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Lymphopenia at intensive care unit admission does not predict 28-day mortality in older adults

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Abstract

Absolute lymphocyte count has often been proposed as a practical prognostic variable in critical illness. In older adults, however, immunosenescence and long-term immune remodeling may lower baseline lymphocyte levels and weaken their relationship with outcomes. We therefore examined whether lymphopenia at ICU admission predicts 28-day mortality in geriatric patients and whether it improves commonly used prognostic models. We undertook a retrospective cohort analysis of 202 consecutive ICU admissions of patients aged ≥ 65 years in a tertiary university hospital between January and December 2019. Admission lymphopenia was defined as an absolute lymphocyte count < 1100 × 10^3/μL. The primary outcome was 28-day mortality. Independent predictors were assessed using multivariable logistic regression, and discriminative performance was evaluated using ROC curve analysis. Lymphopenia was present in 76.2% of patients and showed no significant association with 28-day mortality (p = 0.209). Mortality was independently related to ward admission, higher APACHE II and Charlson Comorbidity Index scores, lower Glasgow Coma Scale score, and the need for mechanical ventilation and renal replacement therapy. Adding lymphopenia to multivariable models did not improve discrimination (AUROC 0.752 – 0.897; all p > 0.9). In geriatric ICU patients, lymphopenia at admission is frequent but does not independently predict short-term mortality and does not provide incremental value beyond established severity indicators. These findings support prioritizing validated clinical severity scores and organ support variables over isolated immune-cell counts when stratifying mortality risk in older ICU populations.

Keywords: Lymphopenia, geriatrics, intensive care, 28-day mortality, prognostic marker

Introduction

Low lymphocyte counts are frequently encountered at the onset of critical illness and have been linked to adverse outcomes across a range of ICU populations [1]. In mixed-age cohorts, lymphopenia has been viewed as a surrogate of immune dysfunction and systemic inflammation, and associations with mortality have been described in sepsis, trauma, COVID-19, and general ICU admissions [2]. Because lymphocyte count is inexpensive, rapidly available, and routinely measured, it has been suggested as a pragmatic marker for early risk stratification at ICU entry [3].

However, the prognostic implications of lymphopenia may not be consistent across all patient groups. Older adults represent a distinct population characterized by high multimorbidity, broad biological heterogeneity, and age-related immune changes, yet they remain relatively underrepresented in studies evaluating lymphopenia as a mortality marker [4]. Importantly, immunosenescence may lower baseline lymphocyte counts

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through impaired production and altered redistribution, which may weaken the link between admission lymphocyte values and acute illness severity [5]. In geriatric critical care, frailty, comorbidity burden, and reduced physiological reserve often outweigh isolated laboratory abnormalities in determining outcomes. Therefore, biomarkers that perform well in younger cohorts may have limited prognostic utility when applied to older ICU patients.

In this context, we investigated whether lymphopenia at ICU admission independently predicts 28-day mortality in critically ill patients aged ≥ 65 years. We expected that any observed association would not persist after accounting for illness severity and organ support requirements.

Material and Methods

Study Design and Ethical Approval

This retrospective cohort study was performed in the ICU of a tertiary university hospital. The study protocol was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee on November 23, 2020 (Approval No. 2020/28-43).

Patient Selection

All consecutive medical ICU admissions of patients aged ≥ 65 years to the Internal Medicine and Anesthesiology ICUs between January 1 and December 31, 2019, were reviewed. Inclusion required a complete blood count and an ICU stay of at least 24 hours. We excluded patients with chronic lymphocytic leukemia or lymphoma, those receiving immunosuppressive therapy, had missing laboratory data required for the analyses, stayed in the ICU for < 24 hours, or died within 24 hours after admission. Excluding deaths during the first 24 hours was intended to reduce bias related to terminal presentations at ICU entry, consistent with prior geriatric ICU cohorts [6,7].

Definitions

The analysis period comprised the first 28 days after ICU admission. Lymphopenia was defined using the admission (day 1) absolute lymphocyte count; values < $1100 \times 10^3/\mu L$ were classified as lymphopenic. The laboratory reference interval for lymphocytes was $1100 – 3500 \times 10^3/\mu L$ [8].

Data Collection

Demographic and clinical data were extracted from the hospital's electronic medical record system. Recorded baseline variables included age, sex, admission diagnosis, and comorbidities. Admission diagnoses were grouped into acute respiratory failure, circulatory shock, sepsis, postoperative admission, and return of spontaneous circulation (ROSC). Comorbid conditions included hypertension, coronary artery disease, congestive heart failure, diabetes mellitus, and chronic obstructive pulmonary disease.

Clinical severity and ICU course variables were also collected, including APACHE II score, Charlson Comorbidity Index, mechanical ventilation requirement, vasopressor-free days, renal replacement therapy (RRT), ICU length of stay, hospital length of stay, discharge status, and 28-day mortality. ICU length of stay was included in regression analyses to reflect early death versus prolonged survival rather than as a baseline predictor. Lymphocyte counts were recorded on ICU day 1 and repeated on days 7 and 14; the primary exposure definition relied solely on the day 1 value. Mortality outcomes were verified using the national electronic death notification system. Although lymphocyte counts on ICU days 7 and 14 were recorded, the primary analysis focused on the admission value because the purpose of the study was to evaluate the early prognostic usefulness of lymphopenia at the time of ICU entry. Later measurements may be affected by treatment exposure, nosocomial complications, evolving organ failure, and survivorship bias, and were therefore not included in the primary model.

Study Outcomes

The primary outcome was 28-day mortality and its association with lymphopenia at ICU admission (day 1) among patients aged ≥ 65 years. ICU length of stay was evaluated as the secondary outcome.

Statistical Analysis

Continuous variables were reported as mean ± standard deviation when approximately normally distributed, or as median with interquartile range otherwise. Comparisons between survivors and non-survivors were performed using Student's t-test or the Mann – Whitney U test. Categorical variables were summarized as counts and percentages and compared using Chi-square testing, with Fisher's exact test applied when expected cell counts were < 5.

Logistic regression was used to evaluate factors associated with 28-day mortality. Univariable analyses were performed first, followed by multivariable logistic regression to identify independent predictors. To evaluate whether lymphopenia improved prediction, ROC curve analyses were conducted and AUROC values were compared between models with and without lymphopenia.

All analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as a two-sided p-value < 0.05.

Results

Baseline Characteristics

In total, 202 ICU patients aged 65 years and older were analyzed. At 28 days, 96 patients (47.5%) had died, whereas 106 (52.5%) were still alive. Median age was comparable between survivors and non-survivors (75.0 vs. 76.0 years; p = 0.889). A higher proportion of males was observed in the non-survivor group, although the difference narrowly missed statistical significance (63.5% vs. 50.0%; p = 0.053). Admission origin showed a strong relationship with outcome: patients transferred from hospital wards had markedly higher 28-day mortality than those admitted

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from the emergency department (63.5% vs. 31.3%; p < 0.001).

The distribution of admission diagnoses also differed between groups. Acute respiratory failure and circulatory shock were more commonly recorded among patients who died (p = 0.024 and p = 0.002, respectively). No significant differences were found for sepsis, postoperative admission, or ROSC.

With respect to comorbidities, coronary artery disease was significantly more frequent in non-survivors (45.8% vs. 21.7%; p < 0.001). Hypertension, congestive heart failure, diabetes mellitus, and chronic obstructive pulmonary disease were not significantly associated with 28-day mortality.

Admission severity indicators were consistently worse in the non-survivor group. Patients who died had higher APACHE II scores (28.0 vs. 21.0; p < 0.001) and higher Charlson Comorbidity Index values (7.0 vs. 6.0; p = 0.001), together with substantially lower Glasgow Coma Scale scores (3.0 vs. 11.5; p < 0.001).

Admission lymphopenia was highly prevalent in both groups and was numerically more frequent among non-survivors; however, this difference was not statistically significant (80.2% vs. 72.6%; p = 0.207). Indicators of organ support showed clear outcome-related differences: RRT use was higher in the non-survivor group (37.5% vs. 20.8%; p = 0.007), and invasive mechanical ventilation was required in nearly all non-survivors compared with approximately half of survivors (92.7% vs. 47.2%; p < 0.001). Patients who died had a shorter ICU stay than survivors (6.0 vs. 13.5 days; p < 0.001) (Table 1).

Table 1. Baseline characteristics of older adults admitted to the ICU, stratified by 28-day mortality

Variable	Overall n = 202 (100%)	28-day mortality n = 96 (47.5%)	28-day survival n = 106 (52.5%)	p value
Age (year), median (IQR)	75.0 (15.0)	75.0 (12.0)	76.0 (16.0)	0.889
Age 65 – 74 years, n (%)	90 (44.6)	45 (46.9)	45 (42.5)	0.692
Age 75 – 84 years, n (%)	75 (37.5)	37 (38.5)	38 (35.8)	0.528
Age ≥ 85 years, n (%)	37 (18.3)	14 (14.6)	23 (21.7)	0.192
Sex (Male) n (%)	114 (56.4)	61 (63.5)	53 (50.0)	0.053
Admission source, n (%)				
Ward	100 (49.5)	61 (63.5)	39 (36.8)	< 0.001
Emergency department	97 (48.0)	30 (31.3)	67 (63.2)	
Other intensive care unit	5 (2.5)	5 (5.2)	0 (0.0)	
Admission diagnosis, n (%)				
Acute respiratory failure	184 (91.1)	92 (95.8)	92 (86.8)	0.024
Circulatory shock	103 (51.0)	60 (62.5)	43 (40.6)	0.002
Sepsis	40 (19.8)	19 (19.8)	21 (19.8)	0.997
Postoperative admission	20 (9.9)	13 (13.5)	7 (6.6)	0.099
ROSC	17 (8.4)	6 (6.3)	11 (10.4)	0.291
Comorbidities				
Hypertension	118 (58.4)	57 (59.4)	61 (57.5)	0.792
Coronary arter disease	67 (33.2)	44 (45.8)	23 (21.7)	< 0.001
Congestive heart failure	52 (25.7)	28 (29.2)	24 (22.6)	0.289
Diabetes mellitus	76 (37.6)	41 (42.7)	35 (33.0)	0.156
Chronic obstructive pulmonary disease	49 (24.3)	18 (18.8)	31 (29.2)	0.082
Illness severity and support				
CCI med, (IQR)	6.0 (3.0)	7.0 (4.0)	6.0 (3.0)	0.001
GCS med, (IQR)	4.0 (12.0)	3.0 (12.0)	11.5 (12.0)	< 0.001
APACHE II, med (IQR)	26.0 (13.0)	28.0 (9.0)	21.0 (13.0)	< 0.001
Lymphopenia at admission, n (%)	154 (76.2)	77 (80.2)	77 (72.6)	0.207
Requirement for RRT, n (%)	58 (28.7)	36 (37.5)	22 (20.8)	0.007
Need for MV, n (%)	139 (68.8)	89 (92.7)	50 (47.2)	< 0.001
ICU Length of Stay, med (IQR)	10.0 (16.0)	6.0 (10.0)	13.5 (22.0)	< 0.001

Med: median, IQR: interquartile range, ROSC: return of spontaneous circulation, CCI: charlson comorbidity index, GCS: Glasgow coma scale, APACHE II: acute physiology and chronic health evaluation II, RRT: Renal replacement therapy, MV: mechanical ventilation, ICU: intensive care unit

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Logistic Regression Analysis for 28-Day Mortality

On univariable analysis, several predictors were significantly related to 28-day mortality. Compared with emergency department admissions, ward-to-ICU transfer was associated with higher odds of death (OR 3.825; 95% CI 2.181 – 6.707; p < 0.001). Acute respiratory failure (OR 3.500; 95% CI 1.110 – 11.033; p = 0.032) and circulatory shock (OR 2.442; 95% CI 1.386 – 4.303; p = 0.002) were also linked to increased mortality. Among the recorded comorbidities, coronary artery disease was the only condition showing a significant association (OR 3.054; 95% CI 1.656 – 5.631; p < 0.001). Higher Charlson Comorbidity Index (OR 1.183; 95% CI 1.060 – 1.320; p = 0.003) and APACHE II score (OR 1.087; 95% CI 1.047 – 1.129; p < 0.001) were related to an increased risk of death, whereas higher GCS scores were associated with reduced mortality risk (OR 0.881; 95% CI 0.833 – 0.931; p < 0.001). Regarding organ support, RRT (OR 2.291; 95% CI 1.226 – 4.282; p = 0.009) and mechanical ventilation (OR 14.240; 95% CI 6.034 – 33.608; p < 0.001) were among the strongest predictors. ICU length of stay showed an inverse association with mortality (OR 0.929; 95% CI 0.901 – 0.958; p < 0.001), consistent with early death among the most severely ill. Admission lymphopenia was not significant in univariable analysis (OR 1.526; 95% CI 0.790 – 2.950; p = 0.209).

In the fully adjusted model, seven factors remained independently associated with 28-day mortality. Ward admission continued to predict death (OR 3.695; 95% CI 1.579 – 8.646; p < 0.001). Charlson Comorbidity Index (OR 1.213; 95% CI 1.015 – 1.449; p = 0.034), APACHE II score (OR 1.070; 95% CI 1.025 – 1.116; p = 0.002), and GCS score (OR 0.885; 95% CI 0.796 – 0.985; p = 0.025) retained independent associations with outcome. Both RRT (OR 2.444; 95% CI 1.102 – 5.421; p = 0.028) and mechanical ventilation (OR 11.897; 95% CI 4.868 – 29.076; p < 0.001) remained strong predictors. ICU length of stay also remained inversely associated with mortality (OR 0.923; 95% CI 0.894 – 0.952; p < 0.001). Admission lymphopenia did not retain independent prognostic significance (Table 2).

Table 2. Univariable and multivariable logistic regression analysis for the prediction of 28-day mortality in geriatric ICU patients

Variable	28-day mortality			
	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.003 (0.970 – 1.038)	0.846		
Sex (Ref; Female)	1.743 (0.992 – 3.062)	0.052		
Admission source (Ref; ED)	3.825 (2.181 – 6.707)	< 0.001	3.695 (1.579 – 8.646)	< 0.001
Diagnosis				
Acute respiratory failure	3.500 (1.110 – 11.033)	0.032		
Circulatory shock	2.442 (1.386 – 4.303)	0.002		
Comorbidities				
CAD	3.054 (1.656 – 5.631)	< 0.001		
Illness severity and support				
CCI	1.183 (1.060 – 1.320)	0.003	1.213 (1.015 – 1.449)	0.034
GCS	0.881 (0.833 – 0.931)	< 0.001	0.885 (0.796 – 0.985)	0.025
APACHE II	1.087 (1.047 – 1.129)	< 0.001	1.070 (1.025 – 1.116)	0.002
Lymphopenia at admission,	1.526 (0.790 – 2.950)	0.209		
Requirement for RRT	2.291 (1.226 – 4.282)	0.009	2.444 (1.102 – 5.421)	0.028
Need for MV	14.240 (6.034 – 33.608)	< 0.001	11.897 (4.868 – 29.076)	< 0.001
ICU Length of Stay	0.929 (0.901 – 0.958)	< 0.001	0.923 (0.894 – 0.952)	< 0.001

Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using logistic regression; Variables with p < 0.10 in univariable analysis were entered into the multivariable model; The final multivariable model included age, sex, Charlson Comorbidity Index (CCI), Glasgow Coma Scale (GCS), APACHE II score, admission source, renal replacement therapy (RRT), mechanical ventilation (MV), and ICU length of stay; Female sex and emergency department (ED) admission were used as reference categories; Lymphopenia was defined according to admission laboratory reference ranges; A two-sided p < 0.05 was considered statistically significant

Discriminative Performance of Models

To evaluate the incremental predictive value of lymphopenia, ROC analyses were performed (Figure 1). The base model consisting of age, sex, and ICU length of stay demonstrated an AUROC of 0.752 (95% CI 0.686 – 0.819), and the AUROC did not change after lymphopenia was added (p = 0.915). Adding RRT increased the AUROC to 0.785 (95% CI 0.722 – 0.848), but lymphopenia again provided no additional discriminatory benefit (p = 0.932). The most comprehensive model (age, sex, ICU length of stay, RRT, and mechanical ventilation) achieved an AUROC

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of 0.897 (95% CI 0.853 – 0.941); however, lymphopenia still did not improve discrimination (p = 0.976). In contrast, established severity measures increased AUROC significantly: inclusion of GCS increased AUROC from 0.752 to 0.826 (p = 0.003), and inclusion of APACHE II increased AUROC from 0.752 to 0.801 (p = 0.023). Charlson Comorbidity Index increased AUROC numerically but without statistical significance (p = 0.133) (Table 3).

Table 3. Pairwise comparison of ROC curves for baseline and extended models predicting 28-day mortality in geriatric ICU patients

	AUROC (95%CI)		Pairwise analysis 95%CI					
Predicting model	**Without lymphopenia**	**With lymphopenia**	**DBA**	**SE**	**Lower**	**Upper**	**Z statistic**	**p**
Base Model = Age, Sex, ICU length of stay	0.752 (0.686 – 0.819)	0.752 (0.686 – 0.819)	0.000	0.256	-0.004	0.003	-0.107	0.915
Base Model + Requirement for RRT	0.785 (0.722 – 0.848)	0.785 (0.722 – 0.848)	0.000	0.250	-0.004	0.003	-0.086	0.932
Base Model + Requirement for RRT + Need for MV	0.897 (0.853 – 0.941)	0.897 (0.853 – 0.941)	0.000	0.209	-0.003	0.003	-0.030	0.976
Predicting model	**Without GCS**	**With GCS**						
Base Model = Age, Sex, ICU length of stay	0.752 (0.686 – 0.819)	0.826 (0.768 – 0.884)	-0.074	0.250	-0.123	-0.025	-2.979	0.003
Base Model + Requirement for RRT	0.785 (0.722 – 0.848)	0.831 (0.773 – 0.890)	-0.046	0.246	-0.086	-0.007	-2.333	0.020
Base Model + Requirement for RRT + Need for MV	0.897 (0.853 – 0.941)	0.899 (0.853 – 0.945)	-0.002	0.212	-0.018	0.014	-0.256	0.798
Predicting model	**Without CCI**	**With CCI**						
Base Model = Age, Sex, ICU length of stay	0.752 (0.686 – 0.819)	0.779 (0.715 – 0.843)	-0.027	0.254	-0.062	0.008	-1.502	0.133
Base Model + Requirement for RRT	0.785 (0.722 – 0.848)	0.805 (0.744 – 0.865)	-0.020	0.248	-0.047	0.007	-1426	0.154
Base Model + Requirement for RRT + Need for MV	0.897 (0.853 – 0.941)	0.908 (0.869 – 0.948)	-0.011	0.204	-0.028-	0.006	-1.299	0.194
Predicting model	**Without APACHE – II**	**With APACHE – II**						
Base Model = Age, Sex, ICU length of stay	0.752 (0.686 – 0.819)	0.801 (0.739 – 0.863)	-0.049	0.253	-0.091	-0.007	-2.276	0.023
Base Model + Requirement for RRT	0.785 (0.722 – 0.848)	0.804 (0.741 – 0.866)	-0.019	0.250	-0.047	0.009	-1.311	0.190
Base Model + Requirement for RRT + Need for MV	0.897 (0.853 – 0.941)	0.898 (0.854 – 0.942)	-0.001	0.211	-0.009	0.010	-0.131	0.896

Area under the receiver operating characteristic curve (AUROC) values are presented with 95% confidence intervals (CIs); Pairwise comparisons of AUROCs were performed using DeLong's test; DBA indicates the difference between AUROCs of the compared models; SE denotes the standard error of the AUROC difference; Base model included age, sex, and ICU length of stay; extended models sequentially added requirement for renal replacement therapy (RRT), need for mechanical ventilation (MV), Glasgow Coma Scale (GCS), Charlson Comorbidity Index (CCI), APACHE II score, and lymphopenia status as specified; A two-sided $p < 0.05$ was considered statistically significant

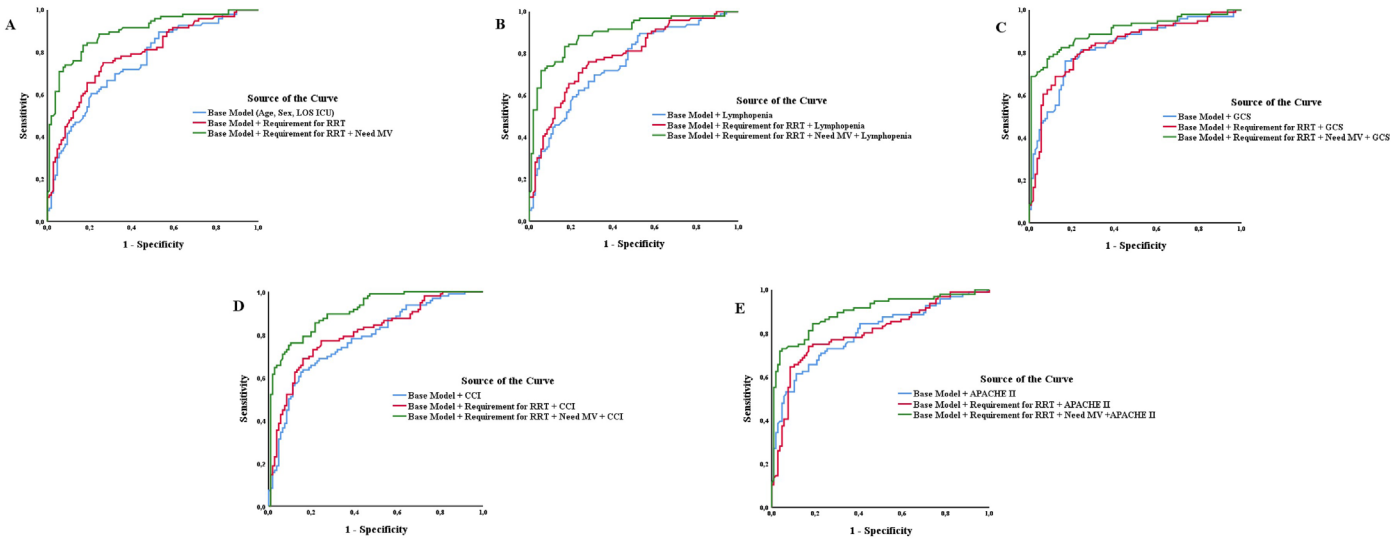

Figure 1. Receiver operating characteristic (ROC) curves for predicting 28-day mortality in geriatric ICU patients using various logistic regression models; Panel A: Base model (Age, Sex, ICU LOS) compared with models including RRT and RRT + Mechanical Ventilation (MV); Panel B: Models incorporating Lymphopenia in addition to base variables and RRT/MV; Panel C: Models incorporating Glasgow Coma Scale (GCS) score; Panel D: Models incorporating Charlson Comorbidity Index (CCI); Panel E: Models incorporating APACHE II score; The addition of MV and RRT consistently improved model performance across all panels, whereas lymphopenia did not enhance discrimination

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Discussion

Among older adults admitted to the ICU, lymphopenia was frequently observed at the time of admission; nevertheless, it did not provide independent prognostic information for 28-day mortality. When adjusted for severity scores and organ support requirements, lymphopenia was no longer associated with mortality and did not improve model discrimination beyond established predictors such as APACHE II, GCS, mechanical ventilation, and RRT. These results indicate that the prognostic value of lymphopenia described in younger or mixed-age ICU populations may be attenuated in older adults, potentially due to baseline lymphocyte decline related to immunosenescence and chronic immune remodeling [1,9,10].

In line with previous evidence, several clinical and physiological parameters were significantly linked to 28-day mortality among older ICU patients in our study [11,12]. As reflected in Table 1, non-survivors showed significantly greater illness severity scores at admission, including APACHE II and Charlson Comorbidity Index, and markedly lower GCS scores. These variables remained significant in multivariable analysis, emphasizing their established prognostic relevance in elderly populations. Furthermore, the requirement for organ support—particularly mechanical ventilation and renal replacement therapy—was considerably higher in non-survivors, underscoring the role of acute organ failure as a central determinant of poor outcomes in this age group. This is consistent with prior studies reporting that invasive support needs, rather than isolated laboratory markers, more accurately reflect mortality risk in older ICU patients [13,14].

Recent evidence also suggests that composite biomarkers integrating inflammation and nutritional status may provide more robust prognostic information than isolated lymphocyte count in geriatric intensive care populations. In a 2025 study conducted in geriatric respiratory ICU patients, Uluç et al. [15] reported that lower HALP scores and higher CRP/albumin and platelet/lymphocyte ratios were associated with mortality, supporting the idea that multidimensional indices may better capture the complex biological vulnerability of older adults. These findings complement our results by suggesting that although absolute lymphocyte count alone may have limited prognostic utility, biomarkers incorporating both immune-inflammatory and nutritional components may offer greater discrimination in geriatric critical care.

A plausible explanation for the limited prognostic value of admission lymphopenia in our cohort is the effect of immunosenescence. Aging is associated with progressive quantitative and functional changes in adaptive immunity, especially within T-cell populations, together with chronic low-grade inflammation [16]. These processes may reduce baseline lymphocyte counts in older adults irrespective of the acute severity of illness, thereby weakening the specificity of lymphopenia as a marker of critical illness – related immune dysfunction [17]. In this context, a low lymphocyte count at ICU admission may reflect pre-existing immune aging rather than an acute prognostic signal, which could explain why lymphopenia did not improve mortality prediction beyond established severity scores and organ support variables in our study.

Interestingly, patients who died had significantly shorter ICU stays, which likely reflects the rapid clinical deterioration observed in severely ill elderly individuals with multi-organ dysfunction. Contrary to what might be assumed in younger cohorts, prolonged ICU length of stay in our study was associated with survival, likely due to the exclusion of early deaths and the limited physiological reserve of geriatric patients at the time of admission. These findings highlight the need for integrating functional and physiological indices—such as frailty status or early organ dysfunction trajectories—rather than relying solely on admission laboratory markers like lymphocyte count.

The multivariable logistic regression analysis further reinforced the limited prognostic value of lymphopenia in elderly ICU patients. While several clinical indicators—such as admission from the ward, higher APACHE II and CCI scores, lower GCS, and the need for mechanical ventilation or renal replacement therapy—were identified as independent predictors of 28-day mortality, lymphopenia failed to retain statistical significance in the final model (Table 2). These findings suggest that, within the geriatric population, physiological severity and acute organ dysfunction carry far greater prognostic weight than isolated immune cell counts.

This result aligns with recent literature questioning the universal applicability of lymphopenia as a mortality marker across different age groups. For instance, Cilloniz et al. [18] demonstrated that in patients aged ≥70, lymphocyte count was no longer an independent risk factor after adjusting for APACHE II and SOFA scores. Similarly, Goyani et al. [19] emphasized that immune parameters such as lymphopenia might be confounded by immunosenescence in elderly individuals, making them less reliable for risk stratification. In contrast, APACHE II and GCS scores, which encapsulate both systemic derangement and neurological function, have consistently demonstrated predictive validity in geriatric critical care settings [20].

Our study confirms that acute organ support variables—particularly the need for MV (OR: 11.9) and RRT (OR: 2.4)—remained the most powerful predictors of mortality, reflecting the burden of respiratory and renal failure in elderly patients. The inverse association between ICU length of stay and mortality also reflects a well-described phenomenon in critical care research, where early deaths often occur before interventions can be fully implemented or evaluated. These results argue against the inclusion of lymphopenia as a standalone prognostic marker in geriatric-specific ICU risk models and favor a multifactorial approach incorporating validated physiological scores and support requirements.

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The findings from the ROC curve analyses in Table 3 further support the limited discriminative utility of lymphopenia for 28-day mortality prediction in critically ill older adults. Across all logistic regression models—ranging from basic models including only demographic variables to extended models incorporating renal replacement therapy and mechanical ventilation—adding lymphopenia as a covariate did not result in any meaningful improvement in the area under the ROC curve (AUROC). For instance, the AUROC of the base model (age, sex, ICU length of stay) remained unchanged at 0.752 after lymphopenia was added ($p = 0.915$). Similarly, in the most comprehensive model including MV and RRT, the AUROC remained stable at 0.897 ($p = 0.976$), (Figure 1).

In contrast, the addition of established severity indicators such as GCS and APACHE II significantly improved model performance, indicating that these parameters provide greater incremental prognostic information. This observation is consistent with recent reports emphasizing that composite severity scores outperform individual laboratory markers in mortality prediction models for older adults [21,22]. The lack of contribution from lymphopenia to model discrimination may reflect both biological and methodological limitations—particularly in the geriatric population, where age-related lymphocyte decline is common and not necessarily indicative of acute immune dysregulation [23].

Taken together, these data suggest that lymphopenia should not be included in mortality prediction models for elderly ICU patients unless it is contextualized within broader immune or frailty-based indices. Clinicians should prioritize comprehensive illness severity scores and early indicators of organ dysfunction when stratifying risk in this population.

Limitations

These findings should be interpreted in the context of several limitations. Because the study was retrospective and conducted at a single institution, the findings may not be fully generalizable to other ICU settings. In addition, although lymphocyte measurements were available at predefined time points, the primary exposure definition relied on admission values, and we did not examine whether longitudinal lymphocyte trajectories were associated with outcome. Frailty and functional status—important determinants of prognosis in older adults—were not available in the dataset. Although we adjusted for multiple covariates, the possibility of unmeasured or residual confounding remains. Finally, lymphopenia was defined using a conventional cut-off; alternative age-adapted thresholds may yield different results and should be explored in future studies.

Conclusion

Among critically ill patients aged 65 years and older, lymphopenia at ICU admission was common but did not independently predict 28-day mortality and did not enhance the discriminative performance of multivariable models. In contrast, established indicators of illness severity and organ failure—including APACHE II, GCS, Charlson Comorbidity Index, mechanical ventilation, and renal replacement therapy—remained strongly associated with short-term mortality. Our results do not justify the routine use of admission lymphopenia as a standalone prognostic marker in geriatric ICU patients. Risk stratification in this population should primarily rely on validated severity measures and early organ support requirements while considering the impact of aging-related immune changes on laboratory interpretation.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Dokuz Eylul University (Approval No. 2020/28-43, approved on 23 November 2020).

Patient Consent

This was a retrospective study using anonymized patient data. Therefore, the requirement for obtaining written informed consent from individual patients was waived by the Dokuz Eylül University Non-Interventional Research Ethics Committee.

Conflict of Interest

The authors confirm the absence of any conflicts associated with this work.

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