REVIEW

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Outcome albumin serum level in cardiac surgery: A systematic review and meta-analysis

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Gieza Ferrani[1*]

[1]Department of Cardiothoracic and Vascular Surgery, Dr. Mohammad Hoesin Hospital, Faculty of Medicine, Sriwijaya University, Palembang, South Sumatera, Indonesia.

*Corresponding to:
Gieza Ferrani;
Department of Cardiothoracic and Vascular Surgery Sriwijaya University, Palembang, South Sumatera, Indonesia;
giezaferrani1609@gmail.com

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ABSTRACT

Introduction: Numerous clinical settings have shown a correlation between preoperative hypoalbuminemia and unfavorable surgical results, suggesting that serum albumin content measured before surgery may be a valuable and accurate predictor of poor surgical outcomes. This study aimed to evaluate the outcome of albumin serum levels in cardiac surgery.

Methods: This PRISMA-guided meta-analysis examined the impact of serum albumin levels on outcomes in cardiac surgery, including mortality, hospital stay, and intubation. A systematic review of studies from significant databases (final search: July 2024) utilized the GRADE system to assess evidence quality and I^2 to analyze heterogeneity. Hypoalbuminemia was linked to increased mortality and prolonged recovery, highlighting serum albumin as a critical biomarker in cardiac surgery care.

Results: The systematic review screened 1,403 publications, ultimately selecting 10 studies examining serum albumin levels and outcomes in cardiac surgery. Study designs included various cohorts, a cross-sectional study, and one randomized controlled trial, with sample sizes ranging from 203 to 842,672 participants and mean ages of 42 to 67 years. Meta-analysis showed hypoalbuminemia significantly increased risks of mortality (OR=7.21; 95%CI=2.08–25.02; I^2=90%) and intubation (OR=2.78; 95%CI=1.76–4.38; I^2=89%), with a less definitive link to more extended length of stays (OR=2.01; 95%CI: 0.70–5.76; I^2=99%).

Conclusion: Low preoperative serum albumin predicts poorer cardiac surgery outcomes. Normalizing levels is recommended, but the roles of malnutrition and supplementation need further study.

Keywords: Albumin, cardiac surgery, hypoalbuminemia.
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INTRODUCTION

Preoperative malnutrition affects 10% to 25% of patients having heart surgery and is linked to higher rates of morbidity and death as well as a worse standard of living following the procedure. To stratify operative risk and perhaps identify patients who can benefit from nutrition optimization before surgery, it is essential to identify patients who are malnourished and awaiting heart surgery. The objective indicator of malnutrition in previous research on patients' nutritional condition after heart surgery has been serum albumin concentration. However, because serum albumin has a lengthy half-life, it is unaffected by recent dietary changes.[1,2]

Albumin is a water-soluble, globular, negatively charged protein produced endogenously by the liver. It is catabolized in the endothelium and degraded in muscle, skin, and other organs.[3,4] According to some research, including albumin in prime fluid might reduce the need for blood products and the amount of water accumulating in the extravascular lungs and the pulmonary shunt fraction. Avoiding albumin usage during the perioperative phase was one of the characteristics linked to a decreased risk of acute kidney damage (AKI) after heart surgery in single-center research. There are no clinically relevant randomized studies with sufficient power to investigate the effects of cardiopulmonary bypass (CPB) prime supplementation on albumin. It is rare to routinely employ human albumin to increase oncotic pressure due to the lack of high-quality data.[5]

Aside from food intake, non-nutritional factors that can impact serum albumin concentration include chronic inflammation, recurrent infections, hepatic failure, renal dysfunction, altered gastrointestinal function, elevated right-sided cardiac pressures, dilution from fluid overload, and medications. After cardiac surgery, reduced albumin levels have been associated with increased procalcitonin, C-reactive protein, α1-antitrypsin, and interleukin-6. Despite its prognostic significance, Gibbs et al. discovered that the preoperative serum albumin testing rate varied widely, ranging from 20% to 98% of patients, with a median testing rate of 60%. When the study was restricted to cases with an ASA score of 3 or above (59% of all cases), the range in the percentage of patients investigated remained considerable (from 27% to 97% of cases, with a median of 72%).[6,7] Therefore, this study aimed to evaluate the impact of serum albumin levels on cardiac surgery outcomes, offering insights to guide clinical practice and future research.

METHODS

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring a systematic and transparent approach to the identification, selection, analysis, and reporting of the included studies.

Identification of relevant literature

A comprehensive search was conducted across databases like PubMed, Lancet, Sage Journals, and Science Direct, with the final search in July 2024 to explore serum albumin levels in cardiac surgery. MeSH terms and keywords related to serum albumin in cardiac surgery were used with Boolean operators, including terms like ("Cardiac surgery") AND ("Albumin") AND ("Hypoalbuminemia") AND ("Outcome"). Eligible studies underwent full-text review after two researchers independently reviewed abstracts and titles. All writers reached a resolution to settle selection discrepancies.

Eligibility Criteria

This meta-analysis included studies on serum albumin levels in cardiac surgery, such as RCTs, observational, quasi-experimental, and case-control designs, with no restrictions on age, gender, or location. Exclusion criteria include studies lacking relevance, original data, or comparison groups. The primary focus is serum albumin level changes, ensuring a comprehensive literature analysis.

Data extraction

The selected studies provided data on key parameters, including the author's name, publication year, country of origin, study design, sample size, average participant age, serum albumin levels, mortality rates, hospital length of stay, and intubation outcomes.

Assessment of risk of bias

The quality of the evidence was evaluated using the GRADE system. Study design restrictions were used to assess the risk of bias; observational studies were regarded as low-quality evidence, and RCTs were considered as high-quality evidence. Every study was examined for flaws, and bias was identified for every result across studies.

Outcome of Interest

Microsoft Excel was used to compile data extracted from studies. The primary outcomes were the effect of hypoalbuminemia on mortality, length of stay, and intubation in patients who underwent cardiac surgery.

Statistical analysis

Heterogeneity was assessed using the I^2; a heterogeneity below 50% represents low heterogeneity, and a heterogeneity of 50% or more will represent high heterogeneity. Fixed effects will be used for low heterogeneity, while high heterogeneity will use the random effects. Further analyses using Peter's tests will be conducted to detect small study biases between included studies because some studies have very few sample sizes. Risk of bias analysis was performed using GRADE. The R Statistical Software v.3.3 was used for all statistical analyses, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Using reputable resources like PubMed, Sage Journal, Lancet, and Science Direct, our research team first gathered 1403 publications. After a comprehensive three-level screening process, only ten papers that were directly connected to the current systematic review were found. These were chosen for additional screening after full-text reading and analysis. Figure 1 displays the selected papers, the years of publication for each, and the distribution of those years.

Based on the critical appraisal table using the GRADE system, studies such as Franco et al. (2020), Montazerghaem et al. (2014), Nipper et al. (2022), Henry et al. (2019), Aksoy et al. (2019), and Aksoy et al. (2021) showed a moderate risk of bias due to failure to meet randomization and blinding parameter, although most

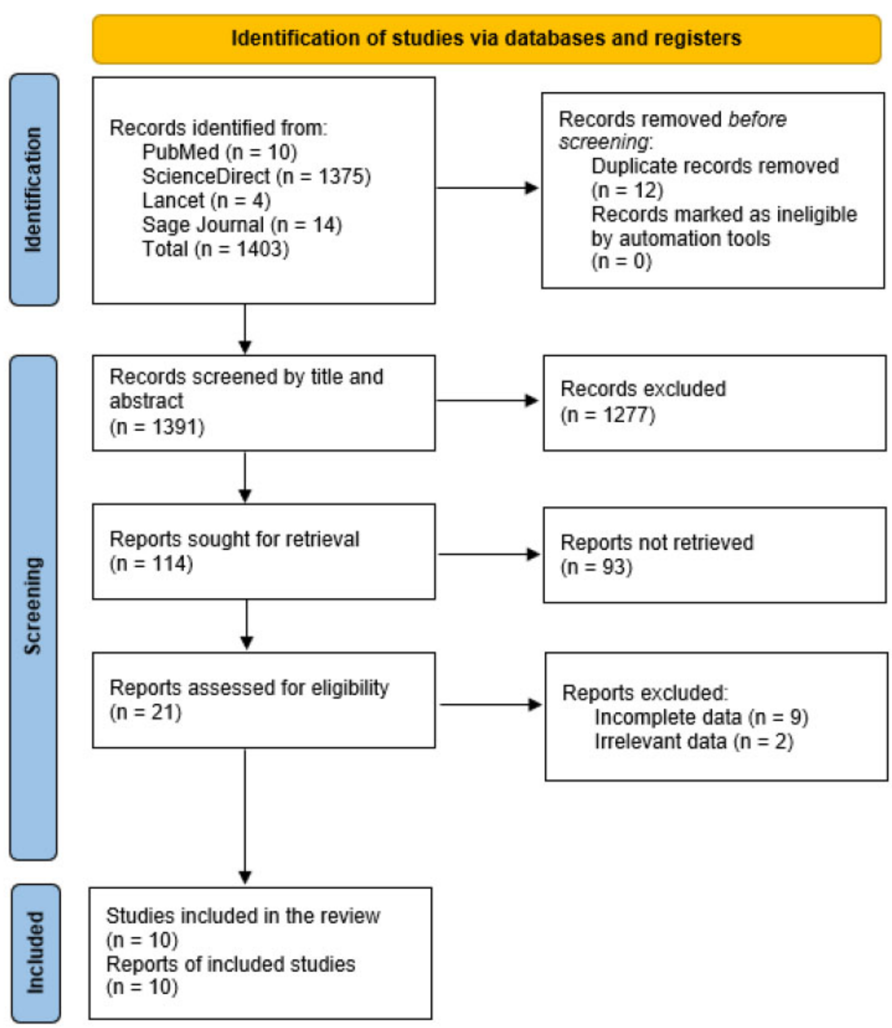

Figure 1. Article search flowchart.

other parameters were met. These studies remain relevant for meta-analysis, but the results must be interpreted cautiously. In contrast, studies such as Matebele et al. (2020), Hendy et al. (2022), Li et al. (2022), and Tharavath et al. (2023) met more parameters, including randomization and methodological consistency, indicating a low risk of bias with a more robust design and more reliable results. Overall, studies with low risk of bias made a stronger contribution, while studies with moderate risk of bias required more consideration in meta-analyses (Table 1).

Most studies used a retrospective cohort design, such as Matebele et al. (2020) in Australia with 3,656 participants, and Nipper et al. (2022) in the United States with the largest sample size, namely 842,672 participants and a mean age of 67.0 years. Prospective designs were applied by Franco et al. (2020) in Spain with 2,818 participants and Tharavath et al. (2023) in India with 580 participants and a mean age of 42.0 years. Montazerghaem et al. (2014) in Iran used a cross-sectional design with 345 participants, while Hendy et al. (2022) in Canada was the only RCT study with 203 participants. Variation in mean age was seen ranging from the youngest age of 42.0 years (India) to the oldest age of 67.0 years (US), although some studies did not report mean age, such as Matebele et al. (2020) and Henry et al. (2019) (Table 2).

Mortality

The forest plot analysis of mortality (Figure 2) demonstrated an odds ratio (OR) of 7.21 (95%CI=2.08–25.02) with a high level of heterogeneity (I^2=90%). According to this, patients who had hypoalbuminemia and were having heart surgery had a 7.21-fold increased risk of dying. The large confidence interval indicates inter-study variation in effect magnitude, which variations in study populations, methods, or hypoalbuminemia classifications may cause. The high I^2 score indicates essential heterogeneity.

Length of Stay

The forest plot analysis of length of stay (Figure 3) showed an OR of 2.01 (95%CI=0.70–5.76) with substantial heterogeneity (I^2=99%). This suggests a potential association between hypoalbuminemia and more extended hospital stays in cardiac surgery patients, though the wide confidence interval and high variability across studies warrant cautious interpretation.

Intubation

The forest plot analysis of intubation duration (Figure 4) showed an OR of 2.78 (95%CI=1.76–4.38) with substantial heterogeneity (I^2=89%). This indicates that cardiac surgery patients with hypoalbuminemia have a 2.78 times higher risk of requiring intubation compared to those without hypoalbuminemia, emphasizing the clinical impact of hypoalbuminemia on postoperative respiratory outcomes.

The study demonstrates a low risk of bias in several areas, including random sequence generation, allocation concealment, participant and staff blinding selective reporting, and other biases. This suggests that the randomization, allocation, and blinding procedures were executed appropriately. However, there are significant concerns regarding detection bias, as the outcome assessors may have yet to be blinded, and attrition bias due to missing data could affect the validity of the results. Overall, while the study shows low risk in most areas, the risks of detection and attrition biases should be carefully considered (Figure 5).

Table 1. Critical appraisal of the study

Author, year	Parameters								
	1	2	3	4	5a	5b	5c	6	7
Franco et al., 2020[8]	√	-	√	-	-	√	√	√	√
Montazerghaem et al., 2014[9]	√	-	√	-	-	√	√	√	√
Matebele et al., 2020[10]	√	√	√	-	√	√	√	√	√
Nipper et al., 2022[11]	√	-	√	-	-	√	√	√	√
Henry et al., 2019[12]	√	-	√	-	-	√	√	√	√
Aksoy et al., 2019[13]	√	-	√	-	-	√	√	√	√
Aksoy et al., 2021[14]	√	-	√	-	-	√	√	√	√
Hendy et al., 2022[15]	√	√	√	-	√	√	√	√	√
Li et al., 2022[16]	√	√	√	-	√	√	√	√	√
Tharavath et al., 2023[17]	√	√	√	-	√	√	√	√	√

DISCUSSION

Albumin is the most common protein in blood, making up around half of all plasma proteins. Albumin, which is produced in the liver, is released right away and is not retained. The two physiological

Table 2. Study characteristics

Author	Country	Study Design	Sample Size	Mean Age
Franco et al., 2020[8]	Spain	Prospective cohort	2818	64.5 ± 11.6 years
Montazerghaem et al., 2014[9]	Iran	Cross-sectional	345	60.7 years
Matebele et al., 2020[10]	Australia	Retrospective cohort	3656	N/R
Nipper et al., 2022[11]	USA	Retrospective cohort	842,672	67.0 (56.0–76.0) years
Henry et al., 2019[12]	USA	Retrospective cohort	203	N/R
Aksoy et al., 2019[13]	Turkey	Retrospective cohort	634	60.59 years
Aksoy et al., 2021[14]	Turkey	Retrospective cohort	207	59.47±10.56 years
Hendy et al., 2022[15]	Canada	Randomized Controlled Trial	203	64.08±9.70 years (control) 63.07 ±10.70 years (treatment)
Li et al., 2022[16]	China	Retrospective cohort	3919	54 years (46-62)
Tharavath et al., 2023[17]	India	Prospective cohort	580	42.0 years (31.0-54.0)

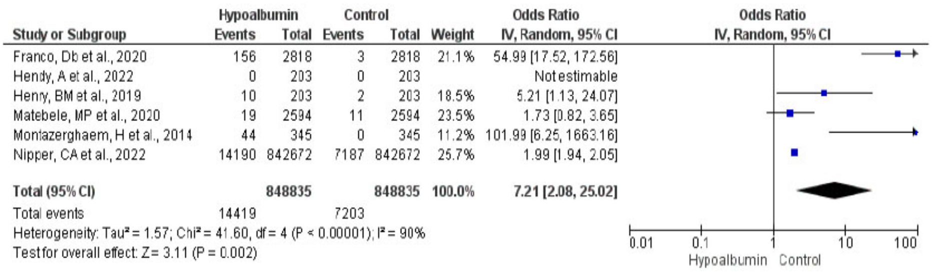

Figure 2. Forest plot of mortality.

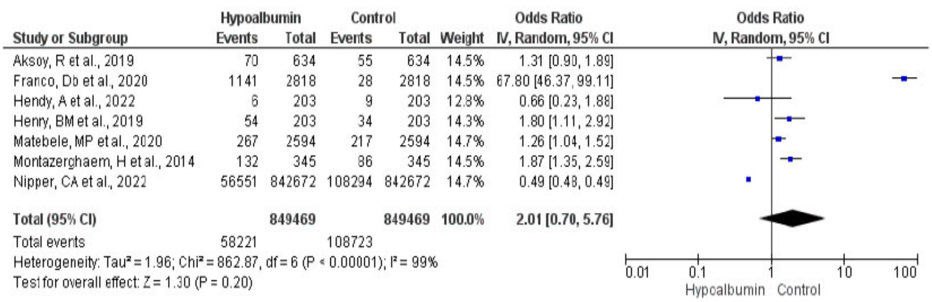

Figure 3. Forest plot of length of stay.

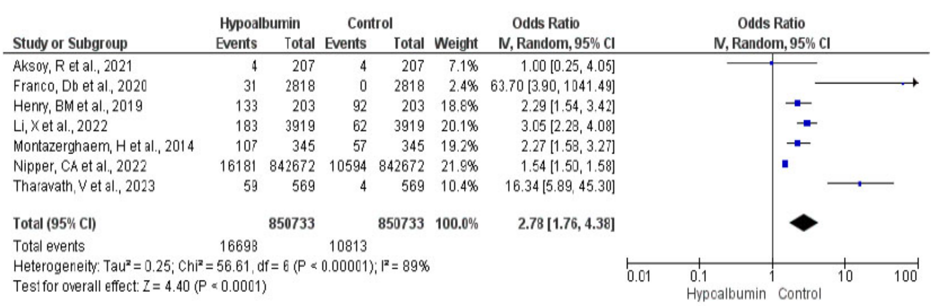

Figure 4. Forest plot of intubation.

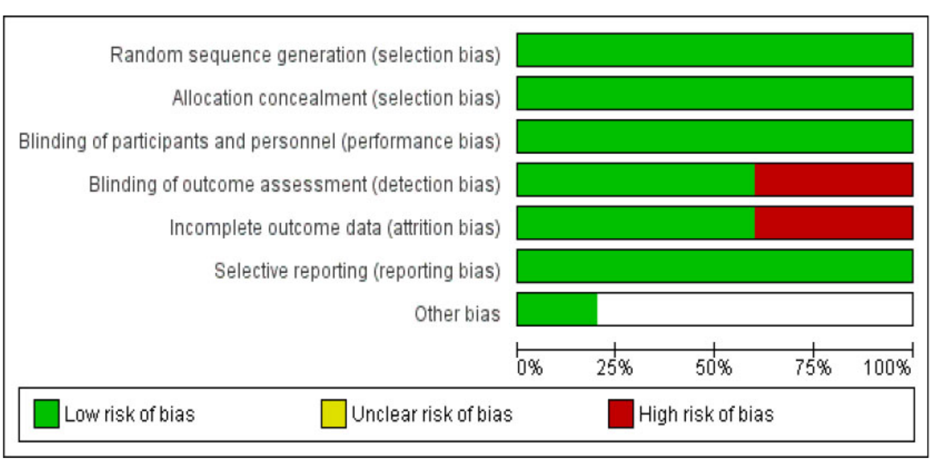

Figure 5. Risk of bias.

factors that control albumin are colloid osmotic pressure and nutritional status. Albumin metabolism depends on its synthesis, diffusion across the interstitium and intravascular region, and excretion. 60% of the total albumin is found in the interstitial space, and the average blood plasma concentration ranges from 3.5 to 5 g/dL. The average half-life is between 28 and 36 days.[18]

Serum albumin predicts poor outcomes in several patient subgroups. It has previously been connected to poor outcomes, such as elevated death rates from cardiovascular disease and cancer. Serum albumin was previously included in intensive care unit ratings, such as the Acute Physiology, Age, and Chronic Health Evaluation III score. It is also included in the frailty criteria and is seen as an indicator of malnutrition. The albumin level is an easy-to-measure marker not influenced by interobserver or inter-observer bias.[19]

Cardiovascular surgery patients require fluid treatment to maintain euvolemia and guarantee tissue perfusion. Hypervolemia prevention is equally important to avoid tissue edema and hemodilution. Relative anemia and subsequent needless red blood cell transfusions brought on by hemodilution might increase morbidity and mortality following heart and vascular surgery. Albumin can treat hypotension during and after cardiovascular surgery, especially after administering intravenous crystalloid solutions. During cardiac surgery, haemodilution occurs when crystalloids, colloids, or both are introduced into the extracorporeal cardiopulmonary bypass circuit (CPB).[20]

Albumin, a 65-kDa protein produced by the liver, makes up around 80% of intravascular oncotic pressure and about 50% of total plasma protein. In addition to its antioxidant properties and role in maintaining microvascular integrity, albumin is involved in transporting medicines, hormones, fatty acids, bile salts, bilirubin, and electrolytes (such as calcium, magnesium, copper, zinc, and so forth). The sterile liquid albumin product, human serum albumin (HSA), is made by pasteurizing and fractionating vast amounts of human plasma. The usage of HAS for medical purposes may have begun around World War II.[4] Patients who have cardiac surgery invariably experience significant alterations, including hemodilution, blood loss, surgical trauma, and a systemic inflammatory reaction. Adult patients following heart surgery have frequently used HSA for purposes such as fluid resuscitation, pump priming, or hypoalbuminemia correction. Regarding the use of HSA in patients undergoing heart surgery, there is still a shortage of data and best practices.[21,22]

Montazerghaem and Safaie Nezhad examined postoperative mortality in 345 patients divided into three groups based on their serum albumin levels before CABG. A significant risk of death after surgery (p-value<0.001), reoperation because of bleeding (p-value<0.001), and prolonged mechanical breathing (p-value=0.019) were linked to low serum albumin levels (2.5, 3.5 g/dl).[23]

One of the first specialties to measure care quality on a broad scale was cardiac surgery. In the USA, data collecting for risk-adjusted mortality rates started in 1987. The database has grown considerably since then. The Society of Thoracic Surgeons (STS) in the US now collects a variety of procedural and outcome indicators, from which a composite score is generated for each physician. Among the individual measures used to rate quality are processes (such as the use of internal mammary artery (IMA) and pre- and postoperative medication), outcomes (such as risk-adjusted mortality, length of stay, and significant morbidity, such as stroke, new renal failure, re-operation, deep sternal wound infection, and prolonged intubation), and one structural measure (participation).[24,25]

The meta-analysis has several limitations, including high heterogeneity across studies, which may affect the reliability of the results. Including various study designs, primarily observational, and the lack of randomized controlled trials limits the ability to establish causality. Potential biases, such as publication and selection bias, should have been addressed, and the variation in sample sizes across studies could lead to underpowered findings or skewed results. Additionally, the studies primarily focus on populations with a mean age that may not fully represent older cardiac surgery patients, limiting the generalizability of the findings. The association between hypoalbuminemia and hospital outcomes like prolonged stays needs to be more consistent, raising concerns about the robustness of these findings. Furthermore, confounding factors, such as comorbidities and variations in surgical procedures, needed to be sufficiently controlled for, and the potential benefits of albumin normalization or supplementation were not directly explored, leaving a gap in actionable recommendations.

CONCLUSION

In conclusion, low preoperative serum albumin is significantly correlated with poorer outcomes after cardiac surgery, including increased mortality, more extended hospital stays, and prolonged intubation times. It is recommended to ensure normal albumin levels before performing cardiac surgery. Further research is needed, considering the level of heterogeneity and the type of cardiac surgery.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

All authors equally contributed to the preparation of this report.

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