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Application of Artificial Intelligence in Predicting Survival Outcomes in Multiple Myeloma Cancer Patients: A Systematic Review

Oyekemi Oyetoro[1]

[1]Department of Bioscience, University of Arkansas at Little Rock, Little Rock, AR, USA

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Abstract: Multiple Myeloma (MM) is a blood disorderliness or malignancy with significant clinical and heterogeneity making it difficult for making strong, reliable, and accurate prognosis. While the usual or conventional staging systems provide significant risk stratification, they are inadequate in the capturing of the complexities of Multiple Myeloma. Artificial Intelligence and Machine Learning tools and models have emerged as capable technologies for the analysis of high dimensional data to improve prognostic accuracy. The study utilized a systematic review approach to investigate the application of Artificial Intelligence and Machine Learning based technologies in the prediction of survival outcomes for Multiple Myeloma patients. PRISMA 2020 framework was adopted for the study. A systematic search of Google scholar for relevant studies was conducted between 2015 to July, 2025. Using relevant inclusion and exclusion criteria, and screening process, a total number of 10 research articles were considered to be very relevant to the study. The study result shows that artificial and machine based models such as Random Forest and Gradient Boosting algorithms demonstrate strong predictive power, with reported Area Under the Curve (AUC) and Concordance Index (C-index) values often ranging from 0.72 to 0.85. The models is capable of integrating different data types, including clinical parameters, laboratory results, high-dimensional genomics, and advanced imaging. The evidence suggests that AI/ML models can significantly enhance risk stratification, identify novel prognostic biomarkers, and offer more personalized survival predictions compared to conventional methods. Integrating AI into clinical practice holds the potential to optimize treatment strategies and improve outcomes for MM patients.

Keywords: *Multiple Myeloma, Artificial Intelligence, Machine Learning, Survival Prediction, Prognosis, Systematic Review.*

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I. INTRODUCTION

The second most prevalent haematological cancer in the world is multiple myeloma (MM), a cancer of the bone marrow's plasma cells. Patient survival varies greatly, from a few months to more than ten years (Cowan et al., 2022). A complex interaction between host factors, tumor biology, and genomic diversity is what causes this heterogeneity. Staging systems such as the International Staging System (ISS) and the Revised-ISS (R-ISS) have been used for decades to guide clinical decision-making. These systems stratify patients into risk groups based on a limited set of clinical and laboratory markers. Although these systems have been helpful, their capacity to offer accurate, personalized prognoses is severely limited. (Padala et al., 2021; Lawanson et al., 2025). Recent evidence suggests that age at diagnosis significantly influences survival outcomes in multiple myeloma, with non-linear effects that may be shaped by comorbidities and treatment access (Lawanson et al., 2025).

Large volumes of complex data, such as proteomic, genomic, and advanced imaging data, have been produced by the introduction of high-throughput technologies. In order to find subtle patterns that are predictive of patient outcomes, traditional statistical methods frequently find it difficult to analyse these high-dimensional datasets. The use of artificial intelligence (AI) and its subfield, machine learning (ML), in oncology has been made possible by this challenge. In order to combine various data types, learn from intricate patterns, and create advanced predictive models that can outperform traditional prognostic tools, AI/ML algorithms are uniquely suited (Gehlot et al., 2021).

AI has the potential to completely transform patient care in the context of MM by providing more precise risk stratification. ML models can more accurately forecast

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important outcomes like Overall Survival (OS) and Progression-Free Survival (PFS) by examining each patient's distinct clinical, genomic, and imaging profile. Clinicians can use this improved predictive ability to better target treatment plans, find high-risk patients who might benefit from more intensive therapies, and guide prognostic conversations with patients and their families. For example, ML can find new biomarker combinations from PET/CT imaging or RNA-sequencing data that are not visible with conventional analysis (Zhong et al., 2023).

The crucial role of the tumour microenvironment (TME) further complicates prognostication. In MM, the bone marrow niche—which is made up of different non-malignant cells that promote tumour growth, angiogenesis, and drug resistance—plays an active role in the disease's progression rather than acting as a passive scaffold. Although they are not included in conventional prognostic models, the intricate signalling and cellular crosstalk within the TME have a substantial impact on patient outcomes. A route to a more comprehensive understanding of MM biology is provided by AI, which is especially well-suited to model these complex interactions (Garcia-Ortiz et al., 2021).

The approval of novel agents, such as immunomodulatory medications, proteasome inhibitors, monoclonal antibodies, and cellular therapies like CAR-T cells, has also significantly changed the therapeutic landscape for multiple myeloma. According to Shah and Mailankody (2020), although these treatments have greatly increased survival, they are also linked to high expenses and possible side effects. By identifying which patients are most likely to respond to particular therapies, AI models can be crucial in personalizing treatment, increasing efficacy while reducing needless side effects and financial burden (Sakemura et al., 2022).

Significant clonal evolution, in which the tumour's genetic makeup varies over time and frequently results in relapse and treatment resistance, is another characteristic of MM. This dynamic nature is not captured by static models used for prognostic evaluations made solely at diagnosis. Dynamic predictive tools that can be updated with longitudinal data over the course of a patient's journey are desperately needed in order to provide risk assessment in real time. In order to map a patient's changing risk profile and provide a more precise and timely clinical management guide, AI models are uniquely able to integrate serial data points (Maura et al., 2024).

By creating models for a range of predictive tasks, numerous individual studies have shown the promise of AI in MM. To comprehend the current state of the science, determine the best modelling strategies, and identify research gaps, a thorough synthesis of this quickly developing field is necessary. To direct future research and eventual clinical implementation, a thorough assessment of the approaches, data sources, and reported performance of these AI models is necessary. This systematic review aims to identify, appraise, and synthesize the existing literature on the application of AI and ML models for predicting survival outcomes in patients with Multiple Myeloma. By examining the types of data used, the algorithms employed, and the predictive accuracy achieved, this review will provide a clear overview of the current landscape and highlight the potential of these advanced technologies to refine prognostication and personalize medicine in MM.

II. METHODOLOGY

A. Study Design

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The methodology was designed to ensure a transparent, comprehensive, and reproducible process for literature identification, screening, eligibility assessment, and data synthesis.

B. Research Question

The primary research question for this review was: How effective are Artificial Intelligence and Machine Learning models in predicting survival outcomes (Overall Survival or Progression-Free Survival) in patients with Multiple Myeloma?

This question was structured using the Population, Intervention, Comparison, and Outcome (PICO) framework:

- *Population (P)*
  Patients diagnosed with Multiple Myeloma.

- *Intervention (I)*
  Application of an AI or ML model for survival prediction.

- *Comparison (C)*
  Comparison between different AI/ML models or against traditional prognostic systems (where reported).

- *Outcome (O)*
  The predictive performance of the model, measured by metrics such as Area Under the Curve (AUC), Concordance Index (C-index), or accuracy.

C. Eligibility Criteria

Studies were selected based on the following criteria:

- *Inclusion Criteria:*
  - Original research articles (e.g., retrospective or prospective cohort studies).
  - Study population consisted of patients with Multiple Myeloma.
  - The primary objective was the development and/or validation of an AI or ML model.
  - The model predicted a direct survival outcome (OS or PFS).
  - The study reported quantitative performance metrics (e.g., AUC, C-index).
  - Studies published in English between the year 2015 and 2025.

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➢ *Exclusion Criteria:*

- Review articles, meta-analyses, editorials, letters, or case reports.
- Studies where AI was used for diagnosis or treatment selection but not survival prediction.
- Studies that did not report clear performance metrics for the prognostic model.
- Studies for which the full text could not be retrieved.

D. Information Sources and Search Strategy

A systematic search was performed in Google Scholar to identify relevant studies published up to July 2025. The search strategy combined keywords related to the population (Multiple Myeloma), intervention (Artificial Intelligence), and outcome (Survival).

The final search string used for Google Scholar was: intitle: "multiple myeloma" AND intitle:("survival prediction" OR "prognostic model" OR "predicting survival") AND ("artificial intelligence" OR "machine learning" OR "deep learning")

The reference lists of included articles were also manually screened to identify any additional relevant studies.

E. Study Selection

The initial database search in Google Scholar yielded 132 records. These records were screened by title and abstract to 94 studies, after which 35 articles were selected for full-text review. Of these, 28 full-text articles were successfully retrieved. After a detailed assessment of the full texts, 10 studies met all inclusion criteria and were included in the final narrative synthesis. The primary reasons for exclusion at the full-text stage were an incorrect study focus (e.g., focusing on bioinformatics gene signature identification rather than the ML model itself) or the use of traditional statistical models (e.g., nomograms) without a clear AI/ML component. The PRISMA flow diagram detailing this process is shown in Table 1.

Table 1: PRISMA Flow Diagram

Phase	Number of Records
Records identified via Google Scholar	132
Records screened (titles/abstracts)	94
Full-text articles assessed for eligibility	35
Full-text articles retrieved	28
Studies included in final synthesis	10

F. Data Extraction

For the final set of included studies, a structured data extraction form was used to collect the following information: First author and publication year, study objective, sample size (including training and validation cohorts), input data features (e.g., clinical, genomic, imaging), type of AI/ML model(s) used, primary outcome predicted (OS or PFS), key performance metrics and main findings.

G. Ethical Consideration

As this is a secondary synthesis of previously published data, no ethical approval was required. All original studies were assumed to have received ethical clearance from their respective institutions.

III. RESULTS

A. Study Characteristics

The 10 included studies demonstrated a wide range of approaches to AI-driven survival prediction in MM. A summary of their characteristics and key findings is presented in Table 2.

Table 2: Data Extraction Table

Author, Year	Study Objective	Sample Size (Training/Validation)	Input Data Features	AI/ML Model(s) Used	Outcome Predicted	Key Performance Metric
Bao et al., 2022	To develop ML models to predict OS in elderly patients with newly diagnosed MM (NDMM).	487 (Training) / 123 (Validation)	Clinical & Lab data (42 features)	LightGBM, Random Forest, XGBoost, CatBoost	Overall Survival (OS) at 1, 3, 5 years	**AUC: 0.85** (LightGBM)
Ren et al., 2023	To build an ML model to predict both survival and therapeutic response in MM.	1141 (Total)	Clinical & Lab data (27 features)	XGBoost	Overall Survival (OS)	**C-index: 0.77**
Witte et al.,	To predict PFS at	1797 (Total)	Clinical &	XGBoost,	Progression-	**AUC: 0.73**

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2023	24 months in NDMM patients using real-world data from multiple countries.		Treatment data	SHAP	Free Survival (PFS)	
Mosquera Orgueira et al., 2022	To use unsupervised ML to identify novel risk groups in NDMM based on gene expression.	564 (Training) / 306 (Validation)	Genomic (Gene expression)	Unsupervised ML (Consensus Clustering)	Overall Survival (OS) & PFS	N/A (Focus on group separation, not a predictive score)
Zhong et al., 2023	To use radiomic features from PET/CT scans to predict prognosis in MM.	132 (Training) / 57 (Validation)	Radiomics (from PET/CT)	Random Forest, SVM	Overall Survival (OS) & PFS	**C-index: 0.82** (OS)
Sachpekidis et al., 2024	To use AI-based volumetric assessment of PET/CT scans to predict survival in NDMM.	100 (Total)	Radiomics (AI-based volumetric)	N/A (Cox regression on AI-derived feature)	Overall Survival (OS) & PFS	N/A (Focus on hazard ratio of the AI feature)
Shah et al., 2025	To develop ML models from RNA-seq data for prognostication in MM.	599 (Total)	Genomic (RNA-seq)	ElasticNet, Random Forest	Overall Survival (OS)	**AUC: 0.82** (Random Forest)
Belmonte et al., 2025	To predict survival risk in MM patients undergoing hematopoietic stem cell transplantation (HSCT).	1188 (Training) / 397 (Validation)	Clinical & Transplant data	Neural Network	Overall Survival (OS)	**AUC: 0.72**
Zhou et al., 2023	To integrate web data and ML to predict survival in MM.	129 (Total)	Clinical & Web-mined data	Random Forest, Naive Bayes, J48	Overall Survival (OS) & PFS	**AUC: 0.99** (OS, likely overfit)
Guerrero et al., 2022	To use ML on biomarkers to predict MRD negativity and its impact on survival outcomes.	473 (Total)	Clinical, Flow Cytometry, Genomic	Penalized Logistic Regression	Progression-Free Survival (PFS)	**AUC: 0.84** (for MRD pr

B. Narrative Synthesis

➢ *Diversity and Integration of Input Data*

The studies successfully utilized a variety of data sources to build their models. Several studies relied on readily available clinical and laboratory data, including standard prognostic markers like age, beta-2 microglobulin, LDH, and cytogenetic abnormalities. For example, Bao et al. (2022) used 42 such features to predict OS in elderly patients, achieving a high AUC of 0.85 with a LightGBM model. Similarly, Ren et al. (2023) developed a robust model using 27 clinical variables from a large cohort.

A significant number of studies leveraged high-dimensional data to capture deeper biological insights. Shah et al. (2025) built models from RNA-sequencing data, demonstrating that genomic information can yield strong prognostic signals (AUC = 0.82). Another key area was radiomics, where quantitative features are extracted from medical images. Zhong et al. (2023) and Sachpekidis et al. (2024) both showed that features derived from PET/CT scans using AI can effectively predict survival, highlighting the value of non-invasive imaging biomarkers for assessing whole-body tumor burden. Furthermore, some studies integrated novel data types, such as flow cytometry data (Guerrero et al., 2022) and even web-mined data (Zhou et al., 2023), showcasing the flexibility of ML to incorporate diverse information streams.

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➢ *Common and Novel Machine Learning Algorithms*

Supervised learning algorithms is reported to receive increasing research attention. Report shows that among the prominent and seemingly effective models is Tree based ensemble models. The model is effective and has ability to handle complex as well as missing data without any preprocessing. Consequently, Random Forest and gradient machines such as LightGBM, XGBoost among others. Have been identified by studies as one of the most effective algorithms in terms of performance (Bao et al.,2022; Ren et al.,2023; & Zhong et al., 2023). According to Belmonte et al.,(2025) a Neutral Network is also capable of predicting survival outcomes of patients treated with stem cell transplantation. Consequently, unsupervised machine learning has being used to identify novel, data driven patients with unique survival outcomes, thereby enhancing risk stratifications beyond specified clinical cut offs.

➢ Strong and Generalizable Predictive Performance

Artificial intelligence and machine learning models reported in the reviewed studies showed strong predictive power. This is evidenced by their reported AUC and C index values which is considered high within the range of 0.72 to 0.85. For instance, Witte et al., (2023) reported AUC value of 0.73 when predicting PFS in a large, real-world Cohort of over 1,00 patients from five European Countries, suggesting high acceptance rate. The use of separate training and validation cohorts in many of the studies (e.g., Bao et al., 2022; Mosquera Orgueira et al., 2022) is a critical methodological strength that helps to mitigate overfitting and provides stronger evidence of the model's predictive power on unseen data.

➢ *Focus on Specific Populations and Endpoints*

A number of studies customized their models to particular clinical scenarios or patient subgroups, but the majority concentrated on the general MM population. The problem of prognostication in elderly patients, a demographic that is frequently underrepresented in clinical trials, was particularly addressed by Bao et al. (2022). Belmonte et al. (2025) concentrated on the post-transplant environment, which is a crucial stage in the treatment of MM. Additionally, Guerrero et al. (2022) showed how AI can be used to predict Minimal Residual Disease (MRD), an intermediate but highly significant endpoint. Their model offers an early checkpoint for evaluating treatment efficacy and risk by precisely predicting MRD status, which is highly correlated with long-term survival.

IV. DISCUSSION

There appears to be consensus among the selected studies reviewed for this study, particularly on the use of Artificial Intelligence and Machine Learning for the treatment of Multiple Myeloma. This study utilized systematic review approach. There is increasing evidence that Artificial intelligence and machine learning models performed as prognostic devices. Artificial intelligence and machine learning models also substantially enhanced the conventional or traditional technique of investigation of multiple myeloma.

Several of the reviewed studies revealed that different data sources are capable of being integrated by artificial intelligence and machine learning models. Consequently, artificial intelligence and machine learning models integrate data that serves as baseline sources of information for prognosis, is able to complement extremely complex datasets like quantitative random feature taken from PET/CT scans and whole transcription data.

]Artificial intelligence and machine learning performs well in terms of accuracy and reliability in it prognostic predictions. They are capable of integrating several data sources into a single system. The Artificial intelligence and machine learning models is able to capture in it framework patients diseases biology and clinical signs. This serves as an improvement as well as a deviation from reliance on mere few static markers towards dynamic and comprehensive assessment of patient risk. This review revealed the extent of improvement in healthcare and health sector at large. Considering the extent to which AI and ML technologies offer reliable framework for understanding multiple myeloma and application of this framework into the predictions of clinical decision.

A. Interpretation of Key Findings

The ability of the AI/ML models found in this review to handle high-dimensional, heterogeneous data is their main strength. Conventional statistical models frequently only include a few pre-selected variables. On the other hand, machine learning algorithms such as Random Forest and XGBoost are capable of sorting through thousands of features in genomic or radiomic datasets to find new, interactive patterns that are very likely to survive (Shah et al., 2025; Zhong et al., 2023). A more detailed and biologically informed approach to risk stratification is made possible by this capability, which is a major advancement over the R-ISS.

Mosquera Orgueira et al. (2022) are notable for their use of unsupervised learning. This method revealed previously unknown patient subgroups with distinct survival trajectories rather than forecasting a known outcome. This demonstrates AI's capacity to not only forecast the future but also to uncover fresh information about the biology underlying the illness, which may open the door to innovative treatment approaches.

Furthermore, the successful application of AI to radiomics data from PET/CT scans is a major advance. It provides a non-invasive method to assess whole-body tumor burden and metabolic activity, offering prognostic information that is complementary to that derived from invasive bone marrow biopsies (Sachpekidis et al., 2024). This could reduce the burden on patients while providing powerful data for prognostic models.

B. Implications for Clinical Practice and Future Research

According to the data compiled in this review, AI/ML models have the potential to be useful instruments for the clinical treatment of MM. These models can facilitate shared decision-making between patients and clinicians by offering

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more precise, personalized survival predictions. For instance, a patient who has been classified as high-risk by an AI model may be eligible for more aggressive frontline therapies or clinical trials. On the other hand, a low-risk prediction might reassure and encourage the selection of a conventional treatment plan.

However, a number of issues need to be resolved before these models can be widely used. Clinical trust may be hampered by the "black box" nature of some complex models, such as deep neural networks. Thus, it is essential to employ explainable AI (XAI) methods, like the SHAP analysis carried out by Witte et al. (2023). Clinicians can better understand and interpret a model's predictions by using XAI techniques to shed light on how it makes them.

Future research should focus on several key areas. First, there is a need for large-scale, prospective validation of the most promising models to confirm their performance and clinical utility in real-world settings. Second, studies should aim to integrate multi-modal data (e.g., combining clinical, genomic, and imaging features) into a single model, which may offer synergistic predictive power. Finally, research is needed to determine how to best integrate these AI-driven predictions into clinical workflows to ensure they translate into improved patient outcomes.

C. Limitations of the Review

This systematic review has several limitations. First, the search was limited to a single database (Google Scholar), which, while broad, may have missed relevant studies indexed elsewhere. Second, the heterogeneity in study designs, patient populations, input features, and chosen ML models precluded a quantitative meta-analysis. The synthesis was therefore narrative. Third, studies with unfavourable or unimpressive results might have a lower chance of being published, which could lead to publication bias. Finally, as the study by Zhou et al. (2023) may have demonstrated, some of the included studies had relatively small sample sizes, which may have resulted in model overfitting and excessively optimistic performance metrics.

V. CONCLUSION

This systematic review offers strong evidence that machine learning and artificial intelligence models have great potential to enhance multiple myeloma patients' survival prediction. AI/ML algorithms frequently outperform conventional staging systems in predicting Overall and Progression-Free Survival by utilizing complex, multi-modal data. These models' potential to offer a more comprehensive and individualized approach to prognostication is demonstrated by their successful application to clinical, genomic, and imaging data. As the field develops, the use of explainable, prospectively validated AI tools in clinical settings may revolutionize treatment optimization and risk assessment, ultimately improving patient outcomes for those with this complicated illness.

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