

The Clinical Impact of the Controlling Nutritional Status (CONUT) Score in Patients with Multiple Myeloma

Özlem Beyler, Cengiz Demir

Gazi Yaşargil Training and Research Hospital, Department of Hematology, Diyarbakır, Türkiye

Abstract

Introduction: Multiple myeloma (MM) is a blood cancer involving the abnormal growth of clonal plasma cells in the bone marrow. Traditional models for prognosis such as the Revised International Staging System (R-ISS) primarily considers tumor burden and cytogenetic abnormalities, yet it fails to comprehensively capture patients' immune competence and nutritional condition. The CONUT (Controlling Nutritional Status) score is an immuno-nutritional metric derived from measurements of serum albumin, cholesterol concentration, and lymphocyte levels. Our study aimed to investigate the effect of the CONUT score on prognosis in patients with MM.

Methods: Ninety-one patients with a confirmed diagnosis of MM were included in this retrospective analysis. Individuals were assigned to low (score ≤ 4), moderate (score 5–8), or high (score ≥ 9) risk groups based on their CONUT assessment. The relationship between the CONUT score and the R-ISS stage and the presence of plasmacytoma was evaluated using the chi-square test.

Results: According to the CONUT scores, the mean survival time of the patients was 4202 days in the low-risk group, 3665 days in the moderate-risk group, and 987 days in the high-risk group, with the difference between these durations being statistically significant ($p=0.002$). The presence of plasmacytoma was identified as a factor negatively affecting survival.

Conclusion: The CONUT score appears to be a simple and objective parameter that can predict survival in multiple myeloma independently of traditional staging systems. The assessment of nutritional and immunological status, when integrated into risk classification, may contribute to individualized treatment strategies.

Key words: Multiple myeloma; nutritional status; prognosis; plasmacytoma.

Introduction

Multiple Myeloma (MM) is the second most common hematologic cancer resulting from the abnormal infiltration of plasma cells in the bone marrow (1). This disease can lead to abnormal monoclonal immunoglobulin (M protein) production, causing organ damage including elevated calcium levels, low red blood cell count, kidney dysfunction, and bone destruction with lytic lesions (1). In recent years, significant improvements in survival rates for MM patients have been achieved through new treatment options based on immunotherapies such as novel immunotherapies including BCMA (B cell maturation antigen)-targeted antibody-drug conjugates, bispecific T-cell engagers, and CAR-T (chimeric antigen receptor T-cell) treatments (2). However, despite all these advances, MM remains incurable for most patients; the disease often recurs and has a heterogeneous course (the 5-year survival rate is approximately 55%) (3,4).

Therefore, identifying reliable new biomarkers that can predict prognosis in MM is of great importance (5). The patient's systemic inflammation level and nutritional condition have a significant impact on cancer progression and outcome (6). In various cancers, including hematological malignancies, scores reflecting the patient's immune-nutritional status are reported to possess prognostic relevance (7,8). Designed to evaluate nutritional deficiencies in clinical settings, The Controlling Nutritional Status (CONUT) score integrates three laboratory parameters: albumin, total cholesterol, and the absolute lymphocyte count, offering insight into both nutritional and immune function (8,10 9). The CONUT score reflects not only nutritional reserves but also the patient's immune response capacity, serving as a composite indicator of both nutritional and inflammatory status (7,11 10). The CONUT score can be used in the assessment of

*Corresponding Author: Özlem Beyler Gazi Yaşargil Training and Research Hospital Department of Hematology Kayapınar, Diyarbakır, Türkiye Email: drozlembeyler@gmail.com Orcid: Özlem Beyler [0000-0002-2032-8877](https://orcid.org/0000-0002-2032-8877), Cengiz Demir: [0000-0001-9856-184X](https://orcid.org/0000-0001-9856-184X)



patients with hematological and oncological malignancies. Prognostic staging systems commonly utilized in MM are typically constructed upon assessments of tumor load and

Table 1: Parameters and Scoring System Used for Calculation of the CONUT Score

Parameter	Value Range	Score
Serum Albumin (mg/dL)	≥ 3.50	0
	3.00 – 3.49	2
	2.50 – 2.99	4
	< 2.50	6
Absolute Lymphocyte Count (/mm ³)	≥ 1600	0
	1200 – 1599	1
	800 – 1199	2
	< 800	3
Total Cholesterol (mg/dL)	≥ 180	0
	140 – 179	1
	100 – 139	2
	< 100	3

The total CONUT score is calculated as the sum of the scores for albumin, lymphocyte count, and cholesterol levels. Scores of 2–4 are classified as low risk, 5–8 as moderate risk, and 9–12 as high risk.

biological features. The International Staging System (ISS) evaluates risk using serum β_2 -microglobulin and albumin concentrations. In contrast, the revised system (R-ISS) incorporates additional variables such as adverse cytogenetic findings and elevated lactate dehydrogenase levels to improve risk stratification (9–11). Nevertheless, these models fall short in reflecting patients' immunonutritional status. Moreover, albumin levels can be influenced by factors like inflammation and fluid shifts, which constitutes a notable limitation of the ISS. Indeed, in patients with malnutrition or high inflammatory burden, ISS or R-ISS may fail to predict poor clinical outcomes (5,7). Various retrospective analyses and meta-analyses conducted in recent years have shown that MM patients with high CONUT scores have significantly poorer overall survival (12–14). Indeed, it has been reported that the CONUT score predicts survival even in some patients classified as low-risk based on the ISS, and that combining it with the ISS enhances its prognostic discriminatory power (13,14). Despite increasing evidence, the literature still presents conflicting results regarding the role of the CONUT index in outcome prediction (15–17). Therefore, the primary aim of this study is to investigate the value of the CONUT score in predicting survival in patients with multiple myeloma and its potential contribution to existing staging systems.

Materials and Methods

This retrospective cohort study involved patients aged 18 and above who had been diagnosed with multiple myeloma and monitored between January 2021 and May 2025. The diagnosis was made according to the diagnostic criteria updated by the International Myeloma Working Group (IMWG) in 2014. Data were retrospectively obtained from the hospital automation system and patient files. Total cholesterol, serum albumin and complete blood count were recorded at the time of diagnosis. The CONUT score was calculated using laboratory values at the time of diagnosis. The CONUT score was evaluated on a scale of 0–12 points based on serum albumin level, total cholesterol level, and absolute lymphocyte count. Patients were categorized into CONUT-based risk groups as follows: low risk for scores up to 4, moderate risk for scores ranging from 5 to 8, and high risk for scores of 9 and above (7) (Table 1). Clinical parameters such as patients' demographic characteristics, R-ISS stage, presence of plasmacytoma and lytic lesions, and autologous stem cell transplantation (ASCT) were recorded. All participants gave written consent, and the study was conducted in alignment with the ethical standards set forth in the Declaration of Helsinki. The study received ethical clearance from the Clinical Research Ethics Board of Gazi Yaşargil Training and Research Hospital on May 23, 2025 (Decision No: 498).

Statistical analysis: Basic statistical descriptors were utilized to outline the demographic and clinical features. Survival time was calculated as the period from the date of diagnosis to the last

follow-up date or date of death. Survival outcomes were analyzed by generating Kaplan–Meier curves, with group comparisons evaluated through the Log-Rank test, considering variables

Table 2: Demographic and Clinical Characteristics of Patients with Multiple Myeloma

Characteristic	Category	Number (n)	Percentage (%)
Gender	Female	37	40.7
	Male	54	59.3
R-ISS Stage	1	22	24.2
	2	60	65.9
	3	9	9.9
CONUT Category	Low	53	58.2
	Moderate	28	30.8
	High	10	11.0
ASCT Treatment	No	43	47.3
	Yes	48	52.7
Plasmacytoma	Absent	62	68.1
	Present	29	31.9
Lytic Lesion	Absent	32	35.2
	Present	59	64.8
Survival Status	Alive	77	84.6
	Exitus	14	15.4

such as CONUT groups and the presence of plasmacytoma. The relationship between the CONUT score and the presence of plasmacytoma was evaluated using the chi-square test. IBM SPSS Statistics 25.0 was used for data analysis, and statistical significance was defined as a p-value less than 0.05.

Results

The study included 91 patients with MM. Fifty-nine point three percent of the patients were male (n=54) and 40.7% were female (n=37). According to the R-ISS, 24.2% of patients (n=22) were classified as stage 1, 65.9% (n=60) as stage 2, and 9.9% (n=9) as stage 3. According to the CONUT score, 58.2% (n=53) were in the low-risk group, 30.8% (n=28) were in the medium-risk group, and 11.0% (n=10) were in the high-risk group (Table 1). 52.7% (n=48) of patients had received ASCT treatment, while 47.3% (n=43) had not. The presence of plasmacytoma as an extramedullary disease finding was detected in 31.9% (n=29) of patients. Lytic lesions were present in 64.8% of patients (n=59). During the follow-up period, 14

patients (15.4%) died, and 77 patients (84.6%) survived. The distributions of these data are presented in Table 2. In the survival analysis conducted using the Kaplan–Meier method according to CONUT categories, a statistically meaningful variation was observed across the groups (Log-Rank $\chi^2 = 12.352$, $p = 0.002$). The estimated mean survival durations were 4,202 days (95% CI: 3,694–4,710) for the low-risk category, 3,665 days (95% CI: 2,681–4,649) for the moderate-risk group, and 987 days (95% CI: 738–1,237) for patients classified as high risk. The comparison between the low- and moderate-risk groups revealed a significant difference ($p = 0.023$), whereas the contrast between the low- and high-risk categories demonstrated a highly significant disparity ($p = 0.000$). On the other hand, no statistically relevant difference was found between the moderate- and high-risk groups ($p = 0.208$) (Figure 1) (Table 3). A Kaplan–Meier analysis based on the presence of plasmacytoma also revealed a significant difference in survival (Log-Rank $\chi^2=4.328$, $p=0.037$). The mean survival time for patients without plasmacytoma was 3756

days (SD: 325), while for patients with plasmacytoma, it was 3382 days (SD: 579). The median survival time was determined to be 3780 days in patients without plasmacytoma, while the median survival time in patients with plasmacytoma could not be calculated due to the

lack of events during the follow-up period. Although no statistically significant relationship was demonstrated in the chi-square analysis conducted to evaluate the relationship with the CONUT score and the presence of plasmacytoma (Pearson chi-square = 4.372, $p = 0.112$), the

Table 3: Comparison of Survival Time Between CONUT Score Groups (Kaplan–Meier Analysis and Log-Rank Test Results)

CONUT Risk Group	Mean Survival (days)	95% Confidence Interval	Number of Events (n)	Log-Rank p
Low	4202	3694 – 4710	2	Ref
Moderate	3665	2681 – 4649	6	0.023*
High	987	738 – 1237	3	0.001*
All groups	4002	3316 – 4689	11	0.002†

* Statistically significant difference compared to the low-risk group in pairwise comparisons

† Overall comparison result among the three groups (Log-Rank test)

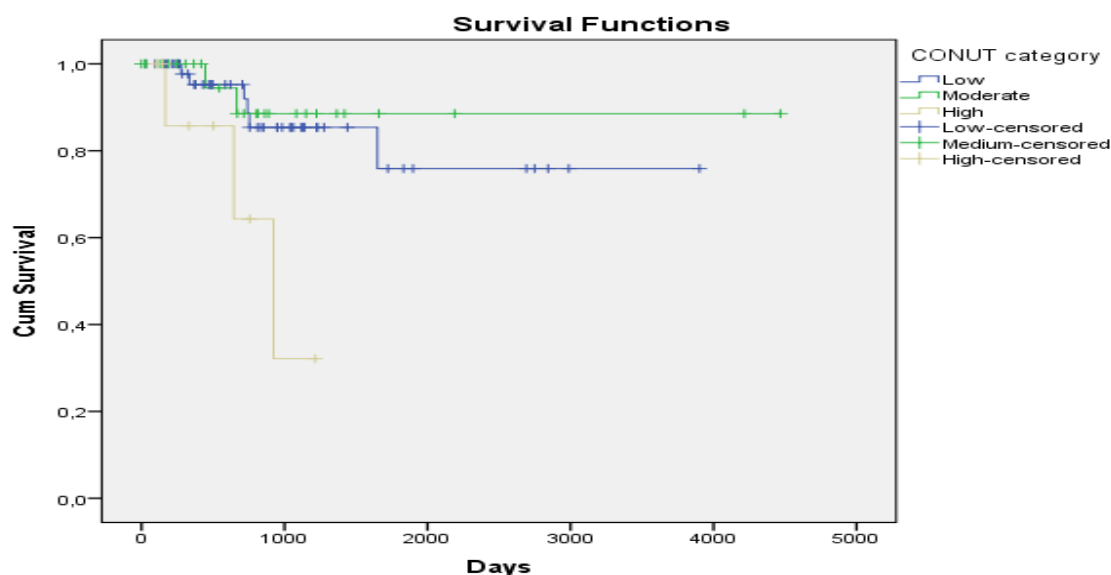


Figure 1: Kaplan–Meier Survival Curves According to CONUT Score Groups

The patients were classified into low-, moderate-, and high-risk groups based on their CONUT scores. A statistically significant difference in survival was observed among the groups (Log-Rank $p = 0.002$).

incidence of plasmacytoma was higher (60%) in patients in the high CONUT group.

Discussion

In this retrospective study, the prognostic effect of the CONUT score, which reflects the immunonutritional status of multiple myeloma patients, on survival was evaluated. Our findings revealed that survival time was significantly shorter, especially in patients with high CONUT scores. This result is consistent with data from

previous studies (12-14). The CONUT score provides a comprehensive assessment of systemic status by incorporating parameters that reflect both nutritional and immune response capacity, such as albumin, cholesterol, and lymphocyte levels (8,10). In our study, the fact that the average survival time of patients in the low CONUT score group was significantly longer than that of other groups suggests that the immunonutritional status may be an important predictor of MM prognosis. This finding is consistent with

the results of Okamoto and colleagues' study, which demonstrated that the CONUT score, a marker of immune-nutritional status, has independent prognostic significance (13). The observed survival difference between patients in the low- and moderate-risk CONUT categories indicates that even mild to moderate levels of immunonutritional compromise, not just advanced malnutrition, may have a detrimental effect on prognosis. This observation aligns with evidence from several meta-analyses, which have demonstrated that the CONUT index is linked to poorer outcomes not only at high scores but also at intermediate levels across various types of malignancies (15). The lack of a significant difference between the moderate and high groups may be explained by the limited number of patients, particularly in the high CONUT group. Indeed, it is thought that this relationship may become clearer in studies with larger sample sizes. Additionally, this situation suggests that patients currently classified as having a moderate risk score may have a prognosis as poor as those with a high risk score. The presence of plasmacytoma has also been identified as a negative prognostic factor for survival. This finding supports studies showing that extramedullary involvement is associated with disease aggressiveness (1,3). The presence of plasmacytoma is an indicator of the ability of myeloma cells to spread outside the bone marrow and is often associated with poor-risk cytogenetics (1). Although no direct statistical relationship was found between the CONUT score and the presence of plasmacytoma, the increased frequency of plasmacytoma in patients with high CONUT scores is a notable observation. It is hypothesized that deterioration in immunonutritional condition might play a role in the pathogenesis of extramedullary involvement (8). Extramedullary disease, including plasmacytomas, has been associated with aggressive disease biology and poor prognosis in multiple myeloma patients (16). These observations suggest that a higher CONUT score, reflecting compromised immunonutritional status, may predispose to extramedullary spread. However, since this did not achieve statistical significance in our research, it should be validated by larger, prospective studies.

Strengths of the study: One of the main strengths of this study is the evaluation of the CONUT score, an easily obtainable immunonutritional index, in a well-defined cohort of patients with multiple myeloma. The analysis incorporated both survival outcomes and disease-related features such as the presence of

plasmacytoma, providing a broader clinical perspective. Additionally, the study included patients across all R-ISS stages and assessed the potential association between the CONUT score and extramedullary disease, an area that has been scarcely addressed in the literature. The use of real-world data from a single tertiary center also enhances the applicability of the findings to routine clinical practice.

Study limitations: This investigation is subject to some constraints, notably its retrospective design and the low representation of individuals in the high CONUT risk category. In addition, immunonutritional parameters were assessed only at the time of diagnosis, and dynamic changes during treatment could not be monitored.

Conclusion

This study demonstrates that the CONUT score may serve as a practical, low-cost, and clinically applicable tool for predicting survival in multiple myeloma patients. Evaluating the CONUT score alongside existing prognostic models (ISS, R-ISS) may contribute to the development of individualized risk classifications. However, these findings require validation in larger, multicenter, and prospective cohorts.

Ethical approval: Ethics committee approval for this study was obtained from the Clinical Research Ethics Committee of Gazi Yaşargil Training and Research Hospital with the decision number 498, dated May 23, 2025.

Conflict of interest: The authors declare that they have no conflict of interest related to this study.

Financial disclosure: No financial support was received for the conduct or publication of this study.

Author contributions: Concept and Design: ÖB, CD; Data Collection and/or Processing: ÖB, CD; Analysis and/or Interpretation: CD, ÖB; Writing – Original Draft Preparation: ÖB; Writing – Review and Editing: CD

Acknowledgement: None.

References

1. Van de Donk NWCJ, Pawlyn C, Yong KL. Multiple myeloma. *Lancet* 2021; 397(10272):410-427.
2. Manier S, Ingegnere T, Escure G, Prodhomme C, Nudel M, Mitra S, et al. Current state and next-generation CAR-T cells in multiple myeloma. *Blood Rev* 2022; 54:100929.

3. Pinto V, Bergantim R, Caires HR, Seca H, Guimarães JE, Vasconcelos MH. Multiple myeloma: available therapies and causes of drug resistance. *Cancers (Basel)* 2020; 12(2):407.
4. Podar K, Leleu X. Relapsed/refractory multiple myeloma in 2020/2021 and beyond. *Cancers (Basel)* 2021; 13(20):5154.
5. Wallington-Beddoe CT, Mynott RL. Prognostic and predictive biomarker developments in multiple myeloma. *J Hematol Oncol* 2021; 14(1):151.
6. Li B, Lu Z, Wang S, Hou J, Xia G, Li H, et al. Pretreatment elevated prognostic nutritional index predicts a favorable prognosis in patients with prostate cancer. *BMC Cancer* 2020 Apr 29; 20(1):361.
7. Zhou X, Lu Y, Xia J, Mao J, Wang J, Guo H. Association between baseline controlling nutritional status score and clinical outcomes of patients with multiple myeloma. *Cancer Biomark* 2021; 32(1):65-71.
8. Takagi K, Buettner S, Ijzermans JNM. Prognostic significance of the controlling nutritional status (CONUT) score in patients with colorectal cancer: a systematic review and meta-analysis. *Int J Surg* 2020; 78:91-96.
9. Jeon CH, Park KB, Jung YJ, Seo HS, Park CH, Song KY, et al. Modified controlling nutritional status score: a refined prognostic indicator depending on the stage of gastric cancer. *Surg Oncol* 2020; 34:261-269.
10. Takemura K, Yuasa T, Fujiwara R, Ito M, Suzuki H, Yonese J, et al. Prognostic significance of the controlling nutritional status (CONUT) score in patients with advanced renal cell carcinoma treated with nivolumab after failure of prior tyrosine kinase inhibitors. *J Urol* 2020; 204(6):1166-1172.
11. Palumbo A, Avet-Loiseau H, Oliva S, Lokhorst HM, Goldschmidt H, Rosinol L, et al. Revised international staging system for multiple myeloma: a report from International Myeloma Working Group. *J Clin Oncol* 2015; 33(26):2863-2869.
12. Kamiya T, Ito C, Fujita Y, Ogura S, Mizuno K, Sakurai A, et al. The prognostic value of the controlling nutritional status score in patients with multiple myeloma. *Leuk Lymphoma* 2020; 61(8):1894-1900.
13. Okamoto S, Ureshino H, Kidoguchi K, Kusaba K, Kizuka-Sano H, Sano H, et al. Clinical impact of the CONUT score in patients with multiple myeloma. *Ann Hematol* 2020; 99(1):113-119.
14. Liang F, Dong XY, Tang GF, Qi KM, Chen W, Sang W, et al. Influence of prognostic nutritional index and controlling nutritional status on the prognosis of patients with multiple myeloma. *Chin J Hematol* 2021; Apr 14;42(4):332-337.
15. Lu C, Chen Q, Fei L, Wang J, Wang C, Yu L. Prognostic impact of the controlling nutritional status score in patients with hematologic malignancies: a systematic review and meta-analysis. *Front Immunol* 2022; 13:952802.
16. Usmani SZ, Heuck C, Mitchell A, Szymonifka J, Nair B, Hoering A, et al. Extramedullary disease portends poor prognosis in multiple myeloma and is over-represented in high-risk disease even in the era of novel agents. *Haematologica* 2012;97(11):1761-1767.