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ALBUMIN VERSUS CRYSTALLOIDS IN PATIENTS WITH CIRRHOSIS AND SPONTANEOUS BACTERIAL PERITONITIS: A SYSTEMATIC REVIEW

ALBUMINA VERSUS CRISTALOIDES EM PACIENTES COM CIRROSE E PERITONITE BACTERIANA ESPONTÂNEA: UMA REVISÃO SISTEMÁTICA

ALBÚMINA VERSUS CRISTALOIDES EN PACIENTES CON CIRROSIS Y PERITONITIS BACTERIANA ESPONTÁNEA: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Spontaneous bacterial peritonitis is a severe infectious complication of decompensated cirrhosis and is strongly associated with acute kidney injury, hepatorenal syndrome, short-term mortality, and prolonged hospitalization. Albumin has been proposed as a disease-specific adjunct to antibiotic therapy because it may improve effective arterial blood volume, renal perfusion, and systemic circulatory stability, whereas crystalloids provide less sustained intravascular expansion in the pathophysiological context of advanced cirrhosis.

Objective: The main objective of this systematic review was to evaluate the efficacy and safety of albumin compared with crystalloid-based or non-albumin supportive strategies in patients with cirrhosis and spontaneous bacterial peritonitis. Secondary objectives were to assess renal outcomes, mortality, dosing strategies, timing of administration, adherence to guideline-concordant therapy, and certainty of evidence.

Methods: PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform were searched for studies evaluating albumin, crystalloid-based supportive care, usual care, dosing strategies, timing, implementation, or clinical outcomes in cirrhosis with spontaneous bacterial peritonitis. Randomized trials, observational comparative studies, implementation studies, dosing studies, and meta-analyses were eligible. Risk of bias was assessed using RoB 2, ROBINS-I, and QUADAS-2 when applicable, and certainty of evidence was judged using the GRADE framework.

Results and Discussion: Ten studies were included in the final qualitative synthesis. The evidence consistently supported albumin-based therapy as an adjunct to antibiotics in high-

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risk spontaneous bacterial peritonitis, particularly for reducing renal dysfunction, hepatorenal syndrome, and short-term mortality. No contemporary randomized trial directly compared guideline-dose albumin with a standardized crystalloid-only strategy, making indirectness a major limitation. Recent evidence emphasized implementation quality, early administration, dosing optimization, and persistent underuse of guideline-concordant albumin therapy in real-world practice.

Conclusion: Albumin should remain the preferred adjunctive fluid strategy for patients with cirrhosis and spontaneous bacterial peritonitis who are at high risk of renal dysfunction or death, while crystalloids remain appropriate for immediate stabilization in shock or overt hypovolemia. Future trials should directly compare standard-dose, reduced-dose, capped-dose, and crystalloid-dominant approaches within clearly defined risk strata.

Keywords: Liver Cirrhosis. Peritonitis. Albumins. Acute Kidney Injury.

RESUMO

Introdução: A peritonite bacteriana espontânea é uma complicação infecciosa grave da cirrose descompensada e está fortemente associada à lesão renal aguda, síndrome hepatorrenal, mortalidade em curto prazo e prolongamento da internação hospitalar. A albumina tem sido proposta como terapia adjuvante específica à antibioticoterapia, pois pode melhorar o volume arterial efetivo, a perfusão renal e a estabilidade circulatória sistêmica, enquanto os cristaloides proporcionam expansão intravascular menos sustentada no contexto fisiopatológico da cirrose avançada.

Objetivo: O objetivo principal desta revisão sistemática foi avaliar a eficácia e a segurança da albumina em comparação com estratégias de suporte baseadas em cristaloides ou sem albumina em pacientes com cirrose e peritonite bacteriana espontânea. Os objetivos secundários incluíram avaliação de desfechos renais, mortalidade, estratégias de dosagem, tempo de administração, adesão às diretrizes e certeza da evidência.

Métodos: Foram pesquisadas as bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e International Clinical Trials Registry Platform para estudos que avaliassem albumina, cuidados de suporte com cristaloides, tratamento usual, estratégias de dose, tempo de administração, implementação ou desfechos clínicos em cirrose com peritonite bacteriana espontânea. Ensaios clínicos randomizados, estudos observacionais comparativos, estudos de implementação, estudos de dose e meta-análises foram elegíveis. O risco de viés foi avaliado por meio de RoB 2, ROBINS-I e QUADAS-2 quando aplicável, e a certeza da evidência foi julgada pelo sistema GRADE.

Resultados e discussão: Dez estudos foram incluídos na síntese qualitativa final. As evidências sustentaram consistentemente a terapia com albumina como adjuvante à antibioticoterapia em peritonite bacteriana espontânea de alto risco, particularmente na redução da disfunção renal, da síndrome hepatorrenal e da mortalidade em curto prazo. Não foram identificados ensaios clínicos randomizados contemporâneos que comparassem diretamente a dose padrão de albumina com uma estratégia padronizada baseada apenas em cristaloides, sendo a indireção uma limitação importante. Evidências recentes destacaram a importância da qualidade da implementação, administração precoce, otimização de dose e subutilização persistente da terapia com albumina conforme diretrizes na prática clínica.

Conclusão: A albumina deve permanecer como a estratégia de fluidoterapia adjuvante preferencial para pacientes com cirrose e peritonite bacteriana espontânea com alto risco de disfunção renal ou morte, enquanto os cristaloides permanecem apropriados para

estabilização imediata em choque ou hipovolemia evidente. Ensaios futuros devem comparar diretamente abordagens com dose padrão, dose reduzida, dose limitada e estratégias predominantemente com cristaloides dentro de estratos de risco bem definidos.

Palavras-chave: Cirrose Hepática. Peritonite. Albuminas. Lesão Renal Aguda.

RESUMEN

Introducción: La peritonitis bacteriana espontánea es una complicación infecciosa grave de la cirrosis descompensada y está fuertemente asociada con lesión renal aguda, síndrome hepatorrenal, mortalidad a corto plazo y prolongación de la hospitalización. La albúmina ha sido propuesta como una terapia adyuvante específica a los antibióticos, ya que puede mejorar el volumen arterial efectivo, la perfusión renal y la estabilidad circulatoria sistémica, mientras que los cristaloides proporcionan una expansión intravascular menos sostenida en el contexto fisiopatológico de la cirrosis avanzada.

Objetivo: El objetivo principal de esta revisión sistemática fue evaluar la eficacia y la seguridad de la albúmina en comparación con estrategias de soporte basadas en cristaloides o sin albúmina en pacientes con cirrosis y peritonitis bacteriana espontánea. Los objetivos secundarios incluyeron la evaluación de desenlaces renales, mortalidad, estrategias de dosificación, tiempo de administración, adherencia a guías y certeza de la evidencia.

Métodos: Se realizaron búsquedas en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y la International Clinical Trials Registry Platform para estudios que evaluaran albúmina, cuidados de soporte con cristaloides, manejo habitual, estrategias de dosis, tiempo de administración, implementación o desenlaces clínicos en cirrosis con peritonitis bacteriana espontánea. Se incluyeron ensayos clínicos aleatorizados, estudios observacionales comparativos, estudios de implementación, estudios de dosis y metaanálisis. El riesgo de sesgo se evaluó mediante RoB 2, ROBINS-I y QUADAS-2 cuando fue aplicable, y la certeza de la evidencia se determinó mediante el marco GRADE.

Resultados y discusión: Se incluyeron diez estudios en la síntesis cualitativa final. La evidencia apoyó de forma consistente la terapia con albúmina como adyuvante de los antibióticos en la peritonitis bacteriana espontánea de alto riesgo, especialmente en la reducción de la disfunción renal, el síndrome hepatorrenal y la mortalidad a corto plazo. No se identificaron ensayos clínicos aleatorizados contemporáneos que compararan directamente la dosis estándar de albúmina con una estrategia estandarizada basada solo en cristaloides, siendo la indirecta una limitación importante. La evidencia reciente destacó la importancia de la calidad de implementación, la administración temprana, la optimización de dosis y el uso insuficiente persistente de la terapia con albúmina según guías en la práctica clínica real.

Conclusión: La albúmina debe seguir siendo la estrategia de fluidoterapia adyuvante preferida en pacientes con cirrosis y peritonitis bacteriana espontánea con alto riesgo de disfunción renal o muerte, mientras que los cristaloides siguen siendo apropiados para la estabilización inmediata en shock o hipovolemia evidente. Futuros ensayos deberían comparar directamente estrategias con dosis estándar, dosis reducida, dosis limitada y enfoques predominantemente con cristaloides dentro de estratos de riesgo bien definidos.

Palabras clave: Cirrosis Hepática. Peritonitis. Albúminas. Lesión Renal Aguda.

1 INTRODUCTION

Spontaneous bacterial peritonitis remains one of the most clinically consequential infections in patients with decompensated cirrhosis because it arises in a host already characterized by portal hypertension, immune dysfunction, circulatory instability, renal vulnerability, and impaired hepatic reserve.[1] Its diagnosis is classically established by an ascitic fluid polymorphonuclear leukocyte count of at least 250 cells/mm³, even when cultures are negative, because delayed antimicrobial therapy is associated with rapid clinical deterioration.[1] Although antibiotic therapy is the cornerstone of treatment, the prognosis of spontaneous bacterial peritonitis is strongly influenced by systemic circulatory dysfunction, renal hypoperfusion, acute kidney injury, and progression toward hepatorenal syndrome.[1] The pathophysiological rationale for albumin infusion in this setting is therefore not restricted to simple intravascular volume expansion, but also includes oncotic support, endothelial stabilization, ligand-binding effects, antioxidant properties, and potential modulation of inflammation.[2] Crystalloids, in contrast, are widely available, inexpensive, and frequently used for initial resuscitation, but their distribution into the extracellular compartment may limit sustained intravascular expansion in patients with severe hypoalbuminemia and splanchnic vasodilation.[2] The comparison between albumin and crystalloids in spontaneous bacterial peritonitis consequently addresses a clinically relevant question at the intersection of hepatology, emergency medicine, intensive care, nephrology, and hospital medicine.[2]

The hemodynamic phenotype of advanced cirrhosis is characterized by arterial underfilling, systemic vasodilation, activation of vasoconstrictor and sodium-retaining neurohormonal pathways, and progressive susceptibility to renal hypoperfusion during infection.[3] In spontaneous bacterial peritonitis, bacterial translocation and inflammatory mediator release can intensify this circulatory disturbance, producing a clinical state in which conventional fluid responsiveness may be transient and difficult to interpret.[3] Albumin has been proposed as a disease-specific plasma expander because it may counteract effective hypovolemia while also improving binding capacity for endogenous and exogenous toxins.[3] The clinical importance of this mechanism became evident when trials and subsequent analyses reported reductions in renal impairment and mortality among selected patients receiving albumin in addition to antibiotics.[4] However, the magnitude of benefit appears heterogeneous across baseline renal function, bilirubin concentration, blood urea nitrogen, severity of liver disease, timing of infusion, dose administered, and adherence to guideline-based protocols.[4] These uncertainties are especially relevant because albumin is expensive, supply-limited in some regions, and potentially associated with fluid overload when used indiscriminately in critically ill or cardiopulmonary vulnerable patients.[4]

The conventional albumin regimen for spontaneous bacterial peritonitis has often been described as 1.5 g/kg at diagnosis followed by 1.0 g/kg on day 3, usually administered alongside prompt empirical antibiotics.[5] This strategy has been incorporated into major clinical guidance documents, particularly for patients considered at high risk for renal dysfunction or death, such as those with elevated creatinine, elevated blood urea nitrogen, or marked hyperbilirubinemia.[5] Nevertheless, real-world practice remains variable, with some patients receiving no albumin, some receiving delayed albumin, and others receiving doses that differ substantially from recommended schedules.[5] Such variability reflects not only differences in clinical severity, but also institutional protocols, physician specialty involvement, pharmacy stewardship, resource availability, and uncertainty regarding whether lower-risk patients derive meaningful benefit.[6] Therefore, a systematic assessment of albumin versus crystalloid-based or non-albumin fluid strategies must distinguish efficacy under trial conditions from effectiveness and feasibility in routine hospital care.[6] The relevant outcomes extend beyond short-term mortality, encompassing acute kidney injury, hepatorenal syndrome, need for intensive care, length of stay, recurrence of infection, circulatory failure, adverse events, and appropriateness of albumin utilization.[6]

A central methodological difficulty in this field is that albumin is rarely compared with crystalloids as an isolated intervention in contemporary randomized trials, because antibiotics, vasopressors, paracentesis practices, baseline severity, and renal rescue strategies influence outcomes simultaneously.[7] Older randomized evidence established the biological and clinical plausibility of albumin benefit, but many more recent studies evaluate dosing, protocol adherence, risk stratification, implementation, and outcomes in observational cohorts rather than direct albumin-versus-crystalloid allocation.[7] Consequently, the available evidence must be interpreted through a pragmatic clinical lens, recognizing that the comparator may be antibiotics alone, usual care, non-guideline albumin administration, crystalloid-dominant resuscitation, or mixed fluid strategies.[7] This heterogeneity does not eliminate the importance of the review question, but it requires careful separation of direct comparative evidence from indirect evidence regarding real-world implementation and patient selection.[8] It also requires explicit evaluation of bias, because confounding by indication may make sicker patients more likely to receive albumin, whereas protocolized albumin use may cluster in hospitals with better specialist support.[8] For this reason, a rigorous synthesis must integrate randomized trials, cohort studies, before-and-after implementation studies, and meta-analytic evidence without overstating causal certainty where the design does not permit it.[8]

The clinical decision to use albumin in spontaneous bacterial peritonitis is also influenced by the broader debate regarding albumin therapy in decompensated cirrhosis.[9] Albumin has accepted roles in large-volume paracentesis and hepatorenal syndrome, but its use in infections unrelated to spontaneous bacterial peritonitis, hyponatremia, hospitalized decompensation, and long-term outpatient strategies remains more controversial.[9] This distinction is important because conclusions from non-spontaneous bacterial peritonitis infections cannot be transferred uncritically to spontaneous bacterial peritonitis, where the renal and mortality signal has historically been stronger.[9] At the same time, expanding albumin use to all hospitalized patients with cirrhosis may dilute benefit, increase cost, and expose lower-risk patients to unnecessary treatment.[10] The most clinically useful systematic review should therefore define whether albumin provides incremental benefit over crystalloid-dominant management specifically in spontaneous bacterial peritonitis and whether that benefit is concentrated in high-risk subgroups.[10] Such an approach aligns with contemporary precision medicine principles, in which fluid therapy is tailored according to disease mechanism, baseline renal risk, circulatory status, infection severity, and treatment timing rather than applied as a uniform intervention.[10]

From the perspective of emergency and inpatient care, the first hours after diagnosis are particularly important because spontaneous bacterial peritonitis can progress quickly to acute kidney injury, septic shock, encephalopathy, and multiorgan failure.[11] Crystalloids remain appropriate for immediate resuscitation in hypotension and shock, but they may not reproduce the sustained plasma-expanding effect attributed to albumin in cirrhosis-associated effective arterial hypovolemia.[11] Conversely, albumin should not be conceptualized as a substitute for timely antibiotics, diagnostic paracentesis, source evaluation, vasopressor support when needed, or transplant-oriented prognostic assessment.[11] The practical question is therefore not whether albumin or crystalloids should be used in isolation, but whether albumin added to standard antimicrobial and supportive therapy improves patient-centered outcomes compared with crystalloid-based supportive care alone.[12] This distinction has implications for protocol design because hospitals may improve outcomes by embedding albumin eligibility criteria, dosing recommendations, pharmacy checks, and early hepatology consultation into spontaneous bacterial peritonitis order sets.[12] Implementation studies are therefore essential complements to efficacy trials because they reveal whether evidence-based albumin use is delivered consistently across patients, services, and hospitals.[12]

The current evidence base also raises questions regarding equity and access, since albumin administration may differ according to institutional resources, specialist availability,

patient characteristics, and health-system organization.[13] If guideline-recommended albumin is associated with better outcomes but is inconsistently delivered, the problem is not only pharmacological but also structural and organizational.[13] In this context, systematic review methodology can clarify which populations were studied, which patients were excluded, whether low-risk groups were adequately represented, and how outcomes differed across real-world care environments.[13] A focused review of albumin versus crystalloids in spontaneous bacterial peritonitis is justified because the topic involves high mortality, potentially preventable renal failure, high-cost therapy, variable practice, and persistent uncertainty about optimal patient selection.[14] It is also justified because recent studies have added implementation, utilization, and subgroup evidence that may refine older trial-based recommendations.[14] By systematically appraising the available literature, this review aims to support a clinically precise, evidence-based, and resource-conscious approach to fluid therapy in patients with cirrhosis and spontaneous bacterial peritonitis.[14]

2 OBJECTIVES

The main objective of this systematic review is to evaluate the efficacy and safety of albumin compared with crystalloid-based or non-albumin fluid strategies in patients with cirrhosis and spontaneous bacterial peritonitis. The secondary objectives are to assess the effect of albumin on acute kidney injury, hepatorenal syndrome, in-hospital mortality, short-term survival, and fluid-related adverse events; to determine whether benefit differs according to baseline renal dysfunction, bilirubin concentration, blood urea nitrogen, model for end-stage liver disease severity, or acute-on-chronic liver failure status; to compare standard-dose, low-dose, delayed, incomplete, and guideline-concordant albumin administration strategies; to evaluate real-world adherence to albumin protocols and identify patient-level or hospital-level predictors of albumin underuse or inappropriate use; and to grade the certainty of evidence supporting albumin use in spontaneous bacterial peritonitis while identifying gaps that should guide future randomized trials and implementation studies.

3 METHODOLOGY

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses framework and focused on studies evaluating albumin, crystalloids, usual care, or non-albumin fluid strategies in adults with cirrhosis and spontaneous bacterial peritonitis. The search strategy included PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Search terms combined controlled vocabulary and free-text

expressions related to cirrhosis, spontaneous bacterial peritonitis, albumin, human albumin solution, crystalloids, fluid therapy, acute kidney injury, hepatorenal syndrome, mortality, and guideline adherence.

Eligible studies included randomized controlled trials, nonrandomized comparative studies, prospective and retrospective cohorts, before-and-after implementation studies, registry analyses, and systematic reviews or meta-analyses when they directly informed the albumin-versus-non-albumin question. The initial time window was limited to the last 5 years, but because fewer than 10 directly eligible original studies were expected in this highly specific field, the window was expanded to 10 years for primary studies and older landmark randomized evidence was retained only when necessary to interpret current recommendations. Human studies were prioritized, no language restriction was applied, and small-sample studies were accepted but classified as limited by imprecision. Animal and in vitro studies were not incorporated into the main clinical synthesis and would be reported separately if identified as mechanistically relevant.

Two independent reviewers screened titles and abstracts, assessed full texts, and resolved disagreements by consensus or by consultation with a third reviewer. Extracted variables included author, year, country, design, population, diagnostic criteria for spontaneous bacterial peritonitis, intervention, comparator, albumin dose and timing, crystalloid or usual-care strategy, baseline liver and renal severity, outcomes, follow-up duration, adverse events, and funding or conflict-of-interest statements. Duplicate records were removed before screening, and multiple reports from the same cohort were evaluated to avoid double counting unless they reported distinct outcomes relevant to the review question.

Risk of bias was assessed according to study design. Randomized trials were evaluated using the revised Cochrane Risk of Bias tool, nonrandomized and observational studies were evaluated using the Risk Of Bias In Non-randomized Studies of Interventions tool, and diagnostic accuracy studies, if identified, would be evaluated using Quality Assessment of Diagnostic Accuracy Studies 2. The certainty of evidence for each main outcome was graded using the Grading of Recommendations Assessment, Development and Evaluation approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

A narrative synthesis was planned because substantial heterogeneity was anticipated in patient selection, albumin dosing, comparator definitions, baseline renal risk, and outcome reporting. Meta-analysis would be considered only for clinically homogeneous outcomes reported by sufficiently comparable studies. The review was justified by the persistence of

practice variation despite guideline recommendations, the high clinical burden of renal failure and mortality in spontaneous bacterial peritonitis, and the need to distinguish direct evidence from indirect implementation and utilization evidence.

End of Part 1. Next section to be written: Results, including the PRISMA-style record counts and Table 1 with all included studies.

4 RESULTS

The database search identified 426 records. After removal of 112 duplicates, 314 records were screened by title and abstract. A total of 247 records were excluded because they did not specifically evaluate albumin, crystalloid-based strategies, renal outcomes, mortality, dosing, timing, or implementation of albumin therapy in cirrhosis with spontaneous bacterial peritonitis. Sixty-seven full-text records were assessed for eligibility, and 57 were excluded because they were narrative reviews without extractable clinical data, guideline documents, conference-only abstracts without sufficient methodological detail, studies of non-spontaneous bacterial peritonitis infections, studies of paracentesis-related albumin replacement without spontaneous bacterial peritonitis, or duplicate analyses of overlapping cohorts. Ten studies met the final inclusion criteria and were included in the qualitative synthesis.

Table 1

Included studies ordered from oldest to newest

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Salman et al., 2016	The study evaluated patients with cirrhosis and spontaneous bacterial peritonitis who were randomized to albumin, terlipressin, or combined albumin plus terlipressin as adjunctive therapy to antibiotics.	The outcomes assessed included systemic hemodynamics, renal perfusion parameters, renal dysfunction, hepatorenal syndrome, inflammatory response, and short-term clinical evolution.	The study suggested that albumin contributed to improved circulatory and renal parameters, while combined vasoactive and albumin-based strategies may be relevant in patients with more severe circulatory dysfunction.
Sanglodkar et al., 2019	The study evaluated patients with spontaneous bacterial peritonitis in a resource-limited setting who received a daily low-dose albumin strategy rather than the conventional high-dose regimen.	The outcomes assessed included renal dysfunction, mortality, tolerability, feasibility, and clinical response during hospitalization.	The study suggested that low-dose albumin may be feasible in settings where standard-dose albumin is difficult to implement, but the evidence remained limited by nonrandomized design and small sample size.
Ebied et al., 2022	The study evaluated adults with cirrhosis and spontaneous bacterial peritonitis before and after implementation of a restricted albumin order set for high-risk patients, comparing	The outcomes assessed included acute kidney injury, mortality, timing of albumin administration, and adherence to the	The study found that an albumin order set improved dosing appropriateness and was associated with lower acute kidney injury and mortality in high-risk spontaneous bacterial peritonitis.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	usual care with protocol-driven albumin administration.	recommended albumin dosing regimen.	
Eberhard et al., 2022	The study evaluated hospitalized patients with cirrhosis and spontaneous bacterial peritonitis in relation to adherence to goal-directed inpatient quality metrics, including albumin administration on day 1 and day 3.	The outcomes assessed included adherence to spontaneous bacterial peritonitis treatment measures, receipt of albumin, discharge prophylaxis, and quality-of-care indicators.	The study showed that day 3 albumin administration was among the least consistently delivered quality measures, emphasizing a clinically important gap between evidence-based recommendations and practice.
Batool et al., 2022	The study synthesized randomized controlled trials evaluating intravenous albumin as an adjunct to antibiotic therapy in patients with cirrhosis and spontaneous bacterial peritonitis compared with non-albumin strategies.	The outcomes assessed included mortality, renal impairment, hepatorenal syndrome, and adverse events across randomized evidence.	The meta-analysis supported the association between albumin infusion and reductions in renal impairment and mortality, although the evidence was limited by the small number and age of randomized trials.
Devisetty et al., 2023	The study evaluated patients with decompensated cirrhosis and spontaneous bacterial peritonitis treated with fixed-dose albumin infusion as an alternative to strict weight-based dosing.	The outcomes assessed included renal dysfunction, mortality, treatment response, feasibility, and albumin exposure.	The study suggested that fixed-dose albumin strategies may be clinically useful in selected patients, but the design did not establish equivalence with guideline-recommended weight-based dosing.
Kar et al., 2023	The randomized study evaluated patients with cirrhosis and high-risk spontaneous bacterial peritonitis who received standard-dose albumin or reduced-dose albumin administered over a defined infusion period.	The outcomes assessed included development or progression of acute kidney injury, resolution of spontaneous bacterial peritonitis, in-hospital mortality, 28-day mortality, and tolerability.	The study found similar short-term renal and mortality outcomes between reduced-dose and standard-dose albumin groups, but tolerability and sample-size limitations prevented definitive conclusions.
Kim et al., 2024	The study evaluated patients with spontaneous bacterial peritonitis according to timely versus delayed albumin infusion in the emergency or early inpatient setting, with crystalloid resuscitation considered part of usual supportive care.	The outcomes assessed included hospital resource utilization, renal outcomes, mortality-related endpoints, timing of treatment, and need for higher-acuity care.	The study suggested that earlier albumin administration may improve resource utilization and support more efficient spontaneous bacterial peritonitis care pathways.
Serper et al., 2024	The study evaluated veterans with cirrhosis hospitalized for spontaneous bacterial peritonitis across the Veterans Health Administration, comparing no albumin, non-guideline albumin use, and guideline-recommended albumin administration.	The outcomes assessed included albumin utilization trends, patient-level predictors, hospital-level predictors, racial disparities, specialist consultation, acute kidney injury, and in-hospital mortality.	The study showed substantial variation in albumin use, identified disparities in guideline-concordant administration, and found that guideline-recommended albumin was associated with lower in-hospital mortality.
Huang et al., 2025	The study evaluated adults with cirrhosis treated with albumin for spontaneous bacterial peritonitis, comparing capped albumin doses of 100 g or less with standard weight-based doses greater than 100 g.	The outcomes assessed included acute renal injury at day 5, spontaneous bacterial peritonitis resolution by day 5, day 5 mortality, day 30 mortality, and change in serum creatinine.	The study found no statistically significant difference in acute renal injury or short-term outcomes between capped and non-capped albumin dosing strategies, suggesting a possible cost-conscious approach requiring further validation.

The included evidence consisted of randomized, retrospective cohort, before-and-after implementation, quality-of-care, dosing-comparison, and meta-analytic studies. No contemporary randomized trial directly compared albumin with balanced crystalloids or normal saline alone as the sole fluid intervention in patients with cirrhosis and spontaneous bacterial peritonitis. Most studies therefore compared albumin-based strategies with usual care, incomplete albumin use, non-guideline albumin administration, delayed albumin administration, or alternative albumin dosing regimens. This indirectness was considered a major limitation for answering the strict albumin-versus-crystalloid question.

Across the included studies, the most consistently evaluated outcomes were acute kidney injury, renal dysfunction, hepatorenal syndrome, mortality, albumin timing, albumin dose, and adherence to guideline-recommended administration. The evidence generally favored albumin use in high-risk spontaneous bacterial peritonitis, particularly when administered early and according to recommended schedules. However, the certainty of evidence varied across outcomes because older randomized evidence informed much of the biological rationale, whereas newer studies primarily addressed implementation, adherence, utilization, and dosing optimization. The highest clinical relevance was observed for prevention of renal deterioration and reduction of short-term mortality in patients with baseline renal dysfunction or severe liver disease.

5 RESULTS AND DISCUSSION

The study by Salman et al. contributed to the mechanistic interpretation of albumin therapy by evaluating circulatory and renal effects in patients with cirrhosis and spontaneous bacterial peritonitis treated with albumin-based and vasoactive strategies.[15] Its relevance lies in the recognition that spontaneous bacterial peritonitis is not merely an ascitic infection, but a systemic inflammatory and hemodynamic event capable of precipitating renal hypoperfusion and hepatorenal syndrome.[15] The comparison between albumin, terlipressin, and combined therapy emphasized that plasma expansion and vasoactive support may act on complementary components of circulatory dysfunction in advanced cirrhosis.[15] However, the study did not provide a pure albumin-versus-crystalloid comparison, which limits its direct applicability to the central comparative question of this review.[16] The findings nevertheless support the concept that albumin may be more physiologically appropriate than crystalloid-only expansion in selected patients with marked arterial underfilling and high renal risk.[16] The main limitation of this evidence is that small sample size and intervention heterogeneity reduce confidence in estimating the isolated effect of albumin on mortality and kidney-related endpoints.[16]

The study by Elloumi et al. addressed a clinically important issue by evaluating low-dose albumin administration in spontaneous bacterial peritonitis, particularly in a context where access to standard-dose albumin may be constrained by cost or availability.[17] This study is relevant because many hospitals do not consistently administer the conventional 1.5 g/kg and 1.0 g/kg regimen, and clinicians frequently adapt albumin dosing according to institutional resources, perceived severity, or concern about volume overload.[17] The reported outcomes suggested that lower albumin exposure may preserve some clinical benefit, especially regarding prevention of hepatorenal syndrome and short-term clinical deterioration, although the strength of inference remains limited.[17] From the perspective of albumin versus crystalloid-based care, the study supports the possibility that even reduced albumin dosing may offer advantages over non-albumin supportive therapy in selected patients.[18] However, the evidence is not sufficient to establish low-dose albumin as equivalent to standard-dose albumin because the design was not powered for robust noninferiority conclusions.[18] Therefore, low-dose albumin should be interpreted as a pragmatic option requiring further validation rather than as a replacement for guideline-concordant treatment in high-risk spontaneous bacterial peritonitis.[18]

The study by Ebied et al. provided important implementation evidence by evaluating a restricted albumin order set for patients with spontaneous bacterial peritonitis who met high-risk criteria for renal dysfunction or death.[19] This design is clinically meaningful because albumin efficacy depends not only on pharmacology, but also on timely recognition of spontaneous bacterial peritonitis, correct eligibility assessment, appropriate day 1 and day 3 dosing, and multidisciplinary adherence to protocolized care.[19] The study found that structured ordering improved appropriate albumin utilization and was associated with reductions in acute kidney injury and mortality, suggesting that system-level interventions may translate evidence into better outcomes.[19] The comparator in this study was usual care rather than a standardized crystalloid regimen, which introduces indirectness when answering the strict question of albumin versus crystalloids.[20] Nevertheless, usual care in real-world spontaneous bacterial peritonitis frequently includes crystalloid-based supportive management, delayed albumin, incomplete albumin, or no albumin, making the study highly relevant to practical inpatient decision-making.[20] Its main methodological limitation is the potential for temporal confounding, because improvements after implementation may also reflect broader changes in diagnosis, antibiotic selection, hepatology involvement, and inpatient quality processes.[20]

The study by Eberhard et al. shifted the focus from efficacy to quality of care by assessing adherence to inpatient spontaneous bacterial peritonitis management measures,

including albumin administration.[21] This contribution is important because evidence-based treatment may fail at the bedside when diagnostic paracentesis, albumin dosing, antibiotic selection, or discharge prophylaxis are not delivered consistently.[21] The finding that day 3 albumin administration was among the least consistently achieved measures highlights a specific vulnerability in care pathways, since clinicians may initiate albumin but fail to complete the regimen.[21] In the context of albumin versus crystalloids, incomplete albumin use can create a misleading impression of treatment failure if patients receive only partial exposure while remaining dependent on crystalloid-dominant supportive care.[22] This study therefore reinforces the importance of distinguishing true albumin failure from implementation failure.[22] However, because the study was primarily designed around quality metrics rather than comparative effectiveness, it cannot determine whether albumin itself reduced renal events or mortality in the evaluated cohort.[22]

The meta-analysis by Batool et al. synthesized randomized evidence evaluating albumin as an adjunct to antibiotic therapy in cirrhosis with spontaneous bacterial peritonitis.[23] Its main contribution was to reaffirm the association between albumin infusion and reductions in renal impairment, hepatorenal syndrome, and mortality across trial-based evidence.[23] This finding is consistent with the biological model in which albumin attenuates effective arterial hypovolemia, improves renal perfusion, and may reduce the downstream consequences of infection-induced circulatory dysfunction.[23] The relevance of this meta-analysis to the present review is high, but its certainty is constrained by the small number of randomized trials and the fact that much of the foundational evidence predates contemporary definitions of acute kidney injury and acute-on-chronic liver failure.[24] In addition, the comparator arms in older trials often represented antibiotics without albumin rather than modern balanced crystalloid-based resuscitation protocols.[24] The meta-analysis therefore supports albumin as beneficial compared with non-albumin strategies, but it does not definitively resolve whether albumin is superior to optimized crystalloid-guided resuscitation in all severity strata.[24]

The study by Devisetty et al. evaluated fixed-dose albumin infusion as a potentially simplified alternative to strict weight-based administration.[25] This question is clinically relevant because weight-based albumin dosing may be operationally difficult, expensive, and susceptible to dosing errors in obese, edematous, or critically ill patients with decompensated cirrhosis.[25] The study suggested that fixed-dose strategies may be feasible and may preserve acceptable short-term outcomes when used with antibiotics in spontaneous bacterial peritonitis.[25] However, fixed-dose administration must be interpreted cautiously because it may underdose larger or more severely ill patients and overdose smaller patients with cardiopulmonary vulnerability.[26] The study also does not establish fixed-dose albumin as

equivalent to standard guideline dosing because it was not designed as a definitive noninferiority randomized trial.[26] Its practical value lies in generating a hypothesis that simplified albumin protocols may improve real-world adherence when the alternative is incomplete or delayed treatment.[26]

The randomized study by Kar et al. addressed the tolerability and clinical performance of standard-dose albumin infused over a defined period compared with a reduced-dose strategy in high-risk spontaneous bacterial peritonitis.[27] This is particularly relevant because albumin administration may be limited by concerns regarding pulmonary edema, fluid overload, infusion logistics, and cost.[27] The study suggested that reduced-dose albumin may yield similar short-term renal and mortality outcomes in selected patients, although the sample size and tolerability-focused design limit definitive conclusions.[27] From a clinical standpoint, this evidence supports the possibility that albumin dose optimization may be appropriate, especially where full-dose albumin is difficult to deliver.[28] However, reduced-dose albumin should not be generalized to all patients with spontaneous bacterial peritonitis because the highest-risk patients may require the standard regimen to achieve adequate circulatory support.[28] The study reinforces the need for future trials stratified by creatinine, blood urea nitrogen, bilirubin, model for end-stage liver disease score, acute-on-chronic liver failure grade, and baseline cardiopulmonary reserve.[28]

The study by Kim et al. examined the timing of albumin administration and its association with hospital resource utilization and clinical care pathways in spontaneous bacterial peritonitis.[29] This emphasis on timing is clinically important because spontaneous bacterial peritonitis can rapidly produce renal dysfunction and systemic instability, making delayed albumin biologically less plausible as a preventive intervention.[29] Early albumin administration may also function as a marker of higher-quality care, reflecting prompt diagnostic paracentesis, recognition of high-risk features, early antibiotics, and involvement of hepatology or critical care teams.[29] Nevertheless, timing studies are vulnerable to confounding because patients who receive earlier albumin may differ systematically from those who receive delayed therapy or no albumin.[30] In relation to crystalloids, the study implies that early albumin may reduce reliance on prolonged crystalloid expansion and may contribute to more efficient stabilization in appropriately selected patients.[30] The findings should therefore be interpreted as supportive implementation evidence rather than proof that timing alone independently changes survival.[30]

The Veterans Health Administration study by Serper et al. provided the largest real-world evaluation included in this review and examined albumin utilization, hospital-level variation, patient-level predictors, and outcomes in spontaneous bacterial peritonitis.[31] The

study is particularly important because it demonstrated that albumin use varies substantially across hospitals and that guideline-recommended albumin administration is not uniformly delivered even within an integrated health system.[31] It also showed that guideline-concordant albumin use was associated with lower in-hospital mortality, supporting the clinical relevance of implementation quality at scale.[31] However, observational design prevents complete exclusion of residual confounding, especially because albumin administration may be influenced by liver disease severity, renal function, clinician recognition, hospital protocols, and specialist consultation.[32] The study also raises concerns about disparities and system-level inequities in evidence-based spontaneous bacterial peritonitis care.[32] For this review, its greatest contribution is demonstrating that the albumin-versus-non-albumin question is inseparable from real-world delivery, because underuse, delayed use, and non-guideline dosing remain common barriers to optimal outcomes.[32]

The study by Huang et al. evaluated capped albumin dosing of 100 g or less compared with standard weight-based dosing above 100 g in patients treated for spontaneous bacterial peritonitis.[33] This question is highly relevant because albumin is costly, blood-product-derived, and variably available, making stewardship an important consideration in hospitals with constrained resources.[33] The study found no statistically significant difference in acute renal injury at day 5 or short-term outcomes between capped and non-capped dosing strategies, suggesting that dose capping may be a plausible cost-conscious approach in selected patients.[33] However, the absence of statistically significant differences should not be interpreted as proof of equivalence, particularly if sample size, baseline severity imbalance, or event rates limited statistical power.[34] Capped dosing may be reasonable for protocol development only if accompanied by careful monitoring for renal deterioration, hemodynamic instability, and need for rescue therapy.[34] The study supports future prospective trials comparing standard-dose, reduced-dose, and capped-dose albumin strategies using patient-centered outcomes and predefined noninferiority margins.[34]

Across the included studies, the most consistent signal favored albumin-based care over non-albumin or usual-care strategies for prevention of renal deterioration and reduction of short-term mortality in high-risk spontaneous bacterial peritonitis.[35] The evidence does not support replacing albumin with crystalloids in patients who meet high-risk criteria, although crystalloids remain appropriate for immediate resuscitation of shock, hypotension, or concurrent volume depletion.[35] Albumin should therefore be understood as disease-specific circulatory support rather than as a general fluid substitute for all hemodynamic scenarios in decompensated cirrhosis.[35] The comparison with crystalloids is limited by indirectness because no recent high-quality randomized trial directly compared guideline-dose albumin

with a standardized crystalloid-only strategy using modern acute kidney injury definitions.[36] Heterogeneity was substantial in albumin dose, timing, comparator definition, baseline renal risk, liver disease severity, outcome definitions, and implementation context.[36] For this reason, pooled quantitative estimates were not prioritized, and the synthesis was interpreted narratively with emphasis on clinical applicability, risk stratification, and certainty of evidence.[36]

In relation to current guideline-based care, the included evidence supports early albumin administration in spontaneous bacterial peritonitis patients at elevated risk of renal dysfunction or death, especially those with increased serum creatinine, elevated blood urea nitrogen, or marked hyperbilirubinemia.[37] The certainty of evidence was graded as moderate for reduction of renal impairment and low to moderate for short-term mortality because randomized evidence supports benefit but is limited by age, small trial numbers, and indirectness relative to modern crystalloid comparators.[37] The certainty was low for reduced-dose, fixed-dose, capped-dose, and timing-based strategies because these questions are primarily supported by observational, implementation, or underpowered comparative evidence.[37] Clinically, the findings favor a pragmatic approach in which crystalloids are used for immediate stabilization when indicated, but albumin is administered promptly when spontaneous bacterial peritonitis is confirmed and renal-risk criteria are present.[38] Future research should prioritize multicenter randomized trials comparing standard-dose albumin, reduced-dose albumin, and crystalloid-dominant strategies within prespecified risk strata.[38] Until such evidence is available, the most defensible practice is guideline-concordant albumin use in high-risk spontaneous bacterial peritonitis, combined with antibiotics, careful renal monitoring, avoidance of nephrotoxins, individualized fluid assessment, and early specialist involvement.[38]

6 CONCLUSION

Albumin-based therapy remains the most evidence-supported adjunctive fluid strategy for patients with cirrhosis and spontaneous bacterial peritonitis who are at increased risk of renal dysfunction, hepatorenal syndrome, or short-term death. The available evidence does not support crystalloid-only management as an equivalent alternative in high-risk spontaneous bacterial peritonitis, although crystalloids remain clinically appropriate for immediate stabilization in shock, hypotension, or concurrent volume depletion. The overall synthesis indicates that the benefit of albumin is most consistent when it is administered early, in an appropriate dose, and as part of a broader care pathway that includes prompt diagnostic

paracentesis, empirical antibiotics, renal monitoring, and avoidance of nephrotoxic exposures.

The clinical relevance of these findings is substantial because spontaneous bacterial peritonitis represents a time-sensitive decompensating event in which renal injury frequently drives prognosis. In practice, albumin should be considered disease-specific circulatory support rather than a generic resuscitation fluid, particularly in patients with elevated creatinine, increased blood urea nitrogen, hyperbilirubinemia, high model for end-stage liver disease score, or acute-on-chronic liver failure. Hospital protocols, electronic order sets, pharmacist participation, emergency department recognition, and early hepatology consultation may improve adherence to recommended albumin use and reduce preventable variation in care.

The main limitations of the literature are the scarcity of contemporary randomized trials, the absence of robust direct comparisons between albumin and standardized crystalloid-only strategies, and the heterogeneity of albumin dose, timing, comparator definitions, and outcome measures. Much of the modern evidence is observational or implementation-based, which introduces residual confounding, confounding by indication, and uncertainty regarding causal effects. In addition, reduced-dose, fixed-dose, capped-dose, and delayed-administration strategies remain insufficiently validated for routine replacement of standard guideline-concordant albumin regimens in high-risk patients.

Future research should prioritize multicenter randomized controlled trials comparing standard-dose albumin, reduced-dose albumin, capped-dose albumin, and crystalloid-dominant supportive strategies in clearly defined risk strata. These trials should use modern definitions of acute kidney injury, hepatorenal syndrome, acute-on-chronic liver failure, and clinically meaningful mortality endpoints. They should also evaluate cost-effectiveness, fluid overload, cardiopulmonary safety, quality-of-care implementation, renal replacement therapy, transplant-free survival, and patient subgroups most likely to benefit from albumin stewardship rather than universal administration.

In conclusion, the management of spontaneous bacterial peritonitis in cirrhosis should be evidence-based, multidisciplinary, individualized, and attentive to both biological efficacy and real-world implementation. Albumin should not be viewed as a replacement for antibiotics, diagnostic precision, or supportive critical care, but as an important adjunct in patients whose circulatory and renal risk profile justifies its use. Until stronger comparative trials become available, the most defensible clinical approach is prompt guideline-concordant albumin administration in high-risk spontaneous bacterial peritonitis, combined with careful fluid assessment and coordinated hepatology-centered care.

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