Renal Dysfunction in Multiple Myeloma: Mechanisms, Diagnosis, and Pharmacist-Led Interventions

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Background

- Multiple myeloma (MM) is the second most common hematologic malignancy in high-income countries and accounts for approximately 17% of hematologic cancers.
- The incidence of MM has increased by 143% since 1975, with up to 50 %of patients presenting with renal impairment at diagnosis.
- The American Cancer Society estimates 36,110 new cases of MM occurring in the United States this year, resulting in 12,030 deaths.
- Renal dysfunction complicates treatment and independently worsens prognosis, emphasizing the importance of prompt intervention for optimal outcomes.

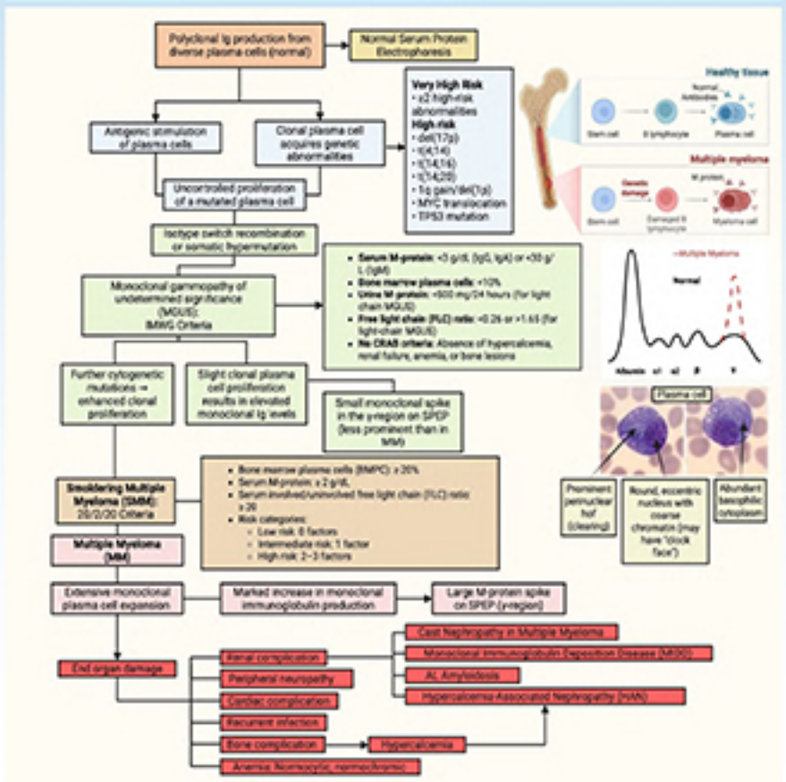
Objectives

- Describe the pathophysiological mechanisms underlying renal dysfunction in multiple myeloma (MM), including cast nephropathy, hypercalcemia-associated nephropathy, and monoclonal immunoglobulin deposition disease (MIDD).
- Identify diagnostic and monitoring strategies for early detection of MM-related renal impairment.
- Evaluate pharmacist-driven interventions to optimize therapy and preserve renal function in MM patients.

Methodology

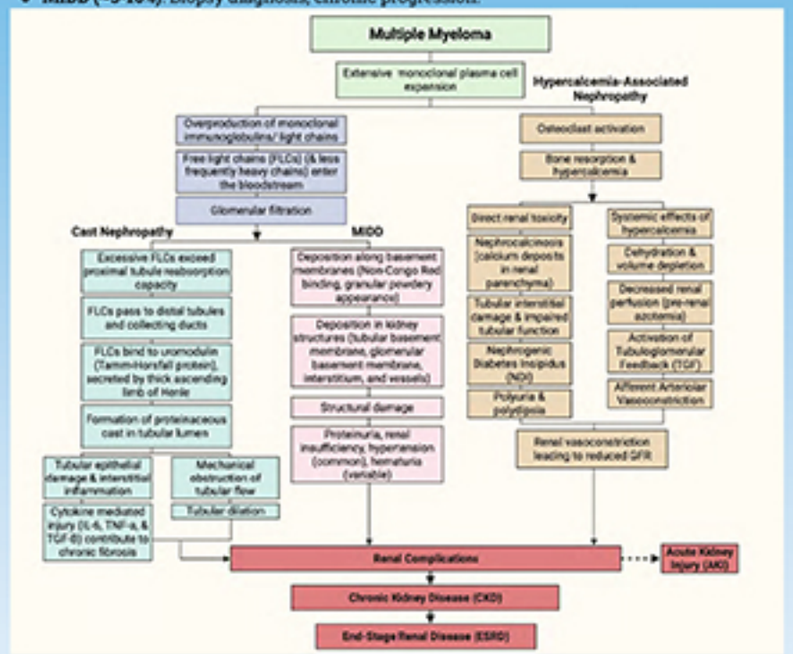
- Comprehensive literature review.
  - Resources relevant to MM diagnosis, pathophysiology, renal impairment, and pharmacotherapy.
- PubMed, NCCN, and IMWG guidelines were utilized to ensure the information was both relevant and accurate.
- Information was collected from retrospective cohort studies, current guidelines, and clinical trials.

Pathophysiology of MM



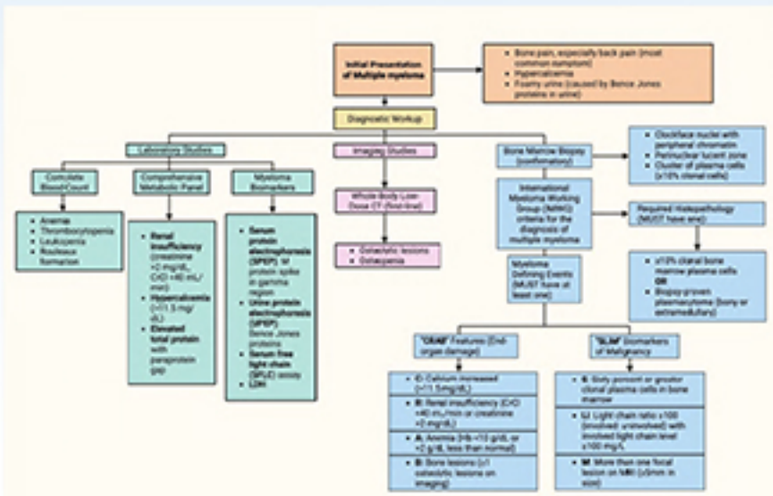
MM-Induced Renal Pathophysiology

- **Cast Nephropathy (~40-60%)**: Leading cause of AKI, poor survival.
- **Hypercalcemia-Associated Nephropathy (~15-20%)**: Nephrocalcinosis, worsens renal decline.
- **MIDD (~5-10%)**: Biopsy diagnosis, chronic progression.



Diagnostic Criteria

- Presence of **monoclonal protein (M-protein)** in serum or urine.
- Evidence of **clonal plasma cells** in bone marrow biopsy.
- End-organ damage (**CRAB:** Hypercalcemia, Renal impairment, Anemia, Bone lesions).
- Free light chain (FLC) assays assist in early detection of cast nephropathy.



NCCN Guidelines

Line of Therapy	Preferred Regimen	Clinical Consideration	Key Notes
First-Line (Hematopoietic Stem Cell Transplantation Eligible)	• Daratumumab/Bortezomib/Lenalidomide/Dexamethasone (Dara-VRd) • Isatuximab-irfc/Bortezomib/Lenalidomide/Dexamethasone (Isa-VRd) • Bortezomib/Lenalidomide/Dexamethasone (VRd)	• Carfilzomib regimens (e.g., KRd) often preferred in renal impairment (Cyclophosphamide is safe) • Melphalan requires dose adjustment • Bortezomib safe in renal dysfunction	• **Early autologous stem cell transplant (ASCT) standard** • **Maintenance**: Lenalidomide (Standard of care); consider bortezomib or Dara in high-risk cytogenetics
First-Line (Hematopoietic Stem Cell Transplantation Ineligible)	• Daratumumab/Lenalidomide/Dexamethasone (Dara-Rd) • Daratumumab/Bortezomib/Lenalidomide/Dexamethasone (Dara-VRd) → (for <80-year-old non-frail patient) • Isatuximab-irfc/Bortezomib/Lenalidomide/Dexamethasone (Isa-VRd) → (for <80-year-old non-frail patient) • Bortezomib/Lenalidomide/Dexamethasone (VRd) • Daratumumab/Bortezomib/Melphalan/Prednisone (D-VMP) • Cyclophosphamide/Bortezomib/Dexamethasone (CyBorD)	• Dose adjusted lenalidomide in renal impairment • Cyclophosphamide is safe • Bortezomib does not require renal dose adjustment	• Frailty-adjusted regimens recommended for older adults • Continuous therapy improves outcomes • **Maintenance**: Lenalidomide until progression or intolerance
Second-Line (Relapsed/Refractory after 1–3 prior therapies)	• Carfilzomib/Lenalidomide/Dexamethasone (KRd) • Pomalidomide/Bortezomib/Dexamethasone (PVd) • Daratumumab/Carfilzomib/Dexamethasone (Dara-KRd) • Daratumumab/Lenalidomide/Dexamethasone (Dara-Rd) • Isatuximab-irfc/Carfilzomib/Dexamethasone (Isa-Kd) • Daratumumab/Bortezomib/Dexamethasone (Dara-Vd) • Daratumumab/Lenalidomide/Dexamethasone (D-Rd) • Isatuximab/Lenalidomide/Dexamethasone (IRd) • Selinexor/Bortezomib/Dexamethasone (SVd)	• Avoid carfilzomib in unstable cardiac/renal disease • Pomalidomide requires renal dose adjustment	• Regimen selection depends on prior exposure & refractoriness • Switch drug classes (Immunomodulatory Drug, Proteasome Inhibitor, anti-CD38)
Third-Line (Relapsed/Refractory after 1–3 prior therapies)	• Chimeric Antigen Receptor T-cell Therapies (idecabtagene vicleucel, ciltacabtagene autoleucel) (CAR-T) • Bispecific antibodies (Teclistamab-cqyv, Elranatamab-bcmm, Talquetamab-tgls, Linvoseltamab-gnpt) (BsAbs) • Selinexor/Dexamethasone (Sd)	• Eligible if adequate organ function • Renal impairment not an absolute contraindication	**Clinical trial enrollment strongly encouraged** • Cellular therapies or bispecifics preferred when available • Maintenance not standard, but retreatment may follow remission

Pharmacist Role

Conclusion & Future Directions

- Renal complications in MM are **multifactorial but often reversible** with early, targeted intervention. **Pharmacists play a central role** by optimizing therapy, monitoring renal function, and counseling patients.
- Active pharmacist involvement in **multidisciplinary teams** improves adherence and guideline-supported care which may reduce complications.
- Future research should evaluate **standardized protocols** integrating extracorporeal therapies with novel MM agents.
- Expanding pharmacist-led interventions may further **enhance patient quality of life and long-term outcomes**.

References