Diagnostic Hospitalization and Associated Costs in Patients with Amyloid Light-Chain Amyloidosis

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BACKGROUND & OBJECTIVES

- Light-chain (AL) amyloidosis is a rare, fatal disease due to the extracellular deposition of misfolded, insoluble immunoglobulin light chains[1]
- Clinical experience suggests some patients are diagnosed with AL amyloidosis during an acute admission for organ dysfunction[2]
- Delayed diagnosis is associated with early mortality due to disease progression and resulting organ dysfunction[1,3,4]
- Study aim: Estimate the rate of diagnostic events among hospitalized patients and measure associated healthcare utilization and costs

METHODS

Study Design and Data Source

- Retrospective analysis using 2017-2020 data from the Premier® Healthcare Database

Patient Population

- Hospitalized patients aged ≥18 years were identified if they:
  - Had ≥1 inpatient claim for AL amyloidosis (*International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] code E85.81) in any diagnosis field during the study period (10/1/2017-12/31/2020)
  - Without a diagnosis for other amyloidosis types (E85.0x-E85.3x) or certain chronic inflammatory disease
- Patients were stratified into diagnostic and other hospitalization
- Diagnostic hospitalization was defined as a hospitalization with diagnostic biopsy (bone marrow, kidney, liver, abdominal fat pad, salivary gland, gingival, or endomyocardial) without solid organ or hematopoietic stem cell transplant (HSCT)

Study Measures

- In-hospital mortality, APR-DRG severity of illness, hospitalization costs (in 2020 USD) and length of stay (LOS)

Statistical Analysis

- Means, standard deviations (SD), and relative frequencies and percentages were reported for continuous and categorical data, respectively
- To compare between diagnostic vs other hospitalizations, t-test and Chi-square (or exact Chi-square if <5) tests were performed
- Cost estimates were converted to 2020 US dollars using the Consumer Price Index to adjust for inflation
- Data transformations and statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC)

RESULTS

Demographic and Hospital Characteristics (Table 1)

- Of 1,341 hospital admissions, 234 (17.6%) were diagnostic admissions
- Diagnostic admissions did not differ from non-diagnostic hospitalizations regarding characteristics such as patient demographics, payer type, and hospital location

Table 1. Demographic of Hospitalized Patients with AL Amyloidosis, Hospital Characteristics, and Physician Specialty, Stratified by Type of Hospitalization

	Type of Hospitalization			All Adult AL Amyloidosis Hospitalization
	Diagnostic[c] N (%) = 234 (17.6)	Other N (%) = 1,107 (82.4)	*P* Value	N = 1,341
Age, mean (SD) [median]	67.7 (11.1) [68]	67.1 (11.2) [67]	0.490	67.2 (11.2) [68]
Female, n (%)	114 (48.7)	478 (43.2)	0.121	592 (44.1)
Race, n (%)			0.570	
White	147 (62.8)	715 (64.6)		862 (64.3)
African American	50 (21.4)	256 (23.1)		306 (22.8)
Other	25 (10.7)	99 (8.9)		124 (9.2)
Asian	4 (1.7)	15 (1.4)		19 (1.4)
Unable to determine	8 (3.4)	22 (2.0)		30 (2.2)
Primary payer type, n (%)			0.623	
Medicare	154 (65.8)	683 (61.7)		837 (62.4)
Medicaid	23 (9.8)	105 (9.5)		128 (9.5)
Commercial	14 (6.0)	86 (7.8)		100 (7.5)
Self-pay	4 (1.7)	11 (1.0)		15 (1.1)
Managed care	32 (13.7)	187 (16.9)		219 (16.3)
Other	7 (3.0)	35 (3.2)		42 (3.1)
Year of hospitalization			0.317	
2017[a]	20 (8.5)	60 (5.4)		80[a] (6.0)
2018	63 (26.9)	322 (29.1)		385 (28.7)
2019	80 (34.2)	389 (35.1)		469 (35.0)
2020	71 (30.3)	336 (30.4)		407 (30.4)
Admission type			0.050	
Elective	20 (8.5)	146 (13.2)		166 (12.4)
Urgent/emergent	214 (91.5)	961 (86.8)		1,175 (87.6)
Hospital type			0.547	
Teaching	142 (60.7)	695 (62.8)		837 (62.4)
Non-Teaching	92 (39.3)	412 (37.2)		504 (37.6)
Diagnostic biopsies,[b] n (%)				
Bone marrow biopsy	186 (79.5)	2 (0.2)*	<0.001	188 (14.0)
Abdominal fat pad biopsy	4 (1.7)	0 (0.0)	<0.001	4 (0.3)
Liver biopsy	3 (1.3)	0 (0.0)	0.005	3 (0.2)
Kidney biopsy	105 (44.9)	0 (0.0)	<0.001	105 (7.8)
Endomyocardial biopsy	5 (2.1)	0 (0.0)	<0.001	5 (0.4)

AL: Systemic light chain; SD: standard deviation.
[a] ICD-10-CM code E85.81 for AL amyloidosis not available until 10/1/2017.
[b] Zero patients identified with salivary gland or gingival biopsy (results not shown).
[c] Defined as presence of bone marrow, kidney, liver, abdominal fat pad, salivary gland, gingival, or endomyocardial biopsy and absence of solid organ or HSCT.
* These patients had SCT during the episode thus their episode was not considered diagnostic.

Healthcare Utilization and Costs (Table 2, Figure 1)

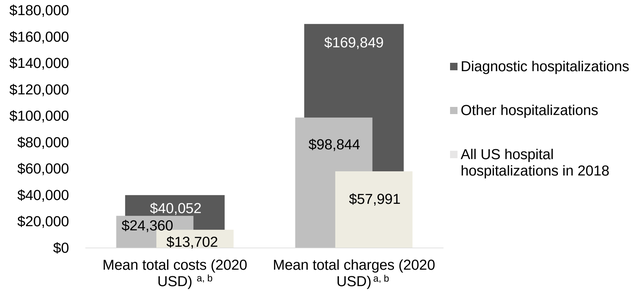
- Patients with a diagnostic hospitalization had more severe disease
- Compared to non-diagnostic AL amyloidosis hospitalizations, diagnostic hospitalizations were characterized by:
  - Higher proportion of in-hospital death
  - Longer LOS (mean: 14.5 vs. 8.4 days, *P*<0.001; median: 11.0 vs. 5.0)
  - Higher cost ($40,052 vs. $24,360, *P*<0.001; $26,346 vs. $13,224)
  - Higher total charges ($169,849 vs. $98,844, *P*<0.001; $116,530 vs. $51,578)
- Diagnostic hospitalization costs and charges were about three times the costs and charges of the average US hospitalization in 2018.

Table 2. In-Hospital Death, Length of Stay, and Hospital Costs and Charges, Stratified by Type of Hospitalization

	Type of Hospitalization			All Adult AL Amyloidosis Hospitalization
	Diagnostic[c] N (%) = 234 (17.6)	Other N (%) = 1,107 (82.4)	*P* Value	N = 1,341
In-hospital mortality, n (%)	21 (9.0)	86 (7.8)	0.536	107 (8.0)[d]
APR-DRG severity of illness,[a] n (%)			<0.001	
Minor	1 (0.4)	5 (0.5)		6 (0.4)
Moderate	20 (8.5)	183 (16.5)		203 (15.1)
Major	126 (53.8)	637 (57.5)		763 (56.9)
Extreme	87 (37.2)	282 (25.5)		369 (27.5)
Overall length of stay (days), mean (SD) [median]	14.5 (11.7) [11.0]	8.4 (8.9) [5.0]	<0.001	9.5 (9.7) [6.0]
ICU,[b] n (%)	51 (21.8)	218 (19.7)	0.466	269 (20.1)
Length of ICU [b] stay among utilizers, mean (SD) [median]	7.0 (6.4) [4.0]	6.4 (7.9) [3.0]	0.593	6.5 (7.6) [3.0]
ED,[b] n (%)	165 (70.5)	750 (67.8)	0.410	915 (68.2)
Length of ED [b] stay among utilizers, mean (SD) [median]	1.1 (0.3) [1.0]	1.3 (3.3) [1.0]	0.065	1.3 (3.0) [1.0]

AL: Systemic light chain; APR-DRG: All Patients Refined Diagnosis Related Groups; ICU: intensive care unit; SD: standard deviation.
[a] APR-DRG Severity of Illness subclasses is a measure of disease burden based on the extent of organ system loss of function or physiologic decompensation. Categories (minor, moderate, major, and extreme) are generated by a proprietary algorithm using a set of diagnosis codes and surgical procedure codes. (https://www.hcup-us.ahrq.gov/db/nation/nis/APR-DRGsV20MethodologyOverviewandBibliography.pdf)
[b] Care units identified through hospital billing records, based on any charge for room and board.
[c] Defined as presence of bone marrow, kidney, liver, abdominal fat pad, salivary gland, gingival, or endomyocardial biopsy and absence of solid organ or HSCT.
[d] 95% CI of death during hospitalization: 6.5%-9.4%.

Figure 1. Hospital Costs and Charges, Stratified by Type of Hospitalization



[a] Difference in cost and charges for diagnostic hospitalization and non-diagnostic hospitalization (*P*<0.001).
[b] Total costs and charges do not include professional fees for the services received in hospitals by physicians and other skilled health care professionals licensed for independent practice.

LIMITATIONS

- As diagnostic admissions were identified based on the presence of specific biopsies, patients diagnosed in the hospital based on other findings may have been excluded; additionally, patients diagnosed previously but underdoing biopsies for other reasons may have been included
- Database limitations include possible miscoding and lack of data from federally funded hospitals (e.g., Veteran Affairs)

CONCLUSIONS

- This study provides insight into AL amyloidosis hospitalizations:
  - Approximately 1 in 6 hospitalizations with AL amyloidosis are associated with the initial diagnosis
  - Of diagnostic admissions, 1 in 5 spent time in the ICU and 1 in 13 died before discharge
- Healthcare utilization and costs are high among patients hospitalized with AL amyloidosis, and are particularly high for those who have not been diagnosed prior to being admitted for an acute event
  - Healthcare costs are about three times higher among diagnostic hospitalizations for AL amyloidosis compared to the average US hospitalization

REFERENCES

1. Elsayed M, et al. *J Hematol.* 2021. 2. McCausland KL, et al. *The Patient.* 2018. 3. Gertz MA, et al. *J Clin Oncol.* 2016. 4. Renz M, et al. *Amyloid.* 2016.

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