ORIGINAL RESEARCH

Hospitalization Rates, Prevalence of Cardiovascular Manifestations, and Outcomes Associated With Sarcoidosis in the United States

Nirav Patel, MD; Rajat Kalra, MBChB; Rajkumar Doshi, MBBS, MPH; Harpreet Arora, MBBS; Navkaranbir S. Bajaj, MD, MPH; Garima Arora, MD, MRCP; Pankaj Arora, MD

***Background*—**Recent trends of hospitalizations and in-hospital mortality are not well defined in sarcoidosis. We examined aforementioned trends and prevalence of cardiovascular manifestations and explored rates of implantable cardioverter-defibrillator implantation in hospitalizations with sarcoidosis.

***Methods and Results*—**Using data from the National Inpatient Sample, a retrospective population cohort from 2005 to 2014 was studied. To identify sarcoidosis, an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis code was used. We excluded hospitalizations with myocardial infarction, coronary artery disease, and ischemic cardiomyopathy. Cardiovascular manifestations were defined by the presence of diagnosis codes for conduction disorders, arrhythmias, heart failure, nonischemic cardiomyopathy, and pulmonary hypertension. A total of 609 051 sarcoidosis hospitalizations were identified, with an age of 55±14 years, 67% women, and 50% black. The number of sarcoidosis hospitalizations increased from 2005 through 2014 (138 versus 175 per 100 000, $P_{trend}<0.001$). We observed declining trends of unadjusted in-hospital mortality (6.5 to 4.9 per 100 sarcoidosis hospitalizations, $P_{trend}<0.001$). Overall ≈31% (n=188 438) of sarcoidosis hospitalizations had coexistent cardiovascular manifestations of one or more type. Heart failure (≈16%) and arrhythmias (≈15%) were the most prevalent cardiovascular manifestations. Rates of implantable cardioverter-defibrillator placement were ≈7.5 per 1000 sarcoidosis hospitalizations ($P_{trend}=0.95$) during the study period. Black race was associated with 21% increased risk of in-hospital mortality (odds ratio, 1.21; 95% confidence interval, 1.16–1.27 [$P<0.001$]).

***Conclusions*—**Sarcoidosis hospitalizations have increased over the past decade with a myriad of coexistent cardiovascular manifestations. Black race is a significant predictor of in-hospital mortality, which is declining. Further efforts are needed to improve care in view of low implantable cardioverter-defibrillator rates in sarcoidosis. **(*J Am Heart Assoc*. 2018;7:e007844. DOI: 10.1161/JAHA.117.007844.)**

Key Words: cardiovascular outcomes • implantable cardioverter-defibrillator • sarcoidosis

Sarcoidosis is a systemic granulomatous disease[1,2] with a predilection towards the cardiovascular system.[2] Most patients with sarcoidosis either remain clinically silent or present with nonspecific constitutional symptoms.[3] Only 5% of patients with sarcoidosis present with cardiovascular manifestations attributable to cardiac sarcoidosis.[4] However, biopsy-proven cardiac sarcoidosis has been reported in up to 25% of asymptomatic sarcoidosis autopsy studies.[5,6] Patients with sarcoidosis with concomitant cardiovascular manifestations have more complications and a greater risk of sudden death.[7,8] Thus, there is considerable interest in identifying patients with sarcoidosis with concomitant cardiovascular manifestations.[9,10]

In 2006, the Japan Society of Sarcoidosis and Other Granulomatous Disorders revised their diagnostic guidelines for cardiac sarcoidosis by creating "histologic" and "clinical"

From the Division of Cardiovascular Disease, University of Alabama at Birmingham, AL (N.P., H.A., N.S.B., G.A., P.A.); Cardiovascular Division, University of Minnesota, Minneapolis, MN (R.K.); Department of Cardiology, North Shore University Hospital, Northwell Health, Manhasset, NY (R.D.); Division of Cardiovascular Medicine (N.S.B.), Department of Radiology (N.S.B.), Brigham and Women's Hospital and Harvard Medical School, Boston, MA; Section of Cardiology, Birmingham Veterans Affairs Medical Center, Birmingham, AL (P.A.).

Accompanying Tables S1 and S2 are available at http://jaha.ahajournals.org/content/7/2/e007844/DC1/embed/inline-supplementary-material-1.pdf

Correspondence to: Pankaj Arora, MD, Division of Cardiovascular Disease, 1670 University Boulevard, Volker Hall B140, University of Alabama at Birmingham, Birmingham, AL 35294-0019. E-mail: parora@uabmc.edu

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Clinical Perspective

What Is New?

- Rates of hospitalizations of sarcoidosis have increased from 2005 to 2014.
- In-hospital mortality associated with sarcoidosis has decreased over the same period.
- Heart failure and arrhythmias were the most prevalent cardiovascular manifestations in sarcoidosis followed by pulmonary hypertension, nonischemic cardiomyopathy, and conduction disorder.
- Notwithstanding the increasing hospitalizations with sarcoidosis, rates of implantable cardioverter-defibrillator implantation are low, and have not shown any upward trend from 2005 through 2014.
- Black race was significantly associated with in-hospital mortality.
- In a propensity match subgroup, blacks with sarcoidosis had higher in-hospital mortality and cardiac arrest compared with whites.

What Are the Clinical Implications?

- Cardiovascular manifestations are prevalent in sarcoidosis hospitalizations, and aggressive screening and risk stratification of patients with sarcoidosis for cardiovascular manifestations could be beneficial.
- Implantable cardioverter-defibrillator devices may be underutilized for prevention of sudden cardiac death in patients with sarcoidosis.
- Racial disparities in outcomes may exist in sarcoidosis.

groups.[11,12] Rather than placing additional emphasis on histologic diagnoses of cardiac sarcoidosis, the updated guidelines highlighted the presence of cardiovascular manifestations (eg, atrioventricular block and ventricular arrhythmias) to diagnose sarcoidosis with presumed cardiac involvement.[11,12] In addition, the 2014 Heart Rhythm Society consensus statement highlighted the utilization and role of implantable cardioverter-defibrillators (ICDs) for the primary and secondary prevention of sudden cardiac death in patients with sarcoidosis as an important direction for future research.[10] Since these guidelines were implemented, data reporting hospitalization trends and outcomes in sarcoidosis are lacking.

In view of the gaps in the existing literature base, a retrospective study was conducted to determine trends of hospitalizations and outcomes in sarcoidosis during 2005–2014. Furthermore, we examined rates of ICD, cardiac resynchronization therapy (CRT), and permanent pacemaker (PPM) placement, and factors associated with in-hospital mortality. We also examined racial disparities in outcomes in sarcoidosis hospitalizations in a propensity matched subgroup.

Methods

Data, Materials, and Code Disclosure Statement

The National Inpatient Sample (NIS) database is publicly available online at the following link (URL: https://www.distributor.hcup-us.ahrq.gov/). Additional information on the data, analytic methods, and study materials will be made available on request from the corresponding author to other researchers for purposes of reproducing the results or replicating the procedure.

Data Source

Our study records were derived from the NIS.[13,14] The details regarding the NIS data have been previously published.[15] The NIS is a subset of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality.[16] The NIS is the largest publicly available all-payer inpatient care database in the United States, including data on ≈7 to 8 million discharges per year, and is a stratified 20% sample of discharges from the United States community hospitals, excluding rehabilitation and long-term acute-care hospitals.[17] Our study sample spans from 2005 through 2014. To represent national estimates, weights were calculated using discharge weights provided by the sponsor (ie, Agency for Healthcare Research and Quality). The NIS constitutes data from 44 states participating in the Healthcare Cost and Utilization Project, representing more than 95% of the United States hospitalizations.

The study cohort was derived from a deidentified publicly available database. Hence, the study was considered exempt from formal review by the University of Alabama at Birmingham's (Birmingham, AL) institutional review board.

Study Population

The *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) was used to identify our study population. We queried the NIS database using the *ICD-9-CM* diagnostic code of 135 for sarcoidosis in the primary or secondary diagnosis fields.[9,18,19] Hospitalizations with any present or past history of myocardial infarction, coronary artery disease, or ischemic cardiomyopathy were excluded using *ICD-9-CM* diagnostic codes to avoid influence of ischemic heart disease on trends and outcomes (Table S1).

We examined sarcoidosis hospitalizations free of prevalent ischemic heart disease. Cardiovascular manifestations were defined by the presence of the following disease classes in the primary or secondary diagnosis fields: conduction disorders, arrhythmias, heart failure, nonischemic cardiomyopathy, and pulmonary hypertension (Table S2).[18,20–22] The NIS variables were used to identify demographic and baseline

characteristics of sarcoidosis hospitalizations. Comorbidities used in our study were derived from Elixhauser method for quantification of comorbidities.[14] A cardiac arrest (*ICD-9-CM* diagnosis code 427.5) was identified from the disease class of arrhythmias.[23] We identified all discharges who came or required new ICD implantation or replacement while hospitalized (*ICD-9-CM* procedure codes-37.94, 37.95, and 37.96), CRT implantation or replacement (*ICD-9-CM* procedural code-00.50, 00.51), or PPM implantation (*ICD-9-CM* procedural code-37.7, 37.8) by using primary and secondary procedural fields.

Outcomes

The primary outcomes of our study were the trends of hospitalizations, and in-hospital mortality associated with sarcoidosis. Trends of hospitalizations and in-hospital mortality associated with sarcoidosis. Additional analyses performed in sarcoidosis were: (1) trends of ICD, CRT, and PPM use; (2) factors associated with in-hospital mortality; and (3) propensity score–matched analyses between blacks and whites in a subgroup of the overall sarcoidosis hospitalizations.

Statistical Analysis

Primary analyses

SAS 9.4 (SAS Institute Inc) was used to analyze the NIS database. The initial study cohort derived from the NIS was 20% stratified. To generate nationally representative estimates, discharge weights provided by the sponsor (ie, Agency for Healthcare Research and Quality) were utilized. All analyses were performed in the weighted study cohort to minimize biases. Categorical data were presented as weighted frequency in percentages. Continuous data were presented as mean±SD. Trends of sarcoidosis hospitalizations were calculated using number of sarcoidosis hospitalizations divided by total number of hospitalizations in a given year per 100 000. Furthermore, trends of in-hospital mortality were calculated as total number of events per 100 sarcoidosis hospitalizations. The trend analyses were performed using Jonckheere-Terpstra test. Rates of ICD, CRT, and PPM implantation were calculated by number of these procedures per 1000 sarcoidosis hospitalizations. In addition, we identified factors associated with in-hospital mortality by using a mixed effect logistic regression model.

Subgroup analyses

A propensity score–matched model was generated to compare in-hospital outcomes between whites and blacks. Hospitalizations identified from a different race other than black or white were removed before propensity matching. A logistic regression model was performed for age, sex, and all baseline characteristics to calculate a propensity score for each hospitalization. Next, we matched all hospitalizations using a one-to-one scheme without replacement using the nearest number matching method. The primary outcome of incident in-hospital mortality was assessed using McNemar test. Development of in-hospital cardiac arrest in whites and blacks was also compared using the McNemar test. Paired *t* test was used to calculate hospital stay.

Results

Trends of Sarcoidosis Hospitalizations and In-Hospital Mortality

We identified 740 762 sarcoidosis hospitalizations from 2005 to 2014. All sarcoidosis hospitalizations with any present or past history of myocardial infarction, coronary artery disease, or ischemic cardiomyopathy were excluded (n=131 711). A total of 609 051 sarcoidosis hospitalizations were included in our final study cohort (Figure 1). Of which 188 438 hospitalizations (≈31%) were coded as having cardiovascular manifestations of one or more type.

Table 1 demonstrates baseline characteristics of sarcoidosis hospitalizations. The mean age of the overall cohort with sarcoidosis was 55±14 years. However, the mean age of the cohort with cardiovascular manifestations was higher (59±14 years) compared with the cohort without cardiovascular manifestations (53±13 years) (Table 1). Among the study cohort with sarcoidosis, ≈67% were women and ≈33% were men. The distribution of sex was similar in sarcoidosis hospitalizations with or without cardiovascular manifestations. Sarcoidosis hospitalizations were more frequent (49%) in blacks as compared with the other races (Table 1). Both hospitalization groups with and without cardiovascular manifestations had a preponderance of blacks (≈54% and ≈47%). Comorbidities including diabetes mellitus, hypertension, fluid and electrolyte disorders, coagulopathy, anemia, pulmonary circulation disorder, and renal failure were more prevalent in sarcoidosis hospitalizations who had co-existing cardiovascular manifestations (Table 1). The Southern United States (Table 1) reported the majority (≈40%) of sarcoidosis hospitalizations. Approximately 91% of sarcoidosis hospitalizations occurred in urban hospitals (Table 1).

Overall, hospitalizations for sarcoidosis substantially increased from 2005 to 2014 (P_{trend}<0.001) (Figure 2). The number of sarcoidosis hospitalizations increased from ≈138 to ≈175 per 100 000 (relative increase ≈26%) (Figure 2). However, rates of in-hospital mortality of sarcoidosis significantly decreased from 2005 to 2014 (6.5 versus 4.9 per 100 sarcoidosis hospitalizations) (relative decrease ≈26%, P_{trend}<0.001) (Figure 2).

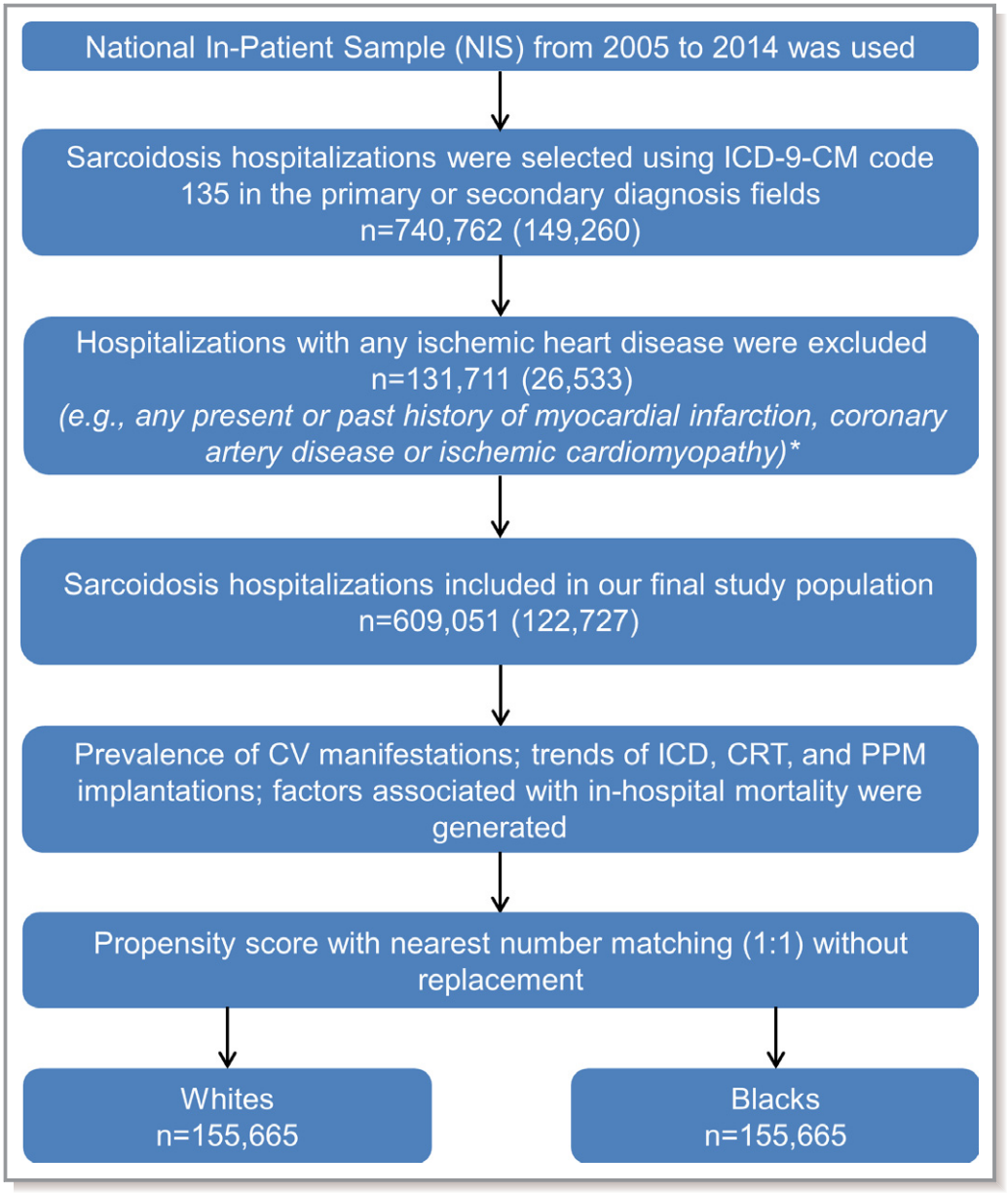

Figure 1. Flow chart of the study design and cohort selection. Sample size presented in weighted numbers (unweighted numbers). *Presence of the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes 410.1-410.9, 411.1, 411.8, 412, 414.00-414.07, and 414.8 in the primary or secondary diagnosis fields. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator; NIS, National Inpatient Sample; PPM, permanent pacemaker.

Prevalence of Cardiovascular Manifestations and Rates of ICD, CRT, and PPM Implantation

The percentage prevalence of cardiovascular disease class in sarcoidosis is shown in Figure 3. Overall, we found ≈31% (n=188 438) of sarcoidosis hospitalizations (n=609 051) had one or more of these cardiovascular manifestations. The overall prevalence of heart failure was ≈15.5%, any arrhythmias ≈14.7%, pulmonary hypertension 8.6%, nonischemic cardiomyopathy 6.7%, and conduction disorder 2.5% among sarcoidosis hospitalizations (Figure 3). Rates of ICDs were steady at ≈7.5 per 1000 sarcoidosis admissions during the study period (P_{trend}=0.95). We observed decreased utilization of CRT (P_{trend}=0.007), and increased placement of PPMs (P_{trend}<0.001) during the study period (Figure 4).

Factors Associated With In-Hospital Mortality

Factors associated with in-hospital mortality are shown in Table 2. Age was an independent factor associated with in-hospital mortality (odds ratio [OR], 1.03; 95% confidence interval [CI], 1.03–1.04 [P<0.001]). After considering white

Table 1. Baseline Characteristics of Sarcoidosis Hospitalizations Stratified by With and Without Cardiovascular Manifestations

Variable Name	Overall Sarcoidosis (N=609 051)	With Cardiovascular Manifestations (n=188 438)	Without Cardiovascular Manifestations (n=420 613)
Age, y	55±14	59±14	53±13
Sex, %			
Male	32.8	33.9	32.3
Female	67.2	66.1	67.7
Race, %			
White	43.9	40.5	45.4
Black	49.5	54.3	47.3
Other	6.6	5.2	7.3
Comorbidities, %			
Diabetes mellitus	24.9	29.3	22.9
Hypertension	52.9	58.5	50.4
Liver disease	4.5	4.2	4.7
Fluid and electrolyte disorder	24.2	29.2	22
Neurological disorder	6.8	6.6	6.9
Coagulopathy	4.6	5.7	4.1
Chronic pulmonary disease	29.0	35.8	25.9
Anemia	18.1	20.8	16.9
Solid tumor with metastasis	1.4	1.3	1.4
Metastatic cancer	1.6	1.2	1.8
Pulmonary circulation disorders	6.3	18.9	0.6
Renal failure	12.2	19.4	9.0
Hospital region, %			
Northeast	25.1	23.5	25.7
Midwest	24.1	24.9	23.8
South	40.4	40.8	40.2
West	10.4	10.8	10.3
Hospital type, %			
Urban	91.3	91.8	91.0
Rural	8.7	8.2	9.0

Data are presented as mean±SD or percentage.

race as a reference, black race was associated with a 21% higher risk of in-hospital mortality (OR, 1.21; 95% CI, 1.16–1.27 [P<0.001]) among sarcoidosis (Table 2). Fluid and electrolyte disorders, liver disease, neurological disorders, coagulopathy, history of heart failure, metastatic cancer, history of pulmonary circulation disorder, and renal failure were all associated with a greater risk of in-hospital mortality (Table 2). In contrast, female sex was associated with 17% lower risk of in-hospital mortality (OR, 0.83; 95% CI, 0.80–0.87 [P<0.001]). Chronic diseases such as diabetes mellitus, hypertension, and anemias were associated with lower risk of in-hospital mortality (Table 2). Assuming Northeast region as a reference, other regions had significantly lower risk of in-hospital mortality among sarcoidosis (Table 2).

Propensity-Matched Analyses of in-Hospital Outcomes Between Blacks and Whites

As black race was an independent factor associated with in-hospital mortality in sarcoidosis, we compared in-hospital outcomes in propensity-matched whites (n=155 665) and blacks (n=155 665) (Table 3). Black race was associated with higher in-hospital mortality (1.8% versus 1.5%) (OR, 1.20; 95% CI, 1.14–1.27 [P<0.001]) and cardiac arrest (0.5% versus 0.3%) (OR, 1.67; 95% CI, 1.49–1.87 [P<0.001]) compared with white race (Table 3). Moreover, median length of hospitalization stay was higher in blacks compared with whites (median 4 [interquartile range, 2–6] days versus 3 [interquartile range, 2–6] days, P<0.001) (Table 3).

Discussion

Our study highlights numerous key trends in the overall sarcoidosis population. By exploring the largest national hospitalization database available, we found that sarcoidosis hospitalizations are more frequent in urban as compared with rural hospitals, blacks as compared with other races, and in Southern United States as compared with other regions. We observed a ≈26% increase in hospitalizations of sarcoidosis from 2005 to 2014. Notwithstanding the increasing hospitalizations, we observed a ≈26% reduction in the rates of in-hospital mortality in sarcoidosis over the same time period. We found that heart failure and arrhythmias were most prevalent cardiovascular manifestations in sarcoidosis hospitalizations. Furthermore, we observed a steady rate of implantation of ICDs, increasing trends of PPM implantation, and decreasing trends of implantation of CRT among sarcoidosis hospitalizations. Lastly, we observed evidence of racial disparities, with blacks having higher odds of in-hospital cardiac arrest and mortality than whites in a propensity-matched cohort derived from the study cohort.

We noted that sarcoidosis hospitalizations are more prevalent in blacks. It follows that the geographical variation may be attributable to the higher concentrations of blacks in the Southern United States.[24,25] The rural-urban hospital

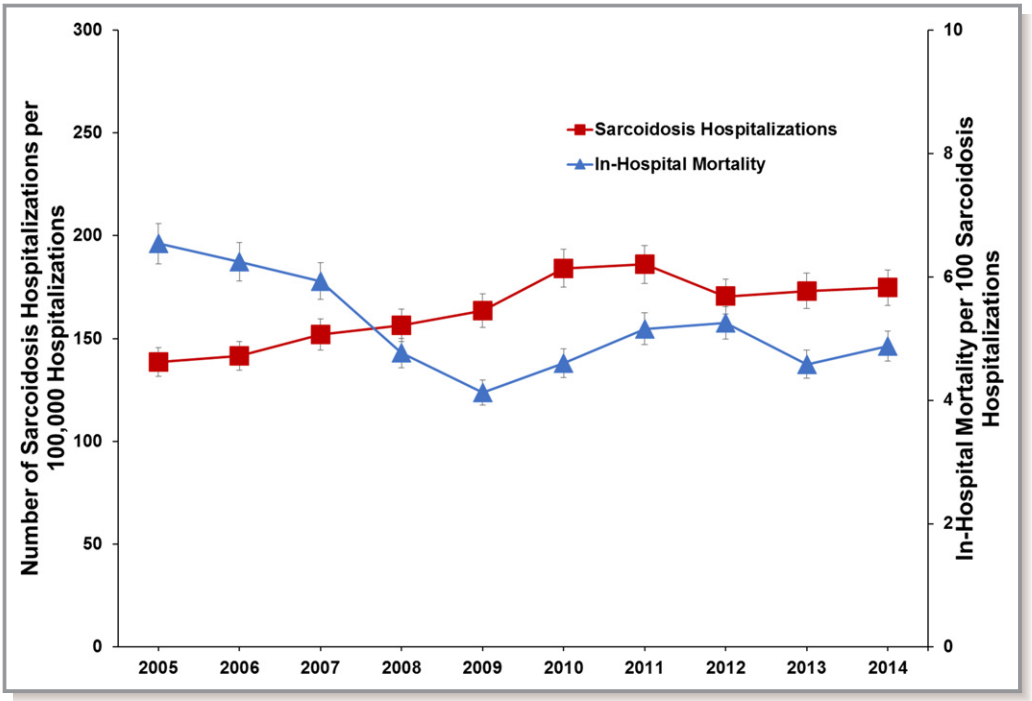

Figure 2. Rate of hospitalizations and in-hospital mortality in sarcoidosis hospitalizations from 2005 to 2014. Figure shows estimated sarcoidosis hospitalizations per 100 000 (red square), and unadjusted in-hospital mortality per 100 sarcoidosis hospitalizations (blue triangle) in the given year. The error bars represent percentage errors. Trend $P<0.001$ by Jonckheere-Terpstra test for both.

variations of sarcoidosis observations may be somewhat expected given that urban hospitals are more likely to have an advanced referral network of primary and secondary care centers. They may also have more diagnostic resources (eg, magnetic resonance imaging and positron emission tomography) for the early detection of sarcoidosis.

There are several possible reasons for the hospitalization statistics of sarcoidosis in the past decade. The publication of 2 sets of formalized guidelines[10,11] during the study period (2005–2014) offered clinicians a more organized and algorithmic method for the diagnostic workup of sarcoidosis, especially with cardiovascular involvement. The availability of these guidelines has also been complemented with rapid and landmark advances in myocardial imaging modalities. The development of the guidelines and imaging techniques has undoubtedly served to enhance the early detection of sarcoidosis, thus increasing the incidence of this disease.[10,11,26,27]

There are multiple mechanistic explanations for the mortality trends and statistics seen in our investigation. It is well recognized that age is perhaps the most significant role player in the development of clinical cardiovascular disease.[28,29] Thus, it follows with sarcoidosis. Moreover, the decreasing trend (from 2005 to 2014) of in-hospital mortality in sarcoidosis can partly be explained by the overall increasing survival from cardiovascular diseases especially from cardiac arrest. This is probably attributable to a combination of enhanced public awareness of cardiac arrest and sudden cardiac death, multiple important process- and systems-based advances in cardiac arrest care in health care, and the publication of at least 3 sets of targeted consensus guidelines addressing cardiopulmonary resuscitation and post-arrest care.[30–32] Hence, patients with longstanding sarcoidosis are now living longer, and potentially experiencing more complications from sarcoidosis that require admission to hospital settings.

Demographic factors such as older age,[29] male sex,[33] and black race[9] were associated with in-hospital mortality. Our findings are in agreement with an informative study that examined sarcoidosis mortality from 1988 to 2007 at a population level using data from the National Center for Health Statistics.[34] Comorbidities such as liver diseases, fluid and electrolyte imbalance, neurological disorders, coagulopathy, cancer, and renal failure were significant factors associated with in-hospital morality. Unexpectedly, we observed that hypertension, diabetes mellitus, and anemia were associated with reduced risk of in-hospital mortality. We believe that these observations are likely attributable to coding errors in the reporting of chronic comorbidities, and have been inadvertently seen as protective in previous NIS-based investigations.[35,36]

Our findings also add to the existing literature on sarcoidosis. Gerke et al[19] reported a 2-fold increase in hospitalizations among sarcoidosis using the NIS from 1998

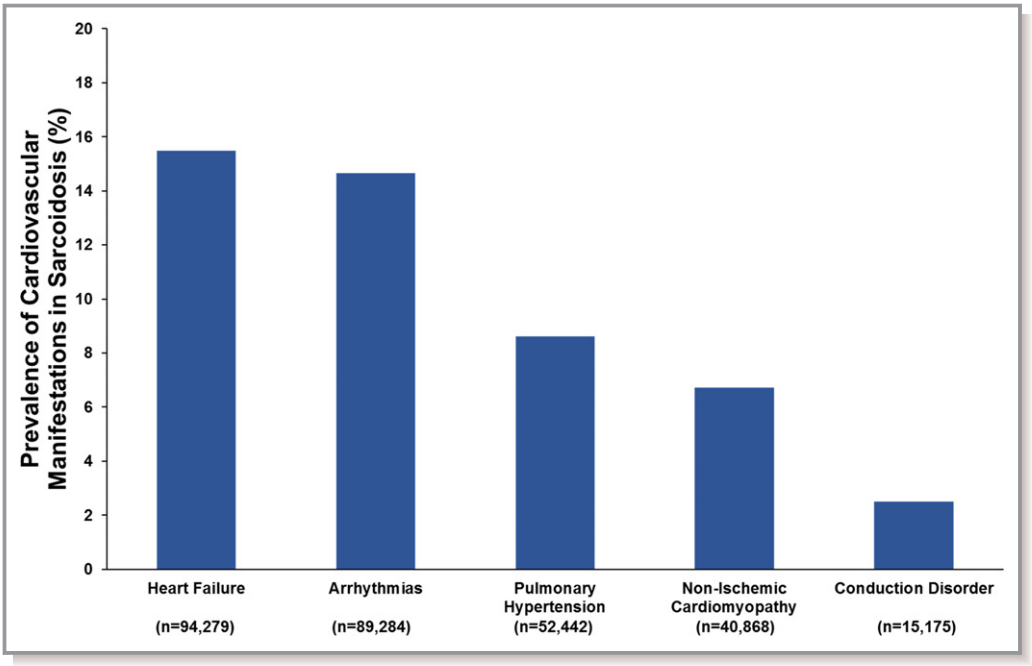

Figure 3. Prevalence of cardiovascular manifestations in sarcoidosis. Data are represented in the percentage. Overall, ≈31% (n=188 438) of sarcoidosis hospitalizations (n=609 051) had cardiovascular manifestations. Individual cardiovascular manifestation may have overlapped with the other. Prevalence of cardiovascular manifestations in sarcoidosis was classified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes (Table S2).

to 2008. By quantifying prevalence of cardiovascular manifestations in sarcoidosis, we added more precision on clinical reasoning of increasing sarcoidosis hospitalizations. Our investigation helps to reiterate some of the prior findings in the field and estimate the prevalence of these conditions in the contemporary era.[20]

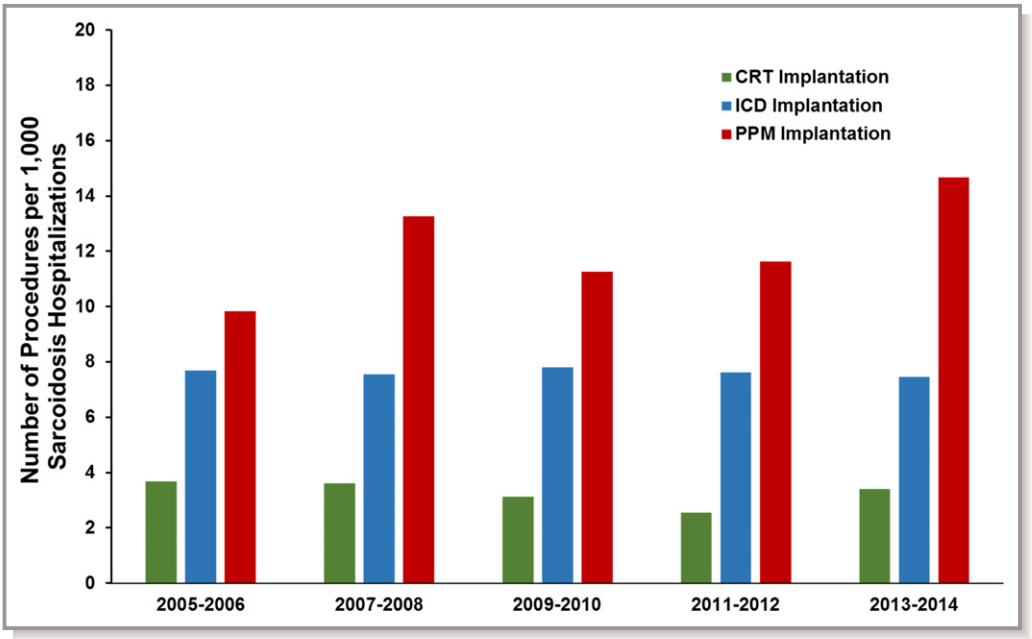

Figure 4. Implantable cardioverter-defibrillator (ICD), cardiac resynchronization therapy (CRT), and permanent pacemaker (PPM) implantations per 1000 hospitalizations of sarcoidosis from 2005 to 2014. Trend P=0.95 for ICD implantation; trend P=0.007 for CRT implantation; and trend P<0.001 for PPM implantation by Jonckheere-Terpstra test.

Table 2. Factors Associated With In-Hospital Mortality in Sarcoidosis Hospitalizations

Variable Name	OR (95% CI)	*P* Value
Age*	1.03 (1.03–1.04)	<0.001
Female vs male	0.83 (0.80–0.87)	<0.001
Race		
White	Referent	
Black	1.21 (1.16–1.27)	<0.001
Other	1.25 (1.19–1.32)	<0.001
Comorbidities†		
Diabetes mellitus	0.88 (0.84–0.92)	<0.001
Hypertension	0.60 (0.58–0.63)	<0.001
Liver disease	1.44 (1.34–1.54)	<0.001
Fluid and electrolyte disorder	2.69 (2.59–2.79)	<0.001
Neurological disorder	1.34 (1.26–1.43)	<0.001
Coagulopathy	3.14 (2.98–3.31)	<0.001
Chronic pulmonary disease	1.10 (1.05–1.14)	<0.001
Congestive heart failure	1.98 (1.89–2.08)	<0.001
Anemia	0.80 (0.77–0.84)	<0.001
Solid tumor with metastasis	1.58 (1.41–2.78)	<0.001
Metastatic cancer	3.76 (3.49–4.09)	<0.001
Pulmonary circulation disorders	2.39 (2.27–2.52)	<0.001
Renal failure	1.54 (1.46–1.61)	<0.001
Hospital region		
Northeast	Referent	
Midwest	0.79 (0.75–0.84)	<0.001
South	0.92 (0.88–0.97)	<0.001
West	0.91 (0.85–0.97)	0.005

Data are presented in odds ratio with 95% confidence interval.
CI indicates confidence interval; OR, odds ratio.
*Age is a continuous variable.
†Reference group is not present for these variables.
C statistic 0.78.

Table 3. Propensity Score Matched Cohort (1:1) of Sarcoidosis Hospitalizations Between Blacks and Whites

Variable Name	Blacks (n=155 665)	Whites (n=155 665)	*P* Value
Age, y	54.2±12.3	54.3±12.6	0.11
Sex, %			
Female	75.8	75.8	0.71
Male	24.2	24.2	
Comorbidities, %			
Diabetes mellitus	24.2	24.2	0.71
Hypertension	52.5	52.8	0.09
Liver disease	3.1	3.2	0.32
Fluid and electrolyte disorder	22.1	22.1	0.88
Neurological disorder	5.2	5.4	0.17
Coagulopathy	3.0	2.8	0.40
Chronic pulmonary disease	27.6	27.5	0.33
Congestive heart failure	6.6	7.0	0.22
Anemia	14.8	15	0.06
Solid tumor with metastasis	1.4	1.3	0.70
Metastatic cancer	1.6	1.7	0.15
Pulmonary circulation disorders	3.8	3.9	0.16
Renal failure	9.3	9.4	0.28
In-hospital outcomes			
In-hospital mortality	1.8	1.5	<0.001
Length of stay, median (IQR)*	4 (2–6)	3 (2–6)	<0.001
Cardiac arrest, %	0.5	0.3	<0.001
In-hospital outcomes, OR (95% CI)			
In-hospital mortality	1.20 (1.14–1.27)		<0.001
Cardiac arrest	1.67 (1.49–1.87)		<0.001

Data are presented as mean±SD or number (percentage) or percentage. CI indicates confidence interval; OR, odds ratio.
*Interquartile range (IQR) is from Q1 to Q3.

Our investigation also addresses important issues relating to racial disparities in sarcoidosis. Mirsaeidi et al[9] previously reported that blacks have a mortality rate that is 12 times higher than whites with sarcoidosis in their age-adjusted model. Their investigation used the Centers for Disease Control and Prevention database with evaluating death certificate (the immediate cause of death) in patients with sarcoidosis.[9] We expand on their work by using the NIS with propensity matching on a number of demographic and clinical variables to help further define the increased risk of mortality in blacks with sarcoidosis. Mirsaiedi et al also reported that incident cardiac arrest occurred at a higher rate in blacks compared with whites.[9] This is consistent with our study findings in a much larger sample, making it more generalizable.

The results of our investigation have important implications for clinical practice and public health. On the most basic level, we hope to inform clinicians that the co-occurring of cardiovascular manifestations in sarcoidosis are devastating and could be a leading cause of death. Our investigation also highlights that aggressive primary and secondary prevention of comorbid cardiovascular and pulmonary conditions is critical for patients with sarcoidosis. Our investigation also serves as a stark reminder of the need to aggressively pursue these preventive measures to ameliorate these longstanding cardiovascular racial disparities. We hope that our investigation offers an impetus for clinical

groups to achieve the aforementioned prevention through greater clinical collaboration by forming specialist sarcoidosis with cardiovascular manifestations clinics and/or specialist centers. Finally, our data again emphasize that clinicians and investigators alike have an important responsibility to proactively investigate this condition. Consequently, we hope that the need and motivation for further observational and randomized controlled trial data are renewed through our investigation, consistent with the Heart Rhythm Society's visions for the future.[10]

Limitations

We recognize that our analysis also has limitations. Retrospective studies have well-known limitations. However, the use of a retrospective analysis in this investigation affords us the opportunity to access a large group of hospitalizations with a disease that has relatively low incidence and prevalence rates. Large administrative databases such as the NIS are lacking readmission status and cause of death and are prone to coding errors. There can be misinterpretation of procedure volumes and underreporting of comorbid conditions.[23,35] We have identified prevalence of cardiovascular manifestations in sarcoidosis by presence of concurrent diagnosis codes. Although we excluded all hospitalizations with old or present myocardial infarction, coronary artery disease, and ischemic cardiomyopathy, we cannot validate that the cardiovascular manifestations were caused by cardiac sarcoidosis in the absence of histologic evidence. Also, the *ICD-9-CM* procedural code 37.94 is used to describe both the implantation and replacement of ICDs. The *ICD-9-CM* procedural code 00.51 is used for implantation and replacement of CRT. Similarly, *ICD-9-CM* procedural code 37.7 and 37.8 are used for implantation and replacement of PPM. We may not know whether the admission was for an ICD or CRT or PPM implantation or replacement. Elective implantation of an ICD, CRT, or PPM may not have been captured completely in our investigation.

Conclusions

This NIS-based retrospective investigation shows that hospitalizations of sarcoidosis have increased considerably over the past decade with declining in-hospital mortality. Furthermore, our study summarizes the prevalence of cardiovascular manifestations, rate of device placement, and factors associated with in-hospital mortality in sarcoidosis hospitalizations. Subgroup analyses in a propensity-matched cohort show that blacks had a higher incidence of in-hospital mortality and cardiac arrest compared with whites. Aggressive screening of patients with sarcoidosis for cardiovascular manifestations should be considered for prevention of cardiac arrest in sarcoidosis.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Codes Used to Exclude Sarcoidosis Hospitalizations with Ischemic Heart Diseases

Diagnosis	**ICD-9 CM Codes**
ST Segment Elevated Myocardial Infarction (n=3,455)	410.1, 410.2, 410.3, 410.4, 410.5, 410.6, 410.8, 410.9
Non-ST Segment Elevated Myocardial Infarction (n=10,802)	410.7
Unstable Angina (n=8,774)	411.1, 411.8
Old Myocardial Infarction (n=28,374)	412
Coronary Artery Disease (n=114,086)	414.00-414.07
Ischemic Cardiomyopathy (n=9,498)	414.8

*Each hospitalization may have one or more diagnosis codes.

Table S2. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Codes Included to Identify Cardiovascular Manifestations in Sarcoidosis

Diagnosis	**ICD-9 CM Codes**
Conduction Disorder	426.0, 426.10, 426.11, 426.12, 426.13, 426.2, 426.3, 426.4, 426.5, 426.6, 426.7, 426.8, 426.81, 426.82, and 426.9
Arrhythmias	427.0, 427.1, 427.2, 427.31, 427.32, 427.41, 427.42, 427.5, 427.6, 427.8, and 427.9
Heart Failure	428.0, 428.1, 428.2, 428.3, 428.4, and 428.9
Pulmonary Hypertension	416.0, 416.8, and 416.9
Cardiomyopathies	425