Untangling Hospitalizations in Systemic Amyloidosis: Patient Characteristics, Economic Cost, and Clinical Outcomes

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INTRODUCTION

- The amyloidoses are a group of rare protein-folding disorders characterized by extracellular tissue disposition of misfolded and aggregated autologous proteins as β-pleated sheet fibrils.[1]
- Although many organs can be affected, the heart is frequently involved in two forms of systemic amyloidosis: light chain (AL) and transthyretin (ATTR) amyloidosis.[2,3]
- Patients with systemic amyloidosis frequently require hospital care.

OBJECTIVE

To understand patient characteristics, economic cost, and clinical outcomes associated with systemic amyloidosis treated in U.S. hospitals.

METHODS

Study Design and Data Source

- Retrospective, cohort study using 2014-2016 data from Premier Perspective™ Database
  - Covering over 45 million hospital discharges and includes data on complete clinical coding, hospital cost, and patient billing data from close to 600 hospitals throughout the United States out of 5,500 total[4]

Study Population

- Hospitalized patients aged ≥18 years were identified during calendar years 2014-2016 if they had:
  - ≥1 inpatient claim consistent with systemic amyloidosis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] code 277.30 or 277.39; *International Classification of Diseases, Tenth Revision, Clinical Modification* [*ICD-10-CM*] code E85.4x, E85.8x, or E85.9x) in any diagnosis field;
  - and in patients with multiple qualifying hospitalizations, the first hospitalization was included.
- Patients with evidence of other types of amyloidosis (*ICD-9-CM* codes: 277.31; *ICD-10-CM* codes: E85.0x-E85.3x) or chronic inflammatory diseases that may lead to other types of amyloidosis were excluded.

Study Measures

- Patient demographics and clinical characteristics
  - Demographics (age, gender, race); payment source (Medicare, Medicaid, commercial, or other); concomitant conditions [Charlson Comorbidity Index (CCI), multiple myeloma (MM), monoclonal gammopathy of undetermined significance (MGUS)]
- Hospital characteristics
  - Admission type (elective vs. non-elective); region (Northeast, Midwest, West, South); bed size (0-199, 200-499, 500+); hospital type (teaching vs. non-teaching); and location (rural vs. urban)
- Economic cost and clinical outcomes
  - Hospitalization costs (in 2016 US$), length of stay (LOS), intensive care unit (ICU) use, and mortality

Statistical Analysis

- Means, standard deviations (SD), and relative frequencies and percentages for continuous and categorical data, respectively, were reported
- Data transformations and statistical analyses were performed using SAS© version 9.4.

RESULTS

- The overall study sample was made up of 7,533 hospitalized patients with a diagnosis consistent with systemic amyloidosis.
- *Patient demographics and clinical characteristics* **(Figure 2a-2c)**
  - Mean (SD) age was 72.8 (11.7) years, 46.3% were female, 68.0% were White.
  - Medicare was the primary payer for 78.0% of patients.

- *Patient demographics and clinical characteristics continued*
  - The mean (SD) CCI was 3.2 (2.1), and 10.6% had a code for MM and 2.6% for MGUS. **(Table 1)**
  - 59.5% of patients had either, or both, cardiac involvement or renal disease.
    - Among patients with cardiac involvement, 74.6% had congestive heart failure.
- *Hospital characteristics* **(Figure 3a-3c)**
  - 90.1% of patients had a non-elective (e.g. urgent or emergent) hospital admission, with majority (75.9%) being referred by their physician.
  - Admissions to hospitals from all regions of the U.S. were represented.
  - 46.2% of hospitals had a bed size between 200-499 beds.
  - 93.3% of admissions were to hospitals in urban settings; 51.9% of hospitals were teaching hospitals.
- *Economic costs and clinical outcomes* **(Table 2)**
  - The mean (SD) total hospitalization cost was $18,110.70 (25,245.78), with a mean (SD) LOS of 7.4 (9.9) days.
  - During the hospital stay, 30.7% of patients were admitted to the ICU, with a mean (SD) ICU LOS of 4.1 (5.4) days.
  - In-hospital mortality was 6.7%.

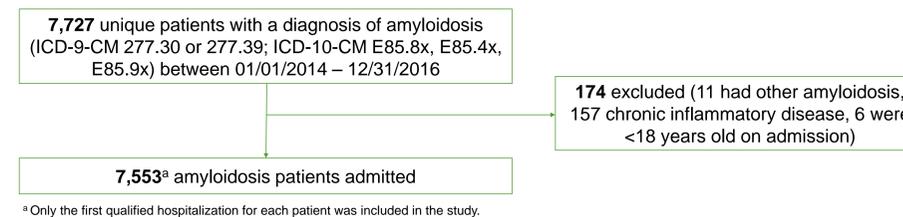**Figure 1.** Patient attrition diagram for identifying hospitalized patients.

7,727 unique patients with a diagnosis of amyloidosis (ICD-9-CM 277.30 or 277.39; ICD-10-CM E85.8x, E85.4x, E85.9x) between 01/01/2014 – 12/31/2016

174 excluded (11 had other amyloidosis, 157 chronic inflammatory disease, 6 were <18 years old on admission)

7,553[a] amyloidosis patients admitted

[a] Only the first qualified hospitalization for each patient was included in the study.

Table 1. Comorbidities and disease manifestations

	All
N	7,553
Charlson Comorbidity Index, mean (SD) [median]	3.2 (2.1) [3.0]
Other Comorbidities, n (%)	
Multiple myeloma (MM)	803 (10.6)
MGUS[a]	195 (2.6)
Manifestations, n (%)	
Carpal tunnel syndrome	20 (0.3)
Hepatomegaly	43 (0.6)
Purpura	722 (9.6)
Claudication	337 (4.5)
Stroke	2,200 (29.1)
Peripheral neuropathy	174 (2.3)

[a] Monoclonal Gammopathy of Undetermined Significance

Table 2. Hospital utilization and cost

|	All
N	7,553
Overall length of stay in days, mean (SD) [median]	7.4 (9.9) [5.0]
Intensive care unit (ICU), n (%)	2,318 (30.7)
Length of stay in days, mean (SD) [median]	4.1 (5.4) [2.0]
Total cost, mean (SD) [median]	$18,110.70 ($25,245.78) [$10,667.26]
Discharge status, n (%)	
Home	3,972 (52.6)
Expired	509 (6.7)
Transferred (hospice, rehab center, nursing home)	2,799 (37.1)
Other	273 (3.6)

Figure 2a. Selected Patient Characteristics: Age

- 18-34 (1%)
- 35-54 (7%)
- 55-64 (13%)
- 65 or older (79%)
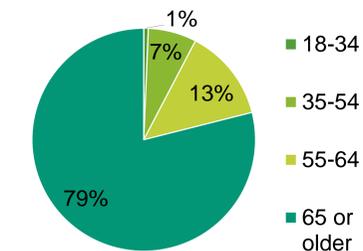
Figure 2b. Selected Patient Characteristics: Race

- White (68%)
- African American (18%)
- Other (13%)
- Unknown (1%)
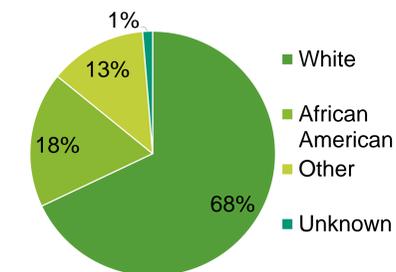
Figure 2c. Selected Patient Characteristics: Primary Payer Type

- Medicare (78%)
- Medicaid (5%)
- Commercial (3%)
- Self-Pay (1%)
- Managed Care (11%)
- Other (2%)
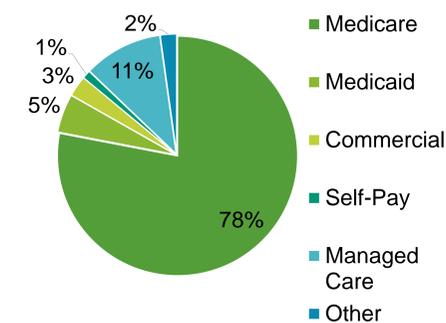
Figure 3a. Selected Hospital Characteristics: Hospital Region

- Northeast (23%)
- Midwest (18%)
- West (20%)
- South (39%)
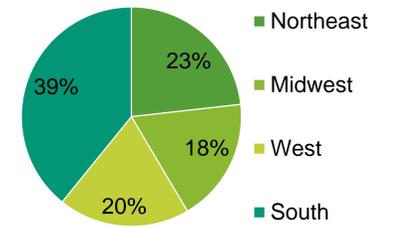
Figure 3b. Selected Hospital Characteristics: Bed Size

- 0-199 (11%)
- 200-499 (46%)
- 500+ (43%)
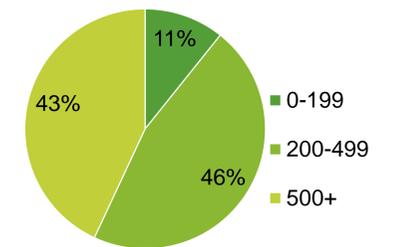
Figure 3c. Selected Hospital Characteristics: Hospital Location

- Rural (7%)
- Urban (93%)
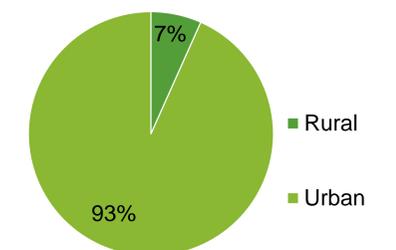
CONCLUSION

- Disease burden and hospital costs associated with AL or ATTR amyloidosis are high.
- Based on hospital discharge records, almost 60% of patients had cardiac and/or renal disease.
- Mean hospitalization costs were >$18,000 per patient and many patients were admitted to ICU.
- New therapies aimed at improving organ response have the potential to extend survival, reduce disease burden, and yield substantial cost savings.
- Limitations
  - Systemic amyloidosis was identified using coded data, not clinical records, leading to errors because codes are primarily applied to support billing, not research.
  - Privacy restrictions that permit the use of coded data explicitly prevented us from seeking additional data on patients, so pathology, laboratory, or other clinical notes could not be used.

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