RISK STRATIFICATION OF ACUTE KIDNEY INJURY IN WALDENSTRÖM MACROGLOBULINEMIA: MACHINE LEARNING-DERIVED CLINICAL PHENOTYPES FROM A NATIONAL INPATIENT DATABASE

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Physicians Regional Healthcare System

SOHO ANNUAL MEETING 2026

INTRODUCTION

Waldenström macroglobulinemia (WM) is a lymphoplasmacytic lymphoma characterized by IgM monoclonal gammopathy and bone marrow involvement. Renal dysfunction, including acute kidney injury (AKI), affects approximately 30% of symptomatic patients and is an independent adverse prognostic factor, yet distinct AKI phenotypes remain poorly characterized.

AIM

To identify and characterize distinct clinical phenotypes of acute kidney injury (AKI) among hospitalized patients with WM who had no pre-existing chronic kidney disease, using unsupervised machine learning applied to a national inpatient database.

METHOD

- Using the National Inpatient Sample (NIS, 2016–2023), adult WM hospitalizations were identified via ICD-10 codes. Patients with pre-existing chronic kidney disease (CKD), end-stage renal disease (ESRD), dialysis dependence, or COVID-19 were excluded. Distinct clinical phenotypes were derived using unsupervised machine learning incorporating UMAP dimensionality reduction and k-means clustering.

  Variables included:
  - **Demographics & socioeconomic:** age, sex, insurance type, income quartile, weekend vs. weekday admission
  - **Hospital characteristics:** urban/rural and teaching status
  - **Comorbidity burden:** Charlson index, frailty
- • **WM-specific / hematologic:** anemia, thrombocytopenia, amyloidosis, plasmapheresis
- • **Metabolic:** hypercalcemia
- • **Acute illness severity:** sepsis, acidosis, vasopressor use, mechanical ventilation
  - **Treatment:** antineoplastic use
  - **Outcome:** acute kidney injury (AKI)

RESULTS

STUDY OVERVIEW

Among **7,399** WM hospitalizations without prior CKD/ESRD

(mean age 74.7 years),

the overall AKI rate was **15.9%**

Unsupervised clustering (UMAP + k-means) identified **3** distinct clinical phenotypes

(p<0.001), summarized at right.

PHENOTYPE 1

ACUTELY ILL, TREATMENT-INTENSIVE

n = 2,177 | AKI RATE **17.4%**

AKI appears driven by acute illness and treatment toxicity.

PATIENT PROFILE

- Youngest Patients — Mean Age **70.8** years
- Lower Frailty & Comorbidity Burden — Frailty **21.0%** | Charlson Index **3.0**

KEY CLINICAL FEATURES

SEPSIS	ACIDOSIS	ANTINEOPLASTIC USE	MECHANICAL VENTILATION
15.1%	20.1%	18.2%	7.3%

AKI in this phenotype is primarily associated with **acute illness severity** and **treatment** exposures.

UMAP + k-means clustering identified this distinct clinical phenotype (p < 0.001).

PHENOTYPE 2

FRAIL, MULTIMORBID

n = 4,319 | AKI RATE **14.4%**

Despite the greatest frailty burden, this group had the **lowest** AKI rate.

PATIENT PROFILE

Oldest Patients Mean Age	Highest Frailty	Highest Comorbidity Burden	Anemia	Thrombocytopenia
77.2 years	38.8%	Charlson Index 3.51	13.0%	15.6%

KEY CLINICAL FEATURES

SEPSIS	ACIDOSIS	ANTINEOPLASTIC USE	MECHANICAL VENTILATION	LENGTH OF STAY (MEDIAN)
11.2%	13.4%	10.8%	3.6%	4 DAYS

AKI in this phenotype is associated with **frailty, multimorbidity,** and **disease burden,** rather than acute illness or treatment toxicity.

UMAP + k-means clustering identified this distinct clinical phenotype (p < 0.001).

PHENOTYPE 3

IGM-MEDIATED RENAL INJURY

n = 903 | AKI RATE **19.5%**

Highest AKI rate despite no prior CKD/ESRD. Findings implicate direct **IgM-mediated** mechanisms over acute illness.

PATIENT PROFILE

Mean Age	Frailty	Charlson Index	Anemia	Thrombocytopenia
74.1 years	27.3%	3.21	11.8%	12.1%

KEY CLINICAL FEATURES

AMYLOIDOSIS	HYPERCALCEMIA	SEPSIS	ANTINEOPLASTIC USE	ACIDOSIS
16.1%	17.2%	7.4% (Low)	6.0% (Minimal)	9.8%

This phenotype is characterized by **IgM-related renal pathology** and metabolic derangements, with minimal contribution from acute illness or treatment exposures.

UMAP + k-means clustering identified this distinct clinical phenotype (p < 0.001).

CONCLUSIONS

Three distinct AKI phenotypes were identified in WM patients without baseline CKD or ESRD:

- Acutely ill, treatment-intensive, AKI driven by acute illness and treatment toxicity (highest AKI rate among illness-driven groups, 17.4%).
- Frail, multimorbid — highest frailty and comorbidity burden, yet the lowest AKI rate (14.4%), suggesting frailty alone does not independently drive AKI.
- IgM-mediated renal injury — highest overall AKI rate (19.5%), driven by amyloid deposition and hypercalcemia-induced tubular injury rather than acute illness.

Phenotype-specific risk stratification may guide tailored management of WM-associated AKI.

ACKNOWLEDGEMENTS

Thank you HCUP/AHRQ for providing access to the National Inpatient Sample used in this analysis. The authors declare no conflicts of interest and report no external funding for this study

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https://hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp

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