advantage of the NIS database that collects information on hospitalized patients from over 4,000 hospitals across the country. Therefore, the data are truly representative of all hospitalized patients with sarcoidosis in the USA, unlike studies from single or few centers that often have a problem with referral bias. The number of patients in the database is also large, allowing a more precise estimation of the inpatient prevalence, expenditures, and magnitude of association between variables. The analysis of comorbidities and expenditures has the advantage of the propensity score matching, which ensures that the baseline characteristics of both groups (patients with sarcoidosis and patients without sarcoidosis) are similar. This better allows to appreciate that the observed difference was truly a result of the presence or absence of sarcoidosis.

Nonetheless, the NIS has several limitations that should be acknowledged. Firstly, since this dataset is fully dependent on ICD-9 CM coding, exposure to mis-coding bias may be a concern. A recently published study found that ICD-9 CM coding for sarcoidosis has only a fair accuracy, with the positive predictive value of approximately 60% [27]. Since the database does not allow for tracking specific patients across time, multiple coding (such as two or more Sarcoidosis ICD-9 CM codes being sustained more than 6 months) cannot be used to further improve the accuracy of the diagnosis. Secondly, the NIS is an inpatient database and, therefore, the observations do not reflect the burden and characteristics of sarcoidosis in the general population. This is of particular importance for the analysis of comorbidities,

as it is possible that patients with sarcoidosis in this cohort have a higher disease burden, as all of them are hospitalized. Therefore, the observed increased risk of cardiac abnormalities may not be generalizable to all patients with sarcoidosis. Another potential limitation of the analysis of comorbidities is the cross-sectional nature of it, in that the temporal relationship between sarcoidosis and other comorbidities cannot be accurately established. It is possible that the coded cardiac abnormalities occurred prior to the onset of sarcoidosis and that there is no causal relationship between them. Lastly, hospital admissions reflected on the NIS database are not necessarily new cases, as the database does not allow for tracking of specific patients. For this reason, it is not possible to know when sarcoidosis was originally diagnosed. For the same reason, inpatient incidence could not be calculated and the term "inpatient prevalence" was used instead. In this way, multiple admissions per patient cannot be tracked, which may contribute to the higher-than-expected inpatient prevalence.

Conclusion

Sarcoidosis was responsible for a non-negligible number of hospitalizations in the USA and was associated with higher hospitalization costs and charges compared to hospitalizations of patients without sarcoidosis. Analysis of comorbidities found significantly higher odds of several cardiac comorbidities, although the possibility of selection bias and the cross-sectional nature of the study are limitations. Prospective cohort studies are still required to investigate the causality of this association.

Compliance with Ethical Standards

Conflict of interest The authors have no financial or non-financial potential conflicts of interest to declare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Judson MA, Boan AD, Lackland DT (2012) The clinical course of sarcoidosis: presentation, diagnosis, and treatment in a large white and black cohort in the United States. Sarcoidosis Vasc Diffuse Lung Dis 29:119–127
2. Israel-Biet D, Valeyre D (2013) Diagnosis of pulmonary sarcoidosis. Curr Opin Pulm Med 19:510–515
3. Mirsaedi M, Machado RF, Schraufnagel D et al (2015) Racial difference in sarcoidosis mortality in the United States. Chest 147:438–449
4. Rybicki BA, Major M, Popovich J Jr et al (1997) Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. Am J Epidemiol 145:234–241
5. Brito-Zeron P, Sellares J, Bosch X et al (2016) Epidemiologic patterns of disease expression in sarcoidosis: age, gender and ethnicity-related differences. Clin Exp Rheumatol 34:380–388
6. Ungprasert P, Carmona EM, Utz JP et al (2016) Epidemiology of sarcoidosis 1946–2013: a population-based study. Mayo Clin Proc 91:183–188
7. Gribbin J, Hubbard RB, Le Jeune I et al (2006) Incidence and mortality of idiopathic pulmonary fibrosis and sarcoidosis in the UK. Thorax 61:980–985
8. Arkema EV, Grunewald J, Kullberg S et al (2016) Sarcoidosis incidence and prevalence: a nationwide register-based assessment in Sweden. Eur Respir J 48:1690–1699
9. Morimoto T, Azuma A, Abe S et al (2008) Epidemiology of sarcoidosis in Japan. Eur Respir J 31:372–379
10. Park JE, Kim YS, Kang MJ et al (2018) Prevalence, incidence and mortality of sarcoidosis in Korea, 2003–2015: a nationwide population-based study. Respir Med 144S:S28–S34
11. Gerke AK, Yang M, Tang F et al (2012) Increased hospitalizations among sarcoidosis patients from 1998 to 2008: a population-based cohort study. BMC Pulm Med 12:19
12. Foreman MG, Mannino DM, Kamugisha L et al (2006) Hospitalization for patients with sarcoidosis: 1979–2000. Sarcoidosis Vasc Diffuse Lung Dis 23:124–129
13. Pohle S, Baty F, Brutsche M (2016) In-hospital disease burden of sarcoidosis in Switzerland from 2002 to 2012. Plos ONE 11:e0151940
14. Gorham ED, Garland CF, Garland FC et al (2004) Trends and occupational associations in incidence of hospitalized pulmonary sarcoidosis and other lung diseases in Navy personnel: a 27-year historical prospective study, 1975–2001. Chest 126:1431–1438
15. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 45:613–619
16. Judson MA, Thompson BW, Rabin DL et al (2003) The diagnostic pathway to sarcoidosis. Chest 123:406–412
17. Zoller B, Li X, Sundquist J et al (2012) Risk of subsequent coronary heart disease in patients hospitalized for immune-mediated diseases: a nationwide follow-up study from Sweden. PloS ONE 7:e33442
18. Ungprasert P, Crowson CS, Matteson EL (2017) Risk of cardiovascular disease among patients with sarcoidosis: a population-based retrospective cohort study, 1976–2013. Eur Respir J 49:1601290
19. Yatsynovich Y, Dittoe N, Petrov M et al (2018) Cardiac sarcoidosis: a review of contemporary challenges in diagnosis and treatment. Am J Med Sci 355:113–125
20. Montecucco F, Mach F (2009) Common inflammatory mediators orchestrate pathophysiological processes in rheumatoid arthritis and atherosclerosis. Rheumatology 48:11–22
21. Raggi P, Genest J, Giles JT et al (2018) Role of inflammation in the pathogenesis of atherosclerosis and therapeutic interventions. Atherosclerosis 276:98–108
22. Hansson GK (2005) Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 352:1685–1695
23. Xu J, Lupu F, Esmon CT (2010) Inflammation, innate immunity and blood coagulation. Hamostaseologie 30:8–9
24. Esmon CT (2005) The interactions between inflammation and coagulation. Br J Haematol 131:417–430
25. Da Silva JA (2011) Safety of glucocorticoids—clinical trials. Clin Exp Rheumatol 29:S99–S103

26. Tukey MH, Berman JS, Boggs DA et al (2013) Mortality among African American women with sarcoidosis: data from the Black Women's Health Study. Sarcoidosis Vasc Diffuse Lung Dis 30:128–133
27. Ungprasert P, Matteson EL, Crowson CS (2017) Accuracy of diagnostic coding for sarcoidosis in electronic databases: a population-based study. Lung 195:713–715

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