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# Albumin serum as a predictor of prognosis in patients with peripheral artery disease post angioplasty: A Systematic Review and Meta-Analysis

Octavia So Hangrainy<sup>1\*</sup>, Bermansyah<sup>2</sup>, Gama Satria<sup>2</sup>, Ahmat Umar<sup>2</sup>,  
Aswin Nugraha<sup>2</sup>, Arie H.L Tobing<sup>2</sup>, Indra Hakim Nasution<sup>2</sup>

## ABSTRACT

**Introduction:** Peripheral artery disease (PAD) refers to a pathological condition marked by narrowing the artery diameter, the most common cause of atherosclerosis. Serum albumin levels are related to atherosclerosis and increase the risk of hospitalization and death. This study aims to systematically review and conduct a meta-analysis of albumin serum as a predictor of prognosis in patients with peripheral arterial disease (PAD) post-angioplasty.

**Methods:** Use reputable resources like PubMed, Sage Journal, Lancet, and Science Direct with diverse study designs (randomized controlled trials (RCTs), observational studies, quasi-experimental approaches, and case-control studies) to investigate relevant studies. RevMan software from the Cochrane Collaboration was used to do a meta-analysis. In the meta-analysis, the 95% confidence interval (CI) was utilized as a measure of effect size. The degree of heterogeneity across studies was assessed by applying the Chi-square test and the  $I^2$  statistic. A fixed-effect model was employed for data synthesis when heterogeneity was minimal ( $p > 0.1$  or  $I^2 < 50\%$ ), whereas a random-effects model was deemed more appropriate for cases with substantial heterogeneity ( $I^2 > 50\%$ ). Statistical significance was defined by a p-value less than 0.05.

**Results:** A thorough three-level screening strategy was used to identify only five articles out of 1499 directly related to the current systematic review. This study shows that hypoalbumin has a greater risk of mortality (OR 4.21 [2.79, 6.34]), a longer length of stay in hospital (MD 3.80 [2.17, 5.44]), and a higher risk of morbidity (OR 5.87 [2.51, 13.72]).

**Conclusion:** Preoperative hypoalbuminemia is significantly correlated with increased in-hospital mortality and severe postoperative complications in patients undergoing both open and endovascular lower extremity interventions. Given that most procedures are elective, careful evaluation is warranted to postpone elective surgeries until albumin levels are adequately corrected.

**Keywords:** angioplasty, peripheral artery disease, serum albumin.

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<sup>1</sup>Resident of Cardiothoracic and Vascular Surgery, Dr. Moh. Hoesin Hospital, Faculty of Medicine Sriwijaya University, Palembang, Indonesia;

<sup>2</sup>Department of Cardiothoracic and Vascular Surgery, Dr. Moh. Hoesin Hospital, Faculty of Medicine Sriwijaya University, Palembang, Indonesia.

\*Corresponding to:  
Octavia So Hangrainy;  
Resident of Cardiothoracic and Vascular Surgery, Dr. Moh. Hoesin Hospital,  
Faculty of Medicine Sriwijaya University,  
Palembang, Indonesia;  
octaroosevelt@gmail.com

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## INTRODUCTION

Peripheral arterial disease (PAD) encompasses a spectrum of non-coronary arterial disorders characterized by structural and functional abnormalities in the arteries providing the brain, visceral organs, and limbs. While various pathophysiological mechanisms can lead to stenosis or aneurysm development in the peripheral vasculature, atherosclerosis is the most prevalent pathology affecting the aorta and its branches. Globally, PAD is estimated to impact 12–14% of the population, equating to around 202 million individuals. Its prevalence rises

with age, affecting 10–25% of individuals over 55 years and 40% of those over 80 years, contributing substantially to morbidity, mortality, and decrease quality of life.<sup>1,2</sup>

In pre-operative evaluations of patients undergoing cardiac, trauma, and general operations, serum albumin is often used as a biochemical and nutritional marker. Emerging evidence has highlighted a significant association between serum albumin levels and the development of atherosclerosis. Lower albumin levels have been shown to exacerbate atherosclerotic changes, potentially influencing vascular

health and contributing to adverse clinical outcomes. These findings suggest that hypoalbuminemia is a predictor of poor prognoses in patients undergoing major surgeries, as it is linked with higher rates of postoperative complications, prolonged hospitalizations, and increased mortality risk, irrespective of underlying medical conditions.<sup>3,4</sup>

The objective of this study is to do a systematic review and meta-analysis to evaluate the role of serum albumin as a prognostic biomarker in patients with peripheral arterial disease (PAD) post-angioplasty.

## METHODS

This systematic review and meta-analysis stick to the standards outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. The research question was formulated in advance using the Population, Intervention, Comparator, and Outcomes (PICO) methodology. Population: Individuals at risk of or diagnosed with PAD. Intervention: Angioplasty. Comparison: Serum albumin. Outcome: Mortality, morbidity, length of stay in hospital.

### Eligibility Criteria

Studies with diverse designs will be considered for inclusion in this systematic review and meta-analysis on the exploration of albumin serum as a predictor of prognosis in patients with PAD post-angioplasty. This includes randomized controlled trials (RCTs), observational research, quasi-experimental approaches, and case-control investigations.

The target population comprises individuals in whom serum albumin levels are used as a prognostic indicator for patients with PAD post-angioplasty, without limitations regarding age, sex, or geographic region. Studies were excluded if they were not directly pertinent to the research question, consisted solely of reviews without original data, or did not specifically investigate serum albumin as a prognostic factor in PAD patients post-angioplasty.

### Data sources and search strategy

A comprehensive search strategy was deployed to explore albumin serum as a predictor of prognosis in patients with PAD post-angioplasty. The authors conducted a thorough search of pertinent bibliographic databases, such as PubMed, Lancet, Sage, and ScienceDirect. The search was finalized in July 2024. Relevant MeSH terms associated with serum albumin as a prognostic marker in patients with PAD following angioplasty, along with articles containing these terms in their titles or abstracts, were identified.

### Study selection

Two independent investigators conducted title and abstract screening for eligibility.

Studies that fulfilled the inclusion criteria were chosen, and their full-text articles were retrieved and examined. Any disagreements regarding study selection were resolved through a consensus decision among all authors.

### Statistical techniques

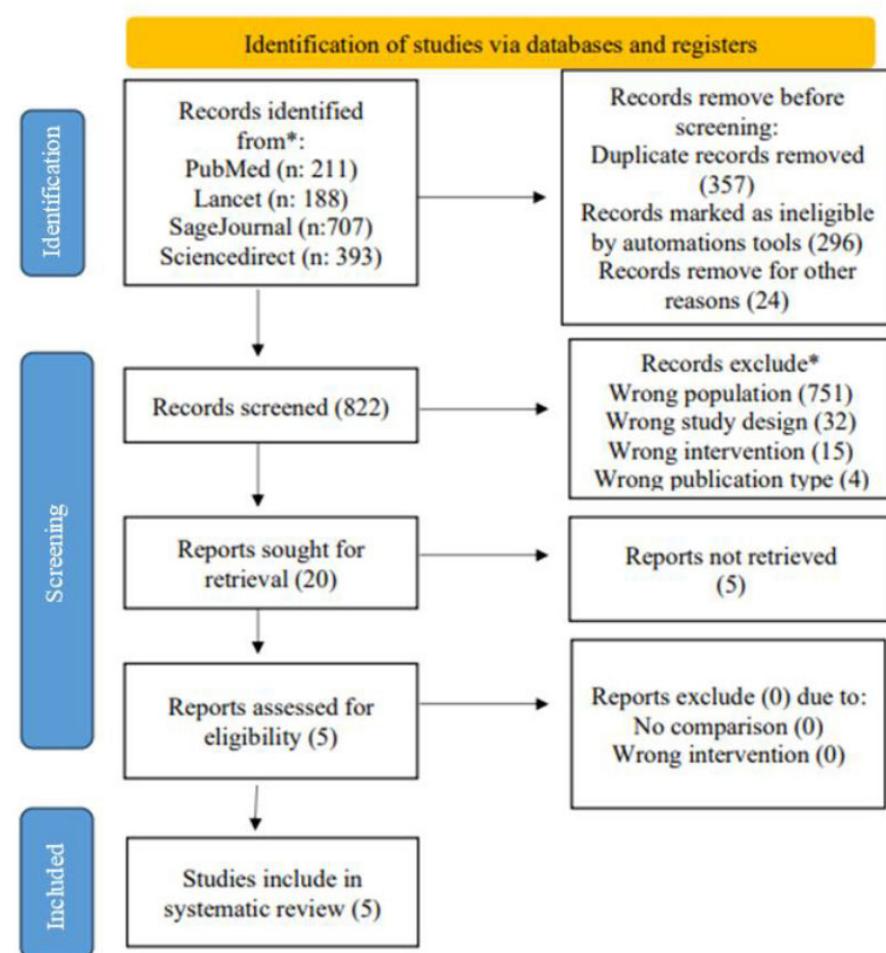
Review Manager (Version 5.4, Cochrane Collaboration, Software Update, Oxford, United Kingdom) was used for all data processing and visualization in the comparative meta-analysis of albumin serum as a prognostic predictor; a p-value of less than 0.05 was deemed statistically significant. For dichotomous variables, the odds ratio (OR) and 95% confidence intervals (CI) were computed, and for continuous variables, the mean difference (MD) and 95% confidence intervals (CI) were computed. Using the  $I^2$  test, heterogeneity across several studies was assessed.

Statistical heterogeneity was considered

current when the p-value in the Cochran Q test was  $<0.05$  and the  $I^2$  statistic was  $>50\%.$ <sup>5</sup> If the heterogeneity was acceptable ( $p>0.10$  or  $p\leq0.10$  but  $I^2 \leq50\%$ ), a fixed-effect model was used. If otherwise, a random effects model was used.

## RESULTS

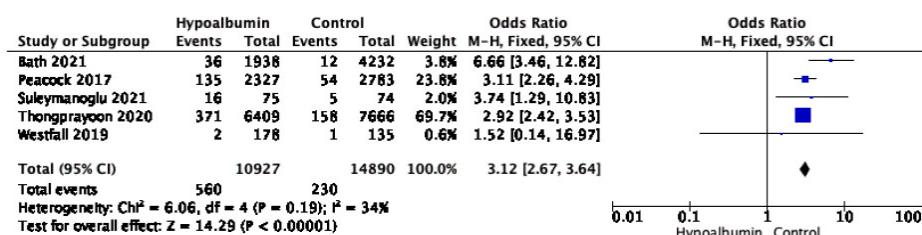
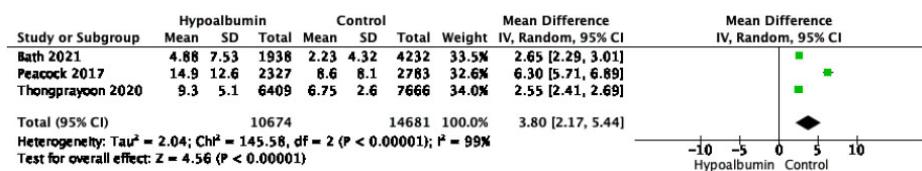
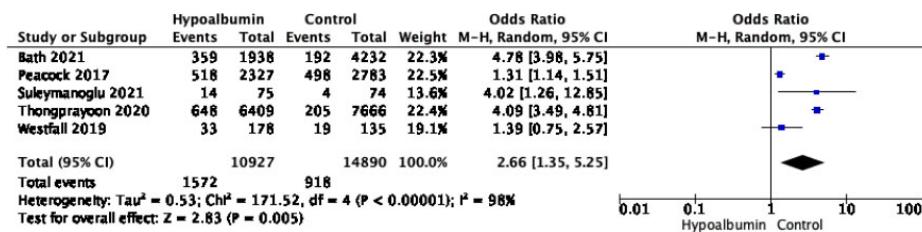
Using reputable resources like PubMed, Sage Journal, Lancet, and Science Direct, our research team first gathered 1499 publications. A comprehensive three-tiered screening process was employed to identify and select only five articles directly relevant to the studies included in this systematic review. These articles were then subjected to a thorough full-text evaluation and analysis for further consideration. The selected articles, along with their publication years and the distribution of these years, are presented in Figure 1. The characteristics of the studies included are shown in Table 1.



**Figure 1.** PRISMA schematic of the search strategy.

**Table 1.** Characteristics of studies included

Author (year)/Country	Study period	Method	Sample Size	Result
Bath, J et al. <sup>6</sup> (2020)/Columbia	2008 - 2015	Observational	6170 patients, 1938 hypoalbumin, 4232 normal albumin	48 patients died, 551 patients had morbidity, and the length of stay for patients with pre-operative hypoalbumin was $4.88 \pm 7.53$ days, with pre-operative normal albumin $2.23 \pm 4.32$ days.
Suleymanoglu, M et al. <sup>7</sup> (2021)/ Turkey	Jan 2015 - Jan 2020	Observational	149 patients, 75 hypoalbumin, 74 normal albumin	21 patients died, and 18 patients had morbidity.
Peacock, M et al. <sup>8</sup> (2017)/	2005 - 2012	Prospective	Total 5110 patients, with 2327 hypoalbumin and 2783 normal albumin	189 patients died, 1,016 patients had morbidity, and the length of stay for patients with pre-operative hypoalbumin was $14.9 \pm 12.6$ days, with pre-operative normal albumin $8.6 \pm 8.1$ days.
Thongprayoon, C et al. <sup>9</sup> (2020)/ USA	Jan 2009 - Dec 2013	Observational	Total 14,075 patients, with 6409 hypoalbumin and 7666 normal albumin	529 patients died, 853 patients had morbidity, and the length of stay for patients with pre-operative hypoalbumin was $9.3 \pm 5.1$ days; with pre-operative normal albumin $6.75 \pm 2.6$ days.
Westfall, JC et al. <sup>10</sup> (2019)/ Boston	2007 - 2017	Observational	Total 313 patients, with 178 hypoalbumin and 135 normal albumin	3 patients died, and 52 patients had morbidity.

**Figure 2.** Forest Plot of Mortality.**Figure 3.** Forest Plot of Length of Stay.**Figure 4.** Forest Plot of Morbidity.

### Mortality

Mortality was measured in 5 trials. The mortality trials involved 25,817 patients,

with 10,927 in the hypoalbumin group and 14,890 in the control group. No significant heterogeneity was observed ( $I^2 = 34\%$ ,  $p =$

0.19). Based on the Z value of 14.29 and p value  $<0.00001$ , hypoalbumin impacts mortality rates (Figure 2).

### Length of Stay

The length of stay was reported in three trials. The  $I^2$  value of 99% indicated high heterogeneity. Based on the Z value of 4.56 and p value  $<0.00001$ , there is a significant impact of hypoalbumin on patients' length of stay after angioplasty in PAD (Figure 3).

### Morbidity

Morbidity was taken as an important index in five trials. Remarkably, The degree of heterogeneity was considerable ( $I^2 = 98\%$ ), necessitating the use of a random-effects model for analysis. Based on the Z value of 2.83 and p value of 0.005, there is an impact of hypoalbumin on the morbidity rate of angioplasty on PAD (Figure 4).

### DISCUSSION

Peripheral arterial disease (PAD) is a chronic, lifelong condition that requires ongoing management. An effective care strategy for PAD patients involves

regular clinical assessments by healthcare professionals experienced in vascular care. The primary focus of treatment is to reduce cardiovascular risks through pharmacological interventions, improve functional capacity through structured exercise, and, when appropriate, pursue revascularization procedures. The care approach is tailored based on whether the patient has undergone revascularization. It is important to consider potential regional differences in the Asia-Pacific area concerning the epidemiology of PAD, the accessibility of diagnostic and therapeutic resources, clinical practices, and possibly even patient responses to treatment, which may necessitate a reassessment of the relevance and applicability of international guidelines.<sup>11,12</sup>

The current study found correlations between prognostic patients with peripheral arterial disease and pre-operative serum albumin following angioplasty. In adults, the typical reference range for serum albumin is between 3.5 and 5.0 g/dL, with levels below 3.5 g/dL classified as hypoalbuminemia. Following open and endovascular lower extremity PAD procedures, a low albumin level has been linked with unfavorable postoperative results, such as mortality and morbidity. Predicting this scenario is critical to managing therapy and preventing health issues. According to this meta-analysis, patients with pre-operative serum albumin levels below normal had a greater death rate (OR 4.21 [2.79, 6.34]) than patients with normal serum albumin levels. Additionally, compared to patients with normal pre-operative serum albumin, those with low pre-operative serum albumin have a greater risk of morbidity (OR 5.87 [2.51, 13.72]). It has been demonstrated that lower serum albumin levels raise cardiovascular disease mortality and morbidity.<sup>13,20</sup>

The most common protein in circulation, serum albumin, is essential for several vital physiological processes. It has been demonstrated that it affects atherosclerosis primarily due to changes in the inflammatory response, platelet aggregation, antioxidant capacity, and the connection to nutritional status. Evidence suggests that albumin is a highly reliable indicator of cardiovascular

risk in some patient populations. Individuals with peripheral artery disease, ischemic stroke, heart failure, hypertension, atrial fibrillation, those undergoing revascularization procedures, patients with aortic stenosis undergoing transcatheter aortic valve replacement, as well as those with congenital heart disease and/or endocarditis, may all experience the protective benefits of albumin.<sup>14,15</sup>

In the observational registry study, Ding et al. found that lower serum albumin was associated with the prevalence of PAD. A significant inverse relationship was observed between serum albumin levels and PAD (per standard deviation increase; OR: 0.83; 95% CI: 0.72, 0.94). The findings of this study indicate that lower serum albumin concentrations are strongly associated with an increased likelihood of PAD.<sup>16</sup>

Bath et al. reported that low albumin levels had been associated with mortality and morbidity, and low pre-operative albumin levels are correlated with increased in-hospital mortality, extended hospitalization, and severe morbidity. Patients with low albumin levels undergo a longer hospital stay (4.9 days vs 2.2 days for those with normal levels;  $P < .0001$ ), higher in-hospital mortality (1.9% compared to 0.3% in those with normal levels;  $P < .0001$ ), and a higher rate of 30-day readmission (15% vs 12.7%;  $P < .02$ ). Multivariable regression analysis revealed a strong relationship between low albumin levels and in-hospital death, with an OR of 5.23 95% CI, 2.00–13.70.<sup>6</sup>

Chahrour et al. also found a relationship between pre-operative serum albumin levels and postoperative mortality. In Kurtul et al. study, low albumin was found to be linked with in-hospital death.<sup>17,18</sup>

Peacock et al. conducted one of the studies examining the impact of albumin levels on morbidity and mortality in patients undergoing lower extremity bypass surgery. The authors found that, postoperatively, patients with low albumin levels undergo higher mortality rates, greater likelihood of requiring reoperation, and longer hospital stays compared to those with normal albumin levels.<sup>8</sup>

This study shows that more patients with low pre-operative serum albumin have longer lengths of stay than patients

with normal pre-operative serum albumin (OR 6.12 [5.09,7.36]).

Multiple mechanisms could explain the connection. Above all, serum albumin has been connected to atherosclerosis due to its antioxidant and anti-inflammatory qualities. Reduced blood albumin levels were linked to a higher risk of inflammation, the primary cause of compromised vascular function. Serum albumin is an antioxidant by scavenging reactive oxygen and nitrogen species due to its high thiol group content. Additionally, albumin may bind to some compounds with antioxidant qualities, like bilirubin and nitric oxide, adding to the body's defense against oxidative stress.

Low serum albumin also causes diminished inhibition of platelet aggregation and attenuated fibrinolysis, which can result in thrombogenesis or atherosclerotic plaque development. Moreover, low albumin levels might reduce the deformability of erythrocytes, which in turn raises blood viscosity.<sup>17</sup>

Nevertheless, research exploring the association between serum albumin levels and the risk of PAD remains infrequent. Furthermore, no prior study has thoroughly examined the factors that potentially adjust the relationship between serum albumin and PAD.<sup>16,19</sup>

## CONCLUSION

Low pre-operative albumin levels are linked with higher rates of in-hospital mortality, longer hospitalization, and significant morbidity following both open and endovascular lower extremity surgeries. Given that many of these procedures are elective, it is crucial to carefully evaluate the option of delaying surgery until serum albumin levels are adequately optimized.

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## CONFLICT OF INTEREST

All authors stated there is no conflict of interest.

## AUTHOR CONTRIBUTION

All authors contributed to this study.

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