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Evaluation of factors associated with mortality after major lower extremity amputation: implications for intensive care

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ABSTRACT

Aims: Amputations performed proximal to the ankle level are defined as major lower extremity amputation (MLEA) and are associated with high postoperative mortality. This study aimed to evaluate the clinical characteristics, laboratory findings, and postoperative complications associated with 30-day and six-month mortality in patients undergoing MLEA for different etiologies.

Methods: The electronic medical records of 419 patients aged 18 years or older who underwent surgery for MLEA between November 2022 and November 2025 were retrospectively analyzed. Patients' demographic data, American Society of Anesthesiologists (ASA) physical status classification, comorbidities, laboratory parameters, length of hospital stay, and 30-day and six-month mortality data were recorded. For the 30-day and six-month analyses, patients were grouped separately by survival status at the end of each follow-up period.

Results: Data from 419 patients were analyzed. Thirty-day mortality occurred in 54 patients (12.9%), and 6-month mortality occurred in 109 patients (26.0%). In the multivariable analysis, postoperative pulmonary complications (adjusted OR, 3.16; 95% CI, 1.77-5.64; p<0.001), older age (adjusted OR, 1.05; 95% CI, 1.03-1.07; p<0.001), higher preoperative creatinine levels (adjusted OR, 1.21; 95% CI, 1.04-1.40; p=0.013), and higher C-reactive protein-to-albumin ratio (CAR) (adjusted OR, 1.08; 95% CI, 1.02-1.14; p=0.005) were independently associated with 6-month mortality. Older age (adjusted OR, 1.030; 95% CI, 1.005-1.056; p=0.019), postoperative pulmonary complications (adjusted OR, 3.993; 95% CI, 2.042-7.806; p<0.001), and higher CAR (adjusted OR, 1.097; 95% CI, 1.030-1.169; p=0.004) were independently associated with 30-day mortality.

Conclusion: Advanced age, elevated preoperative CAR, and postoperative pulmonary complications were independently associated with both early- and intermediate-term mortality after MLEA.

Keywords: Amputation; surgical, lower extremity, mortality

INTRODUCTION

Major lower extremity amputation (MLEA) refers to amputation performed above the level of the ankle.[1] It is often required as a life-preserving procedure in patients with severe limb trauma, peripheral arterial disease, or advanced diabetes-related complications.[2] Despite improvements in vascular treatment, perioperative care, and risk assessment, mortality and morbidity following MLEA remain substantial.[3] A clearer understanding of the factors related to mortality may therefore help improve perioperative assessment and clinical management in this high-risk population.

Outcomes after MLEA are associated with several interacting clinical and perioperative factors. Advanced age, coexisting diseases, impaired renal function, systemic inflammation, poor nutritional status, and postoperative complications have all been linked to adverse outcomes.[4] The C-reactive protein-to-albumin ratio (CAR) combines two routinely measured laboratory parameters and may provide a practical estimate of inflammatory activity and nutritional reserve.[5] Pulmonary complications are also clinically relevant after MLEA, as they may prolong recovery and contribute to poorer survival.[6]

Most previous studies have focused on patients undergoing amputation for a single indication, most often diabetes or peripheral arterial disease, or have examined mortality at a single time point.[3,7,8] Evidence addressing early and six-month mortality within the same cohort, while considering clinical characteristics, laboratory findings, and postoperative complications together, remains limited. The present study therefore investigated the factors associated with 30-day and six-month mortality among patients undergoing MLEA for various indications.

METHODS

Ethics

This study was conducted with the approval of the No. 2 Scientific Researches Evaluation and Ethics Committee of

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Ankara Etlik City Hospital (Date: 30.06.2026, Decision No: AESH-BADEK2-2026-531). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The requirement for informed consent was waived by the ethics committee because of the retrospective design of the study. The study population was identified by reviewing the electronic records of adult patients who underwent MLEA at a tertiary referral hospital between November 2022 and November 2025.

Patients were eligible if they were 18 years of age or older and underwent their first MLEA during the study period. Cases with incomplete data for the planned analyses or insufficient information in the medical records were excluded. Repeated entries for the same patient were identified and removed. Demographic and clinical data collected from the records included age, gender, American Society of Anesthesiologists (ASA) physical status, comorbidities, anesthesia technique, use of a peripheral nerve block, level of amputation, and indication for surgery.

Laboratory measurements obtained at the initial hospital admission were used in the analyses. The recorded variables were complete blood count parameters, creatinine, urea, albumin, C-reactive protein (CRP), glucose, calcium, sodium, potassium, international normalized ratio (INR), aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct bilirubin, and red cell distribution width. The CRP-to-albumin ratio (CAR) was calculated by dividing CRP expressed in mg/L by albumin expressed in g/L.

Complications occurring during the postoperative hospital stay were grouped as pulmonary complications, sepsis, or other complications. Pneumonia, atelectasis, and pulmonary thromboembolism were categorized as pulmonary complications. The sepsis category included cases of sepsis secondary to nonpulmonary infections. Cardiac events, bleeding, electrolyte disturbances, and delirium were included under other complications. When a patient experienced more than one complication, each event was entered separately. Intensive care unit admission, duration of intensive care unit stay, and total hospital length of stay were also documented.

Vital status and date of death were determined from hospital records and the national registry system. Survival time was measured from the date of amputation to the date of death. Death from any cause within 30 days of surgery was considered early mortality, and death within 180 days was considered six-month mortality. For the 30-day analysis, patients who died during the first 30 days were compared with those who remained alive at day 30. The same approach was used for the six-month analysis, with patients classified according to their vital status at 180 days. Follow-up data for at least 180 days were available for every patient included in the study.

The primary outcome was all-cause mortality within six months after MLEA. Thirty-day all-cause mortality was evaluated as the secondary outcome. Clinical characteristics, laboratory findings, and postoperative events associated with each mortality endpoint were subsequently examined using regression analyses.

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro-Wilk test. Variables with a normal distribution were expressed as mean±standard deviation (SD) and compared using the independent samples t-test. Non-normally distributed variables were presented as median (interquartile range [IQR]) and compared using the Mann-Whitney U test. Categorical variables were reported as frequencies and percentages and compared using the Pearson Chi-square test or Fisher's exact test, as appropriate. Factors associated with 30-day and 6-month mortality were examined using univariate and multivariable logistic regression analysis. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. The performance of the final multivariable model for 6-month mortality was assessed by receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated. All statistical analyses were performed using IBM SPSS Statistics for Windows (Version 22.0; IBM Corp., Armonk, NY, USA), and a two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 419 patients who met the inclusion criteria during the study period were included in the final analysis. The mean age of the study population was 66.1±15.7 years, 66.1% were male, and 58.7% were classified as ASA physical status III-IV. At least one comorbidity was present in 87.1% of the patients. The most common comorbidities were diabetes mellitus (74.5%), hypertension (48.2%), and coronary artery disease (32.7%). Below-knee amputation was performed in 82.6% of the patients, whereas 17.4% underwent above-knee amputation. The most common indication for amputation was diabetes mellitus-related disease (n=250, 59.7%), followed by peripheral arterial disease/ischemia (n=104, 24.8%) and trauma (n=53, 12.6%). Postoperative complications occurred in 104 patients (24.8%), with pulmonary complications being the most frequent (n=72, 17.2%). Thirty-day mortality was observed in 54 patients (12.9%), whereas 6-month mortality was observed in 109 patients (26.0%). Detailed demographic, clinical, and laboratory characteristics of the study population are presented in **Table 1**.

Patients who died within 6 months (non-survivors) were older than survivors and were more likely to have ASA physical status III-IV (both p<0.001). The presence of at least one comorbidity was also more common among non-survivors than survivors (92.7% vs. 85.2%, p=0.044). In the preoperative laboratory evaluation, non-survivors had higher CAR [4.88 (7.38) vs. 3.47 (5.71); p=0.007] and creatinine levels [1.40 (1.64) vs. 1.01 (0.70); p=0.005]. Postoperative complications occurred more frequently in non-survivors than in survivors (37.6% vs. 20.3%, p<0.001), with pulmonary complications being more common among non-survivors (31.2% vs. 12.3%). Overall, 95.4% of non-survivors had been admitted to the intensive care unit, and both ICU and hospital lengths of stay were significantly longer in this group (both p<0.05). In addition, non-survivors had lower calcium, albumin, hemoglobin, platelet, lymphocyte, monocyte, and

Table 1. Demographic and clinical characteristics of the study population

Variable	Overall (n=419)
Age, years	66.1±15.7
Gender, n (%)	
Male/female	277 (66.1)/142 (33.9)
ASA physical status, n (%)	
I-II	173 (41.3)
III-IV	246 (58.7)
Indication for amputation, n (%)	
Diabetic foot infection	250 (59.7)
Peripheral arterial disease/ischemia	104 (24.8)
Trauma	53 (12.6)
Other (pyoderma gangrenosum, burn, vasculitis, malignancy, non-diabetic infection)	12 (2.8)
Amputation level, n (%)	
Below-knee amputation	346 (82.6)
Above-knee amputation	73 (17.4)
Type of anesthesia, n (%)	
Spinal anesthesia	175 (41.8)
General anesthesia	244 (58.2)
Peripheral nerve block, n (%)	69 (16.5)
Comorbidities, n (%)	365 (87.1)
Diabetes mellitus	312 (74.5)
Hypertension	202 (48.2)
Coronary artery disease	137 (32.7)
Peripheral artery disease	93 (22.2)
Chronic kidney disease	72 (17.2)
Cerebrovascular disease	40 (9.5)
Chronic obstructive pulmonary disease	34 (8.1)
Heart failure	29 (6.9)
Hyperlipidemia	25 (6.0)
Arrhythmia	21 (5.0)
Cancer	17 (4.1)
Dementia	12 (2.9)
Thyroid disease	10 (2.4)
Parkinson disease	3 (0.7)
Epilepsy	3 (0.7)
Rheumatoid arthritis	2 (0.5)
Cirrhosis	1 (0.2)
Postoperative complications, n (%)	104 (24.8)
Pulmonary complications	72 (17.2)
Sepsis	21 (5.0)
Other (cardiac complications, hemorrhage, delirium)	11 (2.6)
ICU admission, n (%)	326 (77.8)
Length of hospital stay, days	12 (19)
Length of ICU stay, days	3 (7)
30-day mortality, n (%)	54 (12.9)
6-month mortality, n (%)	109 (26.0)
Calcium, mg/dl	8.44±0.90
Sodium, mmol/L	135.6±5.3
Potassium, mmol/L	4.50±0.76
Albumin, g/L	30.4±6.85
Hemoglobin, g/dl	10.65±2.36
Hematocrit, %	33.61±7.0
Platelet count, $\times10^9$/L	349±140
CRP, mg/L	111 (155.4)
Glucose, mg/dl	156 (123)
Serum creatinine, mg/dl	1.05 (0.98)
Urea, mg/dl	49.3 (44.9)
AST, U/L	19 (21)
ALT, U/L	15 (17)
Total bilirubin, mg/dl	0.42 (0.34)
Direct bilirubin, mg/dl	0.19 (0.18)
INR	1.09 (0.17)
WBC, $\times10^9$/L	12.9 (9.4)
Neutrophil count, $\times10^9$/L	10.1 (9.35)
Lymphocyte count, $\times10^9$/L	1.44 (1.0)
Monocyte count, $\times10^9$/L	0.83 (0.52)
RDW-CV, %	14.8 (3.0)
CAR	3.80 (1.40-7.37)

Data are presented as mean±standard deviation (SD), median (interquartile range [IQR]), or number (percentage), as appropriate. ASA: American Society of Anesthesiologists, ICU: Intensive care unit, CRP: C-reactive protein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, INR: International normalized ratio, WBC: White blood cell count, RDW-CV: Red cell distribution width-coefficient of variation, CAR: C-reactive protein-to-albumin ratio, SD: Standard deviation, IQR: Interquartile range

hematocrit levels, whereas INR, RDW, urea, total bilirubin, and direct bilirubin levels were higher (all p<0.05) (**Table 2**).

In the univariate logistic regression analysis, older age, female gender, ASA physical status III–IV, lower calcium, albumin, hemoglobin, and platelet levels, higher CAR, RDW-CV, INR, urea, serum creatinine, total bilirubin, and direct bilirubin levels, and the presence of cerebrovascular disease were significantly associated with 6-month mortality (**Table 3**).

Multivariable logistic regression analysis identified pulmonary complications (adjusted OR, 3.16; 95% CI, 1.77-5.64; p<0.001), older age (adjusted OR, 1.05; 95% CI, 1.03-1.07; p<0.001), higher preoperative creatinine levels (adjusted OR, 1.21; 95% CI, 1.04-1.40; p=0.013), and higher CAR (adjusted OR, 1.08; 95% CI, 1.02-1.14; p=0.005) were independently associated with 6-month mortality (**Table 4**). The area under the receiver operating characteristic curve (AUC) for the multivariable model was 0.738 (95% CI, 0.684-0.792; p<0.001).

To identify factors associated with short-term (30-day) mortality, logistic regression analyses were performed. Older age (adjusted OR, 1.030; 95% CI, 1.005-1.056; p=0.019), pulmonary complications (OR, 3.993; 95% CI, 2.042-7.806; p<0.001), and higher CAR (OR, 1.097; 95% CI, 1.030-1.169; p=0.004) were identified as independent factors in the multivariable analysis. Although ASA physical status III-IV and hematocrit were significantly associated with 30-day mortality in the univariate analysis, they did not retain statistical significance in the multivariable model (**Table 5**).

DISCUSSION

In this retrospective cohort, 30-day and six-month mortality after MLEA were 12.9% and 26.0%, respectively. Multivariable analysis showed that older age, postoperative pulmonary complications, and higher CAR values were independently associated with mortality at both follow-up points. Higher

Table 2. Comparison of demographic and clinical characteristics according to 6-month mortality

Variable	Survivors (n=310)	Non-survivors (n=109)	p[a]
Age, years	64.1±15.7	72.9±13.8	<0.001*
ASA physical status, n (%)			
I-II	144 (46.5)	29 (26.6)	
III-IV	166 (53.5)	80 (73.4)	<0.001
Gender, n (%)			
Male	214 (69)	63 (57.8)	
Female	96 (31)	46 (42.2)	0.035
Peripheral nerve block, n (%)	50 (16.1)	19 (17.4)	0.765
Type of anesthesia, n (%)			
Spinal anesthesia	127 (41)	48 (44)	
General anesthesia	183 (59)	61 (56)	0.575
Comorbidities, n (%)	264 (85.2)	101 (92.7)	0.044
Diabetes mellitus	229 (73.9)	83 (76.1)	0.639
Hypertension	142 (45.8)	60 (55)	0.097
Coronary artery disease	96 (31)	41 (37.6)	0.203
Peripheral artery disease	66 (21.3)	27 (24.8)	0.452
Chronic kidney disease	45 (14.5)	27 (24.8)	0.015
COPD	24 (7.7)	10 (9.2)	0.638
Cerebrovascular disease	23 (7.4)	17 (15.6)	0.012
Heart failure	19 (6.1)	10 (9.2)	0.281
Hyperlipidemia	18 (5.8)	7 (6.4)	0.815
Arrhythmia	12 (3.9)	9 (8.3)	0.071
Cancer	12 (3.9)	5 (4.6)	0.779
Dementia	7 (2.3)	5 (4.6)	0.313
Thyroid disease	3 (1)	7 (6.4)	0.004
Rheumatoid arthritis	2 (0.6)	0	1.000
Parkinson disease	2 (0.6)	1 (0.9)	1.000
Epilepsy	3 (1)	0	0.571
Cirrhosis	0	1 (0.9)	0.260
Amputation level, n (%)			
Below-knee amputation	261 (84.2)	85 (78)	
Above-knee amputation	49 (15.8)	24 (22)	0.094
Indication for amputation, n (%)			
Diabetic foot infection	184 (59.4)	66 (60.6)	
Peripheral arterial disease/ischemia	72 (23.2)	32 (29.4)	
Trauma	46 (14.8)	7 (6.4)	0.107
Other (pyoderma gangrenosum, burn, vasculitis, malignancy, non-diabetic infection)	8 (2.6)	4 (3.7)	
Postoperative complications, n (%)	63 (20.3)	41 (37.6)	
Pulmonary complications	38 (12.3)	34 (31.2)	
Sepsis	18 (5.8)	3 (2.8)	<0.001
Other (cardiac complications, hemorrhage, delirium)	7 (2.3)	4 (3.7)	
ICU admission, n (%)	222 (71.6)	104 (95.4)	<0.001
Calcium, mg/dl	8.52±0.88	8.23±0.90	0.003*
Sodium, mmol/L	135.6±5.0	135.9±6.2	0.644*
Potassium, mmol/L	4.51±0.74	4.44±0.82	0.447*
Albumin, g/L	31.38±6.71	27.62±6.45	<0.001*
Hemoglobin, g/dl	10.87±2.36	10.02±2.23	0.001*
Hematocrit, %	34.25±6.87	31.81±7.04	0.002*
Platelet count, ×10^9/L	356.5±137.3	325.8±146.0	0.048*
CRP, mg/L	108.8 (152.74)	126.0 (155.87)	0.069**
CAR	3.47 (5.71)	4.88 (7.38)	0.007**
Glucose, mg/dl	153 (127.5)	160 (101.0)	0.339**
Serum creatinine, mg/dl	1.01 (0.70)	1.40 (1.64)	0.005**
Urea, mg/dl	44.4 (40.70)	60.9 (63.10)	<0.001**
AST, U/L	19.0 (20.25)	20 (23.00)	0.915**
ALT, U/L	15 (16.50)	14 (16.00)	0.134**
Total bilirubin, mg/dl	0.40 (0.33)	0.45 (0.41)	0.031**
Direct bilirubin, mg/dl	0.18 (0.17)	0.21 (0.24)	0.035**
INR	1.08 (0.15)	1.14 (0.23)	<0.001**
WBC, ×10^9/L	13.19 (8.79)	12.54 (12.57)	0.784**
Neutrophil count, ×10^9/L	10.04 (8.80)	10.15 (13.09)	0.407**
Lymphocyte count, ×10^9/L	1.59 (1.08)	1.19 (0.85)	<0.001**
Monocyte count, ×10^9/L	0.85 (0.56)	0.74 (0.49)	0.008**
RDW-CV, %	14.6 (2.85)	15.3 (3.10)	0.006**
Length of ICU stay, days	2 (5)	6 (14)	<0.001**
Length of hospital stay, days	11 (18)	18 (24)	0.002**

Data are presented as mean±standard deviation (SD), median (interquartile range [IQR]), or number (percentage), as appropriate. ASA: American Society of Anesthesiologists, COPD: chronic obstructive pulmonary disease, ICU: intensive care unit, CRP: C-reactive protein, CAR: C-reactive protein-to-albumin ratio, AST: aspartate aminotransferase, ALT: alanine aminotransferase, INR: international normalized ratio, WBC: white blood cell count, RDW-CV: red cell distribution width-coefficient of variation, SD: Standard deviation, IQR: Interquartile range, a: Chi-square test or Fisher's exact test, as appropriate, *: independent samples t-test; **: Mann-Whitney U test; Statistically significant p-values (p<0.05) are shown in bold.

Table 3. Univariate logistic regression analysis of factors associated with 6-month mortality

Variable	OR (95% CI)	p-value
Age	1.044 (1.026-1.062)	<0.001
Gender (male vs female)	0.614 (0.392-0.963)	0.034
ASA physical status III-IV	2.39 (1.48-3.86)	<0.001
Cerebrovascular disease (no vs. yes)	0.434 (0.222-0.847)	0.014
Calcium	0.685 (0.532-0.883)	0.003
Albumin	0.918 (0.887-0.951)	<0.001
CAR	1.064 (1.015-1.115)	0.009
Hemoglobin	0.849 (0.767-0.939)	0.001
Platelet count (×10^9/L)	0.998 (0.997-1.000)	0.049
RDW-CV	1.125 (1.040-1.216)	0.003
INR	8.451 (2.696-26.490)	<0.001
Urea	1.009 (1.005-1.014)	<0.001
Serum creatinine	1.240 (1.080-1.424)	0.002
Total bilirubin	1.801 (1.124-2.884)	0.014
Direct bilirubin	1.899 (1.086-3.318)	0.024
Pulmonary complications (yes vs no)	3.245 (1.912-5.508)	<0.001

Statistically significant p-values (p <0.05) are shown in bold. OR: odds ratio, CI: confidence interval, ASA: American Society of Anesthesiologists, CAR: C-reactive protein-to-albumin ratio, RDW-CV: Red cell distribution width-coefficient of variation, INR: International normalized ratio

preoperative creatinine was additionally associated with six-month mortality, whereas no independent association was observed for 30-day mortality.

During the six-month follow-up period, approximately one-quarter of the patients died, and approximately half of these deaths occurred within the first 30 days. This finding indicates

Table 4. Multivariable logistic regression analysis of factors associated with 6-month mortality

Variable	Adjusted OR (95% CI)	p-value
Age	1.05 (1.03-1.07)	<0.001
Pulmonary complications (yes vs no)	3.16 (1.77-5.64)	<0.001
Serum creatinine	1.21 (1.04-1.40)	0.013
CAR	1.08 (1.02-1.14)	0.005

Only variables retained in the final multivariable logistic regression model are presented. OR: Odds ratio, CI: confidence interval, CAR: C-reactive protein-to-albumin ratio

that mortality was concentrated in the early postoperative period, but that deaths continued in the following months. Similarly, Morton et al.[4] reported a six-month mortality rate of 25% after MLEA, comparable to that observed in our study. The higher rate of 32.4% reported by Reisoğlu et al.[8] may be explained, at least in part, by the inclusion of patients undergoing amputation exclusively because of diabetes mellitus or peripheral arterial disease. Early mortality rates reported in previous studies range from 4% to 28%.[9-11] Differences in amputation level and indication, patient age, comorbidity profile, study population, geographical setting, and perioperative care may contribute to this wide variation. Therefore, when interpreting mortality rates after MLEA, the region in which the study was conducted and the demographic and clinical characteristics of the patients should be considered together.

In our study, advanced age was independently associated with both 30-day and six-month mortality. For each additional year of age, the odds of 30-day mortality increased by approximately 3%, while the odds of six-month mortality increased by approximately 5%. This association may be explained by frailty and the age-related loss of organ reserve. Frailty reflects a diminished ability to re-establish homeostasis after an acute physiological insult. In older patients, the surgical and metabolic burden of MLEA may therefore exceed the capacity of already compromised organ systems, increasing vulnerability to postoperative complications.[12,13] This vulnerability was particularly relevant in our cohort, in which 87.1% of patients had at least one comorbidity, most commonly diabetes mellitus, hypertension, coronary artery disease, or peripheral arterial disease. These conditions frequently coexist with endothelial dysfunction, chronic inflammation, oxidative stress, and widespread atherosclerosis. Consequently, vascular impairment may extend beyond the affected limb to the coronary, cerebral, and renal circulations, further limiting the ability to tolerate perioperative stress.[14] Age-related deterioration in endothelial function, microcirculation, angiogenesis, immune regulation, and cellular repair may also interfere with stump healing and predispose patients to wound infection, tissue necrosis, and repeat intervention.[15] Rehabilitation may be further restricted by the greater energy expenditure required after amputation, particularly in older patients with limited cardiopulmonary reserve.[16] These age-related physiological and clinical disadvantages may account for the higher mortality observed in older patients after MLEA.

CAR is considered to reflect systemic inflammation and nutritional status together. CRP is an indicator of systemic inflammation, whereas albumin is one of the indicators of nutritional status and the physiological impact of disease.[5,17,18] Therefore, a high CAR may indicate the coexistence of increased inflammatory activity and inadequate nutritional status and may be associated with reduced tolerance to surgical stress. Our findings are consistent with previous studies linking higher CAR values to adverse outcomes in patients with peripheral arterial disease and in those undergoing major amputation for diabetic foot disease.[5,17-19] The presence of this association for both 30-day and six-month mortality suggests that CAR may reflect the impact of inflammatory and nutritional status at admission on short- and intermediate-term prognosis. Among the preoperative laboratory findings, elevated creatinine levels were also associated with mortality; however, unlike CAR, this association was observed only for six-month mortality. Aulivola et al.[20] similarly reported markedly poorer survival among patients with serum creatinine concentrations above 2 mg/dl, including those without end-stage renal disease. Renal dysfunction commonly accompanies systemic vascular disease and may adversely affect prognosis through anemia-related impairment of tissue oxygen delivery, immune dysfunction, and greater susceptibility to infection.[21,22] Elevated creatinine may therefore reflect both reduced renal reserve and a broader burden of systemic disease. Its association with six-month mortality supports the inclusion of renal function in preoperative risk assessment and may help identify patients who require closer follow-up after amputation.

Postoperative pulmonary complications were strongly associated with mortality in our cohort. Patients who developed a pulmonary complication had nearly fourfold higher odds of 30-day mortality, and almost half died within six months. Brix et al.[6] likewise identified pneumonia as an important complication contributing to mortality after MLEA. Similar findings have been reported in other surgical populations. Canet et al.[23] found that postoperative pulmonary complications were independently related to prolonged hospitalization and higher mortality, while Piccioni et al.[24] demonstrated a significant association between pulmonary complications and death after major abdominal

Table 5. Univariate and multivariable logistic regression analyses of factors associated with 30-day mortality

Variable	Univariate OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	1.025 (1.004-1.046)	0.017	1.030 (1.005-1.056)	0.019
ASA physical status III-IV	2.205 (1.160-4.194)	0.016	1.514 (0.726-3.156)	0.269
Pulmonary complications (yes vs no)	4.392 (2.308-8.357)	<0.001	3.993 (2.042-7.806)	<0.001
CAR	1.096 (1.036-1.159)	0.001	1.097 (1.030-1.169)	0.004
Hematocrit	0.952 (0.911-0.994)	0.024	0.965 (0.921-1.012)	0.144

Statistically significant p-values (p <0.05) are shown in bold. OR: Odds ratio, CI: Confidence interval, ASA: American Society of Anesthesiologists, CAR: C-reactive protein-to-albumin ratio

surgery. Several factors may predispose patients undergoing MLEA to respiratory complications. Severe postoperative pain, opioid-related respiratory depression, prolonged immobilization, and delayed mobilization can impair deep breathing and coughing, promote secretion retention, and increase the risk of atelectasis.[25,26] The consequences may be particularly severe in older or frail patients and in those with limited cardiopulmonary reserve. Once a pulmonary complication develops, hypoxemia, increased respiratory workload, infection, and systemic inflammation may further compromise pre-existing cardiac or renal dysfunction.[24-26] Therefore, the prevention, early recognition, and appropriate treatment of pulmonary complications in patients undergoing MLEA are important for prognosis.

Limitations

This study has several limitations. First, owing to its retrospective design, it was not possible to evaluate all potential confounding variables, and the observed associations could not be interpreted within a causal framework. Some clinical variables that may affect prognosis, such as smoking and alcohol use, body-mass index, frailty level, preoperative mobility, and physical performance, could not be included in the analysis because they were not routinely documented in patient records. Similarly, the limited availability of data on prosthesis use, ambulatory status after amputation, and living conditions prevented a more comprehensive evaluation of long-term outcomes. The inability to determine the exact causes of death limited the detailed investigation of the mechanisms underlying mortality. In addition, the single-center design provided some standardization of perioperative practice but may limit the generalizability of the findings to other centers and patient populations.

CONCLUSION

As a result, advanced age, elevated preoperative CAR, and the development of postoperative pulmonary complications were independently associated with early- and intermediate-term mortality after MLEA. The combined evaluation of these variables may assist in perioperative risk stratification after MLEA.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the No. 2 Scientific Researches Evaluation and Ethics Committee of Ankara Etlik City Hospital (Date: 30.06.2026, Decision No: AESH-BADEK2-2026-531).

Informed Consent

The requirement for written informed consent was waived by the ethics committee because of the retrospective design and the use of anonymized data. No additional intervention was performed, and there was no direct patient contact.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: FA; Design: FA; Control: FÖS; Resources: FA, FÖS; Materials: FA, FÖS; Data Collection and/or Processing: FA, FÖS; Analysis and/or Interpretation: FA, FÖS; Literature Review: FA; Article Writing: FA, FÖS; Critical Review: FÖS.

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