Lung involvement in systemic sclerosis is associated with adverse hospital outcomes: insights from the National Inpatient Sample

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ABSTRACT

This study aimed to compare outcomes of systemic sclerosis (SSc) hospitalizations with and without lung involvement. The primary outcome was inpatient mortality while secondary outcomes were hospital length of stay (LOS) and total hospital charge. Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 database. This database is the largest collection of inpatient hospitalization data in the USA. The NIS was searched for SSc hospitalizations with and without lung involvement as principal or secondary diagnosis using International Classification of Diseases 10th Revision (ICD-10) codes. SSc hospitalizations for patients aged ≥18 years from the above groups were identified. Multivariate logistic and linear regression analysis was used to adjust for possible confounders for the primary and secondary outcomes, respectively. There were over 71 million discharges included in the combined 2016 and 2017 NIS database. 62,930 hospitalizations were for adult patients who had either a principal or secondary ICD-10 code for SSc. 5095 (8.10%) of these hospitalizations had lung involvement. Lung involvement group had greater inpatient mortality (9.04% vs 4.36%, adjusted OR 2.09, 95% CI 1.61 to 2.73, p<0.0001), increase in mean adjusted LOS of 1.81 days (95% CI 0.98 to 2.64, p<0.0001), and increase in mean adjusted total hospital charge of $31,807 (95% CI 14,779 to 48,834, p<0.0001), compared with those without lung involvement. Hospitalizations for SSc with lung involvement have increased inpatient mortality, LOS and total hospital charge compared with those without lung involvement. Collaboration between the pulmonologist and the rheumatologist is important in optimizing outcomes of SSc hospitalizations with lung involvement.

Significance of this study

What is already known about this subject?

- Systemic sclerosis (SSc) is known to cause pulmonary complications such as pulmonary hypertension, interstitial lung disease, pulmonary fibrosis, and so on.
- It is, however, unclear if lung involvement adversely worsens hospital outcomes of SSc hospitalizations.

What are the new findings?

- Patients with SSc with lung involvement have worse hospital outcomes such as inpatient mortality, hospital length of stay and total hospital charge compared with patients with SSc without lung involvement.

How might these results change the focus of research or clinical practice?

- A collaborative approach between the rheumatologist and the pulmonologist is needed to ensure the best possible outcomes for SSc with lung involvement hospitalizations.

INTRODUCTION

Systemic sclerosis (SSc), previously called scleroderma, is a complex rheumatologic disease characterized by immune-mediated vasculopathy, fibrosis of the skin, and internal organs, commonly the lungs and gastrointestinal tract.[1–3] It affects about 0.01% of the population, predominantly women. The disease can occur at any age, but it is most common among middle-aged women.[4] Classification of SSc is divided into 2 main groups: limited and diffuse disease. The limited form is characterized by skin thickening that is confined to areas distal to the elbows and knees and generally associated with less severe internal organ involvement. The diffuse form involves skin thickening proximal to the elbows and knees as well as distal areas and is associated with more severe organ damage.[5]

The lungs are commonly involved in scleroderma, ranking only behind the skin, the peripheral vasculature, and the esophagus in frequency of organ involvement. SSc is associated with high mortality owing to internal organ complications, and lung disease is one of the leading causes of SSc-associated death. The most notable pulmonary complications in SSc are fibrosis and pulmonary arterial hypertension.[6 7] Studies have consistently shown a substantially increased mortality in SSc,

predominantly due to cardiopulmonary complications. A better understanding of risk factors for mortality holds the promise of improving outcomes in this devastating multi-organ autoimmune disease.[8]

There is a shortage of studies of outcomes of SSc hospitalizations with and without lung involvement using US large national population-level data. As a result, this study aimed to compare outcomes and baseline characteristics of SSc hospitalizations with and without lung involvement. We queried the National Inpatient Sample (NIS) database to answer this clinically relevant question.

METHODS

Data source

Data were obtained from the NIS 2016 and 2017 database. The NIS was searched for SSc hospitalizations with and without lung involvement as principal or secondary diagnosis using International Classification of Diseases 10th Revision (ICD-10) codes 'M34' and 'M34.81', respectively. NIS is the largest US inpatient database.[9–12] NIS is a 20% sampling of different strata, designed to represent the entire US population.[13] Diagnosis in NIS can be the principal diagnosis or up to 30–40 secondary diagnoses depending on NIS year used.[14 15] NIS 2016 can have up to 30 secondary diagnoses while NIS 2017 can have up to 40 secondary diagnoses. The principal diagnosis is the main ICD-10 code diagnosis or reason for hospitalization while a secondary diagnosis is any other diagnosis apart from the principal diagnosis.[16 17]

Inclusion criteria

We included all hospitalizations for patients ≥18 years with principal or secondary diagnosis of SSc. We used ICD-10 codes to identify diagnoses and procedures: SSc with lung involvement: all 'M3481' codes, SSc without lung involvement: all 'M34' codes excluding 'M3481' codes. See online supplemental table for complete list of ICD-10 codes used.

Outcomes

The primary outcome was inpatient mortality. Hospital length of stay (LOS) and total hospital charges were secondary outcomes of interest.

Statistical analysis

Analyses were performed using Statistics and Data (STATA, V.16; StataCorp, Texas, USA). A univariate logistic regression analysis using all variables and comorbidities in table 1 was used to calculate unadjusted ORs for the primary outcome (which is a categorical outcome). All variables with p values <0.2 were included in a multivariate logistic regression model. P values <0.05 were considered significant in the multivariate analysis. Literature review was used to select confounders. Charlson Comorbidity Index (CCI) was used to control for comorbidity complexity. CCI categorizes comorbidities of patients. Categories are weighted based on the adjusted risk of mortality. The higher the score, the higher the adjusted risk of mortality. Multivariate linear regression using all variables and comorbidities in table 1 was used to adjust for confounders for the secondary outcomes (which are continuous outcomes).

Table 1 Baseline characteristics of systemic sclerosis hospitalizations with and with lung involvement

	SSc (n=62,930)		
Variables	Without lung (n=57,835)	With lung (n=5095)	P value
Mean age (y)	62.95	59.91	<0.0001
Female (%)	84.97	79.96	<0.0001
Race (%)			<0.0001
White	68.37	56.63	
Black	15.17	22.51	
Hispanic	11.10	13.16	
Asian	1.80	3.08	
Native Americans	0.83	0.82	
Others	2.74	3.80	
Charlson Comorbidity Index (%)			0.4973
0			
1	25.02	25.02	
2	24.12	25.71	
≥3	50.86	49.26	
Hospital bed size (%)			<0.0001
Small	16.98	13.84	
Medium	26.52	21.10	
Large	56.51	65.06	
Hospital teaching status (%)			<0.0001
Non-teaching	26.94	18.94	
Teaching	74.06	81.06	
Hospital location (%)			0.1798
Rural	6.74	5.59	
Urban	93.26	94.41	
Expected primary payer (%)			0.0125
Medicare	65.26	60.28	
Medicaid	9.72	10.83	
Private	23.47	26.78	
Self-pay	1.56	2.11	
Median household income (quartile) (%)			0.2261
1st (0th–25th)	25.74	28.37	
2nd (26th–50th)	25.11	22.62	
3rd (51st–75th)	25.04	24.50	
4th (76th–100th)	24.11	24.50	
Hospital region (%)			0.0679
Northeast	20.31	23.26	
Midwest	23.93	19.92	
South	35.26	36.51	
West	20.51	20.31	
Dyslipidemia (%)	30.67	25.12	0.0005
Old MI (%)	5.85	5.20	0.4234
Atrial fibrillation/flutter (%)	13.30	15.80	0.0293
COPD (%)	18.99	18.65	0.8090
Carotid artery disease (%)	1.13	0.98	0.6578
Old stroke (%)	6.62	4.81	0.0241
Hypertension (%)	37.05	29.15	<0.0001
Peripheral vessel disease (%)	5.38	3.04	0.0012
Hypothyroidism (%)	25.08	21.30	0.0090
DM type 1 and type 2 (%)	15.97	14.13	0.1399
Obesity (%)	8.54	8.34	0.8297
CHF (%)	24.70	33.79	<0.0001
CKD (%)	21.92	21.59	0.8167

Continued

Table 1 Continued

Variables	SSc (n=62,930) Without lung (n=57,835)	With lung (n=5095)	P value
Liver disease (%)	7.95	6.18	0.0317
Maintenance hemodialysis (%)	3.54	3.34	0.7336
Smoking (%)	23.44	27.38	0.0060
Anemia (%)	41.10	39.94	0.4861

Median household income refers to median household income for patient's zip code.
CHF, congestive heart failure (chronic); CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; MI, myocardial infarction; SSc, systemic sclerosis.

RESULTS

There were over 71 million discharges included in the combined 2016 and 2017 NIS database. Up to 62,930 hospitalizations were for adult patients (aged 18 years or above), who had either a principal or secondary ICD-10 code for SSc. A total of 5095 (8.10%) and 57,835 (91.90%) of these SSc hospitalizations were with and without lung involvement, respectively. Lung involvement group were younger (59.91 vs 62.95 years, p<0.0001), had more Blacks, atrial fibrillation/flutter, congestive heart failure (CHF), smokers, and more likely to be admitted to a large bed-size and teaching hospital compared with the group without lung involvement (table 1).

A total of 2980 adult SSc hospitalizations (4.74%) resulted in inpatient mortality. Four hundred and sixty (9.04%) of the deaths occurred in SSc with lung involvement versus 2520 (4.36%) without lung involvement (p<0.0001). The adjusted OR for inpatient mortality for SSc with lung involvement compared with SSc without lung involvement was 2.09 (95% CI 1.61 to 2.73, p<0.0001). Mean LOS of hospitalization for SSc with lung involvement was 8.38 vs 5.97 days without lung involvement. SSc with lung involvement hospitalizations had a mean increase in adjusted LOS of 1.81 days (95% CI 0.98 to 2.64, p<0.0001) compared with SSc without lung involvement. Total hospital charges for SSc with lung involvement were $109,565 vs $65,187 for SSc without lung involvement. SSc with lung involvement hospitalizations had an increase in mean adjusted total hospital charge of $31,807 compared with SSc without lung involvement (95% CI 14,779 to 48,834, p<0.0001). See table 2 for complete details of outcomes between both groups.

DISCUSSION

The sociodemographic comparison in this study showed that patients who had SSc complicated by lung disease formed the minority of individuals with SSc with a mean age of 59.91 years. There were less females with lung involvement compared with those without lung involvement; however, both groups comprised predominantly females. This is in keeping with studies by Yazawa *et al* which showed that SSc was more common in middle-aged women.[4] SSc with lung involvement had less Whites and more Blacks compared with those without lung involvement. However, both groups were made up predominantly of Whites, followed by Blacks. Similar findings were noted in a study carried out in 2003 by Mayes *et al* which established baseline estimates of SSc occurrence and characteristics in a large US cohort consisting primarily of White and Black adults.[18]

Comorbidities affect prognosis, therapy, and outcome, and are associated with worse health outcomes. Comorbidity indexes identify comorbid diseases and subsequently apply pathophysiologic severity ratings for these diseases. CCI is the most extensively studied comorbidity index for predicting mortality.[19 20] Predictive validity of CCI was confirmed by finding many significant relationships of CCI with various outcomes such as mortality and LOS.

Patients with SSc with and without lung involvement did not have statistically significant difference in CCI. However, the majority of patients in both groups had a high CCI (≥3) which correlates with increased risk of mortality and prolonged hospital stay. This has a great impact on hospital resources such as healthcare costs, as patients with SSc are most likely to incur high costs in subsequent years of treatment. This is further buttressed in a study by Charlson *et al* which showed that CCI predicted health costs in subsequent years. CCI can also be used prospectively to identify patients who are likely to incur high costs.[21] A larger proportion of patients with SSc with pulmonary involvement presented to teaching and large bed-size hospitals compared with those without lung involvement. This may be accounted for by the high level of specialist care required with these patients.

Atrial fibrillation/flutter, CHF and smoking were more common in patients with SSc with lung involvement compared with those without lung involvement. This is not surprising, as smoking and cardiovascular disorders are more prominent in patients with pulmonary conditions.[22 23] These comorbidities are influential factors that must be considered in models of health-related quality of life in SSc.[24]

Table 2 Outcomes of systemic sclerosis hospitalizations with and without lung involvement

	SSc with lung involvement % (95% CI)	SSc without lung involvement % (95% CI)	Adjusted OR (AOR) (95% CI)	P value
Primary outcome				
In-hospital mortality	9.04	4.36	2.09 (1.61 to 2.73)	<0.0001
Secondary outcomes				
			Adjusted mean difference	
LOS, mean (d)	8.38	5.97	1.81 (0.98 to 2.64)	<0.0001
Total charge, mean (US$)	109,565	65,187	31,807 (14,779 to 48,834)	<0.0001

LOS, length of stay (hospital); SSc, systemic sclerosis.

SSc with lung involvement had higher odds of inpatient mortality when compared with those without lung disease after adjusting for confounders. We postulated that the increased mortality in the SSc with lung involvement group may be associated with the longer LOS and higher hospitalization charges seen in this group of patients. This is similar to the finding in a study done by Fischer *et al* in 2018 that SSc resulted in substantial increases in healthcare cost, which was more prominent in those with lung disease.[25]

The large sample size which increases the study power is a major strength of our study. Due to the nature of the NIS database, we can delineate important sociodemographic characteristics of a relatively rare disease such as SSc. Our study, however, has some limitations: (1) we included hospitalizations and clinical events based on ICD-10 codes which were created for billing purposes[26]; (2) ICD-10 codes do not grade severity, therefore, we cannot discern if SSc disease severity may have had affected outcomes of hospitalizations; (3) NIS database contains reports on hospitalizations, rather than individual patients[27]; (4) data on immunosuppressant use and medication compliance are not available in NIS[28 29]; (5) causation cannot be obtained from NIS studies, only association can be obtained; (6) duration of illness such as lung involvement cannot be obtained from NIS studies.[30]

CONCLUSION

Hospitalizations for SSc with lung involvement have both statistical and clinically significant increased inpatient mortality, LOS and total hospital charge compared with those without lung involvement. Interdisciplinary approach involving the pulmonologist and the rheumatologist is important in optimizing outcomes of SSc hospitalizations with lung involvement.

Correction notice Since Online First publication, author name 'Chukwudi Charles Modijeje' has been corrected to 'Chukwudi Charles Muojieje'.

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