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Clinical Perspectives on Long-Term Albumin Therapy in Decompensated Cirrhosis: A Nationwide Delphi Survey in Spain—The ALBA Study

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ABSTRACT

Background and Aims: Albumin is well established for some acute indications in decompensated cirrhosis, but its long-term use remains controversial. The ALBA study explored expert clinical perspectives, barriers, and current practices regarding long-term albumin therapy in Spain.

Methods: A two-round national Delphi study was conducted among 47 hepatology experts from Spanish hospitals with broad geographic coverage. The survey included 40 Delphi statements and 14 items on opinion, attitude, and behaviour across five domains. Consensus was defined as Tastle's coefficient ≥ 0.8. Items with moderate consensus (0.7–0.79) and $< 70\%$ agreement, or < 0.7, were re-evaluated in round two.

Results: Long-term albumin was reportedly used in 25.5% of centers. However, panellists broadly supported its potential benefit in preventing ascites-related complications and endorsed its use regardless of transplant eligibility. It was prioritised for patients with difficult-to-control ascites (89.3%) and renal impairment (55.2%), though benefits were perceived as lower in late-stage disease. Day hospitals were seen as the most appropriate setting, despite strain. Main barriers included evidentiary limitations, institutional logistics, and pharmacy restrictions. Therapy was viewed as overall safe, with dose-dependent cardiac risk, and considered cost-effective. Strong support was expressed for a national registry to guide implementation.

Abbreviations: ACLF, acute-on-chronic liver failure; AKI, acute kidney injury; CI, confidence interval; CLIF-C AD, chronic liver failure consortium acute decompensation score; HRS-AKI, hepatorenal syndrome—acute kidney injury; IL-6, interleukin 6; MELD, model for end-stage liver disease; MELD-Na, MELD score adjusted for serum sodium; OAB, opinion, attitude, and behaviour; pro-BNP, pro–B-type natriuretic peptide; RCT, randomised controlled trial; SBP, spontaneous bacterial peritonitis; SD, standard deviation.

Conclusions: Panellists considered long-term albumin administration to be clinically beneficial and prioritised its use for patients with advanced-stage disease, regardless of transplant candidacy. However, integration into routine practice remains limited due to a lack of robust supporting evidence, along with institutional and logistical barriers. A national registry and targeted strategies to optimise use and resource allocation were endorsed.

1 | Introduction

Albumin is the most abundant plasma protein in humans and is exclusively synthesised by the liver. Its synthesis is markedly reduced in cirrhosis, particularly in the decompensated stage. Moreover, albumin undergoes conformational and functional changes secondary to systemic inflammation and oxidative stress, which severely impair its physiological activity. As a result, the potential benefits of exogenous albumin administration in advanced liver disease have been widely explored [1, 2].

Current guidelines endorse albumin use for specific well-established indications, such as volume replacement after large-volume paracentesis, prevention of acute kidney injury (AKI) in spontaneous bacterial peritonitis (SBP), and the initial management of AKI and treatment of hepatorenal syndrome-AKI (HRS-AKI) [3–11]. These indications typically involve short-term, high-dose albumin therapy administered in hospital settings.

In contrast, the use of long-term albumin therapy in patients with decompensated cirrhosis and ascites, that involves lower weekly doses administered in the outpatient setting, remains highly controversial [1]. As illustrated in Figure 1, following the initial negative findings by Wilkinson and Sherlock [12], two subsequent Italian trials reported a reduced recurrence of ascites, with one of them also suggesting a potential survival benefit [13, 14]. However, methodological limitations hindered the widespread adoption of this strategy.

Interest in long-term albumin therapy has resurged with two recent landmark randomised controlled trials (RCTs) showing conflicting results: The ANSWER study demonstrated significant survival benefits and a reduced incidence of complications in patients receiving long-term albumin [15], while the MATCH trial failed to replicate these outcomes [16]. Differences in dosing regimens, treatment duration, and disease severity have been proposed to explain these discrepancies [1]. Additional data from observational studies support a potential benefit [17–21], even in patients with refractory ascites [22]. Post hoc analyses of the ANSWER trial suggest that achieving serum albumin >4.0 g/dL after one month of treatment may improve survival, support individualised dosing strategies, and indicate effectiveness in patients with diabetes mellitus [23, 24]. In contrast, the ATTIRE trial, which focused on short-term, high-dose albumin administration in acutely decompensated patients, showed no benefit. However, it did not evaluate the chronic use of albumin [25].

Meta-analyses of RCTs have shown that long-term albumin administration reduces portal hypertension–related complications, but does not improve survival, with the overall quality of evidence rated as low [26–29]. Unsurprisingly, while countries like Italy and Australia have incorporated long-term albumin into clinical practice [30, 31], most major societies

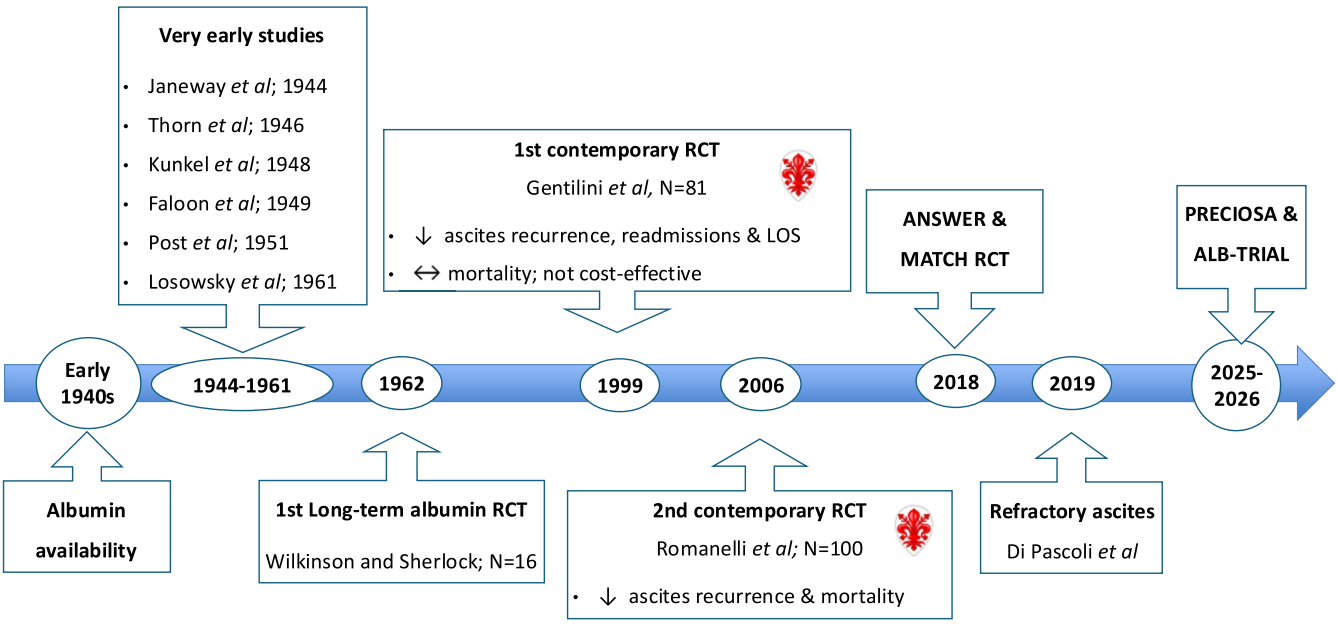

FIGURE 1 | Timeline of key clinical studies evaluating albumin use in cirrhosis. Early studies in the mid-20th century focused on short-term albumin administration for acute complications. The first randomised trial of long-term albumin (Wilkinson and Sherlock [12]) showed negative results. Interest later resurfaced with two Italian trials in the 1990s–2000s suggesting clinical benefit, followed by high-impact randomised controlled trials in the past decade, including ANSWER and MATCH. Ongoing trials such as PRECIOSA and ALB-TRIAL aim to clarify the therapeutic role of long-term albumin in decompensated cirrhosis.

Summary

- Long-term albumin therapy in decompensated cirrhosis remains controversial and inconsistently used in clinical practice.
- In this Delphi study, hepatology experts in Spain globally supported its benefits, but identified key institutional and logistical barriers to implementation.
- A national registry was strongly endorsed to optimise patient selection, guide practice, and support wider adoption.

have not endorsed its routine use [4–11]. The PRECIOSA trial (NCT03451292) and the ALB-TRIAL [32] are expected to help resolve this controversy. Nevertheless, the implementation of long-term albumin use could be limited by several factors, including high cost, the need for intravenous access, potential complications, and dependence on healthcare system resources.

In this context, we conducted a study combining a Delphi panel and an Opinion, Attitude, and Behaviour (OAB) survey to explore current use, attitudes, and barriers related to long-term albumin therapy in routine clinical practice across Spain.

2 | Material and Methods

2.1 | Study Design

In the initial phase, a scientific committee was established, composed of the five hepatologist authors of this manuscript. All members have recognised clinical and research expertise in cirrhosis. This committee oversaw panel selection, literature review, questionnaire development, and the global interpretation of study findings.

The study was conducted across Spain in two online rounds using a mixed-method approach that combined a Delphi consensus technique with an OAB survey. This methodology is widely used in health research to explore consensus among professionals with direct clinical experience, particularly in complex and heterogeneous practice settings. Both Delphi rounds were conducted through a secure, password-protected online platform that ensured full anonymity. No personal identifiers or IP data were collected. To minimise any potential risk of re-identification, demographic and professional characteristics were stored in a separate file and could not be linked back to individual responses. Consequently, subgroup analyses by these variables were not feasible. A summary of the study workflow is presented in Figure S1.

2.2 | Participants

In accordance with the structure of hepatology care in Spain, the expert panel was composed of hospital-based physicians actively involved in the management of patients with cirrhosis.

To ensure a broad representation of perspectives, panellists were selected to reflect geographic diversity and the range of the different levels of care, hospital types and resources across the national healthcare system. The scientific committee initially identified 70 eligible specialists. From this group, a final sample of 47 experts was selected using non-probabilistic cluster sampling, ensuring a representative cross-section of clinical practice in cirrhosis management.

All participants were invited in advance and voluntarily confirmed their participation, minimising the likelihood of attrition and ensuring strong engagement throughout the study. Demographic and professional characteristics were collected at baseline, along with information on albumin use across different clinical indications.

2.3 | Questionnaire Development and Delphi Procedure

The questionnaire included 54 items—40 Delphi-type statements and 14 complementary OAB questions—distributed across three thematic blocks:

1. *Clinical Perceptions and Practices*: Included 15 Delphi statements and 11 OAB questions aimed at understanding clinicians' general stance, awareness, and reported practices regarding both long-term albumin therapy and established acute indications.
2. *Implementation challenges*
   a. *Institutional Organisation*: 5 Delphi statements and 2 OAB questions addressing institutional and organisational challenges.
   b. *Treatment Safety*: 7 Delphi and 1 OAB question on safety and risk perceptions.
   c. *Impact on Quality of Life*: 8 Delphi items on patient burden, experience, and adherence.
3. *Economic Impact*: 5 Delphi items on cost-related considerations influencing treatment decisions.

All Delphi items were rated on a 5-point Likert scale (1 = strongly disagree, 5 = strongly agree). OAB questions included multiple formats: single/multiple choice, ranking, and knowledge/use recognition.

In round one, all participants completed the full questionnaire. A feedback report with aggregated results and commentary from the scientific committee was then circulated. Items without consensus based on predefined criteria were reviewed by the committee, and most were selected for re-evaluation in round two. Participation remained anonymous in both rounds to reduce bias and promote independent judgement. The first round was conducted in September 2021, followed by the second in August 2022.

2.4 | Statistical Analysis

For the OAB questions, descriptive statistics were used. Quantitative variables were summarised using measures of

central tendency (mean, median) and dispersion (standard deviation, 95% confidence intervals), and categorical variables were reported as frequencies and percentages.

For the Delphi statements, group-level measures (mean, median, and standard deviation) were calculated, and agreement was assessed using Tastle's consensus coefficient, based on Shannon entropy. Values ≥0.8 indicated strong consensus, while values between 0.7 and 0.79 were considered moderate. To assess the direction and strength of agreement, all Delphi items were additionally grouped into three response categories on the 5-point Likert scale—Disagree (scores 1–2), Neutral (score 3), and Agree (scores 4–5). Items with a consensus coefficient <0.7, as well as those with moderate consensus but <70% agreement at either end of the scale (i.e., combined Agree or Disagree <70%), were considered for re-evaluation in the second round. At the authors' discretion, and to optimise participation and prevent potential attrition, the most relevant statements were prioritised for reassessment. Associations between Delphi and related OAB responses were explored to better understand contextual influences on agreement patterns.

All analyses were performed using Stata v17.0 and R v4.0.5.

2.5 | Ethical Considerations

The study did not involve patient data, clinical interventions, or treatment allocation. Therefore, informed consent and formal ethics committee approval were not required, in accordance with applicable Spanish regulations. Data were handled in compliance with EU Regulation 2016/679 on data protection and stored in a secured database.

3 | Results

3.1 | Characteristics of the Expert Panel

All 47 specialists completed the first-round questionnaire, while 38 (81%) also participated in the second round. The panel was composed primarily of gastroenterologists (96%), with a minority from internal medicine (4%). About 60% were over 45 years old, 55% were men, and nearly two-thirds had more than 15 years of clinical experience. Experts were geographically distributed across 13 of Spain's 17 autonomous communities.

Most worked in hospitals with over 300 beds (89%). Institutional resources varied: 89% had a hepatology unit, 64% had day hospital services, and nearly half could provide home-based intravenous albumin therapy. These data are presented in Table 1 and Figure S2.

TABLE 1 | Expert panel characteristics.

Characteristic	Value[a]
Total participants	47
Geographic coverage (number of autonomous communities)	13 (76.5)
Specialty	
Gastroenterology and hepatology	45 (95.7)
Internal medicine	2 (4.3)
Sex—Female	21 (44.7)
Age range (years)	
30–45	19 (40.4)
46–55	14 (29.8)
56–65	13 (27.7)
>65	1 (2.1)
Years of clinical experience	
5–9	7 (14.9)
10–14	10 (21.3)
15–19	5 (10.6)
20–24	11 (23.4)
25–29	5 (10.6)
30–34	4 (8.5)
35–39	5 (10.6)
Managerial roles	
No	29 (61.7)
Head of Section	12 (25.5)
Head of Department	6 (12.8)
Hospital size	
100–200 beds	2 (4.3)
201–300 bed	3 (6.4)
>300 beds	42 (89.4)
Hospitals with hepatology unit	42 (89.4)
Hospitals with day hospital services	30 (63.8)
Home-based intravenous administration available	23 (48.9)

[a]Qualitative data are given as numbers and percentages.

3.2 | Reported Indications for Albumin Use Across Centers

As shown in Table 2, most centers reported using albumin for guideline-endorsed indications such as large-volume paracentesis (100%), prevention of AKI in high-risk SBP (91.5%), and treatment of AKI and HRS-AKI (80.9% and 91.5%, respectively). Nonetheless, a substantial proportion also reported its use in non-approved scenarios. Notably, 25.5% of centers indicated they currently administer long-term albumin therapy in patients with cirrhosis and ascites.

3.3 | Block 1—Clinical Perceptions and Practices

Findings for this block are presented in Table 3, which summarises the Delphi statements, and in Table S1 (OAB 1–10) and S2 (OAB 11), which compile responses to the OAB questions.

TABLE 2 | Reported indications for albumin use across centers.

Indication	*N* (% of centers)
Prevention of circulatory dysfunction after large-volume paracentesis (> 5 L)	47 (100)
Treatment of HRS-AKI	43 (91.5)
Prevention of AKI in high-risk SBP (e.g., urea > 60 mg/dL, creatinine > 1 mg/dL, serum bilirubin > 4 mg/dL)	43 (91.5)
Treatment of AKI 1b, 2 and 3 in cirrhotic patients	38 (80.9)
Prevention of AKI in low-risk SBP	31 (66)
Treatment of severe dilutional hyponatremia (< 125–127 mEq/L)	24 (51.1)
Prevention of circulatory dysfunction after low-volume paracentesis (< 5 L) in patients with ACLF	24 (51.1)
Prevention of circulatory dysfunction after evacuating thoracentesis in patients with hepatic hydrothorax	23 (48.9)
Hyponatremia and/or AKI 1a secondary to diuretic treatment in cirrhotic patients with significant edema or anasarca	22 (46.8)
Prevention of circulatory dysfunction after low-volume paracentesis (< 5l) in patients without ACLF	19 (40.4)
Long-term treatment of patients with cirrhosis and ascites	12 (25.5)
Prevention of acute kidney injury in other infections (non-SBP)	12 (25.5)
Treatment of septic shock	12 (25.5)
Treatment of hepatic encephalopathy	4 (8.5)

Abbreviations: ACLF, acute-on-chronic liver failure; AKI, acute kidney injury; HRS-AKI, hepatorenal syndrome—acute kidney injury; MELD, model for end-stage liver disease; SBP, spontaneous bacterial peritonitis.

3.3.1 | Use of Albumin in Guideline-Supported Indications

There was strong consensus regarding the benefit of albumin administration in the management of SBP (Q1, consensus coefficient 0.96) and both HRS-AKI and AKI (Q2, 0.94; OAB 1, 97.9% of respondents). Moreover, most respondents reported administering albumin in clinical practice regardless of the risk of HRS-AKI in SBP (OAB 2, 83%) or the stage of AKI (OAB 3, 46.8%).

3.3.2 | Perspectives on Long-Term Albumin Therapy

Experts widely recognised hypoalbuminemia as a poor prognostic factor (Q3, 0.95) and agreed on the potential clinical benefit of long-term albumin administration (Q4, 0.78), particularly its role in preventing ascites-related complications such as refractory ascites, SBP, and HRS-AKI (OAB 4). These benefits were attributed to both oncotic and non-oncotic mechanisms (OAB 5; Q5, 0.88), with half of the experts supporting the need to monitor treatment response using a combination of routine biomarkers (OAB 6) and advanced cardiac function tools, especially echocardiography (OAB 7), consistent with the relevance of circulatory status in cirrhosis (Q6, 0.88).

3.3.3 | Target Populations and Treatment Strategy

Panellists prioritised long-term albumin therapy for patients with more advanced disease profiles, including those with difficult-to-control ascites (89.3%), renal impairment (53.2%), and unstable decompensation (55.3%) (OAB 8–9; Q7, 0.74). However, they also acknowledged that these populations might derive more limited benefit from treatment (Q8, 0.83; Q9, 0.88). Most experts favoured initiating therapy regardless of transplant eligibility (Q10, 0.30; Q2.1, 0.83) and endorsed the dosing schedule used in the ANSWER study (Q11, 0.74). In terms of safety, there was unanimous agreement that a prior episode of heart failure linked to albumin administration constitutes a contraindication (OAB 10, 100%). Notably, patient age was not considered a limiting factor by the panel. Finally, there was strong consensus on the need for a national real-world registry to support decision-making and improve patient selection (Q12, 0.90; OAB 11-Table S2).

3.3.4 | Refinements in Second Round

Initial agreement on using serum albumin levels to guide treatment was limited (Q13, 0.70), likely due to the strict phrasing. A revised version, presenting it as a potentially useful tool, reached strong consensus (Q2.2, 0.87). Similarly, uncertainty around the use of peripherally inserted central catheters (Q14, 0.65) was resolved by reframing the item to focus on evaluating venous access (Q2.3, 0.80). While consensus was not reached on requiring treatment in referral centers (Q15, 0.68; Q2.4, 0.61), strong agreement supported supervision by such centers (Q2.5, 0.82).

3.4 | Block 2A—Implementation Challenges: Institutional Organisation

Findings are summarised in Table 4. Two of the five Delphi items in this block did not reach consensus. There was uncertainty about the feasibility of home-based administration (Q16, 0.50), which was subsequently reformulated in the second round without reaching consensus either (Q2.6, 0.64). Similarly, no consensus was reached on the need for direct medical supervision in day hospital units (Q17, 0.54).

Moderate consensus was reached regarding the potential burden on day hospital units (Q18, 0.75), which were nonetheless identified as the most suitable setting (OAB 12, 91.5%). Panellists agreed that implementation would not increase medical consultations (Q19, 0.74) but would require formal protocols and pharmacy approval (Q20, 0.76).

Economic restrictions from hospital pharmacy services, logistical challenges, and limited supporting evidence were

TABLE 3 | Delphi statements related to albumin use in cirrhosis—Block 1.

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q1	Albumin administration in patients with SBP reduces the risk of kidney failure and improves survival	0.96	0/2.1/97.9
Q2	Albumin administration in patients with HRS-AKI improves treatment response and survival	0.94	0/0/100
Q3	Hypoalbuminemia is a poor prognostic factor in patients with decompensated cirrhosis	0.95	0/2.1/97.9
Q4	Long-term albumin use in decompensated cirrhosis is associated to fewer complications and improved survival	0.78	6.4/17.0/76.6
Q5	Systemic inflammation may improve with restored albumin levels and function. Biomarkers beyond serum concentration should be explored to guide therapy	0.88	0/2.1/97.9
Q6	Ventricular dysfunction and circulatory decline worsen prognosis. Advanced monitoring may be important	0.88	0/6.4/93.6
Q7	Should PREDICT classification[d] guide initiation of long-term albumin therapy?	0.74	10.6/10.6/78.7
Q8	In the ANSWER study, patients with MELD 12–13 and non-refractory ascites were included. Patients with more advanced disease may therefore derive less benefit	0.83	0/8.5/91.5
Q9	The potential benefit of chronic albumin in patients with refractory ascites requiring repeated paracentesis, regardless of replacement dosing, should be explored	0.88	0/2.1/97.9
Q10	Continuous albumin administration is not indicated in patients who are not liver transplant candidates	0.30	80.9/14.9/4.3
Q2.1	The decision to administer long-term albumin therapy is independent of liver transplant indication	0.83	14/6/78
Q11	In the absence of definitive data, albumin should be administered following the ANSWER study schedule (40 g twice weekly for 2 weeks, then 40 g weekly)	0.74	8.5/17.0/74.5
Q12	A registry led by the Spanish Association for the Study of the Liver is needed to capture real-world practice and address knowledge gaps	0.90	2.1/6.4/91.5
Q13	Serum albumin levels during treatment should guide therapy	0.70	17.0/17.0/66.0
Q2.2	Serum albumin levels during treatment may be useful to guide therapy	0.87	14/6/78
Q14	Weekly long-term albumin administration does not require long-term central venous access	0.65	17.0/36.2/46.8
Q2.3	Long-term albumin therapy requires careful assessment of venous access	0.80	11/4/85
Q15	Long-term albumin candidates are often potential transplant recipients. Despite limited short-term benefit, treatment programs should be implemented in reference centers	0.68	21.3/21.3/57.4

(Continues)

TABLE 3 | (Continued)

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q2.4	Given the frequent transplant indication in patients eligible for long-term albumin therapy, treatment should be implemented in reference centers	0.61	62/15/23
Q2.5	Long-term albumin therapy should be supervised by the reference hospital, regardless of the administration setting	0.82	8/8/84

Abbreviations: HRS-AKI, hepatorenal syndrome–acute kidney injury; MELD, model for end-stage liver disease; SBP, spontaneous bacterial peritonitis.
[a]Questions re-evaluated in the second Delphi round are labelled as Q2.x, where "x" corresponds to the order in that round.
[b]Consensus Coefficient: Calculated using Tastle's method. Values ≥0.8 indicate strong consensus; values between 0.7 and 0.79 indicate moderate consensus.
[c]Agreement: Responses were grouped into three categories based on a 5-point Likert scale: Disagree (1–2), Neutral (3), and Agree (4–5). Items with moderate consensus were re-evaluated in the second round if fewer than 70% of responses clustered at either end of the scale (i.e., Agree or Disagree <70%).
[d]See reference [33].

identified as the main barriers to long-term albumin administration (OAB 13).

3.5 | Block 2B—Implementation Challenges: Treatment Safety

Findings are summarised in Table 5. There was strong consensus on the overall safety of long-term albumin therapy (Q21, 0.82), as well as on the low risk of hypersensitivity reactions (Q22, 0.86) and infectious disease transmission (Q23, 0.89).

Moderate consensus was reached that albumin does not increase the risk of variceal bleeding (Q24, 0.76), while the impact on other bleeding complications—such as portal hypertensive gastropathy—remained inconclusive (Q25, 0.33). Complementary OAB responses (OAB 14) suggested that in patients unable to tolerate beta-blockers, endoscopic variceal band ligation should be considered.

No consensus was reached regarding whether the dosing regimen used in the ANSWER study (Q26, 0.45) or higher doses (Q27, 0.64) increase the risk of heart failure. However, when the question was reformulated to assess a potential dose-dependent risk, strong agreement was achieved (Q2.7, 0.84).

3.6 | Block 2C—Implementation Challenges: Impact on Quality of Life

Findings are summarised in Table 6. Moderate consensus was reached that long-term albumin therapy improves quality of life in cirrhotic patients with ascites (Q28, 0.75) and reduces hospitalisation and length of stay (Q29, 0.80). In line with earlier OAB-4 responses, strong consensus supported that albumin decreases the need for paracentesis and related complications such as HRS-AKI and SBP (Q30, 0.83). Consistently, there was also moderate agreement that long-term albumin lowers diuretic-related side effects (Q31, 0.77) and reduces the required diuretic dose to manage ascites (Q32, 0.76).

In contrast, no consensus was reached regarding its impact on reducing the risk of severe hepatic encephalopathy (Q33, 0.68) or infections other than SBP (Q34, 0.68). Similarly, concerns around long-term treatment adherence remained unresolved (Q35, 0.54), even after the reformulated item in the second round (Q2.8, 0.67).

3.7 | Block 3—Economic Impact

Findings are summarised in Table 7. The panel reached moderate consensus that only a small proportion of outpatients with cirrhosis are appropriate candidates for long-term albumin therapy (Q36, 0.73). Although the reformulated version of Q37 (0.60) addressing resource impact showed moderate consensus (0.71), agreement did not meet the predefined threshold for directional agreement (Q2.9, 61%). However, there was strong consensus on the need to implement local strategies to reduce inappropriate use and optimise resource allocation (Q38, 0.83).

Although moderate consensus supported the notion that treatment costs might be offset by reductions in hospital admissions and cirrhosis-related complications (Q39, 0.79), there was no clear agreement on whether frequent visits impose a meaningful economic burden (Q40, 0.54), and the reformulated item (Q2.10, 0.70; 63% agreement) also failed to reach consensus.

4 | Discussion

This national Delphi study, complemented by an OAB survey, provides a comprehensive assessment of clinician perspectives on the controversial indication of long-term albumin therapy in cirrhosis in the Spanish healthcare system. The panel included experienced hepatologists from a wide range of care settings and geographic areas across the country. While the overall perception of long-term albumin use was favourable, our findings highlight evidence gaps, along with institutional and logistical barriers that hinder its widespread implementation in routine practice. The following sections discuss the most relevant findings of the study.

4.1 | Clinical Practice Patterns

Albumin has been used in patients with cirrhosis for decades, with its therapeutic applications evolving alongside advances

TABLE 4 | Implementation challenges: Block 2A–institutional organisation.

(A) Delphi statements

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q16	Home-based albumin administration by nursing staff is feasible in my healthcare area	0.50	51.1/21.3/27.7
Q2.6	In my healthcare area, long-term home administration of albumin would be feasible	0.64	38/20/42
Q17	Albumin administration should be performed under medical supervision in day hospital units	0.54	48.9/19.1/31.9
Q18	Implementing this new albumin indication would significantly burden day hospital units	0.75	17.0/10.6/72.3
Q19	Weekly long-term albumin does not increase medical visits aside from dispensing albumin	0.74	14.9/12.8/72.3
Q20	Implementing this albumin use requires off-label protocols and Pharmacy Committee approval	0.76	17.0/12.8/70.2

(B) Opinion, attitude, and behaviour responses[d]

	Frequency (*n*)	Response (%)	Cases (%)
OAB 12: In which setting would continuous albumin administration be most suitable in your clinical practice? (Select all that apply)			
• Inpatient setting	0	0	0
• Day hospital	43	63.2	91.5
• Emergency department	0	0	0
• At home	23	33.8	48.9
• Primary care	2	2.9	4.3
OAB 13: What are the main limitations of continuous albumin administration in cirrhosis patients? (Select all that apply)			
• Economic or pharmacy-related restrictions	26	23.4	55.3
• Logistics of repeated albumin administration	31	27.9	66.0
• Reduced quality of life from frequent treatment visits	23	20.7	48.9
• Risk of adverse effects	7	6.3	14.9
• Lack of sufficient scientific evidence to support its use	24	21.6	51.1

[a]Questions re-evaluated in the second Delphi round are labelled as Q2.x, where "x" corresponds to the order in that round.
[b]Consensus Coefficient: Calculated using Tastle's method. Values ≥0.8 indicate strong consensus; values between 0.7 and 0.79 indicate moderate consensus.
[c]Agreement: Responses were grouped into three categories based on a 5-point Likert scale: Disagree (1–2), Neutral (3), and Agree (4–5). Items with moderate consensus were re-evaluated in the second round if fewer than 70% of responses clustered at either end of the scale (i.e., Agree or Disagree < 70%).
[d]"Frequency (*n*)" is the number of times that response was selected, "Response (%)" is the percentage of total responses, and "Cases (%)" refers to the percentage of participants who selected that option.

in the understanding of both its oncotic and non-oncotic properties [1]. Reflecting this evolution, the panel agreed on the prognostic influence of hypoalbuminemia in decompensated cirrhosis and on the efficacy of albumin in managing SBP, AKI, and HRS-AKI, consistent with current clinical guidelines [3–11]. Importantly, considerable heterogeneity in clinical practice was observed. Many clinicians reported the use of albumin in scenarios where supporting evidence is limited or not explicitly endorsed by clinical guidelines—such as SBP with low risk of HRS-AKI, AKI stage 1A, low-volume paracentesis (with or without acute-on-chronic liver failure [ACLF]) and hyponatremia. Among these, long-term albumin therapy emerged as one of the least frequently used indications, underscoring the controversy of its use in clinical practice.

TABLE 5 | Implementation challenges: Block 2B—treatment safety.

(A) Delphi statements

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q21	Long-term albumin treatment is safe and associated with few adverse effects	0.82	2.1/6.4/91.5
Q22	The risk of hypersensitivity reactions is low	0.86	0/6.4/93.6
Q23	The risk of infectious disease transmission is low	0.89	0/6.4/93.6
Q24	Variceal bleeding risk should not limit chronic albumin use, as no current studies have shown increased risk	0.76	12.8/8.5/78.7
Q25	Long-term albumin treatment increases the risk of other portal hypertension-related bleeding (e.g., portal hypertensive gastropathy)	0.33	76.6/21.3/2.1
Q26	Albumin at 40 g biweekly for 2 weeks, then weekly, increases the risk of fluid overload and heart failure	0.45	63.8/19.1/17.0
Q27	Albumin at 1.5 g/kg every 8–12 days increases the risk of fluid overload and heart failure	0.64	27.7/17.0/55.3
Q2.7	Long-term albumin therapy carries some risk of heart failure that may depend on the dose administered	0.84	11/0 / 89

(B) Opinion, attitude, and behaviour responses[d]

	Frequency (*n*)	Response (%)	Cases (%)
OAB 14: Given the high mortality of bleeding, which of the following factors should be considered? (Select all that apply)			
• Reduced tolerance or contraindications to beta-blockers are common in these patients	36	42.4	76.6
• Band ligation is advised if drug prophylaxis is insufficient	34	40	72.3
• Special caution should be exercised with the use of anticoagulants in cases of portal vein thrombosis	15	17.6	31.9

[a]Questions re-evaluated in the second Delphi round are labelled as Q2.x, where "x" corresponds to the order in that round.
[b]Consensus Coefficient: Calculated using Tastle's method. Values ≥0.8 indicate strong consensus; values between 0.7 and 0.79 indicate moderate consensus.
[c]Agreement: Responses were grouped into three categories based on a 5-point Likert scale: Disagree (1–2), Neutral (3), and Agree (4–5). Items with moderate consensus were re-evaluated in the second round if fewer than 70% of responses clustered at either end of the scale (i.e., Agree or Disagree < 70%).
[d]"Frequency (*n*)" is the number of times that response was selected, "Response (%)" is the percentage of total responses, and "Cases (%)" refers to the percentage of participants who selected that option.

4.2 | Perceived Efficacy and Target Populations

Despite its limited use, long-term albumin therapy was generally viewed positively by the expert panel, who emphasised its potential to reduce key ascites-related complications—such as refractory ascites, SBP, HRS-AKI, and the need for paracentesis or hospitalisation—through both oncotic and non-oncotic mechanisms. Interestingly, clinicians prioritised its use in more complex clinical settings such as unstable decompensation, renal dysfunction, or difficult-to-control ascites, even recognising that these subgroups may be less likely to derive substantial benefit from albumin infusion. This paradox may reflect a pragmatic approach to manage high-risk patients in which therapeutic options are limited. Moreover, the differences between the trial population of the ANSWER study (i.e., patients with uncomplicated ascites) and real-world patients underscore the need for more nuanced guidance tailored to sicker patient cohorts. Experts also supported individualised therapy using serum albumin levels and echocardiographic markers of circulatory function, suggesting a shift toward more personalised care. Finally, while transplant candidacy did not influence therapeutic decisions, the preference for referral centers' oversight indicates the perceived complexity of this intervention.

4.3 | Implementation Challenges and Future Directions

Long-term albumin therapy was broadly perceived as safe and beneficial for improving quality of life in decompensated cirrhosis. Fluid overload was the only relevant safety concern—viewed as dose-dependent and particularly important in patients with prior episodes of heart failure, which were considered a clear contraindication. In contrast, commonly considered barriers such as treatment adherence, hospital visit burden, or reduced albumin availability—were not considered major obstacles. Notably, most clinicians considered the treatment to be cost-effective, echoing the conclusions of economic evaluations conducted in Spain, Mexico, and Brazil based on the ANSWER trial [34–36].

TABLE 6 | Delphi statements on implementation challenges: Block 2C—impact on quality of life.

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q28	Long-term albumin treatment improves quality of life in cirrhotic patients with ascites	0.75	0/27.7/72.3
Q29	Long-term albumin treatment reduces hospitalizations and length of stay	0.80	2.1/17.0/80.9
Q30	Long-term albumin treatment reduces the need for paracentesis and ascites-related complications (e.g., HRS-AKI and SBP)	0.83	2.1/8.5/89.4
Q31	Long-term albumin treatment reduces diuretic-related side effects	0.77	4.3/17.0/78.7
Q32	Long-term albumin treatment reduces the dose of diuretics required to control ascites	0.76	4.3/19.1/76.6
Q33	Long-term albumin treatment reduces the risk of severe hepatic encephalopathy (West Haven grade 3–4)	0.68	10.6/34.0/55.3
Q34	Long-term albumin treatment reduces the risk of infections other than SBP	0.68	8.5/42.6/48.9
Q35	Weekly long-term albumin administration does not present adherence issues for most patients	0.54	40.4/25.5/34.0
Q2.8	Weekly albumin administration entails challenges for long-term treatment adherence	0.67	32/0 / 68

Abbreviations: HRS-AKI, hepatorenal syndrome–acute kidney injury; SBP, spontaneous bacterial peritonitis.
[a]Questions re-evaluated in the second Delphi round are labelled as Q2.x, where "x" corresponds to the order in that round.
[b]Consensus Coefficient: Calculated using Tastle's method. Values ≥0.8 indicate strong consensus; values between 0.7 and 0.79 indicate moderate consensus.
[c]Agreement: Responses were grouped into three categories based on a 5-point Likert scale: Disagree (1–2), Neutral (3), and Agree (4–5). Items with moderate consensus were re-evaluated in the second round if fewer than 70% of responses clustered at either end of the scale (i.e., Agree or Disagree <70%).

TABLE 7 | Delphi statements on the economic impact of long-term albumin use—Block 3.

Question number[a]	Item	Consensus coefficient[b]	Agreement[c] (Disagree/Neutral/Agree) (%)
Q36	Only a small proportion of outpatients with cirrhosis are candidates for long-term albumin therapy	0.73	14.9/12.8/72.3
Q37	This treatment would lower self-sufficiency by increasing reliance on commercial albumin and raise associated costs	0.60	27.7/31.9/40.4
Q2.9	Long-term albumin therapy in cirrhosis would increase usage, reduce availability, and raise costs	0.71	29/10 / 61
Q38	Local strategies are needed to curb inappropriate use and improve albumin self-sufficiency	0.83	4.3/8.5/87.2
Q39	The cost of long-term albumin use is offset by reduced hospital stays, fewer paracenteses, and fewer cirrhosis-related complications	0.79	0/29.8/70.2
Q40	Frequent travel to healthcare facilities is not a significant cost burden for most patients	0.54	42.6/23.4/34.0
Q2.10	The cost and work-related impact of frequent visits to healthcare facilities may be significant for patients	0.70	29/8/63

[a]Questions re-evaluated in the second Delphi round are labelled as Q2.x, where "x" corresponds to the order in that round.
[b]Consensus Coefficient: Calculated using Tastle's method. Values ≥0.8 indicate strong consensus; values between 0.7 and 0.79 indicate moderate consensus.
[c]Agreement: Responses were grouped into three categories based on a 5-point Likert scale: Disagree (1–2), Neutral (3), and Agree (4–5). Items with moderate consensus were re-evaluated in the second round if fewer than 70% of responses clustered at either end of the scale (i.e., Agree or Disagree <70%).

The gap between favourable perceptions of long-term albumin therapy and its limited implementation highlights evidentiary, institutional and health system–level barriers. Experts identified key obstacles, including the lack of robust supporting evidence, limited day hospital capacity, and restrictive pharmacy policies. To address these issues, the panel strongly supported the creation of a national registry to generate real-world data, refine patient selection, and support context-sensitive, feasible implementation strategies.

In parallel, ongoing RCTs such as PRECIOSA and ALB-TRIAL are expected to provide robust clinical data that complement real-world insights. The PRECIOSA trial targets a high-risk population—closely aligned with the profile prioritised by our panel—namely, patients with decompensated cirrhosis and ascites requiring hospitalisation (excluding ACLF), and a CLIF-C AD score > 50. The study evaluates high-dose albumin (1.5 g/kg every 10 days for 12 months). Preliminary results showed no significant improvement in 1-year transplant-free survival, but a significant benefit at 3 months (HR 0.58 [95% CI: 0.34–0.99]; $p = 0.044$). The study also reported lower rates of SBP and HRS-AKI, and confirmed the safety of long-term high-dose albumin [37]. The final results will be essential to determine its potential clinical impact. Meanwhile, the ALB-TRIAL will offer complementary insights by using a biomarker-guided strategy and a shorter treatment duration (6 months), further informing the debate on the feasibility and optimization of long-term albumin therapy [32].

4.4 | Limitations

First, as with any Delphi study the results reflect expert opinion rather than clinical outcomes and are therefore subject to inherent biases related to perception and experience. Local differences in the availability to prescribe may have influenced how some items—particularly those involving newer or less established indications—were interpreted. Second, although some studies on long-term albumin were published after the survey, the key trials likely to impact clinical practice were already available. Third, as is common in OAB-type surveys, some questions may have offered limited response options or flexibility, which could have constrained the expression and interpretation of more nuanced clinical views. Fourth, because individual responses were fully anonymized and stored separately from participant characteristics, subgroup analyses such as comparing managerial versus non-managerial physicians could not be performed. Finally, although the second round response rate remained high, the attrition of 19% (38 of 47 participants) may affect the generalizability of findings from that round.

5 | Conclusions

This national Delphi and OAB survey highlights significant heterogeneity in clinical practice beyond guideline-endorsed indications. Long-term albumin therapy in decompensated cirrhosis is generally perceived by clinicians as safe and potentially beneficial, and its use is prioritised for patients with advanced-stage disease, regardless of transplant candidacy. However, its adoption remains limited, primarily due to evidentiary, institutional, and logistical barriers. Upcoming results from PRECIOSA and ALB-TRIAL will be pivotal in shaping future clinical practice and clarifying current uncertainties.

Author Contributions

All authors fulfilled the ICMJE criteria for authorship. Study concept and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting of the manuscript: J.I.F. and R.B. Critical revision of the manuscript for important intellectual content: all authors.

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Ethics Statement

This study involved an anonymous survey of physicians and did not include identifiable patient data or medical intervention. In accordance with Spanish regulations and institutional policies, formal ethics committee approval was not required.

Conflicts of Interest

All authors received honoraria from Grifols International S.A. for their involvement in the scientific coordination and manuscript preparation of this project. Additional conflicts of interest are individually presented below: J.I.F.: Served as a speaker for Grifols and received travel support from Gilead. D.R.R.: Nothing to declare. A.A.: Served as a speaker for Grifols. E.S.V.: Nothing to declare. R.B.: Served as a speaker for Grifols.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** liv70429-sup-0001-TableS1-S2-FigureS1-S8.docx.