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Original Article

Understanding the prevalence, in-hospital mortality and readmission rates amongst pulmonary vs cardiac sarcoidosis patients: insights from a nationwide registry

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Abstract: Objectives: Sarcoidosis is a multisystem granulomatous disorder, with pulmonary sarcoidosis (PS) affecting approximately 90% of patients and cardiac sarcoidosis (CS) being less common but associated with severe clinical implications. While PS is primarily characterized by respiratory symptoms, CS can lead to serious complications like heart failure and arrhythmias, contributing to sarcoidosis-related mortality. This study aims to compare the prevalence, in-hospital mortality, 30-day readmission rates, and healthcare costs between PS and CS patients using data from the Nationwide Readmissions Database (NRD). Methods: Data were extracted from the NRD for adult patients diagnosed with PS or CS from January 2016 to December 2020. Baseline demographics, comorbidities, in-hospital outcomes, and 30-day readmission rates were analyzed. Statistical comparisons were made using appropriate tests for categorical and continuous variables. Results: Among 101,365 patients, 96,905 had PS and 4,460 had CS. CS patients experienced significantly higher rates of cardiovascular complications, such as heart failure (77.1% vs. 31.1%) and arrhythmias (75.8% vs. 27.7%), and incurred higher hospital charges ($59,520 vs. $40,249; P < 0.001). In-hospital mortality was similar between groups (CS: 2.4% vs. PS: 2.8%; P = 0.090). The 30-day readmission rate was comparable (CS: 12.9% vs. PS: 11.9%; P = 0.400), but PS patients were more likely to be readmitted for respiratory complications, while CS patients were readmitted primarily for heart failure. Conclusions: This study underscores the distinct clinical profiles of PS and CS. Although CS is less prevalent, it is associated with a higher cardiovascular burden and healthcare costs. Both groups exhibited similar mortality and readmission rates, though their readmission causes differed. These findings highlight the need for targeted management strategies for PS and CS to optimize patient outcomes and resource utilization.

Keywords: Cardiac sarcoidosis, pulmonary sarcoidosis, mortality, readmission

Introduction

Sarcoidosis is a complex multisystem granulomatous disorder characterized by diverse organ involvement, with pulmonary manifestations occurring in the majority of patients (90%) [1, 2]. Pulmonary sarcoidosis (PS), involving the lungs and intrathoracic lymph nodes, typically presents with symptoms such as cough and dyspnea [1, 2]. Radiographic findings commonly include bilateral hilar lymphadenopathy, parenchymal infiltrates, and fibrosis [3-5]. In the United States, the estimated mortality from PS is 2.8 per million, with advanced pulmonary fibrosis being the leading cause of death [6, 7].

Cardiac sarcoidosis (CS), though less common, poses significant clinical challenges due to complications such as atrioventricular block, heart failure, ventricular arrhythmias, and sudden cardiac death [8, 9]. While only 3-10% of sarcoidosis patients exhibit clinical manifestations of CS, autopsy studies suggest a prevalence of up to 30% in confirmed sarcoidosis

cases [10-13]. Despite its rarity, CS accounts for at least 25% of sarcoidosis-related deaths in the United States [14].

The diagnosis of CS is difficult as there are no standardized guidelines. The current diagnostic approach is based on recommendations from the Heart Rhythm Society (HRS) and Japanese Circulation Society (JCS). The 2014 HRS criteria recommends histological confirmation via endomyocardial biopsy with proven extra-cardiac sarcoid or a clinical diagnosis based on evidence of definite extra-cardiac sarcoid plus cardiac involvement [15]. Similarly, the 2016 JCS guidelines emphasize these diagnostic approaches [16]. Advances in imaging modalities including cardiac MRI with gadolinium and cardiac PET FDG are being studied for the use of diagnosing sarcoidosis and are incorporated in the diagnostic recommendations from the American Heart Association (AHA) [17-19].

PS and CS are both systemic manifestations of sarcoidosis. Although CS has a lower prevalence than PS, cardiac involvement, such as ventricular arrhythmias and sudden cardiac death, is known to significantly impact the mortality and morbidity of sarcoidosis [15]. Comparative data on hospitalized PS versus CS patients remain limited. This study aims to address this gap by evaluating the prevalence, in-hospital mortality, and readmission rates between these groups using the National Readmission Database (NRD).

Methods

Data source

Data for this study were sourced from the NRD covering the period from January 1, 2016, to December 31, 2020. The NRD, part of the Healthcare Cost and Utilization Project and funded by the Agency for Healthcare Research and Quality, provides a comprehensive dataset on in-hospital stays and readmissions across 31 U.S. states, representing 62.2% of the U.S. resident population and 60.8% of all hospitalizations nationwide. Each patient in the NRD is assigned a unique, de-identified identifier to track readmissions within the same calendar year across different hospitals. The NRD comprises de-identified data, pre-approved by an ethics committee, thus individual informed consent was not required for this study.

Study population

Our inclusion criteria consisted of patients over 18 years of age with either a primary or secondary diagnosis of pulmonary sarcoidosis (ICD-10 codes: D860, D862) or cardiac sarcoidosis (ICD-10 code: D8685) using the International Classification of Diseases, Tenth Revision (ICD-10) codes. As the NRD does not provide detailed clinical variables, exclusion criteria were limited to cases with missing essential demographic or outcome data.

Study outcomes

The study aimed to assess the prevalence, in-hospital mortality, and 30-day readmission rates among patients admitted with CS compared to PS. Prevalence was determined as the proportion of patients diagnosed with CS or PS within the total hospitalized cohort. In-hospital mortality was defined as death occurring during the index hospitalization, while 30-day readmission was identified based on subsequent hospital admissions within 30 days of discharge from the index hospitalization

Statistical analysis

Categorical variables were reported as frequencies and percentages, while continuous variables, such as age, length of stay, and total charges, were summarized as mean ± standard deviation (SD) or median with interquartile range, as appropriate. Comparisons of continuous variables were conducted using the Student's t-test, one-way analysis of variance (ANOVA), or Wilcoxon rank-sum (Mann-Whitney) test, based on the distribution of data. Categorical variables were analyzed using the Mantel-Haenszel chi-square or Fisher's exact test, as appropriate. For 30-day readmission rate calculations, we excluded patients being discharged in December and those readmitted electively. To identify predictors of in-hospital mortality, we first conducted univariate logistic regression for all relevant clinical and demographic variables. Variables with a p-value < 0.05 in the univariate analysis were included in a multivariable logistic regression model using forward selection. Variables were sequentially added based on statistical significance ($P < 0.05$) and clinical relevance to derive the final model. All analyses were performed on unweighted samples using Stata

Corp. 2023 (Stata Statistical Software: Release 18, College Station, TX: StataCorp LLC).

Results

A total of 101,365 patients were analyzed, comprising 96,905 patients with lung sarcoidosis and 4,460 with CS. Patients with PS were slightly older (median age 62 years, interquartile range (IQR) 52-70) compared to those with CS (58 years, IQR 50-66; P < 0.001). Female predominance was observed in PS (59.6%) but not in CS (40.3%; P < 0.001).

Cardiovascular complications were substantially more prevalent in CS patients. Congestive heart failure (77.1% vs. 31.1%; P < 0.001) and cardiac arrhythmias (75.8% vs. 27.7%; P < 0.001) were markedly more common in CS. Similarly, valvular disease (17.7% vs. 9.9%; P < 0.001), peripheral vascular disorders (43.6% vs. 8.0%; P < 0.001), and hypertension (52.8% vs. 35.6%; P < 0.001) occurred more frequently in CS patients.

Among metabolic conditions, obesity was more common in PS (27.5% vs. 24.3%; P < 0.001). Uncomplicated diabetes was more prevalent in PS (14.8% vs. 11.1%; P < 0.001), while complicated diabetes showed similar rates between groups (lung: 24.0% vs. cardiac: 21.0%; P < 0.001).

Malignancies were generally more prevalent in PS, including lymphoma (1.5% vs. 1.0%; P < 0.001), metastatic cancer (2.2% vs. 0.6%; P < 0.001), and solid tumors without metastasis (4.8% vs. 2.2%; P < 0.001). Coagulopathy was more frequent in CS (11.3% vs. 7.8%; P < 0.001), while depression was more common in PS (15.9% vs. 13.0%; P < 0.001). Alcohol abuse (3.4% vs. 2.9%; P = 0.260) and psychoses (1.4% vs. 1.1%; P = 0.240) showed no significant differences between groups.

The overall burden of comorbidities, as measured by the Elixhauser Comorbidity Index, was higher in CS patients (median 5, IQR 4-7) compared to PS patients (median 4, IQR 3-6; P < 0.001) (**Table 1**).

Outcomes

The in-hospital mortality rate was slightly lower in the CS group (2.4%) compared to the PS group (2.8%), but this difference was not statistically significant (P = 0.090). Acute kidney injury (AKI) was significantly more common in the CS group (32.3%) than in the PS group (25.2%) (P < 0.001).

The 30-day readmission rate was similar between the two groups, with 12.9% in the CS group and 11.9% in the PS group (P = 0.400), indicating no statistically significant difference in readmissions.

Length of stay (LOS) was slightly longer in the CS group, with a median of 4 days (IQR 2-8) compared to 4 days (IQR 2-7) in the PS group, and this difference was statistically significant (P < 0.001). Additionally, the total hospital charges were significantly higher for CS patients, with a median of $59,520 (IQR $24,654-$142,634), compared to $40,249 (IQR $21,651-$78,035) in the PS group (P < 0.001) (**Table 2**).

Predictors of mortality

In patients with PS, several factors were associated with an increased risk of mortality. These included advancing age (aOR 1.02, 95% CI 1.02-1.03, P < 0.001), the presence of congestive heart failure (aOR 2.03, 95% CI 1.74-2.38, P < 0.001), cardiac arrhythmias (aOR 1.82, 95% CI 1.60-2.07, P < 0.001), complicated diabetes (aOR 1.21, 95% CI 1.05-1.39, P = 0.007), coagulopathy (aOR 3.22, 95% CI 2.76-3.76, P < 0.001), and weight loss (aOR 3.23, 95% CI 2.78-3.75, P < 0.001). In the CS group, factors significantly associated with increased mortality risk included age (aOR 1.03, 95% CI 1.00-1.07, P = 0.045), hypertension (aOR 2.21, 95% CI 1.00-4.90, P = 0.05), lymphoma (aOR 4.76, 95% CI 1.21-18.75, P = 0.026), coagulopathy (aOR 3.33, 95% CI 1.78-6.22, P < 0.001), and weight loss (aOR 2.91, 95% CI 1.28-6.61, P = 0.011) (**Table 3**).

30-day readmission

This Kaplan-Meier survival curve (**Figure 1**) represents 30-day readmission rates for patients with PS (blue line) and CS (red line). The curve shows that patients with PS experience a higher cumulative incidence of 30-day readmissions compared to those with CS. The hazard ratio (HR) for readmission between the two groups is 1.86 (95% CI 1.37-2.53, P < 0.001),

Table 1. Baseline characteristics of study population

Characteristic	Pulmonary Sarcoid (n = 96,905)	Cardiac Sarcoid (n = 4,460)	*p*-value
Age (IQR), years	62 (52-70)	58 (50-66)	0.000
Female (%)	59.6	40.3	0.000
Congestive heart failure (%)	31.1	77.1	0.000
Cardiac arrhythmias (%)	27.7	75.8	0.000
Valvular disease (%)	9.9	17.7	0.000
Peripheral vascular disorders (%)	8.0	43.6	0.000
Hypertension (%)	35.6	52.8	0.000
Uncomplicated diabetes (%)	14.8	11.1	0.000
Complicated diabetes (%)	24.0	21.0	0.000
Hypothyroidism (%)	13.9	13.6	0.000
Lymphoma (%)	1.5	1.0	0.000
Metastatic cancer (%)	2.2	0.6	0.000
Solid tumor without metastasis (%)	4.8	2.2	0.000
Coagulopathy (%)	7.8	11.3	0.000
Obesity (%)	27.5	24.3	0.000
Weight loss (%)	7.4	4.8	0.000
Blood loss anemia (%)	0.8	0.6	0.280
Deficiency anemia (%)	6.0	4.8	0.020
Alcohol abuse (%)	3.4	2.9	0.260
Drug abuse (%)	4.7	3.2	0.000
Psychoses (%)	1.4	1.1	0.240
Depression (%)	15.9	13.0	0.000
Elixhauser comorbidity score (IQR)	4 (3-6)	5 (4-7)	0.000

Table 2. Outcome measures

Outcome Measure	Pulmonary Sarcoid (n = 96,905)	Cardiac Sarcoid (n = 4,460)	*p*-value
Death	2.80%	2.40%	0.090
AKI	25.20%	32.30%	0.000
30-day Readmission	11.90%	12.90%	0.400
LOS (IQR), days	4 (2-7)	4 (2-8)	0.000
Total Charge (IQR), dollars	40249 (21,651-78,035)	59520 (24,654-142,634)	0.000

indicating that patients with PS have an 86% higher risk of being readmitted within 30 days than those with CS. The *p*-value ($P < 0.001$) signifies that this difference is statistically significant, suggesting that PS may be associated with an increased likelihood of readmission within 30 days compared to CS in this cohort.

The most common causes of 30-day readmission in CS were heart failure exacerbation (55.62%), sepsis (11.99%), and cardiac implantable electronic device complications (2.74%). Amongst patients with PS, the most common causes of readmission were sepsis (15.46%), heart failure exacerbation (7.13%), and acute on chronic respiratory failure with hypoxia (5.44%).

Discussion

Our study revealed compelling insights into the differences between CS and PS. Despite the significantly lower prevalence of CS (6.3% vs. 93.7% for PS), both groups demonstrated comparable in-hospital mortality and 30-day readmission rates. Additionally, notable differences were observed in predictors of mortality and healthcare costs.

The comparable mortality rates between CS and PS, despite their vastly different prevalence, can be attributed to the severe pathology and life-threatening manifestations of CS. CS predominantly affects the left ventricle and interventricular septum, leading to significant

Table 3. Predictors of mortality

Predictors of Mortality	Pulmonary Sarcoid (aOR, 95% CI, *p*-value)	Cardiac Sarcoid (aOR, 95% CI, *p*-value)
Age	1.02 (1.02-1.03), P < 0.001	1.03 (1.00-1.07), P = 0.045
Congestive Heart Failure	2.03 (1.74-2.38), P < 0.001	2.81 (0.79-9.96), P = 0.109
Cardiac Arrhythmias	1.82 (1.60-2.07), P < 0.001	0.9 (0.46-1.77), P = 0.769
Complicated Diabetes	1.21 (1.05-1.39), P = 0.007	1.71 (0.91-3.22), P = 0.096
Coagulopathy	3.22 (2.76-3.76), P < 0.001	3.33 (1.78-6.22), P < 0.001
Weight Loss	3.23 (2.78-3.75), P < 0.001	2.91 (1.28-6.61), P = 0.011
Hypertension	0.94 (0.80-1.10), P < 0.045	2.21 (1.00-4.90), P = 0.05
Lymphoma	1.15 (0.72-1.83), P = 0.552	4.76 (1.21-18.75), P = 0.026

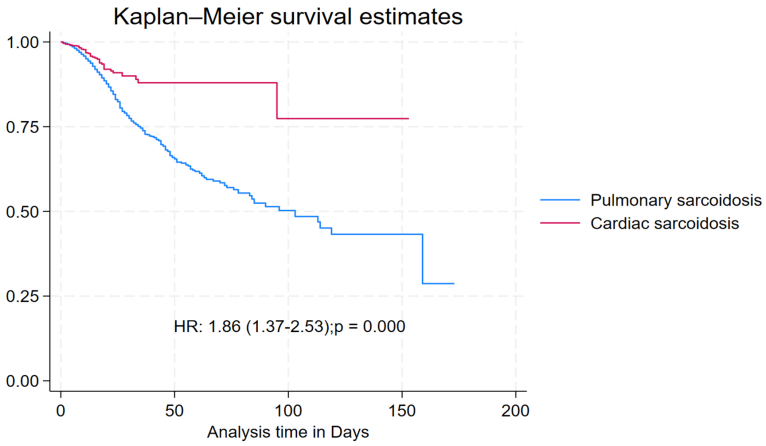

Figure 1. Kaplan-Meier survival estimates. 30-day readmission rates for patients with pulmonary sarcoidosis (blue line) and cardiac sarcoidosis (red line).

structural and conduction system complications [4]. High-grade atrioventricular blocks are often initial symptoms, with ventricular arrhythmias accounting for most fatalities [9, 15]. These findings align with previous research demonstrating a high cardiac burden in CS patients, particularly due to arrhythmias and heart failure [20-23].

Predictors of mortality differed between groups. In PS, significant factors included age, heartfailure,arrhythmias,coagulopathy,andweight loss. For CS, mortality predictors were age, hypertension, lymphoma, coagulopathy, and weight loss. Interestingly, PS patients exhibited more cardiac complications, such as heart failure and arrhythmias, contributing to mortality compared to CS. This may reflect clinically undiagnosed or misdiagnosed cardiac involvement in PS patients. Supporting this, a Finnish nationwide registry reported that two-thirds of sarcoidosis-related deaths were due to undiagnosed or misdiagnosed cardiac involvement [9].

Although overall 30-day readmission rates were comparable, PS patients had a higher cumulative incidence of readmissions (HR 1.86; 95% CI 1.37-2.53, P < 0.001). This is likely driven by progressive lung fibrosis and recurrent respiratory complications. Additionally, chronic immunosuppressive therapy in PS patients, particularly those with advanced fibrosis, may increase susceptibility to severe infections [4].

Readmission patterns differed significantly between groups. CS patients were predominantly readmitted for heart failure (55.62%), sepsis (11.99%), and cardiac implantable device complications (2.72%). Conversely, PS patients' primary readmission causes included sepsis (15.46%), heart failure (7.13%), and respiratory complications (5.44%). The higher rate of congestive heart failure in CS patients (77.8% vs. 31.1%, P < 0.001) underscores the burden of heart failure as a primary manifestation and prognostic predictor in CS [15].

The high readmission rate for heart failure in CS highlights concerns about the adequacy of current diagnostic and treatment guidelines. Studies have noted discordance among diagnostic criteria, leaving many clinically suspected CS cases unclassified [24]. Treatment for CS often extrapolates from general heart failure guidelines [25], but outcomes remain poor. For instance, CS patients with heart failure have a

10-year transplant-free survival rate of only 53%, compared to 83% in the general cohort [8]. Approximately 15% of CS patients progress to end-stage heart failure requiring advanced therapies such as ventricular assist devices or heart transplantation [26, 27].

The financial burden of CS is substantial, with hospital costs averaging $20,000 higher than for PS patients. CS patients also had a longer median length of stay (4 days [IQR 2-8] vs. 4 days [IQR 2-7] for PS; $P < 0.001$). This disparity likely reflects the higher acuity of illness, need for critical care, and involvement of multiple specialties. Prior studies have linked cardiac complications, particularly arrhythmias, with increased healthcare costs in sarcoidosis patients [28].

This study has several limitations inherent to the NRD. The reliance on ICD-10 coding introduces the potential for coding errors and variability across institutions. The NRD is restricted to inpatient encounters within a single calendar year and state, limiting the ability to track cross-state readmissions or long-term outcomes. Additionally, the database lacks clinical details such as disease severity, laboratory values, medication adherence, and outpatient care data. Cost data reflect charges rather than actual costs, and institutional variation in charging practices may affect comparisons. These factors should be considered when interpreting the results.

Conclusion

Our study highlights key differences between PS and CS in hospitalized patients. While CS, though less prevalent, incurred higher cardiovascular complications and healthcare costs, both groups had similar mortality and 30-day readmission rates. PS patients were more likely to be readmitted for respiratory issues, whereas heart failure drove readmissions in CS. These findings emphasize the need for condition-specific management strategies.

Disclosure of conflict of interest

None.

Abbreviations

PS, Pulmonary Sarcoidosis; CS, Cardiac Sarcoidosis; NRD, National Readmission Database; HRS, Heart Rhythm Society; JCS, Japanese Circulation Society; AHA, American Heart Association; SD, Standard Deviation; AKI, Acute Kidney Injury; LOS, Length of Stay; HR, Hazard Ratio.

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