

Who to Suspect of Having Myeloma?

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ABSTRACT

Multiple myeloma (MM) is the second most common haematological malignancy worldwide, yet its non-specific presentation frequently leads to diagnostic delays in primary care. This article highlights the key clinical and laboratory features that should prompt suspicion for MM. Primary care physicians are often the first point of contact for these patients and play a crucial role in early investigation and timely referral. Early identification is essential in preventing irreversible end-organ damage and to enable prompt initiation of treatment, which could substantially improve patient outcomes.

KEYWORDS: multiple myeloma, CRAB features, diagnosis, primary care, early referral

INTRODUCTION

Multiple myeloma is a malignancy of plasma cells characterised by the production of a monoclonal protein and associated end-organ damage, including osteolytic bone lesions, renal impairment, hypercalcaemia, anaemia, and immunosuppression. It is the second most common haematological malignancy in the world, with approximately 100 to 120 people being diagnosed with MM in Singapore per year.¹ Multiple myeloma occurs slightly more often in men than in women and is most commonly diagnosed in individuals aged 65–74 years.²

Rather than reflecting anatomical extent of disease, staging in MM is based on biochemical and genetic markers that indicate tumour burden and disease biology. The primary purpose of staging is to guide prognosis and risk stratification. This helps haematologists determine disease aggressiveness and tailor treatment strategies. Importantly, advanced-stage disease does not preclude a meaningful response to modern treatment and should therefore not preclude referral or treatment consideration.

Treatment outcomes in multiple myeloma have improved dramatically over the past two decades, with many patients now living for years beyond diagnosis. Modern therapy typically combines several novel agents, followed by autologous stem cell transplant in eligible patients and ongoing maintenance therapy, most of which can be delivered in the outpatient setting. Clinical trial data have demonstrated impressive results, with 4-year progression-free survival exceeding 84 percent in transplant-eligible patients³ and median progression-free survival was not yet reached at over 56 months of follow-up in transplant-ineligible patients.⁴ Nevertheless, a proportion of patients still fare poorly, and research efforts continue to focus on improving outcomes for this group.

WHEN TO BE SUSPICIOUS OF MULTIPLE MYELOMA

Multiple myeloma can present with a broad spectrum of non-specific features that frequently mimic common conditions, often resulting in significant diagnostic delays in

primary care. In some cases, it may be entirely asymptomatic, with myeloma first suspected on the basis of incidental laboratory abnormalities.

Importance of Early Detection and Role of Primary Care Physician in Identifying Suspicious Cases

Early detection of multiple myeloma is critical for preventing irreversible end-organ damage and severe complications such as spinal cord compression, pathologic fractures, or advanced renal impairment. In addition, prompt initiation of therapy is associated with improved outcomes.⁵ Increasing awareness of the varied presentations in MM among primary care physicians therefore remains an essential priority.

SIGNS AND SYMPTOMS

Multiple myeloma classically presents with a constellation of features remembered by the acronym CRAB: hyperCalcaemia, Renal impairment, Anaemia, and Bone lesion. Recognising these features early in primary care is crucial, as each reflects significant underlying disease burden and should prompt urgent further investigation.

HyperCalcaemia

Hypercalcaemia in primary care is most often due to hyperparathyroidism, but myeloma must be considered—especially when accompanied by anaemia, unexplained renal impairment, elevated total protein, or a raised ESR. In myeloma, hypercalcemia arises from osteoclastic bone resorption driven by malignant plasma cells. Serum calcium level should be interpreted after correction for albumin.

Renal Impairment

Renal impairment in myeloma is often due to cast nephropathy, where excess monoclonal free light chains combine with Tamm-Horsfall protein to form obstructive tubular casts, causing inflammation and injury. It is one of the most serious complications of myeloma. GPs should refer urgently without waiting for a formal myeloma diagnosis, ensure adequate hydration, and avoid nephrotoxins such as NSAIDs and contrast agents. Rapid reduction of free light chains through prompt myeloma-directed therapy is the key to renal recovery.⁶

Anaemia

Anaemia in myeloma is typically normochromic and normocytic, resulting from plasma cell infiltration suppressing normal bone marrow haematopoiesis. Mild macrocytosis may also be seen.⁷ Peripheral blood film may show rouleaux formation.

Bone Lesion

Many MM patients suffer from bone pain.⁸ Myeloma cells drive osteoclast activity without compensatory bone repair,⁹ producing lytic lesions visible on imaging. Plain X-rays may miss early lytic lesions but can sometimes detect established disease, and thus should be evaluated carefully. A normal X-ray does not exclude myeloma, and further imaging should be sought if suspicion remains. Pathological fractures can occur even at presentation. Vertebral collapse causing spinal cord compression is an oncological emergency requiring immediate assessment.

Immunosuppression/Infection

Recurrent or severe infections are a significant clinical feature of multiple myeloma, arising from the profound immunosuppression.^{10,11}

Constitutional Symptoms

Patients may also present with constitutional symptoms, including malaise, fatigue, or unintentional weight loss.

WHAT CAN PRIMARY CARE PHYSICIANS DO?

The majority of patients with myeloma initially present to primary care, often visiting several times before a haematology referral is made. To prevent diagnostic delays that lead to irreversible organ damage, primary care physicians should initiate directed investigations and early referral when there are suspicious signs and symptoms.

Initial Diagnostic Tests in Primary Care

- **Full Blood Count (FBC):** Screen for unexplained normocytic, normochromic anaemia (typically Hb <10 g/dL), as well as leukopenia or thrombocytopenia.
- **Renal function test and serum biochemistry:** Specifically evaluate renal function (serum creatinine or eGFR), albumin, and corrected calcium.
- **Serum Total Protein:** Be alert for elevated total protein levels.¹² Serum total protein includes both albumin and globulin. In multiple myeloma, the presence of monoclonal protein drives an elevation in globulin levels, consequently raising the total serum protein concentration and affecting the albumin/globulin ratio.
- **Erythrocyte Sedimentation Rate (ESR):** A matched case-control study in UK primary care found that during the year before diagnosis, 85 percent of myeloma patients had an abnormal ESR compared with 46 percent of controls.¹³
- **Imaging:** X-ray or CT scans might show lytic lesions. Early lesions might manifest as focal bone lesion on MRI.

If available, myeloma screening panel, which consists of serum electrophoresis (SPEP), serum immunofixation (IFE), and serum-free light chain, can be sent, and urgent haematology referral should be made. Including serum-free light chain testing in addition to SPEP and IFE is essential, as it substantially improves detection rates, particularly given that approximately 20 percent of myeloma patients produce light chains only, thereby eliminating the need for cumbersome 24-hour urine collection for Bence Jones protein (which represents a homogeneous population of light chains) detection.^{2,14}

Supportive Care and Management

Primary care physicians can provide symptomatic relief while facilitating referral. Bone pain can be managed with analgesia, although nonsteroidal anti-inflammatory drugs (NSAIDs) are generally avoided in MM patients due to their potential to exacerbate renal impairment.¹⁵ Additionally, hydration could be encouraged and infections managed promptly due to patients' underlying immunosuppression.

REFERRAL TO HAEMATOLOGIST

Patients with suspected myeloma should be referred urgently to a haematologist. Some patients might need urgent same-day referral to the emergency department for urgent management, such as for patients with new or worsening neurological deficit suspicious of spinal cord compression, acute kidney injury, or symptomatic hypercalcaemia.

CONCLUSION

Primary care physicians play a pivotal role in the early detection of multiple myeloma. By recognising the key clinical and laboratory features and initiating timely investigations and referrals, primary care physicians can make a meaningful difference to patient outcomes. With modern therapies offering unprecedented survival benefits, every earlier diagnosis is an opportunity to change a patient's trajectory for the better.

Learning Points

- Multiple myeloma often presents with non-specific features, including unexplained anaemia, back pain, hypercalcaemia, and renal impairment, that can mimic common conditions. Familiarity with the CRAB criteria and other features is essential for timely recognition in primary care.
- Initial investigations in primary care should include FBC, renal function, calcium, ESR, and total protein, followed by myeloma screening panel if available.
- Early referral is critical, with same-day emergency referral required for red flag presentations such as spinal cord compression, acute kidney injury, or symptomatic hypercalcaemia.

REFERENCES

1. de Mel S, Tso AC, Soekojo CY, et al. Singapore Myeloma Study Group consensus guidelines for the management of patients with newly diagnosed multiple myeloma. *Ann Acad Med Singap.* 2025 Sep 25;54(9):561–584. doi: 10.47102/annals-acadmedsg.202532. PMID: 41054332.
2. Mikhael J, Bhutani M, Cole CE. Multiple Myeloma for the Primary Care Provider: A Practical Review to Promote Earlier Diagnosis Among Diverse Populations. *Am J Med.* 2023 Jan;136(1):33–41. doi: 10.1016/j.amjmed.2022.08.030. Epub 2022 Sep 20. PMID: 36150517.
3. Sonneveld P, Dimopoulos MA, Boccadoro M, et al. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. *N Engl J Med.* 2024 Jan 25;390(4):301–313. doi: 10.1056/NEJMoa2312054. Epub 2023 Dec 12. PMID: 38084760.
4. Facon T, Kumar SK, Plesner T, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2021 Nov;22(11):1582–1596. doi: 10.1016/S1470-2045(21)00466-6. Epub 2021 Oct 13. PMID: 34655533.
5. Kariyawan CC, Hughes DA, Jayatilake MM, Mehta AB. Multiple myeloma: causes and consequences of delay in diagnosis. *QJM.* 2007 Oct;100(10):635–40. doi: 10.1093/qjmed/hcm077. Epub 2007 Sep 10. PMID: 17846059.

6. Leung N, Rajkumar SV. Multiple myeloma with acute light chain cast nephropathy. *Blood Cancer J.* 2023 Mar 29;13(1):46. doi: 10.1038/s41408-023-00806-w. PMID: 36990996; PMCID: PMC10060259.
7. Eslick R, Talaulikar. Multiple myeloma: from diagnosis to treatment. *Australian Family Physician.* 2013 Oct;42(10).
8. Pietsch C, Engelhardt M, Ihorst G, et al. Analysis of skeletal pain, general symptoms and patient-reported outcome measures and their value in detecting symptomatic progression - An interdisciplinary prospective study in patients with multiple myeloma. *J Bone Oncol.* 2025 May 8;52:100685. doi: 10.1016/j.jbo.2025.100685. PMID: 40475915; PMCID: PMC12138919.
9. Bataille R, Chappard D, Klein B. Mechanisms of bone lesions in multiple myeloma. *Hematol Oncol Clin North Am.* 1992 Apr;6(2):285–95. PMID: 1582975.
10. Malard F, Neri P, Bahlis NJ, et al. Multiple myeloma. *Nat Rev Dis Primers.* 2024 Jun 27;10(1):45. doi: 10.1038/s41572-024-00529-7. PMID: 38937492.
11. Soekojo CY, Chng WJ. The evolution of immune dysfunction in multiple myeloma. *Eur J Haematol.* 2022 Nov;109(5):415–424. doi: 10.1111/ejh.13839. Epub 2022 Sep 19. PMID: 35880386.
12. International Myeloma Foundation. Tests to assess proteins and other substances in the blood. Available at: <https://www.myeloma.org/blood-protein-testing>.
13. Koshariis C, Van den Bruel A, Oke JL, et al. Early detection of multiple myeloma in primary care using blood tests: a case–control study in primary care. *Br J Gen Pract.* 2018 Sep;68(674):e586–e593. doi: 10.3399/bjgp18X698357. Epub 2018 Aug 13. PMID: 30104326; PMCID: PMC6104875.
14. Patel KB, H. Bence Jones Protein. In: *StatPearls.* StatPearls Publishing.
15. International Myeloma Foundation. Multiple Myeloma Pain. Available at: <https://www.myeloma.org/multiple-myeloma-pain>.

Approach to the Diagnosis of Multiple Myeloma

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Abstract

Multiple myeloma (MM) is the second most common haematologic malignancy and is characterised by a clonal proliferation of plasma cells along with specific clinical manifestations. The diagnosis of MM requires the demonstration of a clonal plasma cell infiltrate along with at least one clinical manifestation from among anaemia, renal impairment, bone lesions, and hypercalcaemia. Monoclonal proteins are detected in the majority of patients with MM and require laboratory evaluation for accurate characterisation. Awareness of the clinical presentation of MM and prompt evaluation with a view to obtaining a definitive diagnosis are key steps towards timely initiation of treatment.

Key Words: Multiple myeloma; Diagnosis; Monoclonal protein; Myeloma-Defining Events

INTRODUCTION

Multiple myeloma (MM) is the second most common blood cancer worldwide and affects 100–120 people per year in Singapore.^{1,2} Recognising the clinical manifestations and performing the initial investigations leading to the suspicion of MM are key steps in the diagnostic process. MM is part of a spectrum of plasma cell dyscrasias whereby Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smouldering Multiple Myeloma (SMM) are recognised precursor stages of MM.³ MGUS and SMM are characterised by monoclonal paraproteinaemia and bone marrow plasma cell infiltration at specific levels in the absence of clinical manifestations (known as MM-defining events).⁴ The management of patients with MGUS and SMM currently involves close observation rather than treatment.^{4–6} This review elucidates the current approach to confirming a diagnosis of MM based on the international myeloma working group (IMWG) diagnostic criteria.

INTERNATIONAL MYELOMA WORKING GROUP DIAGNOSTIC CRITERIA FOR MULTIPLE MYELOMA

The diagnosis of MM requires the presence of clonal plasma cells infiltrating the bone marrow (≥ 10 percent), or a histopathologically proven bony or extramedullary plasmacytoma alongside one or more MM-defining events denoted by the acronym “SLiM-CRAB”.^{3,7} The IMWG definitions of MM-defining events are summarised below.

- **S:** Sixty percent or more clonal plasma cells infiltrating the bone marrow
- **Li:** Serum-free light chain ratio (Involved/Uninvolved) ≥ 100
- **M:** Magnetic Resonance Imaging (MRI) based bone lesions (>1 focal bone lesions ≥ 5 mm in size)
- **C:** Hypercalcaemia (>2.75 mmol/L or >0.25 mmol/l greater than the upper limit of normal)
- **R:** Renal impairment (creatinine clearance <40 ml/min or serum creatinine >177 $\mu\text{mol/L}$)
- **A:** Anaemia (Haemoglobin <10 g/dL or >2 g/dl below the lower limit of normal)

- **B:** Bone lesions: One or more osteolytic lesions detected by skeletal imaging

Although monoclonal proteins are found in the majority of patients with MM, their presence is not a requirement for the diagnosis of MM, as a minority of patients have non-secretory disease.⁸ Importantly, the discovery of a monoclonal protein does not equate to a diagnosis of MM, as paraproteins are also found in patients with MGUS, SMM, and other plasma cell disorders such as light chain amyloidosis.⁹ Plasma cell leukaemia is an aggressive variant of MM in which the diagnostic criteria for MM are met along with 5 percent or more circulating plasma cells.¹⁰

DIAGNOSTIC APPROACH TO PLASMA CELL DISORDERS

Screening for Monoclonal Proteins

Monoclonal proteins are detected in approximately 97 percent of patients with MM³ and a systematic approach to their characterisation is crucial for accurate diagnosis. Serum immunofixation (sIFE) is required to confirm monoclonality and the serum-free light chain assay (SFLC) is important in the diagnosis of patients with light chain MM who may have MM-defining events and a negative sIFE.¹¹ The SFLC also plays a role in the prognostication of patients with MGUS and SMM.¹² It is noteworthy that SFLC readings are sensitive to renal impairment and the IMWG has published SFLC reference ranges adjusted for creatinine clearance.¹³

The Singapore Myeloma Study Group (SMSG) currently recommends that serum protein electrophoresis (SPEP), sIFE, and SFLC are used in the format of a screening panel for monoclonal proteins.² When SPEP, sIFE, and SFLC are available, urinalysis for a monoclonal protein is of doubtful added value and is not routinely recommended. While 24-hour urinary protein quantification is used in the assessment of patients with light chain amyloidosis, spot urine IFE, m band quantification, or urine-free light chain assays are not routinely recommended.¹⁴

Confirmation of Bone Marrow Plasma Cell Infiltration and Myeloma-Defining Events

Bone marrow aspiration and trephine biopsy (BMAT) are essential for the diagnosis of MM, with confirmation of plasma cell clonality being demonstrated by immunohistochemistry.³ Flow cytometric immunophenotyping is another means of demonstrating light chain restriction of plasma cells but is not mandatory for the diagnosis of MM.¹⁵ BMAT is particularly important in the 3 percent of patients with non-secretory MM.

The initial evaluation of myeloma-defining events requires a full blood count (FBC), serum creatinine, and corrected calcium, investigations that can be performed in the primary care setting when MM is suspected. Quantification of the serum monoclonal protein by densitometry is required at diagnosis as a baseline for assessment of response to treatment. Quantification of individual immunoglobulins by turbidimetry is recommended in patients with IgA, IgM, or IgD paraproteins, which are not reliably measured by densitometry of the M protein.¹⁶

Confirming the presence of bone lesions is a key step in the diagnostic evaluation for MM. While the whole-body skeletal survey was historically the standard imaging modality, whole-body low dose computed tomography (WBLDCT), whole-body

magnetic resonance imaging (MRI), and positron emission tomography (PET) scans have since been proven as more sensitive options.^{17,18} The SMSG and Asian myeloma network (AMN) consensus currently recommend WBLDCT as the minimal requirement for bone imaging.^{19,20} An MRI of the spine is required in the evaluation of spinal cord compression while whole-body MRI is recommended at the initial diagnosis of SMM as the finding of more than one focal lesion >5 mm will upstage these patients to MM.⁷ The AMN imaging consensus²⁰ and SMSG guidelines² provide more information on each of these modalities and detailed guidance on their use.

Staging and Prognostication

Prognostication of MM was traditionally based on the international staging system (ISS) where albumin and β 2 microglobulin (B2M) were used to calculate a prognostic score.²¹ Genomic information obtained through fluorescent in situ hybridisation (FISH) and conventional karyotyping from the diagnostic bone marrow sample also play a key role in risk stratification.²² Key chromosomal abnormalities driving adverse prognosis including t(4;14) 17p del, t(14;16), t(14;20), 1p loss, and 1q gain²² can be detected by FISH performed on bone marrow samples enriched for plasma cells.²³ The latest international myeloma society/IMWG risk stratification defines high risk MM based on combinations of genomic abnormalities and/or high B2M (>5.5 mg/dl) with normal renal function.²⁴ The recommended investigations for diagnosis and risk stratification of MM are summarised in **Table 1**.

Blood Investigations	Bone Marrow Investigations	Imaging
Serum M protein quantification (In addition to SPEP/SFLC and IFE)	Bone marrow aspirate and trephine biopsy	Whole-body low-dose CT scan (WBLDCT) as the minimum first-line screening modality
FBC, Serum electrolytes, and renal function assessment including urea/creatinine, corrected Calcium	FISH myeloma panel including the following probes: FGFR3/MMSET t(4;14), MAF-B t(14;20), and MAF-C t(14;16) translocations, copy number changes for 17p, 1q, and 1p	Non-Contrasted diffusion weighted whole-body MRI or Non-Contrasted FDG PET-CT to be considered if WBLDCT is not conclusive/unavailable
Serum β 2 microglobulin, albumin, and LDH		MRI whole-body is the modality of choice when evaluating patients with SMM for high-risk biomarkers, which may result in upstaging to active MM

Table 1. Recommended Investigations for Confirmation of Diagnosis and Risk Stratification in Multiple Myeloma

Learning Points

- The diagnosis of multiple myeloma requires the demonstration of a clonal plasma cell infiltrate along with myeloma-defining clinical events.

- Serum immunofixation, electrophoresis, and the serum-free light chain assay are the key investigations required to identify monoclonal proteins.
- The presence of a monoclonal protein is not equivalent to a diagnosis of myeloma as it can be found in the precursor states and other plasma cell disorders.

CONCLUSION

The diagnosis of MM requires awareness of the key clinical manifestations and knowledge of which initial investigations are required. Close collaboration between primary care and specialist haematology services is important for the timely referral and evaluation of patients with suspected plasma cell disorders. Key advancements in the diagnostic process include the advent of mass spectrometry for the detection and monitoring of paraproteins,²⁵ as well as ongoing improvements in imaging techniques.²⁶ The diagnostic landscape is likely to evolve further in the coming years with the integration of these tools into routine clinical practice.

REFERENCES

1. van de Donk NWCJ, Pawlyn C, Yong KL. Multiple myeloma. *Lancet*. 2021 Jan 30;397(10272):410–427. doi: 10.1016/S0140-6736(21)00135-5. PMID: 33516340.
2. de Mel S, Tso AC, Soekojo CY, et al. Singapore Myeloma Study Group consensus guidelines for the management of patients with newly diagnosed multiple myeloma. *Ann Acad Med Singap*. 2025 Sep 25;54(9):561–84. doi: 10.47102/annals-acadmedsg.202532. PMID: 41054332.
3. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol*. 014 Nov;15(12):e538–48. doi: 10.1016/S1470-2045(14)70442-5. Epub 2014 Oct 26. PMID: 25439696.
4. Stern S, Chaudhuri S, Drayson M, et al. Investigation and management of the monoclonal gammopathy of undetermined significance. *Br J Haematol*. 2023 Aug;202(4):734–744. doi: 10.1111/bjh.18866. Epub 2023 May 18. PMID: 37587091.
5. Rajkumar SV. Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. 2022 Aug;97(8):1086–1107. doi: 10.1002/ajh.26590. Epub 2022 May 23. PMID: 35560063; PMCID: PMC9387011.
6. Kyle RA, Durie BG, Rajkumar SV, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. *Leukemia*. 2010 Jun;24(6):1121–7. doi: 10.1038/leu.2010.60. Epub 2010 Apr 22. PMID: 20410922; PMCID: PMC7020664.
7. Dispenzieri A, Stewart AK, Chanan-Khan A, et al. Smoldering multiple myeloma requiring treatment: time for a new definition? *Blood*. 2013 Dec 19;122(26):4172–81. doi: 10.1182/blood-2013-08-520890. Epub 2013 Oct 21. PMID: 24144641; PMCID: PMC3952477.
8. Toscano MP, Nakashima MO. Where are the immunoglobulins? A review of non-secretory multiple myeloma. *J Hematop*. 2025 Aug 6;18(1):39. doi: 10.1007/s12308-025-00652-8. PMID: 40764414; PMCID: PMC12325458.
9. Tan M, Chen Y, Ooi M, et al. AL amyloidosis: Singapore Myeloma Study Group consensus guidelines on diagnosis, treatment and management. *Ann Acad Med Singap*. 2023 Nov 29;52(11):601–624. doi: 10.47102/annals-acadmedsg.2023101. PMID: 38920149.

10. Fernández de Larrea C, Kyle R, Rosiñol L, et al. Primary plasma cell leukemia: consensus definition by the International Myeloma Working Group according to peripheral blood plasma cell percentage. *Blood Cancer J*. 2021 Dec 2;11(12):192. doi: 10.1038/s41408-021-00587-0. PMID: 34857730; PMCID: PMC8640034.
11. Dispenzieri A, Kyle R, Merlini G, et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. *Leukemia*. 2009 Feb;23(2):215–24. doi: 10.1038/leu.2008.307. Epub 2008 Nov 20. PMID: 19020545.
12. Go RS, Rajkumar SV. How I manage monoclonal gammopathy of undetermined significance. *Blood*. 2018 Jan 11;131(2):163–173. doi: 10.1182/blood-2017-09-807560. Epub 2017 Nov 28. PMID: 29183887; PMCID: PMC5757684.
13. Long TE, Indridason OS, Palsson R, et al. Defining new reference intervals for serum free light chains in individuals with chronic kidney disease: Results of the iStopMM study. *Blood Cancer J*. 2022 Sep 14;12(9):133. doi: 10.1038/s41408-022-00732-3. PMID: 36100605; PMCID: PMC9470548.
14. Castillo JJ, Callander NS, Baljevic M, Sborov DW, Kumar S. The evaluation and management of monoclonal gammopathy of renal significance and monoclonal gammopathy of neurological significance. *Am J Hematol*. 2021 Jul 1;96(7):846–853. doi: 10.1002/ajh.26155. Epub 2021 Mar 25. PMID: 33709474; PMCID: PMC8252623.
15. van Dongen JJ, Lhermitte L, Bottcher S, et al. EuroFlow antibody panels for standardized n-dimensional flow cytometric immunophenotyping of normal, reactive and malignant leukocytes. *Leukemia*. 2012 Sep;26(9):1908–75. doi: 10.1038/leu.2012.120. Epub 2012 May 3. PMID: 22552007; PMCID: PMC3437410.
16. Blirup-Jensen S. Protein standardization III: Method optimization basic principles for quantitative determination of human serum proteins on automated instruments based on turbidimetry or nephelometry. *Clin Chem Lab Med*. 2001 Nov;39(11):1098–109. doi: 10.1515/CCLM.2001.175. PMID: 11831625.
17. Hillengass J, Moulopoulos LA, Delorme S, et al. Whole-body computed tomography versus conventional skeletal survey in patients with multiple myeloma: a study of the International Myeloma Working Group. *Blood Cancer J*. 2017 Aug 25;7(8):e599. doi: 10.1038/bcj.2017.78. PMID: 28841211; PMCID: PMC5596388.
18. Wolf MB, Murray F, Kilk K, et al. Sensitivity of whole-body CT and MRI versus projection radiography in the detection of osteolyses in patients with monoclonal plasma cell disease. *Eur J Radiol*. 2014 Jul;83(7):1222–1230. doi: 10.1016/j.ejrad.2014.02.008. Epub 2014 Feb 22. PMID: 24793843.
19. Hillengass J, Usmani S, Rajkumar SV, et al. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders. *Lancet Oncol*. 2019 Jun;20(6):e302–e312. doi: 10.1016/S1470-2045(19)30309-2. Erratum in: *Lancet Oncol*. 2019 Jul;20(7):e346. doi: 10.1016/S1470-2045(19)30423-1. PMID: 31162104.
20. Nagarajan C, Anthony NF, Hillengass J, et al. Imaging in plasma cell disorders—consensus recommendations of the Asian myeloma network bone imaging workgroup. *Lancet Reg Health West Pac*. 2025 Jun 7;59:101597. doi: 10.1016/j.lanwpc.2025.101597. PMID: 40535453; PMCID: PMC12174565.
21. Greipp PR, San Miguel J, Durie BG, et al. International staging system for multiple myeloma. *J Clin Oncol*. 2005 May 20;23(15):3412–20. doi: 10.1200/JCO.2005.04.242. Epub 2005 Apr 4. Erratum in: *J Clin Oncol*. 2005 Sep

- 1;23(25):6281. Harousseau, Jean-Luc [corrected to Avet-Loiseau, Herve]. PMID: 15809451.
22. Chng WJ, Dispenzieri A, Chim CS, et al. IMWG consensus on risk stratification in multiple myeloma. *Leukemia*. 2014 Feb;28(2):269–77. doi: 10.1038/leu.2013.247. Epub 2013 Aug 26. PMID: 23974982.
23. Rajan AM, Rajkumar SV. Interpretation of cytogenetic results in multiple myeloma for clinical practice. *Blood Cancer J*. 2015 Oct 30;5(10):e365. doi: 10.1038/bcj.2015.92. PMID: 26517360; PMCID: PMC4635200.
24. Avet-Loiseau H, Davies FE, Samur MK, et al. International Myeloma Society/International Myeloma Working Group Consensus Recommendations on the Definition of High-Risk Multiple Myeloma. *J Clin Oncol*. 2025 Aug 20;43(24):2739–2751. doi: 10.1200/JCO-24-01893. Epub 2025 Jun 9. Erratum in: *J Clin Oncol*. 2025 Aug;43(22):2553. doi: 10.1200/JCO-25-01367. PMID: 40489728.
25. Murray DL, Puig N, Kristinsson S, et al. Mass spectrometry for the evaluation of monoclonal proteins in multiple myeloma and related disorders: an International Myeloma Working Group Mass Spectrometry Committee Report. *Blood Cancer Journal*. 2021 Feb 1;11(2):24. doi: 10.1038/s41408-021-00408-4. PMID: 33563895; PMCID: PMC7873248.
26. Messiou C, Kaiser M. Precision medicine in myeloma demands precision imaging: is whole body MRI the solution? *Cancer Imaging*. 2026 Mar 11;26(1):37. doi: 10.1186/s40644-026-01017-9. PMID: 41814411; PMCID: PMC12977864.

Why Does It Matter, and What Can We Do for Myeloma Patients

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Abstract

Multiple myeloma has been the poster child for drug development in oncology, with more than 10 new drugs approved in the last two decades. These drugs and their combinations have resulted in deeper responses and longer survival, with generally good tolerability and quality of life for patients. However, the situation is becoming even more promising with the emergence of immunotherapy. These exciting therapeutic agents are producing unprecedented response and survival duration, even in relapse and high-risk disease. More importantly, the treatments are in general well tolerated and patients have good quality of life. It is therefore critical to diagnose myeloma early so that patients can benefit maximally from the improvement in therapy.

Keywords: Myeloma, Therapy, Prognosis, Immunotherapy

INTRODUCTION

What Is Myeloma?

Multiple myeloma is a malignancy arising from post-germinal centre B cells. Phenotypically, most of these cells are plasma cells, which are normally antibody-producing cells that reside in the bone marrow. It is commonly diagnosed in the 6th decade of life or later. We see a rising incidence in Singapore, which is reflective of trends across the world. This is likely due to a combination of factors such as an ageing population and increasing diagnostic awareness.

Patients tend to present with one or more of the following clinical features¹:

- **Hypercalcaemia**, which may result in non-specific pain and changes in mental state
- **Renal impairment**, which may result in non-specific symptoms
- **Anaemia**, which may result in fatigue, breathlessness, dizziness
- **Bone involvement** (plasma cell infiltration or lytic lesions), which may cause pain, pathological fracture, or serious spinal cord compression resulting in bilateral lower limb weakness and loss of sensation

In addition, there should be a measurable clonal fraction in the form of monoclonal proteins measurable in the blood (intact monoclonal immunoglobulin or monoclonal light chain) and clonal plasma cells in the bone marrow. However, the monoclonal immunoglobulins or plasma cells might also be present as a person ages (especially when at lower levels) in conditions such as monoclonal gammopathy of undetermined significance (MGUS) or smouldering myeloma (SMM), which does not require treatment. As some of the above myeloma-defining clinical features are non-specific, it is often important to exclude other potential causes before diagnosing myeloma and instituting treatment.

PROGNOSIS

Outcomes of patients to treatment is quite heterogenous, mainly driven by underlying heterogeneity in biology. One of the key drivers of biological heterogeneity is the genetic aberrations present in the myeloma cells. Some of the recurrent genetic abnormalities such as t(4;14); t(14;16); t(14;20), 1q21 gain, 1p32 loss, and 17p13 loss

have been incorporated into the IMS/IMWG high-risk criteria.² Outcomes of standard risk patients are good, while that of high-risk patients remain a challenge with short disease-free periods and a propensity towards drug resistance. Tumour burden reflected by beta-2-microglobulin is another important prognostic factor.

While the current genetic risk classification is good, it does not take into account some important phenotypic elements that may also be important for prognosis such as age and frailty, response to treatment, extramedullary disease, and presence of significant renal impairment.

GOALS OF TREATMENT

Once the diagnosis of myeloma requiring treatment is made, the goals of the treatment will depend on the age and performance status of the patients, pre-morbid conditions, and transplant eligibility.

In a younger, transplant-eligible patient, the focus is more on getting the patient into remission with a potent treatment that can induce a response quickly and to consolidate with treatment that will get the patient into the deepest remission conceivable and to maintain this for as long as possible. The ideal response is to reach minimal residual disease (MRD)³ negativity at a sensitivity of 10^{-5} . There are standardised methodologies using either flow cytometry or genomic sequencing for the detection of MRD. This may be at a cost of higher toxicity in exchange for treatment that will also produce a longer period of remission and survival. With today's regimen, a proportion of these patients may well be cured with a single line of treatment, yet more will probably die of other conditions rather than myeloma (similar to well-controlled chronic disease such as diabetes).

In older patients who are too frail, or too old for transplant to be considered, the goal will be disease control with a good quality of life. The treatment intensity might be lower, with the aim of providing effective treatment that is less toxic. With this approach, the maximal response might take longer, and the depth of response may not be as much as in the approach for younger patients. As a result, the remission time and survival might also be shorter, but this is acceptable as the time from age of diagnosis to normal expected lifespan is also shorter.

TREATMENT PATHWAYS

Supportive Care

One of the first things is to manage the complications. If there is hypercalcaemia, hydration is started and sometimes a bisphosphonate is needed.

If there is renal impairment, again hydration is important, and likewise avoidance of imaging contrast and nephrotoxic drugs. Sometimes, dialysis support might be necessary.⁴

For anaemia, if this is severe and patient is symptomatic, blood transfusion might be necessary.

For pain related to myeloma bone lesions, analgesia may be needed. If there are fractures in the vertebra or long bone, surgical consult and sometimes a surgical

intervention may be needed to stabilise the bone. If lytic lesions and myeloma bone disease is present, bisphosphonates (mainly zoledronate acid) have been shown to reduce bone events.⁵

Myeloma lesions are very radiosensitive. If there are isolated myeloma lesions (plasmacytomas) that may be causing cord compression or other symptoms, they may be irradiated. If there is cord compression due to vertebral plasmacytomas, this is a medical emergency that requires urgent referral to orthopaedic surgery and radiation oncology. High-dose steroids can be started while waiting for these consults.

Clone Eradication

Once the acute symptoms are managed, consideration should be given to the main myeloma treatment that is effective in eradicating the myeloma clones. For transplant-eligible patients (fit and relatively young), treatment usually includes a 4-drug combination of a monoclonal antibody targeting CD38 (Daratumumab or Isatuximab), a proteasome inhibitor (Bortezomib), an immunomodulatory drug (Lenalidomide or Thalidomide), and Dexamethasone.^{6,7} This combination is given for 4–6 cycles during the induction phase. This is usually followed by an autologous stem cell transplant following high-dose melphalan for consolidation. Subsequently, at least two years of maintenance therapy with lenalidomide will take place.⁸

In patients who do not have high-risk disease and have achieved an MRD-negative response, one can consider stopping maintenance after two years. If patients have high-risk disease or are still MRD positive, it is prudent to continue maintenance.

For transplant-ineligible patients, they are typically treated with a triplet such as Daratumumab plus lenalidomide plus dexamethasone in a continuous manner.⁹ To reduce toxicity, dexamethasone is usually stopped after 3–6 months. The treatment usually continues until progression.

In very frail patients, a 2-drug combination of lenalidomide and dexamethasone can be used. Similar to transplant-eligible patients, if the patient has standard risk disease and manages to achieve MRD negativity, treatment could potentially be stopped after two years.

Follow-up

Whether on treatment or off treatment, myeloma patients should be regularly followed up in clinic to assess for treatment toxicity and response. In patients in remission, they should be followed up for surveillance of relapse so that salvage therapy can be initiated early prior to clinical symptoms.

Lenalidomide is a commonly used drug and often used for prolonged duration in maintenance. It can be associated with increased risk of developing a secondary malignancy.¹⁰ It is therefore important to do cancer surveillance during follow-up.

Management of Relapse Disease¹¹

It is common for myeloma patients to experience relapse. The first period free of progression is highly variable but is 4–5 years on average; however, this may extend to more than 10 years for new patients treated with today's regimen.

When patients progress or relapse, they are usually identified prior to symptomatic relapse. Treatment for relapse disease is usually started before the development of symptoms. Myeloma patients are fortunate that many effective treatments are available. The choice of treatment will depend on a number of factors such as the patient's condition, comorbid medical conditions, their prior treatment and response, how they presented, and if they have high-risk disease.

The development of new immunotherapy such as bispecific T-cell engagers and Chimeric Antigen Receptor (CAR)-T cells, several of which have been approved for the treatment of myeloma, is an important advancement as they are producing very high response rates and deep responses with long progression-free survival even in relapse disease as well as in high-risk patients.

CONCLUSION

With the treatment options available today, the outcomes of myeloma patients and their quality of life during therapy are very good. Access to treatment might pose a challenge as some of the newer treatments can be quite expensive and are not yet on the MOH cancer drug list. Nevertheless, it is important to have myeloma as one of the differential diagnoses to consider in patients, as their symptoms can be non-specific and common in populations of their age, so that they are diagnosed early and can benefit from therapy.

Learning Points

- Tremendous progress has been made in the treatment for multiple myeloma, resulting in a marked improvement in survival of patients.
- Treatment is based on supportive care for affected organs and effective non-chemotherapy-based eradication of tumour cells followed by consolidation to deepen response and maintenance to prevent early relapse.
- Emergence of immunotherapy is heralding an even more exciting era in myeloma treatment, with Bispecific T-cell Engagers and CAR-T targeting BCMA, producing excellent responses and progression-free survival even in advanced disease.
- Treatment is also mainly outpatient-based with favourable toxicity profile, resulting in good quality of life.

REFERENCES

1. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* 2014; 15: e538–48. doi: 10.1016/S1470-2045(14)70442-5. Epub 2014 Oct 26. PMID: 25439696.
2. Avet-Loiseau H, Davies FE, Samur MK, et al. International Myeloma Society/International Myeloma Working Group Consensus Recommendations on the Definition of High-Risk Multiple Myeloma. *J Clin Oncol*. 2025 Aug 20;43(24):2739–2751. doi: 10.1200/JCO-24-01893. Epub 2025 Jun 9. Erratum in: *J Clin Oncol*. 2025 Aug;43(22):2553. doi: 10.1200/JCO-25-01367. PMID: 40489728.
3. Landgren O, Prior TJ, Masterson T, et al. EVIDENCE meta-analysis: evaluating minimal residual disease as an intermediate clinical end point for multiple myeloma. *Blood*. 2024 Jul 25;144(4):359–367. doi: 10.1182/blood.2024024371. PMID: 38768337; PMCID: PMC11418064.

4. Dimopoulos MA, Merlini G, Bridoux F, et al. Management of multiple myeloma-related renal impairment: recommendations from the International Myeloma Working Group. *Lancet Oncol.* 2023 Jul;24(7):e293–e311. doi: 10.1016/S1470-2045(23)00223-1. PMID: 37414019.
5. Terpos E, Zamagni E, Lentzsch S, et al. Treatment of multiple myeloma-related bone disease: recommendations from the Bone Working Group of the International Myeloma Working Group. *Lancet Oncol.* 2021 Mar;22(3):e119–e130. doi: 10.1016/S1470-2045(20)30559-3. Epub 2021 Feb 2. PMID: 33545067.
6. Moreau P, Hulin C, Perrot A, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab and followed by daratumumab maintenance or observation in transplant-eligible newly diagnosed multiple myeloma: long-term follow-up of the CASSIOPEIA randomised controlled phase 3 trial. *Lancet Oncol.* 2024 Aug;25(8):1003–1014. doi: 10.1016/S1470-2045(24)00282-1. Epub 2024 Jun 15. PMID: 38889735; PMCID: PMC12375812.
7. Sonneveld P, Dimopoulos MA, Boccadoro M, et al. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. *N Engl J Med.* 2024 Jan 25;390(4):301–313. doi: 10.1056/NEJMoa2312054. Epub 2023 Dec 12. PMID: 38084760.
8. McCarthy PL, Holstein SA, Petrucci MT, et al. Lenalidomide Maintenance After Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: A Meta-Analysis. *J Clin Oncol.* 2017 Oct 10;35(29):3279–3289. doi: 10.1200/JCO.2017.72.6679. Epub 2017 Jul 25. PMID: 28742454; PMCID: PMC5652871.
9. Facon T, Kumar S, Plesner T, et al. Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma. *N Engl J Med.* 2019 May 30;380(22):2104–2115. doi: 10.1056/NEJMoa1817249. PMID: 31141632; PMCID: PMC10045721.
10. Castillo JJ, Gertz MA. Secondary malignancies in patients with multiple myeloma, Waldenström macroglobulinemia and monoclonal gammopathy of undetermined significance. *Leuk Lymphoma.* 2017 Apr;58(4):773–780. doi: 10.1080/10428194.2016.1217527. Epub 2016 Aug 22. PMID: 27546465.
11. Dimopoulos MA, Terpos E, Boccadoro M, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol.* 2025 Sep;22(9):680–700. doi: 10.1038/s41571-025-01041-x. Epub 2025 Jul 7. PMID: 40624367.

FPSC 134

MCQS ON Maybe it's Multiple Myeloma?

SUBMISSION DEADLINE: 7 July 2026, 12 noon

INSTRUCTIONS

• To submit answers to the following multiple choice questions, you are required to log on to the College Online

Portal (<https://lms.wizlearn.com/cfps/>)

• Please contact sfp@cfps.org.sg if you have not received an email on the LMS account.

• Attempt ALL the following multiple-choice questions.

• There is only ONE correct answer for each question.

• The answers should be submitted to the College of Family Physicians Singapore via the College Online Portal

before the submission deadline stated above.

• There will be NO further extension of the submission deadline

S/N	15 MCQs
1	<p>A 68-year-old man presents with persistent lower back pain, fatigue, and a serum creatinine of 180 $\mu\text{mol/L}$. His full blood count reveals normocytic, normochromic anaemia with Hb 9.2 g/dL. Which acronym best captures the core organ-damage features of multiple myeloma that should guide your clinical assessment?</p> <p>A. CRASH B. CRAM C. CARB D. GRAB E. CRAB</p>
2	<p>A 68-year-old man presents to his GP with a 6-week history of worsening fatigue, diffuse back pain, and decreased urine output over the past 3 days. He has no history of diabetes or prior kidney disease. Blood results show: haemoglobin 8.8 g/dL, creatinine 480 $\mu\text{mol/L}$ (baseline 90 $\mu\text{mol/L}$ 1 year ago), corrected calcium 2.6 mmol/L. He takes ibuprofen regularly for back pain.</p> <p>Which of the following is the most appropriate immediate next step in management?</p> <p>A. Reassure the patient, stop ibuprofen, and arrange a routine nephrology outpatient referral in 4–6 weeks to investigate the renal impairment. B. Order a 24-hour urine collection for Bence Jones protein and review results in 2 weeks before deciding on further action. C. Prescribe oral prednisolone empirically and review in 1 week to assess if renal function improves. D. Stop ibuprofen, same-day emergency department referral for acute kidney injury in the context of suspected multiple myeloma, ensure the patient is adequately hydrated, and avoid nephrotoxins while awaiting urgent haematology review and myeloma-directed therapy.</p>

	<p>E. Start a renal-dose ACE inhibitor to slow progression of renal impairment and schedule a non-urgent haematology referral within the next month.</p>
3	<p>A primary care physician suspects multiple myeloma in a 70-year-old patient with back pain, hypercalcaemia, and a markedly elevated ESR. Which combination of investigations constitutes the most appropriate initial workup in primary care?</p> <p>A. Full blood count, liver function tests, and urine dipstick B. Full blood count, renal function, corrected calcium, ESR, serum total protein, and myeloma screening panel if available C. Bone marrow biopsy, CT chest-abdomen-pelvis, and 24-hour urine collection D. Serum ferritin, thyroid function, and chest X-ray E. Peripheral blood film, reticulocyte count, and direct Coombs test</p>
4	<p>A patient with suspected multiple myeloma develops new-onset bilateral leg weakness and urinary retention. What is the most appropriate next step in management?</p> <p>A. Prescribe NSAIDs for pain relief and review in two weeks B. Arrange an outpatient MRI spine within one month C. Initiate empirical corticosteroids and refer to haematology within one week D. Same-day emergency referral for suspected spinal cord compression E. Order urgent serum free light chains and await results before referring</p>
5	<p>Which of the following statements about anaemia in multiple myeloma is correct?</p> <p>A. It is typically microcytic and hypochromic, consistent with iron deficiency B. It is always macrocytic due to vitamin B12 deficiency from malabsorption C. It is usually normochromic and normocytic, sometimes slightly macrocytic, and the peripheral blood film may show rouleaux formation D. It is caused exclusively by renal failure-related erythropoietin deficiency E. It is rarely seen at initial presentation and usually develops only in advanced disease</p>
6	<p>Which of the following is NOT a myeloma defining event according to the IMWG diagnostic criteria?</p> <p>A. Anemia B. Lytic bone lesions C. Monoclonal protein quantification above 50 g/dl D. Renal impairment</p>

	E. Hypercalcaemia
7	<p>Which of the following is mandatory to make a diagnosis of myeloma?</p> <p>A. Bone marrow plasma cell infiltration of at least 10% or biopsy proven plasmacytoma B. Circulating plasma cells at least 5% C. Presence of a monoclonal protein in the serum D. Presence of a monoclonal protein in the urine E. Monoclonal protein quantification above 30 g/dl</p>
8	<p>Which of the following is recommended as part of the screening panel for monoclonal proteins?</p> <p>A. Serum Immunofixation B. Erythrocyte sedimentation rate C. Total protein D. Albumin E. Globulin</p>
9	<p>How does the IMWG define anaemia as a myeloma-defining event?</p> <p>A. Haemoglobin < 13 g/dL or >1 g/dl below the lower limit of normal. B. Haemoglobin < 10 g/dL or >2 g/dl below the lower limit of normal. C. Haemoglobin < 8 g/dL or >3 g/dl below the lower limit of normal. D. Haemoglobin < 7 g/dL or >2 g/dl below the lower limit of normal. E. E) Haemoglobin < 6 g/dL or >3 g/dl below the lower limit of normal.</p>
10	<p>How does the IMWG define renal impairment as a myeloma defining event?</p> <p>A. Creatinine clearance <30ml/min or serum creatinine > 199 µmol/L. B. Creatinine clearance <20ml/min or serum creatinine > 200 µmol/L.. C. Creatinine clearance <50ml/min or serum creatinine > 160 µmol/L. D. Creatinine clearance <40ml/min or serum creatinine > 177 µmol/L. E. Creatinine clearance <60ml/min or serum creatinine > 100 µmol/L.</p>
11	<p>Myeloma patients survive a median of:</p> <p>A. 1 year B. 3 years C. 5 years D. 10 years E. 20 years</p>
12	<p>Which of the following is true of myeloma treatment?</p> <p>A. Combination cytotoxic chemotherapy is used B. Treatment of newly diagnosed patients need prolonged hospitalization</p>

	<p>C. Treatment usually continues in some form until disease progression</p> <p>D. Stem cell transplant is never use</p> <p>E. Quality of life is very poor</p>
13	<p>Which of these is a medical emergency that may arise from myeloma?</p> <p>A. Toxic Shock Syndrome</p> <p>B. Spinal cord compression</p> <p>C. Hypertensive Crisis</p> <p>D. Stevens Johnson Syndrome</p> <p>E. Respiratory Distress Syndrome</p>
14	<p>Which of the following is not useful imaging to pick up myeloma bone disease?</p> <p>A. Skeletal survey</p> <p>B. Low dose CT whole body</p> <p>C. Whole body PET-CT</p> <p>D. Bone scan</p> <p>E. Whole body MRI</p>
15	<p>Which of the following is an exciting new treatment that is changing the outcome of myeloma patients?</p> <p>A. Daratumumab</p> <p>B. Blinatumumab</p> <p>C. Rituximab</p> <p>D. CD19 CAR-T</p> <p>E. Siltuximab</p>

FPSC 134 10 Readings

Maybe It's Multiple Myeloma? Role of Family Physicians in Improving Patient Outcomes

Sat 2 May 2026, (2.00 pm—5.30 pm (via Zoom))

A Selection of Ten Readings on Related Topics

All are in Free Full Text

Selection of Readings Made by A/Prof Goh Lee Gan

READING 1. RHEOLOGICAL PROPERTIES OF BLOOD IN MULTIPLE MYELOMA PATIENTS

Ptaszek B,¹ Podsiadło S,² Jandziś Z,³ Teległów A,⁴ Piotrowska A,⁴ Czerwińska-Ledwig O,⁴ Jurczyszyn A.⁵ Rheological properties of blood in multiple myeloma patients. *Sci Rep.* 2024 Feb 21;14(1):4260. PMID: 38383860.

doi: 10.1038/s41598-024-54947-4. PMID: 38383860. Free Full Text.

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ABSTRACT

Multiple myeloma (MM) is considered to be one of the haematological malignancies formed by excessive and abnormal proliferation of plasmocytes. Among other parameters, several blood tests are used to diagnose multiple myeloma. The haemorheological profile in multiple myeloma is not widely studied.

Haemorheology includes the study of measuring the deformability and aggregation of erythrocytes, blood viscosity, and sedimentation rate. The degree of deformability of blood cells is necessary to maintain proper vital functions. Proper deformability of red blood cells ensures proper blood circulation, tissue oxidation, and carbon dioxide uptake. The aim of the study was to compare morphology and blood rheology parameters in patients with MM and healthy individuals. The study included 33 patients with MM and 33 healthy subjects of the same age. The haematological blood parameters were evaluated using ABX MICROS 60 haematology analyser. The LORCA Analyser was used to study erythrocyte aggregation and deformability. Patients with MM had lower red blood cell count (RBC) (9.11%) ($p < 0.001$) and half time of total aggregation (T1/2) (94.29%) ($p < 0.001$) values; and higher mean corpuscular volume (MCV) (5.50%) ($p < 0.001$), aggregation index (AI) (68.60%) ($p < 0.001$), total extent of aggregation (AMP) (87.92%) ($p < 0.001$) values than the healthy control group. Aggregation in patients with MM is different compared to healthy individuals.

It was observed that the percentage of cell aggregation is almost 50 percent higher than in the control group. The study of morphology, aggregation, and deformability of erythrocytes in patients with suspected MM might be helpful in making clinical decisions.

READING 2. EPIDEMIOLOGY AND TREATMENT OPTIONS OF MULTIPLE MYELOMA IN ASIA

Chng WJ,^{1,2} Nagarajan C,^{3,4} Huang SY,⁵ Malhotra P,⁶ Hwang YY,⁷ Blunk V,⁸ Singh M,⁹ Wang L.⁹ A systematic review on the epidemiology and treatment options of multiple Myeloma in Asia. *Heliyon*. 2024 Oct 22;10(21):e39698. PMID: 39553611.

doi: 10.1016/j.heliyon.2024.e39698. PMID: 39553611. Free Full Text.

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ABSTRACT

Multiple myeloma (MM) accounts for almost 15 percent of all neoplastic malignancies around the globe. This systematic review intends to analyse data on the treatment and management of MM in selected regions in Asia to identify and prioritise areas that need attention.

A comprehensive review of original articles, published in English from 2005 to 2022 and derived from the PubMed/MEDLINE database, was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

There were 98 studies from select regions of Asia (China, India, Taiwan, Hong Kong, and Singapore) on newly diagnosed MM and relapsed/refractory MM. This review evaluated the trends in disease outcomes with the gradual shift in treatment regimens from doublet to triplet. Additionally, this review also explored autologous stem cell transplant outcome and anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy in MM patients. This is the first systematic review attempting to collect data on the utility and comparison of innovative agents and modifications in treatment regimens in the context of the Asian population. This review established that the body of evidence for the management of MM was generally of poor quality and there is a need for more versatile studies in the region. Novel and innovative drug regimens may help in combating the illness but concerted efforts by researchers, industry partners, policymakers, and the government are key factors in the long-term survival of MM patients.

In the current systematic review, the authors have tried to give a comprehensive account of the available treatments, trends in MM management, and prognosis for MM in Asia.

READING 3. MULTIPLE MYELOMA PRESENTING AS CHRONIC PAIN MIMICKING DEGENERATIVE CONDITIONS

Mo B,¹ Markar J,¹ Sacks S.^{1,2} Unmasking Multiple Myeloma: The Importance of Suspecting Malignancy in Atypical Chronic Pain Mimicking Degenerative Conditions—A Case Report. *Clin Case Rep*. 2025 Jan 16;13(1):e70129. PMID: 39822886.

doi: 10.1002/ccr3.70129. PMID: 39822886. Full Free Text.

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ABSTRACT

Heightened clinical vigilance for multiple myeloma is essential in patients presenting with atypical chronic pain progression. Symptoms may overlap with degenerative musculoskeletal conditions, frequently leading to misdiagnosis. This underscores the necessity of a thorough evaluation when symptoms are refractory to conventional therapies, in order to facilitate timely diagnosis and effective management of malignancy.

READING 4. UNUSUAL PRESENTATION OF MULTIPLE MYELOMA AS LIVER TUMOUR (CASE REPORT)

Abdel-Samad N,¹⁻³ Nahri S,^{1,4} Bharadwaj L,⁵ Ross L.⁵ Unusual Presentation of Multiple Myeloma as a Liver Tumour at Initial Diagnosis: A Case Report. *Am J Case Rep.* 2025 Aug 14;26:e946709. PMID: 40811143.

doi: 10.12659/AJCR.946709. PMID: 40811143. Free Full Text.

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ABSTRACT

BACKGROUND: Multiple myeloma (MM) is a haematologic cancer marked by malignant plasma cells in the bone marrow, often leading to bone pain, anaemia, and renal issues. Rarely, MM presents as extramedullary myeloma in organs such as the liver and is associated with a poor prognosis.

CASE REPORT: We report a 64-year-old woman with a history of aortic stenosis and transient ischaemic attack who presented with severe anaemia, epistaxis, and fatigue. Initial test results showed elevated liver enzymes, hypercalcemia, and kidney injury, with imaging revealing suspected liver metastases. Cancer markers, such as carcinoembryonic antigen, cancer antigen 15-3, and cancer antigen 125 were elevated. Liver biopsy showed plasma cells positive for CD138, CD38, and CD56, confirming MM. Additional tests found IgA kappa monoclonal proteins and 60 percent plasma cells in bone marrow, without bone lesions. The patient required an extended hospital stay, due to recurrent pleural effusions, hypercalcemia, and cholangitis requiring stent placement. After recovery from complications, including COVID-19, she was treated with seven cycles of daratumumab-dexamethasone-lenalidomide and was scheduled for an autologous stem cell transplant. After four months of treatment, the patient had positive clinical outcomes in myeloma parameters and liver lesions. The patient had improved haemoglobin, white blood cells, neutrophils, and platelets. The patient's IgA decreased, hepatic enzymes improved, monoclonal protein bands disappeared, and liver lesions resolved.

CONCLUSIONS: This case highlights an uncommon MM presentation with liver involvement, underscoring the importance of considering MM in the differential diagnosis of atypical liver lesions and of early identification to improve treatment outcomes.

READING 5. PERIPHERAL NEUROPATHY IS A COMMON COMPLICATION OF MULTIPLE MYELOMA

Huang J,¹ Xie Y.¹ **Diagnostic Potential of the Risk Factors Associated with Peripheral Neuropathy in Multiple Myeloma: Evidence from Logistic Regression Analysis.** *Br J Hosp Med (Lond)*. 2025 Nov 25;86(11):1–14. PMID: 41284234.

doi: 10.12968/hmed.2025.0795. PMID: 41284234. Free Full Text.

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ABSTRACT

AIMS/BACKGROUND: Peripheral neuropathy (PN) is a common and debilitating complication in patients with multiple myeloma (MM), which results from both disease-related mechanisms and treatment-induced neurotoxicity.

Despite its clinical significance, comprehensive investigations assessing PN risk in MM, along with examining demographic, clinical, nutritional, and inflammatory factors, remain limited. Therefore, this study aimed to investigate independent risk predictors associated with PN in MM patients using univariate and multivariate logistic regression analysis, thereby enhancing clinical risk management and improving treatment outcomes.

METHODS: This retrospective observational study included 161 MM patients who were treated at Ganzhou People's Hospital between February 2020 and February 2024. Study participants were divided into the PN (n=45) and non-PN (n=116) groups. PN diagnosis was conducted based on new neurological signs and symptoms post-treatment, confirmed through abnormal sensory, motor, autonomic, or nerve conduction assessments. Baseline characteristics, including demographic information, clinical features, and laboratory parameters, were compared between the two groups using Mann-Whitney U and Chi-square tests. Univariate logistic regression analysis evaluated potential parameters associated with PN. Furthermore, a multivariate logistic model was used to assess independent risk predictors. Finally, model performance was evaluated via receiver operating characteristic (ROC) curve analysis.

RESULTS: This study analysed 161 patients, of whom 45 (27.95%) developed PN. Patients in the PN group were significantly older and had higher body mass index (BMI), increased immunoglobulin G (IgG) and interleukin-6 (IL-6) levels, and increased diabetes prevalence than the non-PN group. However, they exhibited lower haemoglobin (Hb) and serum 25-hydroxyvitamin D [25(OH)D] levels ($p < 0.05$). Multivariate logistic regression analysis identified older age (odds ratio [OR] = 1.49, 95% confidence interval [CI]: 1.07–2.08), higher BMI (OR=2.05, 95% CI: 1.01–4.17), reduced 25(OH)D levels (OR=0.54, 95% CI: 0.29–0.97), elevated IgG (OR=1.64, 95% CI: 1.12–2.41), and increased IL-6 (OR=2.07, 95% CI: 1.10–3.88) as independent PN predictors. The model showed excellent discrimination capability (area under the curve [AUC] = 0.998, 95% CI: 0.996–1.000, $p < 0.001$).

CONCLUSION: This study identified older age, higher BMI, vitamin D deficiency, elevated IgG, and increased IL-6 levels as independent risk predictors for PN. Assessing these parameters in the early stages facilitates the identification of high-risk patients, allowing for targeted preventive strategies

and personalised nursing interventions in MM patients, which can reduce PN incidence and enhance overall clinical outcomes.

READING 6. MULTIPLE MYELOMA PRESENTING AS PERICARDIAL EFFUSION—A CASE REPORT

Kebede LM,¹ Woldeamanuel AM,² Mehammed FM,² Girma HG,² Tafa ME,² Abraham YB.² Unmasking multiple myeloma first presentation as pericardial effusion with tamponade physiology: a case report. *J Med Case Rep.* 2026 Jan 18;20(1):89.

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ABSTRACT

BACKGROUND: Multiple myeloma is a malignant plasma cell disorder primarily involving the bone marrow and skeleton, leading to anaemia, renal dysfunction, and lytic bone lesions. Extramedullary disease, seen in about 9 percent of cases, reflects aggressive disease biology with poor prognosis. Common sites include the pleura, liver, and gastrointestinal tract, while pericardial involvement is exceedingly rare and often detected postmortem. Fewer than 25 cases of pericardial effusion or cardiac tamponade due to multiple myeloma have been reported, usually in advanced disease. The mechanism likely involves hematogenous spread or direct extension from adjacent lesions, often associated with high-risk cytogenetic abnormalities. This case presents an unusual first manifestation of multiple myeloma as pericardial effusion with tamponade physiology, emphasising the need to consider haematologic malignancy in unexplained pericardial effusion, especially in resource-limited settings.

CASE PRESENTATION: A 60-year-old Ethiopian man presented with a 6-month history of progressive dry cough, dull chest pain, and worsening shortness of breath. He had been repeatedly treated for pneumonia and pulmonary tuberculosis without improvement. Chest-computed tomography revealed a large pericardial effusion with features of cardiac tamponade. Echocardiography confirmed pericardial fluid causing right atrial and ventricular collapse. Pericardiocentesis drained 800 mL of haemorrhagic fluid, and cytology showed atypical plasma cells. Further evaluation, including serum protein electrophoresis and bone marrow biopsy, confirmed multiple myeloma. The patient was managed with Pericardiocentesis and systemic chemotherapy, showing clinical and radiologic improvement, highlighting the rarity of pericardial involvement as an initial presentation of multiple myeloma.

CONCLUSION: Pericardial involvement in multiple myeloma is an extremely rare and serious manifestation, usually signifying advanced or aggressive disease. While malignant pericardial effusions are commonly due to solid tumours, multiple myeloma should also be considered when no other cause is identified. Early echocardiography-guided pericardiocentesis is lifesaving, and definitive procedures such as a pericardial window may prevent recurrence. This case highlights the importance of suspecting haematologic malignancy in patients with unexplained pericardial effusion or cardiac tamponade. Early recognition and prompt initiation of systemic therapy can improve survival, particularly in resource-limited settings where diagnostic challenges are common.

READING 7. ESTABLISHING A MULTIPLE MYELOMA CLINICAL REGISTRY IN ASIA PACIFIC REGION

Aoki N,¹ Chen PY,¹ Moore E,¹ Oliver L,¹ Waters NA,¹ Wellard C,¹ McQuilten ZK,^{1,11} Chen W,² Chng WJ,³ Gan GG,⁴ Goh YT,⁵ Hou J,⁶ Huang J,⁷ Kim K,⁸ Lee JJ,⁹ Lu J,¹⁰ Min CK,¹² Wood EM,¹³⁻¹⁵ Yeh SP,¹⁶ Spencer A¹⁷⁻¹⁹; APAC MRDR Investigators. The establishment of a multiple myeloma clinical registry in the Asia-Pacific region: The Asia-Pacific Myeloma and Related Diseases Registry (APAC MRDR). *BMC Med Res Methodol.* 2024 May 2;24(1):102.

doi: 10.1186/s12874-024-02227-0.

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ABSTRACT

BACKGROUND: Multiple myeloma (MM) is the second most common haematological cancer worldwide. Along with related diseases including monoclonal gammopathy of undetermined significance (MGUS), plasma cell leukaemia (PCL), and plasmacytoma, MM incidence is rising, yet it remains incurable and represents a significant disease burden. Clinical registries can provide important information on management and outcomes, and are vital platforms for clinical trials and other research. The Asia-Pacific Myeloma and Related Diseases Registry (APAC MRDR) was developed to monitor and explore variation in epidemiology, treatment regimens, and their impact on clinical outcomes across this region. Here we describe the registry's design and development, initial data, progress, and future plans.

METHODS: The APAC MRDR was established in 2018 as a multicentre collaboration across the Asia-Pacific, collecting prospective data on patients newly diagnosed with MM, MGUS, PCL, and plasmacytoma in Korea, Singapore, Malaysia, and Taiwan, with China recently joining. Development of the registry required a multidisciplinary team of clinicians, researchers, legal and information technology support, and financial resources, as well as local clinical context from key opinion leaders in the APAC region. Written informed consent is obtained and data are routinely

collected throughout treatment by hospital staff. Data are stored securely, meeting all local privacy and ethics requirements. Data were collected from October 2018 to March 2024.

RESULTS: Over 1,700 patients from 24 hospitals have been enrolled onto the APAC MRDR to date, with the majority (86%) being newly diagnosed with MM. Bortezomib with an immunomodulatory drug was most frequently used in first-line MM therapy, and lenalidomide-based therapy was most common in second-line. Establishment and implementation challenges include regulatory and a range of operational issues.

CONCLUSION: The APAC MRDR is providing “real-world” data to participating sites, clinicians, and policymakers to explore factors influencing outcomes and survival, and to support high quality studies. It is already a valuable resource that will continue to grow and support research and clinical collaboration in MM and related diseases across the APAC region.

READING 8. DIAGNOSIS AND MANAGEMENT OF MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE

Liu Y,¹ Parks AL.² Diagnosis and Management of Monoclonal Gammopathy of Undetermined Significance: A Review. JAMA Intern Med. 2025 Apr 1;185(4):450–456.

doi: 10.1001/jamainternmed.2024.8124.

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ABSTRACT

IMPORTANCE: Nearly 5 percent of adults have the precursor malignant condition monoclonal gammopathy of unknown significance (MGUS). Management centres on differentiating MGUS from more serious conditions to determine additional diagnostic testing, monitoring, and potential therapy.

OBSERVATIONS: MGUS is defined by the absence of end-organ damage or symptoms, a small amount of monoclonal immunoglobulin (M protein), and low volume of plasma cells. MGUS must be distinguished from overt malignant diseases like multiple myeloma (MM), immunoglobulin light-chain (AL) amyloidosis, and monoclonal gammopathy of clinical significance (MGCS), all of which cause organ damage or symptoms. Although testing for M proteins is often prompted by clinical findings (e.g., osteoporosis or autoimmune disease), recent evidence from screened populations suggests that previous MGUS disease associations were likely overestimated and that testing for M proteins should be reserved for when malignant disease or MGCS is suspected. Risk of progression to malignant disease ranges from 0.5 to 1 percent, meaning most patients have indolent disease. Guideline-concordant management of MGUS is determined by predicted risk of progression to malignant disease, which depends on subtype of immunoglobulin, M protein concentration, and free light chain ratio. Patients with low-risk MGUS can safely defer bone marrow biopsy and advanced imaging, and should undergo periodic laboratory monitoring. Intermediate- and high-risk MGUS should trigger bone marrow biopsy and bone imaging to detect overt MM and shorter monitoring intervals. Advanced molecular testing may improve on current risk stratification to target monitoring and treatment to those with highest risk of malignant progression and avoid overtreatment of those with low-risk disease. Management will also be informed via results of several clinical trials to clarify the risks and benefits of screening, optimal monitoring strategy, predictors of progression, and potential preventive or curative therapies.

CONCLUSIONS AND RELEVANCE: Evidence-based management of MGUS currently rests on separating clinically indolent from high-risk precursor disease. Research using novel detection methods, incorporating molecular testing into risk stratification, and evaluating screening, monitoring, and therapeutic or lifestyle interventions has the potential to improve outcomes.

READING 9. DETECTING SYMPTOMATIC PROGRESSION IN PATIENTS WITH MULTIPLE MYELOMA

Pietsch C,^{1,2} Herget GW,^{1,2} Schmal H,^{1,2} Frodl A,^{1,2} Wäsch R,^{2,3} Engelhardt M,^{2,3} Ihorst G,⁴ Wystrach L,⁵ Jung J,⁶ Terpos E.⁷ Analysis of skeletal pain, general symptoms and patient-reported outcome measures and their value in detecting symptomatic progression—An interdisciplinary prospective study in patients with multiple myeloma. *J Bone Oncol.* 2025 May 8;52:100685.

doi: 10.1016/j.jbo.2025.100685.

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ABSTRACT

Delayed diagnosis of multiple myeloma (MM) and progressive disease (PD) can increase the risk of skeletal complications and thus affects patients' quality of life (QoL).

In this prospective study, we analysed skeletal pain, general symptoms, and patient-reported outcome measures (PROMs) in patients with MM and their value in detecting symptomatic progression. We evaluated 502 patients, 47 with initial diagnosis (ID) of MM and 455 follow-up patients. At ID, 74 percent reported bone pain, mostly in the spine. General symptoms, particularly fatigue, were present in 89 percent of the patients. 88/455 (19%) of the follow-up patients experienced PD. Of these, 65 percent reported skeletal pain and 81 percent exhibited general symptoms, with fatigue being the most common. PD was suspected and confirmed as the cause of clinical symptoms in 59/88 (67%) and not suspected in 29/88 (33%). Occurrence and character of bone pain and general symptoms differed significantly between patients with and without PD, as did QoL and health-related status. Logistic regression analysis demonstrated that bone pain at night, pain in various locations, pain of known character with occurrence in different location, pain in the chest, pelvis, and thigh as well as fatigue and weight loss were associated with an increased risk of PD.

In conclusion, bone pain and general symptoms are helpful in identifying both MM and PD. PROMs can aid in the diagnosis of PD through symptom-based patient assessment. Serologic and,

especially in the case of skeletal complaints, additional radiologic diagnostics are required to confirm suspected and detect unexpected PD.

READING 10. MULTIPLE MYELOMA GROUP CONSENSUS GUIDELINES FOR MANAGEMENT OF NEWLY DIAGNOSED PATIENTS

de Mel S,¹ Soekojo CY,¹ Ooi MG,¹ Chng WJ,^{1,#} Tso AC,² Lee LK,² Cao L,² Lim CC,³ Teo C,⁴ Chen YX,⁵ Tan M,⁵ Manjeri A,⁵ Goh YT,⁵ Nagarajan C,^{5,#} Lee ZY,⁶ Tan D.⁷ Singapore Myeloma Study Group consensus guidelines for the management of patients with newly diagnosed multiple myeloma. *Ann Acad Med Singap.* 2025 Sep 25;54(9):561–584.

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ABSTRACT

Plain Language Summary: Multiple myeloma (MM) is the second most common haematologic malignancy and remains incurable.

Significant advances have been made in both supportive care and definitive therapy for MM, leading to marked improvements in survival and quality of life. The availability of potent novel agent-based induction regimens, as well as methods to assess deeper levels of response, has transformed the landscape of MM therapy. Balancing therapeutic efficacy against toxicities and cost-effectiveness remains a key challenge to be addressed.

Here, the Singapore myeloma study group provides consensus recommendations on the management of newly diagnosed MM, incorporating key developments in diagnostics, response assessment, supportive care, and definitive therapy.