Hospitalization and Mortality of Patients with Systemic Lupus Erythematosus

ESWAR KRISHNAN

ABSTRACT. ***Objective.*** To describe hospitalization and mortality outcomes of patients with systemic lupus erythematosus (SLE) in the general population.

Methods. Hospitalizations of patients with SLE (n = 76,961) were identified from the US Nationwide Inpatient Sample, spanning 5 years from 1998 to 2002. Correlates of mortality were analyzed using logistic regression, while those of hospitalization charges were studied using median regressions.

Results. Overall, 11% of all hospitalizations were for SLE and/or lupus flare. There were 2454 (3.1%) hospitalizations that ended in death. Half of all deaths occurred within 7 days after admission. There were 3 peaks in mortality risk after admission, the first on Day 6, the second Day 33, the third Day 57. Patients in higher income strata and those with private insurance had better mortality outcomes than the rest. Hospitalization charges were expensive, at about US $10,000 per incident. Hospital charges were driven primarily by length of stay and number of medical procedures.

Conclusion. Hospitalizations for SLE are expensive, and 1 in 30 hospitalizations culminates in death. There appears to be a trimodal pattern in the time risk of death following admission. Patients with higher socioeconomic status and those with private insurance were less likely to die in hospital. (First Release July 1 2006; J Rheumatol 2006;33:1770–4)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS HOSPITALIZATION MORTALITY

Systemic lupus erythematosus (SLE) has long been known as a disease of young and middle aged women. While survival from SLE has improved over the years, mortality from this disease remains high compared to the general population[1,2]. Among those with SLE, comorbidities such as infection, renal failure, and cardiovascular disease lead to frequent hospitalizations and sometimes death in hospital. The few studies that have addressed overall hospital utilization and in-hospital mortality are limited to single referral centers, centers known to attract more severe and complicated cases[3,4]. Little population based information is available on the impact of SLE on hospital utilization or in-hospital mortality.

Data are presented from the Nationwide Inpatient Sample (NIS), the largest all-payer hospitalization database in the US. NIS contains annual data from about 7 million hospital stays from a 20% stratified sample of acute care community hospitals in the US[5]. The NIS is the only national hospital database with hospital charge information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, and private insurance, and the uninsured. It contains clinical and resource use information included in a typical discharge abstract, with safeguards to protect the privacy of individual patients, physicians, and hospitals. My objective was to determine mortality outcomes of hospitalizations of patients with SLE regardless of cause of admission, and to identify determinants of healthcare utilization as measured by hospitalization charges among these patients.

MATERIALS AND METHODS

Data source. Data from 1998 through 2002 from the Healthcare Cost and Utilization Project of the NIS were analyzed. The study sample was based on 100% of discharges from a 20% sample of US community hospitals. Collectively they contain records of about 7 million hospital discharges per year.

Study subjects: inclusion and exclusion criteria. Urgent and emergent hospitalizations for all adult (age > 18 yrs) patients with SLE were included in the analysis. Reasons for hospitalization in the data set were coded either as primary diagnosis or as one of 14 secondary diagnoses. Patients with SLE were identified from abstracted discharge diagnoses for 1 of 15 possible discharge diagnosis codes from the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM)[6] rubric 710.0 (systemic lupus erythematosus). Hospitalizations related to maternity and for non-urgent reasons were excluded.

Definitions of outcomes. Two outcomes were studied: (1) in-hospital, all-cause mortality defined as death at any time after admission to hospital, regardless of cause; and (2) hospital charges that reflected the dollar amount charged by the hospital (not the amount collected). In addition, these charges did not include those billed by the physician or medications prescribed at time of discharge.

Definitions of covariates. Since individual patient income was not available from abstracted summaries, we used the median income of the patient's postal zip code as a surrogate. Insurance payers were classified as Medicare, Medicaid, private insurance (including health maintenance organizations), and others (predominantly comprising the uninsured).

From the Division of Rheumatology, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

E. Krishnan, MD, MPH, Assistant Professor of Medicine, University of Pittsburgh.

Address reprint requests to Dr. E. Krishnan, Division of Rheumatology, Department of Medicine, University of Pittsburgh, S709 BST South 3500 Terrace St., Pittsburgh, PA 15261, USA. E-mail: arthritis.md@gmail.com

Accepted for publication April 17, 2006.

Statistical analyses. Student's t test and Pearson's chi-square tests were performed to assess differences in means and proportions, respectively. Pearson's correlation coefficient was used to assess correlation between covariates such as length of stay, hospital charges, and age. In-hospital mortality rate was calculated as number of deaths per 1000 hospitalization days. Time progression of death was studied by plotting mortality risk as a function of length of hospital stay using Nelson-Aalen estimation[7]. In these calculations, only hospitalizations that ended in death were used. Age and other adjustments for relative risk were made using logistic regression models. Median regressions were used to model correlates of hospitalization[8]. Median regression differs from ordinary least-square linear regression in that it fits a line through the data that minimizes the sum of absolute residuals rather than the sum of the squares of the residuals. The median was modeled as opposed to the mean. Because of the sampling and selection of study subjects, the bootstrap procedure to calculate confidence intervals (CI) was used. This procedure makes little assumption about the distribution of data and usually gives a more conservative (wider) estimate of the CI. In these models, with the exception of age, number of procedures, and number of diagnoses, independent variables were treated as categorical variables with appropriate dummy variables used to contrast the different levels of these variables.

Sensitivity analyses. Sensitivity analyses were performed to assess the effect of errors in the diagnosis of SLE and outliers. In large population studies of SLE, epidemiologists depend on surrogate sources of information on the diagnosis and the veracity of these diagnoses depends on the source. Self-reports are likely to have the least positive predictive value, followed by death certificate data. Hospital data bear the diagnosis based on physician attribution. This study depended on physician's identification of a diagnosis of SLE in the discharge summary. It is likely that many patients with inactive or subclinical lupus will not have this diagnosis in the list of discharge diagnoses. On the other hand, some individuals with ill-defined disease and a positive antinuclear antibody test are likely to be labeled as having SLE in the discharge summary. With randomness in misclassification, one can assume an element of nondifferential misclassification bias that can lead to measurement error and regression to the mean. Due to confidentiality issues patients' hospital charts could not be reviewed. However, assuming that analyses were confined to a primary diagnosis of SLE (i.e., first in the list of 15 diagnoses), there would be a sample with nearly 100% specificity, i.e., a positive predictive value of 100%. Such analyses were performed and the results were compared with those done with the entire data set.

To further allay concerns about the effect of outliers, data were reanalyzed excluding brief (one day or less) and prolonged (greater than 90 days) hospitalizations. For sensitivity analyses of hospital charges, extremes (< $1500 and > $152,000) were excluded. These cutoffs were chosen to reflect 1st and 99th percentiles of charges for the entire study group.

Because of confidentiality concerns, individual patient identifiers are not available in the NIS data sets. To minimize the possibility of counting the same individual more than once, an algorithm was used in which hospitalization records with the identical year of admission, age, sex, race, income, health insurance, hospital identification code, and other relevant variables were identified as duplicate/multiple admissions. Among the multiple records, the first was retained and the rest were eliminated.

As government sponsored insurance such as Medicare and Medicaid is provided to younger people only under special circumstances (poverty, disability) and because of the potential for statistical interactions, parallel multivariable analyses were performed on the strata of each of these variables instead of adjusting them in the multivariable models. All analyses were performed using Stata (Stata Corp., College Station, TX, USA). Since this analysis involved publicly available data that does not contain individual patient identifiers, Institutional Review Board approval was not sought.

RESULTS

Sample characteristics. Overall, there were 76,961 hospitalizations with SLE as a discharge diagnosis. Of these, 8710 (11.3%) had SLE as the primary reason for admission. The characteristics of the study sample are given in Table 1. Notably, 50% of all these hospitalizations lasted between 2 and 4 days and 50% had at least one procedure performed during this time.

Patient disposition. The majority of discharges were to home (74%). About 11% were transfers to a nursing home and 8% were discharges with home health services. A small proportion of discharges were against medical advice (1%).

Mortality. There were 2454 (3.1%) deaths in the study sample. Patients with SLE who died were older than survivors (mean 59 yrs vs 51 yrs), had almost double the length of hospitalization (mean 12 days vs 6 days), and had double the number of procedures performed (mean 4 vs 2). All these differences were statistically significant ($p < 0.001$). Among deaths, half occurred within 7 days after admission.

Figure 1 shows the time progression of risk of death with length of hospital stay. Of note, there were 3 peaks in the mortality risk: Day 6, Day 33, and Day 57.

Breakdowns of the proportion of deaths and the mortality rate by age and sex are given in Table 2. Increasing age was associated with higher mortality risk (odds ratio 1.028 per each advancing year, 95% CI 1.026–1.031). After adjusting for age, women had lower post-admission mortality risk (OR 0.72, 95% CI 0.64–0.80). In multivariable analyses (Table 3) higher income, private insurance, and female sex were independently associated with better outcome, while increasing age, higher number of medical diagnoses, and medical procedures were associated with worse risk.

Hospital charges. The median and 99th percentile hospitalization charges were $10,101 and $151,643, respectively, for the entire cohort (all figures US dollars). Among those who died, the charges were substantially higher, median and 99th percentile being $25,585 and $382,728, respectively. Average hospital charges declined with age, especially among those who died (Figure 2). As expected, these charges were most strongly correlated with length of hospitalization (correlation

Table 1. Characteristics of 76,961 hospitalizations for SLE.

Characteristic	
Mean age, yrs (SD)	51.0 (16.7)
Women, %	88.36
Income strata, US$, %	
< 25,000	8.43
25,000–29,999	27.60
30,000–34,999	27.21
≥ 35,000	36.76
Insurance strata, %	
Medicare	43.59
Medicaid	14.63
Private	36.00
Other	5.78
Mean length of hospitalization, days (SD)	6 (8)
Mean number of diagnoses (SD)	7 (3)
Mean number of procedures (SD)	2 (2)

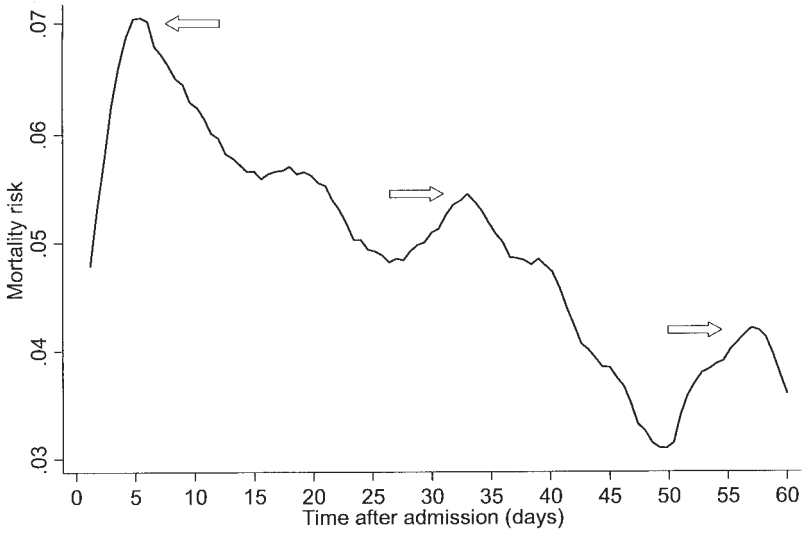

Figure 1. A trimodal pattern of death (arrows) in 2454 in-hospital deaths of patients with SLE.

Table 2. In-hospital mortality among patients with SLE.

Age, yrs	No. of Deaths	No. of Hospitalization Days	Death Rate per 1000 Person-Days of Hospitalization (95% CI)	Hospitalizations Culminating in Death, %
Men				
< 30	20	6,352	3.1 (2.0–4.9)	2
30–49	70	19,925	3.5 (2.8–4.4)	2
50–69	149	20,104	7.4 (6.3–8.7)	5
70–89	165	13,171	12.5 (10.8–14.6)	8
≥ 90	5	415	12.0 (5.0–28.9)	9
Women				
< 30	112	41,771	2.7 (2.2–3.2)	2
30–49	540	159,853	3.4 (3.1–3.7)	2
50–69	756	141,683	5.3 (5.0–5.7)	3
70–89	613	74,333	8.2 (7.6–8.9)	5
≥ 90	23	2,212	10.4 (6.9–15.6)	7

Table 3. Correlates of in-hospital mortality and hospital charges in multivariable regression.

	Mortality		Hospital Charges	
	Odds Ratio	95% CI	Beta coefficient	95% CI
Age (each year)	1.03	1.02–1.03	–12	–15 to –8
Female	0.79	0.70–0.88	–236	–399 to –739
Median income (%)				
< 25,000	1.00			
25,000–29,999	0.96	0.82–1.13	–103	–330 to –124
30,000–34,999	0.92	0.78–1.09	376	145 to 606
≥ 35,000	0.80	0.68–0.95	1087	841 to 1334
No. of medical conditions	1.14	1.12 –1.16	136	115 to 156
No. of medical procedures	1.34	1.32–1.36	2371	2314 to 2430
Health insurance				
Medicare	1.00			
Medicaid	1.03	0.89–1.20	296	192 to 399
Private insurance	0.85	0.76–0.95	602	520 to 684
Other	1.14	0.93–1.40	472	287 to 657

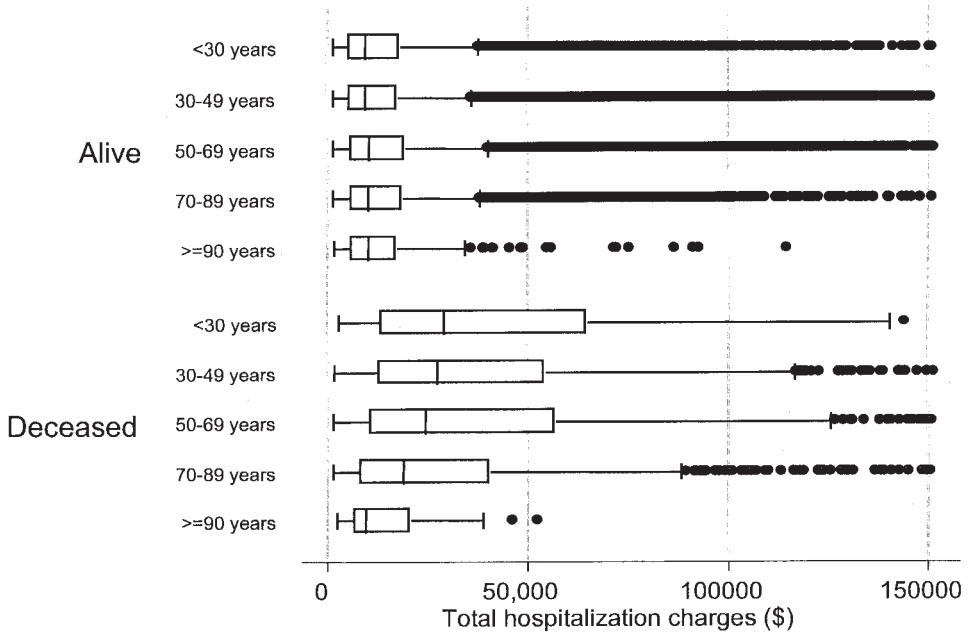

Figure 2. Age distribution of hospital charges in 76,961 admissions of patients with SLE (1998-2002). Box plots indicate 75th/25th percentiles, with outliers (●).

coefficient $r = 0.75$, $p < 0.001$). Other meaningful correlation was with the number of procedures ($r = 0.52$, $p < 0.01$).

In the multivariable median regression, age, female sex, median income, number of procedures, and diagnoses and length of stay were independent correlates of hospitalization charges (Table 3). Compared to Medicare, hospitalizations with other types of insurance were correlated with higher hospitalization charges.

Various sensitivity analyses were performed as described above, and the results remained robust.

DISCUSSION

In-hospital mortality among patients with SLE was found to be low, but significant, with about one in 30 admissions having a fatal outcome. This risk estimate is slightly lower than that reported by Ward (about 5%)[9]. Older age was associated with higher mortality risk. Patients who died were likely to have had almost twice the length of hospital stay, and twice the number of comorbid diagnoses and procedures performed. Overall, there was little difference in mortality risk between men and women. Of note, there were 2 major peaks in mortality risk following hospitalization. The first might be directly related to SLE (flare, infection, and renal failure), while the second might reflect nosocomial problems such as infection and thromboembolism. The smaller peak observed between the first 2 might represent a combination of the others.

In the first half of the 20th century, SLE was described as a progressive and fatal disease, with usual duration of survival from diagnosis less than 1 year[10,11]. Survival from this disease has since improved substantially, and measures of morbidity such as frequency of hospitalizations are useful indicators of disease control. In-hospital mortality, on the other hand, reflects a combination of the frailty of the individual patient (age, number of medical problems, number of medical procedures needed) and the effectiveness of the healthcare process. The latter is a combination of (1) access to care, (2) the quality of general medical care, and (3) quality of care specific to lupus (such as quality of rheumatologists and nephrologists). Age, number of medical problems, and number of medical procedures were found to be independently correlated with risk of death. Income category, a surrogate measure of access to care and ability to purchase medications, was inversely associated with the risk of death. As observed[12],possession of private insurance, often an indicator of relative affluence, was associated with lower mortality risk compared to those with publicly funded insurance such as Medicare and Medicaid. This could reflect better access to and utilization of healthcare resources and access to outpatient rheumatology and nephrology care[13]. It could also indicate that patients with private insurance had less severe disease, as catastrophic illness would have resulted in loss of employment and income, and enrolment in Medicaid and Medicare.

Hospitalization charges were used as a measure of healthcare utilization and not as a part of economic analysis. This metric gives an overall measure of healthcare utilization (since there are no free services in hospitals). In addition, no discounting methods were used, as the objective was not to study costs. Length of hospital stay might have been an alternative outcome, but it is all too often an inaccurate measure of healthcare utilization (e.g., patients staying in hospital for intravenous antibiotics, waiting for test results, etc.). Charges

per day were also used, since overall utilization was the objective of the study, and not intensity of utilization.

SLE was found to be associated with substantial hospital charges, with a median charge of about $10,000. This charge increased by 2.5 times in hospitalizations that ended in death. Increasing age was weakly correlated with hospital charges, number of procedures, and length of stay. The number of procedures was correlated strongly with length of and charges for hospitalization. Overall, the major correlates of hospitalization charges were number of procedures and length of stay: both indicative of severity of disease and intensity of medical care delivered.

The strengths of this study include the large population-based sample and availability of various demographic data as well as information on medical procedures and hospital charges, on type of medical insurance, and on up to 14 comorbid medical conditions. The limitations of the study are the reliance on physician reported diagnoses of SLE and lack of clinical details.

Many complications of SLE are unavoidable. Yet prevention of disease flare and avoidance of excessive immunosuppression can be achieved by appropriate outpatient management as well as self-management strategies. For example, patient noncompliance is an important correlate of poor morbidity outcomes and hospitalizations in SLE[12], and this factor can be addressed by appropriate, culturally sensitive patient education.

REFERENCES

1. Borchers AT, Keen CL, Shoenfeld Y, Gershwin ME. Surviving the butterfly and the wolf: mortality trends in systemic lupus erythematosus. Autoimmun Rev 2004;3:423-53.
2. Trager J, Ward MM. Mortality and causes of death in systemic lupus erythematosus. Curr Opin Rheumatol 2001;13:345-51.
3. Edwards CJ, Lian TY, Badsha H, Teh CL, Arden N, Chng HH. Hospitalization of individuals with systemic lupus erythematosus: characteristics and predictors of outcome. Lupus 2003;12:672-6.
4. Petri M, Genovese M. Incidence of and risk factors for hospitalizations in systemic lupus erythematosus: a prospective study of the Hopkins Lupus Cohort. J Rheumatol 1992;19:1559-65.
5. Steiner C, Elixhauser A, Schnaier J. The healthcare cost and utilization project: an overview. Eff Clin Pract 2002;5:143-51.
6. Hart AC, Hopkins C. ICD-9 CM professional for physicians. 6th ed. Salt Lake City, UT: Ingenix; 2004.
7. Keiding N, Klein JP, Horowitz MM. Multi-state models and outcome prediction in bone marrow transplantation. Stat Med 2001;20:1871-85.
8. Yin G, Cai J. Quantile regression models with multivariate failure time data. Biometrics 2005;61:151-61.
9. Ward MM. Hospital experience and mortality in patients with systemic lupus erythematosus: which patients benefit most from treatment at highly experienced hospitals? J Rheumatol 2002;29:1198-206.
10. Madden J. Acute disseminated lupus erythematosus. Arch Dermatol Syph 1932;12:951-63.
11. Cook CD, Wedgwood RJ, Craig JM, Hartmann JR, Janeway CA. Systemic lupus erythematosus. Description of 37 cases in children and a discussion of endocrine therapy in 32 of the cases. Pediatrics 1960;26:570-85.
12. Petri M, Perez-Gutthann S, Longenecker JC, Hochberg M. Morbidity of systemic lupus erythematosus: role of race and socioeconomic status. Am J Med 1991;91:345-53.
13. Rask KJ, Williams MV, Parker RM, McNagny SE. Obstacles predicting lack of a regular provider and delays in seeking care for patients at an urban public hospital. JAMA 1994;271:1931-3.