Original Article

Association of Pre-Transplant Lymphopenia with Post-Liver Transplantation Complications

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Abstract

Background: Liver transplant is a definitive cure for end-stage liver disease, but organ shortages demand better patient prioritization methods. Absolute lymphocyte count [ALC] may indicate the outcomes, though its role in early post-transplant results needs further study.
Methods: This retrospective study analyzed medical records of 7-month to 75-year-old patients undergoing primary liver transplants at ILBS, New Delhi, from September 2010 to April 2023, excluding cases lacking ALC results or meeting other criteria.
Results: This study included 581 patients, median age 45 years, predominantly male [476], with ethanol-induced chronic liver disease common. MELD 22.7, ascites [378], encephalopathy [211], and CMV positivity [124]. The low ALC group had higher MELD scores, while ascites [73.7%], encephalopathy [38.7%], and CMV positivity [26.8%] were more common in the adequate ALC group. Within 30 days post-LT, bacterial infections were more common in the adequate ALC group [45% vs. 13%], while rejection was more frequent in the low ALC group [19.6% vs. 7%]. Sepsis from gram-negative bacteria was a major cause of death. Persistent post-transplant lymphopenia [ALC $<500/\mu$L at LT and POD30] was associated with 40 of 62 patients experiencing mortality. Culture-positive infections (84.3% vs. 16.6%) and CMV (34.5% vs. 16.6%) were higher in the complication group.
Conclusion: No effect of low ALC on mortality.

Keywords: Absolute lymphocyte count; Post liver transplant; Model for end stage liver disease; Cytomegalovirus; Live donor liver transplant.

Introduction

Transplant of liver is a permanent and ultimate cure for patients with last stage of liver disease [1]. However, a substantial deficit in organ availability persists alongside a growing pool of transplant hopefuls, underscoring the necessity for discovering new, dependable, and readily accessible methods to pinpoint patients who stand to gain the most from LT [2]. The absolute lymphocyte count [ALC], comprising B-cells, T-cells and natural killer [NK] cells, serves as an indicator of both immunocompetence and nutritional status [3, 4]. Studies have illustrated the significance of low ALC [lymphopenia] as a predictive factor for postoperative results among patients with different malignancies [5, 6, 7, 8]. Additionally, research has indicated that pre-LT lymphopenia is indicative of post-LT infections within the initial 2 years [9]. Yet, investigations into the relationship between ALC and early post-LT outcomes, as well as the impact of pre-transplant or post-transplant ALC trends on early post-LT outcomes, remain incomplete.

We assessed the relation between Pre-LT Lymphopenia with early Post-LT outcomes, repercussion of trends in pre-transplant to post-transplant absolute lymphocyte count [ALC] in patients who underwent living donor liver transplant [LDLT] through the Institute, New Delhi, India.

Materials and Methods

Study Design and Ethical Approval

This retrospective study was undertaken in Department of Pathology, New Delhi over 13 years period from September 2010 to April 2023 and was approved by the institutional review board (#IEC/2024/75-1/MA04).

Patient Selection and Eligibility Criteria

The study included pediatric and adult patients, aged 7 months to 75 years, who underwent their first liver transplantation (LT) during the study period. Patients were eligible for inclusion if they underwent primary LT and had documented absolute lymphocyte count (ALC) results at the time of transplantation. The exclusion criteria were: absence of ALC data at LT, re-transplantation, use of a deceased donor graft, split liver grafts, multi-organ transplantation, or intraoperative death.

Immunosuppressive Management Post-Transplant

All patients were managed with a standardized immunosuppressive regimen comprising tacrolimus, mycophenolate mofetil, and corticosteroids. Tacrolimus was administered with a target trough level of 5 to 10 ng/mL during the first month following LT. Mycophenolate mofetil was initiated at a dose of 500 mg twice daily and continued for one year. Steroids were gradually tapered and discontinued by the end of the third month. This treatment protocol was consistently followed, except in cases where biopsy or clinical evidence indicated acute cellular rejection.

Assessment of Post-Transplant Outcomes Based on ALC

Patients were stratified into two groups based on their ALC measured within one month before LT: the low ALC group ($<500/\mu$L) and the adequate ALC group ($\geq 500/\mu$L) [10]. Given that the effect of lymphopenia is most pronounced within 3 to 6 months after transplantation [10, 11], outcomes were primarily assessed at 7, 15, and 30 days post-transplant. The primary outcome was 30-day post-transplant mortality. Cox regression analysis was used to evaluate the association between ALC and mortality, adjusting for confounding variables including sex, liver disease etiology, MELD score, hepatic encephalopathy, ascites, comorbidities (such as diabetes, hypertension, and hypothyroidism), prognostic nutritional index (PNI), and CMV status before LT.

Evaluation of Early Post-Transplant Complications

In addition to mortality, the study compared the incidence of early complications within 30 days post-LT between the low and adequate ALC groups. Sepsis was diagnosed according to international consensus guidelines [12]. Bile leaks were identified through either contrast leakage observed on cholangiography or the presence of bile in surgical drains. Biliary strictures were defined as narrowing of the bile ducts detected through imaging studies [13]. Only bleeding events and biliary complications graded as 3a or higher on the Clavien-Dindo classification were considered for analysis [14]. Bacteremia was confirmed when blood cultures were positive in the presence of clinical signs of infection; common skin contaminants were considered significant only if detected in at least two cultures with clinical correlation [15]. CMV viremia was defined as any positive result on CMV PCR or pp65 antigen testing [16].

Impact of Declining Pre-Transplant ALC

To assess whether declining ALC before LT affected post-transplant outcomes, patients with an ALC $\geq 500/\mu$L 30 days before transplantation were further divided into two groups: a stable group (ALC remained $\geq 500/\mu$L at LT) and a declining group (ALC decreased to $<500/\mu$L at LT). Thirty-day survival and causes of death were compared between these two groups to evaluate the clinical impact of pre-transplant ALC trends.

Statistical analysis

Continuous variables were shown as median with interquartile range [IQR], and discrete variables as percentages. The Mann-Whitney U test and chi-square test were used to compare continuous and discrete variables, respectively. Survival curves were created using the Kaplan-Meier method and compared with the log-rank test. A Cox proportional hazards

model was used to assess the link between ALC and post-LT mortality, with adjustments for relevant covariates. Statistical significance was set at $P < 0.05$. All analyses were performed using SPSS version 25 [IBM].

Results

Patient characteristics

A total of 581 patients, [range 7 months–75 years], and diagnosed with end-stage liver disease, were included based on meeting the specified inclusion criteria. The mean age of the patients was 45 [34, 52] years. There were 476 males and 105 females seen in the study group. Ethanol was the most common cause for chronic liver disease [CLD]. Among comorbidities, Diabetes mellitus was most commonly seen. MELD score of 22.7 [18, 27] was noted at the time of liver transplant among the patients with CLD. Three seventy eight patients presented with ascites, 212 patients with encephalopathy and 127 patients were found to have CMV positivity. The remaining characteristics were detailed in the Table 1.

Categorization according to Pre-transplant ALC

The Table 2 illustrates the pre-liver transplant characteristics of patients categorized by ALC levels into two groups: low [<500/μL] and adequate [≥500/μL]. The median MELD score [P=0.052] was notably higher in the low ALC group [26 [19.3, 35]] compared to the adequate ALC group [22 [17, 27]]. Ascites was most common in the adequate ALC group [73.7%, $P < 0.001$]. Similarly, encephalopathy was more frequent in this group [38.7%, P=0.021], and CMV was also most prevalent in the adequate ALC group [26.8%, $P < 0.001$].

Post-LT complications within 30 days

The incidence of complications within 30 days post-LT was seen among 249 patients. The median age is slightly lower in the complications group [44 years] compared to the no-complications group [46.5 years], but the difference is statistically significant [p=0.074]. The majority of patients in both groups were male, with no significant difference in gender distribution [p = 0.133]. The distribution of primary diseases was broadly similar across the groups, with no statistically significant variation [p = 0.052], although patients with NASH and cryptogenic cirrhosis appeared slightly more represented in the no-complication group.

Median MELD scores were marginally higher in patients who developed complications [22 vs. 21], but this difference did not reach statistical significance [p = 0.471]. The prevalence of common co-morbidities including diabetes mellitus, hypertension, and hypothyroidism was comparable between groups [p = 0.641]. Hepatic encephalopathy was more frequently observed in patients with complications [44.2% vs. 36.1%], approaching statistical significance [p = 0.050]. Ascites was equally prevalent in both groups [71.5% vs. 71.4%, p = 0.979].

A notable difference was seen in the incidence of infections. Culture-positive infections were significantly more frequent in the complication group [84.3% vs. 16.6%, $p < 0.001$], with Klebsiella pneumoniae emerging as the predominant pathogen [82.4% vs. 25.4%]. Similarly, CMV positivity was significantly higher among patients with complications [34.5% vs. 16.6%, $p < 0.001$].

While a higher proportion of patients in the no-complication group had low ALC at baseline (9.6% vs. 7.3%), a declining ALC trend post-transplant was paradoxically more frequent in the no-complication group (66.4% vs. 33.6%, p = 0.0176). This unexpected trend suggests that baseline lymphopenia, rather than post-transplant decline, may have a stronger association with early complications. Patients who experienced complications had a significantly longer median hospital stay (31 vs. 26 days, $p < 0.001$), indicating increased morbidity.

Among hematological and biochemistry parameters, Higher TLC noted in the complications group [4.5 vs. 4, p=0.030]. Elevated total bilirubin reported in the complications group [6 mg/dL vs. 3.4 mg/dL, p=0.002]. Higher AST levels seen in the complications group [74.7 vs. 65, p=0.027]. Slightly lower creatinine present in the complications group [0.6 vs. 0.7, p=0.005]. No significant differences in hemoglobin, platelet count, ALT, albumin, or INR were noted. The details were shown in Table 3.

Sepsis due to gram-negative bacterial infections identified in blood cultures accounted for a higher proportion of deaths in both the low and adequate ALC groups; however, no statistically significant difference was observed between the two groups [p = 0.462]. Increased 30-day post-LT mortality was seen in the adequate ALC group [86 patients, 18.4%] compared to the low ALC group [10 patients, 8.8%], which was statistically significant [p = 0.041]. Among the 96 patients who experienced 30-day post-LT mortality, 27 [21.1%] were CMV-positive and all belonged to the adequate ALC group, while no CMV-positive deaths occurred in the low ALC group [p = 0.009].

The effect of declining ALC in the month before liver transplant on outcomes after the transplant.

Among the 581 patients, 262 [53.8%] had stable ALC values, while 110 [27.5%] belonged to the declining ALC group. The proportion of patients who died due to sepsis was significantly higher in the declining ALC group [105 patients, 50.2%] compared to the ALC group [97 patients, 46.4%], and this difference was statistically significant [$p = 0.038$]. These findings suggest that a declining trend in ALC prior to liver transplantation may be associated with poorer post-transplant outcomes, particularly an increased risk of sepsis-related mortality.

Survival analysis (Kaplan-Meier method) stratified by absolute lymphocyte count (ALC) groups demonstrated significant differences in 30-day post-transplant mortality. The estimated 30-day survival probability was higher in the low ALC group [0.862; 95% CI: 0.746–0.927] compared to the adequate ALC group [0.795; 95% CI: 0.754–0.831]. Among the 581 patients evaluated, 114 were in the low ALC group with 10 deaths [8.8%], while 467 were in the adequate ALC group with 90 deaths [19.3%]. The overall survival difference between groups was statistically significant as shown by the log-rank test [Chi-square = 5.91, df = 1, $p = 0.015$], (Figure 1). Similarly, when stratified by ALC trend group, patients with a stable ALC trend had a higher 30-day survival probability (90.1%) compared to those with a declining trend (80.6%), with a statistically significant difference in survival distributions ($p = 0.008$), suggesting that a declining ALC trend is associated with poorer 30-day post-transplant survival, (Figure 2).

Multivariate Cox proportional hazards analysis revealed that patients in the adequate ALC group had a significantly higher risk of 30-day mortality compared to those with low ALC [Hazard Ratio = 3.63; 95% CI: 1.61–8.20; $p < 0.001$]. Other significant predictors of increased mortality included female sex [HR = 2.26; $p < 0.001$], hepatic encephalopathy [HR = 2.53; $p < 0.001$], elevated total bilirubin [HR = 1.05; $p < 0.001$], and INR [HR = 1.01; $p < 0.001$]. Conversely, the presence of ascites [HR = 0.43; $p < 0.001$] and higher serum albumin levels [HR = 0.53; $p < 0.001$] were associated with reduced mortality risk. CMV positivity showed a protective effect [HR = 0.23; $p < 0.001$], though all CMV-positive cases occurred in the adequate ALC group, possibly reflecting a confounding relationship, (Table 4).

Table 1: Pre-liver transplant characteristics of patients (n = 581)

Variables	Total no. of Patients [n=581]
Age [Years]	45 [34, 52]
Sex, n [%]	
Male	476 [81.9%]
Female	105 [18.1%]
Primary Disease, n [%]	
Ethanol	215 [37%]
NASH	79 [13.6%]
Cryptogenic	47 [8.1%]
Hepatitis	79 [13.6%]
Others*	131 [22.5%]
Co-morbidities, n [%]	
Diabetes Mellitus	179 [30.7%]
Hypertension	56 [9.6%]
Hypothyroidism	84 [14.4%]
Others**	96 [16.5%]
Ascites, n [%]	378 [65%]
Encephalopathy, n [%]	212 [36.5%]
CMV positive, n [%]	127 [21.9%]
MELD Score	22.7 [18, 27]
Hemoglobin, [g/dl]	9.1 [7.9, 10.8]
TLC, [x10^9/L]	4.3 [2.9, 6.6]
Platelet, [x10^9/L]	61 [34, 106]
Total bilirubin, [mg/dl]	4.4 [2.1, 12.4]
Creatinine, [mg/dl]	0.7 [0.5, 0.9]
AST, [IU/L]	71.6 [48.9, 121.9]
ALT, [IU/L]	38.6 [25, 67.8]
Albumin, [g/dl]	2.9 [2.5, 3.3]
INR	1.9 [1.5, 3.1]

Abbreviations: ALC – Absolute Lymphocyte Count, CLD – Chronic Liver Disease, NASH – Non-Alcoholic Steatohepatitis, HCC – Hepatocellular Carcinoma, MELD – Model for End-Stage Liver Disease, CMV – Cytomegalovirus, TLC – Total Leukocyte Count, AST – Aspartate Aminotransferase, ALT – Alanine Aminotransferase, INR – International Normalized Ratio.

*Others: Hepatocellular carcinoma, autoimmune hepatitis, primary biliary cholangitis, biliary atresia, sclerosing cholangitis, Wilson disease, granulomatous hepatitis, ATT-induced liver disease, post-Kasai, inflow vascular pathology.

**Others: Sarcopenia, pulmonary tuberculosis, coronary artery disease, osteomyelitis, ulcerative colitis, portopulmonary hypertension.

Table 2: Comparison of pre-transplant characteristics between low and adequate ALC groups

Variables	Low ALC [ALC <500; n=114]	Adequate ALC [ALC ≥500; n=467]	p-value
Age [Years]	45 [33.8, 52]	45 [34, 52]	0.93
Sex, n [%]			0.474
Male	96 [84.2%]	379 [81.3%]	
Female	18 [15.8%]	87 [18.7%]	
Primary Disease, n [%]			0.427
Ethanol	45 [44.6%]	170 [37.8%]	
NASH	11 [10.9%]	68 [15.1%]	
Cryptogenic	7 [6.9%]	40 [8.9%]	
Hepatitis	11 [10.9%]	68 [15.1%]	
Others*	27 [26.7%]	104 [23.1%]	
Co-morbidities, n [%]			0.258
Diabetes Mellitus	15 [13.1%]	110 [23.5%]	
Hypertension	4 [3.5%]	11 [2.3%]	
Hypothyroidism	9 [7.9%]	35 [7.5%]	
Others**	5 [4.4%]	39 [8.3%]	
Ascites, n [%]	34 [29.8%]	344 [73.7%]	<0.001
Encephalopathy, n [%]	31 [27.2%]	181 [38.7%]	0.021
CMV positive, n [%]	2 [1.7%]	125 [26.8%]	<0.001
MELD Score at LT	26 [19.3, 35]	22 [17, 27]	0.052
Hemoglobin [g/dl]	9 [8, 10.6]	9.1 [7.8, 10.8]	0.61
TLC [x10^9/L]	5.6 [3.8, 10.7]	4.1 [2.9, 6.1]	<0.001
Platelet [x10^9/L]	84.5 [58, 135]	57 [30, 100]	<0.001
Total bilirubin [mg/dl]	6.1 [2.6, 18]	4.1 [2, 11.8]	0.114
Creatinine [mg/dl]	0.7 [0.5, 0.9]	0.7 [0.5, 0.9]	0.981
AST [IU/L]	74.5 [53, 152.3]	70 [48, 119.6]	0.461
ALT [IU/L]	41 [29, 77.3]	38.1 [24.2, 63.2]	0.343
Albumin [g/dl]	2.8 [2.3, 3.2]	3 [2.6, 3.4]	0.001
INR	2 [1.5, 2.6]	1.9 [1.5, 3.6]	0.254

Abbreviations and footnotes same as Table 1.

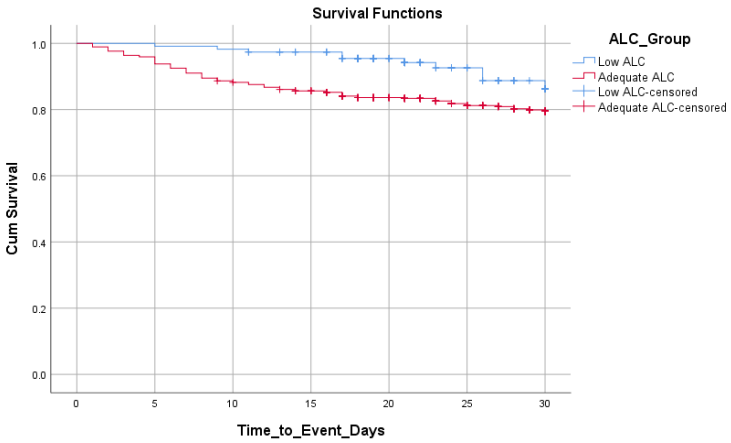

Figure 1: Kaplan–Meier Survival Curve for Low ALC vs. Adequate ALC

Table 3: Post-transplant complications within 30 days of liver transplant

Variables	Complications (n = 249)	No complications (n = 332)	p-value
Age	46 [36, 52]	44 [33, 51]	0.034
Sex, n [%]			0.133
Male	211 [44.4%]	265 [55.8%]	
Female	38 [36.2%]	67 [63.8%]	
Primary Disease, n [%]			0.052
Ethanol	108 [50.2%]	107 [49.8%]	
NASH	28 [35.4%]	51 [64.6%]	
Cryptogenic	15 [31.9%]	32 [68.1%]	
Hepatitis	35 [44.3%]	44 [55.7%]	
Others*	52 [39.7%]	79 [60.3%]	
Co-morbidities, n [%]			0.641
Diabetes Mellitus	58 [55.8%]	74 [54.0%]	
Hypertension	6 [5.8%]	8 [5.8%]	
Hypothyroidism	18 [17.3%]	32 [23.3%]	
Others**	22 [21.1%]	23 [16.8%]	
Culture positive, n [%]			<0.001
Bacterial	47 [25.1%]	140 [74.9%]	
Fungal	3 [15.8%]	16 [84.2%]	
Viral	0 [0%]	9 [100%]	
Bacterial and fungal	11 [26.2%]	31 [73.8%]	
ALC group			<0.001
Low	70 [61.4%]	44 [38.6%]	
Adequate	179 [38.3%]	288 [61.7%]	
Declining	37 [33.6%]	73 [66.4%]	
Stable	90 [34.3%]	172 [65.6%]	0.894
Ascites, n [%]	161 [42.6%]	217 [57.4%]	0.86
Encephalopathy, n [%]	91 [42.9%]	121 [57.1%]	0.98
CMV positive, n [%]	21 [16.5%]	106 [83.5%]	<0.001
MELD	21 [18, 26]	22 [17, 28]	0.471
HB0	9.1 [8, 10.9]	9.1 [7.7, 10.6]	0.368
TLC0	4.3 [2.9, 6.1]	4.3 [2.9, 7.1]	0.471
Platelets0	65 [35.3, 104.8]	59.5 [32, 109.3]	0.343
Totalbilirubin0	3.6 [2.1, 10.2]	5.5 [2.1, 13.9]	0.034
Creatinine0	0.7 [0.5, 0.9]	0.7 [0.5, 0.92]	0.754
AST0	70 [48.6, 117]	72 [49.2, 132]	0.302
ALT0	37 [25, 64]	40 [24.9, 76]	0.294
Albumin0	2.9 [2.5, 3.3]	3 [2.5, 3.3]	0.509
INR0	1.8 [1.5, 2.9]	1.9 [1.5, 3.7]	0.201

Abbreviations and footnotes same as Table 1.

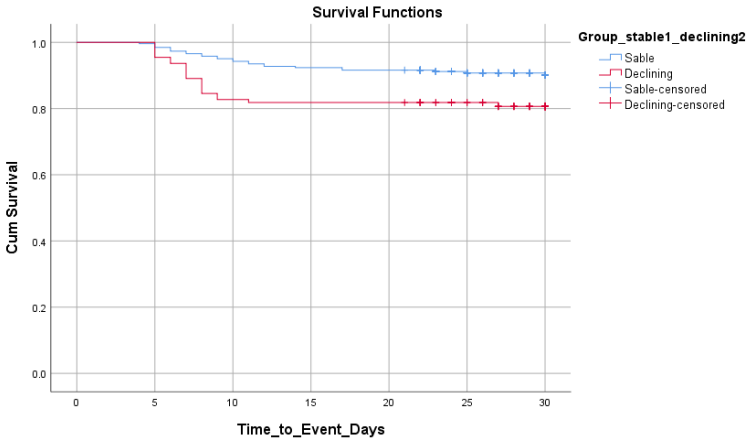

Figure 2: Kaplan–Meier Survival Curve for Stable vs. Declining ALC Trends

Table 4: Multivariable Cox Proportional Hazards Regression Analysis

	Haz. Ratio	$P > z$	**[95% C.I.]**
ALC Group			
Adequate ALC vs Low ALC	3.63	0.00	1.61 – 8.20
Age [Years]	0.99	0.26	0.98 – 1.01
Sex			
Female vs Male	2.26	0.00	1.36 – 3.74
Primary Disease			
NASH vs Ethanol	0.90	0.82	0.36 – 2.26
Cryptogenic vs Ethanol	1.40	0.36	0.68 – 2.85
Hepatitis vs Ethanol	1.29	0.49	0.63 – 2.62
Others* vs Ethanol	1.08	0.81	0.58 – 1.98
Ascites			
Yes vs No	0.43	0.00	0.26 – 0.72
Encephalopathy			
Yes vs No	2.53	0.00	1.59 – 4.02
CMV positive			
Yes vs No	0.23	0.00	0.10 – 0.50
Hemoglobin, [g/dl]	0.95	0.37	0.86 – 1.06
TLC, [x10^9/L]	0.95	0.11	0.90 – 1.01
Total bilirubin, [mg/dl]	1.05	0.00	1.02 – 1.07
AST, [IU/L]	1.00	0.66	1.00 – 1.00
ALT, [IU/L]	1.00	0.19	1.00 – 1.00
Albumin, [g/dl]	0.53	0.00	0.35 – 0.79
INR	1.01	0.00	1.01 – 1.01

Note: Platelet, Creatinine were excluded because of proportional hazard assumption violation.

Discussion

This study investigated the prognostic significance of absolute lymphocyte count (ALC) in predicting 30-day outcomes following living donor liver transplantation (LDLT). Contrary to conventional expectations, patients with low ALC levels ($<$500/μL) at the time of transplant did not exhibit worse 30-day survival. In fact, the survival probability was numerically higher in the low ALC group [86.2%] compared to the adequate ALC group [79.5%], and this difference was statistically significant [log-rank $p = 0.015$]. Furthermore, multivariate Cox regression analysis identified adequate ALC as an independent predictor of increased 30-day mortality [HR = 3.63, 95% CI: 1.61–8.20, $p < 0.001$], while low ALC was not associated with poorer outcomes. These findings challenge the assumption that lymphopenia reflects an immunocompromised state with poor prognosis.

Similarly, when stratified by ALC trend group, patients with a stable ALC trend had a higher 30-day survival probability (90.1%) compared to those with a declining trend (80.6%), with a statistically significant difference in survival distributions (p = 0.008), suggesting that a declining ALC trend is associated with poorer 30-day post-transplant survival. However, among patients who died due to sepsis, a higher proportion belonged to the stable ALC group (30.7%) compared to the declining group (25%), indicating that a declining ALC trend prior to transplant may not necessarily reflect increased vulnerability to sepsis-related mortality in the early post-transplant period.

Despite the adequate ALC group's presumed immunocompetence, a paradoxically higher rate of post-LT bacterial sepsis and CMV positivity was observed. Among the 96 patients who died within 30 days, 27 (21.1%) were CMV-positive—all in the adequate ALC group. Blood culture–positive gram-negative bacterial sepsis was a leading cause of early post-LT mortality in both ALC groups, but no statistically significant difference was found between them in this respect [p = 0.462].

We also analyzed ALC trajectories in the month preceding LT and observed that patients with declining ALC had significantly higher rates of complications and sepsis-related mortality. The declining ALC group showed higher mortality from sepsis [50.2%] compared to those with stable ALC [46.4%, p = 0.038]. This suggests that downward trends in lymphocyte count may serve as early markers of immune exhaustion or disease progression. In contrast, changes in ALC levels before LT were not associated with 30-day mortality, and persistent low ALC (at LT and POD 30) was more strongly associated with mortality than low ALC at a single time point.

Infectious complications and prolonged hospital stays were significantly more common in the complications group. Additionally, elevated bilirubin, total leukocyte count (TLC), and AST levels were more frequently observed in patients who developed complications. CMV positivity and culture-proven bacterial infections were also markedly higher in the complication group, underlining the role of infections in early post-transplant morbidity. Notably, the proportion of patients with low ALC was slightly higher in the complication group, indicating that low ALC alone may be a reliable predictor

of complications. However, declining ALC in the pre-transplant period was more prevalent in the complication group, suggesting that it may be a more sensitive marker for identifying at-risk patients.

Our univariable analysis revealed no significant association between low pre-transplant ALC and clinical features such as hepatic encephalopathy, ascites, or prolonged hospitalization before LT, except for a significant association with higher MELD scores. Previous studies have shown that advanced cirrhosis impairs lymphocyte function due to chronic inflammation, endotoxemia, or malnutrition [9, 10]. Fernandez-Ruiz et al. [11] and Kitajima et al. [12] previously reported that pre-LT ALC predicts post-transplant infections; however, our findings diverge, showing that mortality due to sepsis was similar in both ALC groups but more common in those with declining or persistently low ALC.

Persistent post-transplant lymphopenia, defined as ALC $<500/\mu$L at both LT and POD 30, was strongly associated with 30-day mortality. Among 62 patients with persistent lymphopenia, 40 experienced early mortality, emphasizing its potential as a robust surrogate marker for adverse post-LT outcomes.

Limitations

This study has several limitations. Firstly, the retrospective, single-center design may introduce selection bias and limit the external validity of our findings. Secondly, ALC levels are influenced by various dynamic factors including systemic inflammation, active infections, immunosuppressive therapy, nutritional status, and liver function, which were not fully accounted for due to incomplete longitudinal data. Additionally, the observed paradoxical association between higher ALC and increased mortality may reflect unmeasured confounding variables such as subclinical infections, early immune activation, or differing immunosuppression regimens. Finally, the exclusion of certain parameters from the Cox model (e.g., platelet count, creatinine) due to proportional hazards violations may have limited the comprehensiveness of our multivariable analysis.

Conclusion

Our study demonstrates that absolute lymphocyte count at the time of LDLT is not a straightforward predictor of early post-transplant mortality. Surprisingly, patients with adequate ALC ($\geq 500/\mu$L) had worse 30-day survival and higher rates of sepsis and CMV positivity compared to those with low ALC. Declining ALC in the month preceding LT and persistent post-transplant lymphopenia were associated with increased risk of sepsis and early mortality, indicating their potential utility as dynamic prognostic markers. These findings highlight the importance of longitudinal ALC monitoring over static thresholds, and the need for early infection control strategies in patients with declining or persistently low lymphocyte counts. Future prospective studies are warranted to further clarify the immunologic mechanisms and refine risk stratification models in LDLT recipients.

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