**Hospitalization Rates Are Highest in the First 5 Years of Systemic Sclerosis: Results From a Population-based Cohort (1980–2016)**

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Hello everyone, I'm Ashima Makol, an associate professor in the Division of Rheumatology at Mayo Clinic in Rochester and I'm pleased on behalf of my coauthors, to share an overview of our study recently published in The Journal of Rheumatology.

The study is titled Hospitalization Rates are Highest in the First Five Years of Systemic Sclerosis: Results from a Population-based Cohort 1980 to 2016.

As a background, Systemics Sclerosis, as you know, also known as Scleroderma, is a highly heterogeneous complex, multisystem inflammatory disease, characterized by vascular injury, immune mediated dysfunction, and widespread fibrosis of the skin and internal organs.

It has the highest case fatality of all rheumatic diseases and high health care needs and costs given frequent and severe internal organ involvement. Many of the clinical manifestations of this disease require inpatient care that account for about 31% of annual health care costs in these patients, reported by a study by Furst et al in 2012.

The objective of our study was to compare hospitalization rates between incident cases of systemic sclerosis versus age and sex matched non systemic sclerosis comparators in a geographically based US population over a 36-year period. This was using a population-based cohort in comparison to insurance databases or managed care organization-based studies that have been reported previously.

We also wanted to study indications and risk factors for hospitalization as the presence of interstitial lung disease and other comorbidities, in particular cardiopulmonary disease, have shown a higher risk for hospitalization and inpatient stays in patients from the Australian Scleroderma cohort. We wanted to examine as well length of stay and readmission rates and look at trends over time.

Our study was based in, Olmsted County, Minnesota, where the city of Rochester is located. We identified incident systemic sclerosis cases from Jan 1st, 1980 to December 31st, 2016 using the resources of the Rochester Epidemiology project that links all the inpatient and outpatient healthcare data of every resident in the county together. We also ascertained fulfillment of the scleroderma classification criteria and assigned an index date corresponding to the date of clinical diagnosis of scleroderma for the cases.

A 2:1 cohort of age- and sex-matched non-scleroderma comparators were identified, and those patients had no evidence of other rheumatic diseases either. These were given the same index date as their comparator with Scleroderma.

Here are the study methods. Inpatient hospitalization data through detailed medical record was reviewed beginning 12 months prior to the index or incident date from the period between Jan 1st, 1987 to September 30th, 2018. Patients were followed until death, emigration from Olmsted County or September 30th, 2018 whichever one was later. We identified the primary discharge

diagnosis that was based on the clinical classification system for ICD-9 and 10, which is categorized into 18 chapters where scleroderma lies in Chapter 13. We also manually identified through detailed medical record review of each individual patient to understand if the hospitalization was related to a scleroderma associated indication or not. We defined readmission as occurring within 30 days of discharge.

Outlined below are our statistical methods. These are the results of our study. As you can see, we identified 76 systemic sclerosis patients during this study period which were compared to 155 non-systemic sclerosis comparators. The mean age was similar in both groups at around 56. 91% patients were females in both groups. Majority were Caucasian or white and these patients were followed for a a median of 10.3 years in the systemic sclerosis cohort and the comparators for a median of 12.7 years. There was no difference in the smoking status. The BMI of the systemic sclerosis patients was slightly lower in comparison to the non-scleroderma comparators and this was statistically significantly different. 91% patients with scleroderma fulfilled their 2013 ACR EULAR classification criteria. Majority of these patients had limited cutaneous skin involvement. These are the other clinical characteristics of the cohort. 93% patients had a positive ANA test.

This table outlines the hospitalization rates with and without systemic sclerosis. As we can see that the overall hospitalizations were much higher in the systemic sclerosis population, with 31.9 hospitalizations per hundred person years in comparison to 17.9 in the comparator group.

The hospitalizations were higher for both men and women with systemic sclerosis in comparison to their age and sex matched comparators. Hospitalizations were higher in systemic sclerosis patients among all age groups when compared to their age and sex matched comparators in the general population, and they increased over the calendar year the patients were diagnosed in. The most common indications for hospitalization were cardiopulmonary disease, as well as digestive diseases, and infectious causes.

We look at trends in hospitalization rates over time and when compared to non scleroderma comparators, scleroderma patients had a two fold higher risk of hospitalization within their first five years of disease, which trended lower over time and decreased to the point where they were no longer statistically significantly different for post 15 years after the incidents or index date.

We also identified risk factors for systemic sclerosis associated hospitalizations, and after adjusting by age, sex, and calendar year. A higher risk of inpatient care was associated with the presence of coronary artery disease, presence of diabetes mellitus, hypertension, and pulmonary arterial hypertension.
We noted a lower risk of hospitalization associated with their diffuse cutaneous subgroup compared to those with limited and sine scleroderma.

We did not see any significant association of the risk of hospitalization with the presence of interstitial lung disease, scleroderma specific autoantibodies, digital ischaemia, or smoking status.

We also saw no difference between systemic sclerosis patients and their comparators among the length of stay during inpatient admissions or their readmission rates.

The strengths of our study are the utilization of a population-based incident US cohort of patients over a 36-year period. To our knowledge, this is the most recent study to evaluate inpatient care utilization in a US cohort examining a population-based data. We were able to

identify all the cases and perform a detailed comprehensive medical record review confirming their diagnosis as well as the serial medical history over time. We were able to examine trends over the 36-year period which has not been done before.

The study, of course, had limitations associated with retrospective assessment of data. We had to rely on the primary discharge diagnosis from the hospital stay, which sometimes may not give a true picture of the hospital and hospitalization needs in a complex multi system and disease that may have multiple indications for hospitalization. We did examine each and every medical record or to help stratify and clarify whether the indication was associated with Scleroderma or an infectious etiology at the time of presentation.

The cohort size was small, despite a long study interval and the population was largely white and hence the generalizability to other regions beyond the Midwestern United States, other nations, and healthcare systems is not always possible.

In conclusion, systemic sclerosis patients have a high inpatient burden of care, much higher in comparison to their age and sex matched comparators for all sexes, all age groups, and this increases with the calendar year of diagnosis. There was a three-fold higher risk seen in male patients with Scleroderma compared to females, and presence of coronary artery disease, diabetes mellitus, hypertension, and pulmonary hypertension increased the risk for inpatient care. We also saw that the risk for hospitalization was highest in the first five years, which typically correlates with the highest disease activity in Scleroderma patients and development of comorbidities with rates approaching that of the non-scleroderma group over time. The most common indications for inpatient admission remain cardiopulmonary followed by GI tract issues and infections.

I would like to acknowledge all our patients without whose involvement in the study would not be possible. I would also like to acknowledge our funding sources.

For more details on our study, please review the full paper on The Journal of Rheumatology website. I thank you for your attention.