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Haemoglobin and albumin as predictors of survival in patients undergoing major amputation

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ABSTRACT

INTRODUCTION: Major lower limb amputation is often the last resort procedure for patients with advanced peripheral artery disease and is associated with substantial mortality. Preoperative biomarkers such as haemoglobin and albumin may provide valuable prognostic information by reflecting oxygen-carrying capacity, nutritional status and systemic inflammation. This study aimed to evaluate the association between preoperative haemoglobin and albumin levels and survival among patients undergoing major lower-limb amputation.

METHODS: A retrospective single-centre study was conducted, including all patients who underwent major lower limb amputation between June 2016 and December 2023 at a tertiary vascular surgery centre. Preoperative haemoglobin and albumin levels were collected from medical records. Patients were stratified according to survival status during follow-up. Independent samples t-tests were used to compare mean values between groups. Cox proportional hazards regression was performed to identify independent predictors of mortality, adjusting for relevant comorbidities.

RESULTS: A total of 585 patients were included (mean age 72 ± 12 years; 66% male), with 61% of patients undergoing transfemoral amputation. During follow-up, 66 patients (11.3%) died. Mean preoperative haemoglobin and albumin levels were significantly higher among survivors (haemoglobin: 10.46 vs 10.06 g/dL, p = 0.015; albumin: 3.25 vs 2.94 g/dL, p = 0.019). In multivariable Cox regression analysis, cerebrovascular disease (HR 1.50; p = 0.003), congestive heart failure (HR 1.53; p = 0.007), atrial fibrillation (HR 1.49; p = 0.008), and haemoglobin (HR 0.93 per g/dL; p = 0.048) were independently associated with mortality. As albumin levels were available for only 99 patients, albumin was analysed separately and showed a strong association with improved survival in univariable analysis. (HR 0.488; p = 0.001).

CONCLUSION: Preoperative haemoglobin is an independent predictor of survival following major lower limb amputation, underscoring the importance of preoperative optimisation and risk stratification. Although albumin demonstrated a significant protective association in univariate analysis, further multivariable validation is required. Incorporating these biomarkers into perioperative assessment protocols may improve the identification of high-risk patients and guide targeted interventions.

Keywords: Amputation; Preoperative; Mortality; Haemoglobin; Albumin

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INTRODUCTION

Major amputation is generally considered a procedure of last resort for patients with severe peripheral artery disease, particularly those with critical limb ischemia, non-reconstructible vascular pathology or life-threatening infections. These individuals often present with multiple comorbidities and a compromised clinical status, placing them at an increased risk of mortality. Optimising surgical outcomes requires comprehensive preoperative assessment and targeted interventions to enhance physiological resilience.[1]

Haemoglobin and albumin have been identified as potential prognostic biomarkers in surgical patients, as they provide insights into nutritional status, overall physiological condition, and the body's capacity for recovery. Haemoglobin is a key indicator of oxygen-carrying capacity, with anaemia associated with impaired wound healing, increased cardiovascular strain, and heightened mortality risk. Similarly, serum albumin reflects both nutritional status and systemic inflammation, with hypoalbuminemia consistently linked to a higher incidence of postoperative complications and increased mortality.[2,3]

This study aims to assess the association between preoperative haemoglobin and albumin levels and survival outcomes in patients undergoing major lower limb amputation.

METHODS

A retrospective review was conducted of all patients who underwent major lower-limb amputation performed by vascular surgeons at a tertiary vascular surgery centre between June 2016 and December 2023. This research adheres to the principles of the Declaration of Helsinki, ensuring the confidentiality of patient data. Medical records were reviewed between July and September 2024. All patients were included in the analysis, regardless of prior vascular interventions. Preoperative haemoglobin and albumin levels were extracted from medical records, and patients were stratified into two groups based on survival status throughout the study period.

Data are presented as count and percentage or as mean and standard deviation, as applicable. Independent-samples t-tests were used to compare mean haemoglobin and albumin levels between survivors and non-survivors.

Time-to-event analysis was performed using Cox proportional hazards regression to evaluate factors associated with all-cause mortality during the follow-up. Only variables with a univariable p-value < 0.1 and strong clinical relevance were included in the multivariable model. Albumin was not included because it was available for only 99 patients, which would have significantly reduced the sample size and the number of events, compromising model robustness. Hazard ratios (HR) are reported with 95% confidence intervals (CI), and statistical significance was defined as $p < 0.05$. Potential confounders assessed included diabetes mellitus, hypertension, dyslipidaemia, obesity, HIV infection, cerebrovascular disease, cardiovascular disease, chronic heart failure (CHF), atrial fibrillation, chronic obstructive pulmonary disease (COPD), autoimmune disorders, thrombophilia, dementia, smoking status (current and past), dialysis dependence, and history of organ transplantation. According to the local review board, no ethics committee approval or informed consent was required for this study.

RESULTS

Between 2016 and 2023, 585 patients underwent major amputations; the mean age at the time of amputation was 72 ± 12 years, and the majority of the cases were men, representing 388 (66%) of the cases, Table 1. The most common primary amputation was transfemoral, accounting for 359 (61%) of amputations.

Table 1. Demographic data of patients who underwent major amputation from 2017 to 2023.

		Death	
		No	**Yes**
Sex	**Male**	219 (56%)	169 (44%)
	Female	100 (51%)	97 (49%)
BMI		24,9	24,1

Table 2. Haemoglobin and albumin levels of patients who underwent major amputation, included in this study

	Death		
	No	**Yes**	**p value**
Haemoglobin (g/dL)	10.46 ± 0.12	10.06 ± 0.11	0.015
Albumin (g/dL)	3.25 ± 0.92	2.94 ± 0.08	0.019

The independent samples t-test revealed a statistically significant difference in haemoglobin levels between survivors and non-survivors ($p = 0.015$), with survivors exhibiting higher mean haemoglobin levels (mean difference = 0.40 g/dL; 95% CI [0.08, 0.73]). Similarly, albumin levels were significantly higher among survivors ($p = 0.019$), with a mean difference of 0.31 g/dL (95% CI [0.05, 0.57]). During follow-up, 66 patients (11.3%) died. In the multivariable Cox regression model, cerebrovascular disease (HR 1.50; 95% CI 1.14–1.96; $p = 0.003$), congestive heart failure (HR 1.53; 95% CI 1.13–2.08; $p = 0.007$), atrial fibrillation (HR 1.49; 95% CI 1.11–1.99; $p = 0.008$), and haemoglobin (HR 0.93 per g/dL; 95% CI 0.87–0.99; $p = 0.048$) were independently associated with mortality. Due to the limited availability of albumin measurements (n = 99), a separate subgroup analysis was performed. Univariate Cox regression was used to evaluate the association between albumin levels and all-cause mortality. In this albumin subgroup, higher albumin levels were strongly associated with improved survival (HR 0.488; 95% CI 0.319 – 0.747; $p = 0.001$).

Table 3. Multivariable Cox regression on factors impacting mortality following major amputation, during the whole duration of the study.

Comorbidities/ Risk factors	Hazard Ratio	95% Confidence Interval	p value
Cerebrovascular disease	1.50	1.14 – 1.96	0.003
Coronary artery disease	0.90	0.65 – 1.23	0.497
Chronic heart failure	1.53	1.13 – 2.08	0.007
Atrial fibrillation	1.49	1.11 – 1.99	0.008
Dialysis	1.34	0.97 – 1.85	0.08
Haemoglobin (mean g/dL)	0.93	0.87 – 0.99	0.048

Due to the limited availability of albumin measurements (n = 99), a separate subgroup analysis was performed. Univariate Cox regression was used to evaluate the association between albumin levels and all-cause mortality. In this albumin subgroup, higher albumin levels were strongly associated with improved survival (HR 0.488; 95% CI 0.319 – 0.747; p = 0.001).

DISCUSSION

Preoperative haemoglobin levels emerged as a significant and independent predictor of survival in patients undergoing major lower limb amputation. Lower haemoglobin values were strongly associated with increased postoperative mortality, even after adjustment for a broad spectrum of comorbidities. Specifically, each 1 g/dL increase in haemoglobin was associated with an approximate 6.6% reduction in the hazard of death.

Due to the limited availability of albumin measurements, only a univariate Cox regression was performed, which showed that each 1 g/dL increase in albumin reduced the hazard of death by approximately 51% (HR 0.488; 95% CI 0.319–0.747; p = 0.001), indicating a strong protective effect; however, this requires validation in multivariable analyses.

These findings underscore the importance of preoperative optimisation in this medically complex and vulnerable patient population. The interplay between anaemia and hypoalbuminemia highlights the necessity of a multimodal approach to perioperative risk reduction, emphasising both nutritional support and haematological optimisation as actionable targets for intervention.[4,5] Routine assessment of these biomarkers in preoperative protocols could enhance risk stratification and clinical decision-making, enabling timely interventions that may improve surgical outcomes and survival rates. Despite the study's limitations, including its retrospective design and single-centre scope, the findings provide valuable insights that warrant further investigation. Future prospective multicentre studies with standardised intervention protocols and longitudinal follow-up are essential to validate these results, establish causality, and determine whether targeted correction of hypoalbuminemia and anaemia can translate into improved postoperative survival. By integrating these preoperative biomarkers into clinical practice, this research lays the foundation for optimising perioperative care strategies in patients undergoing major lower limb amputation, ultimately contributing to better patient outcomes and evidence-based surgical management. In fact, Portugal already has a national clinical guideline for perioperative patient blood management, and if albumin is also confirmed as a significant prognostic factor in further studies, this could pave the way for similar evidence-based interventions targeting nutritional status in high-risk surgical patients.

CONCLUSION

This study demonstrates that preoperative haemoglobin is a strong and independent predictor of survival in patients undergoing major lower limb amputation. Lower haemoglobin levels were associated with increased postoperative mortality, emphasising the importance of preoperative optimisation and risk stratification. Although albumin was not included in multivariable adjustment due to limited availability, univariate analysis suggested a protective effect, indicating a potential role that warrants validation in further studies.

Incorporating haemoglobin and albumin assessments into perioperative protocols may facilitate early identification of high-risk patients and enable targeted interventions, potentially improving surgical outcomes and overall survival. Future prospective multicentre studies are essential to validate these findings and to establish evidence-based strategies for optimising preoperative care.

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