

## Critical Review Form Meta-analysis

PGY-4

[Albumin reduces paracentesis-induced circulatory dysfunction and reduces death and renal impairment among patients with cirrhosis and infection: a systematic review and meta-analysis. Biomed Res Int. 2013;2013:295153.](#)

**Objectives:** To “provide a comprehensive and up-to-date overview of the existing evidence regarding the use of albumin in cirrhotic patients.” (p. 2)

**Methods:** This systematic review and meta-analysis was conducted using randomized controlled trials (RCTs) that evaluated the administration of albumin in patients with cirrhosis. RCTs with parallel design comparing albumin administration with either placebo or an alternate volume expander were included. A literature search was conducted in January 2013 using MEDLINE and EMBASE through OvidSP. The bibliographies of included trials and recent review articles were also assessed.

Risk of bias was assessed according to criteria outlined in the [Cochrane Handbook \(Chapter 8\)](#): sequence generation, allocation concealment, blinding of participants/personnel/outcome assessors, incomplete outcome data, selective reporting, and baseline differences in participants. A [random-effects](#) meta-analysis was performed to calculate pooled odds ratios (OR).

The search yielded 16 relevant articles comprising 1518 patients multiple countries. There were 4 studies evaluating albumin vs. no albumin or saline, 8 studies comparing albumin to an alternative plasma expander, and 4 studies comparing antibiotics with albumin to antibiotics without albumin in cirrhotic patients with infection.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. Patients with cirrhosis undergoing large volume paracentesis are at risk for circulatory dysfunction, renal failure, and death as a result of large fluid shifts. Additionally, patients with SBP are also at risk of adverse outcomes. Given the frequency of hypoalbuminemia in such patients, it is reasonable to assess whether the administration of albumin in such patients to increase oncotic pressure and minimize the body’s inflammatory response could reduce adverse events.
2.	Was the search for	No. The authors searched MEDLINE and EMBASE, and did

	relevant studies details and exhaustive?	evaluate the bibliographies of included studies and recent review articles. The authors did not search CINAHL, the Cochrane database, clinicaltrials.gov, or conference abstracts.
3.	Were the primary studies of high methodological quality?	The studies were of moderate quality. Ten of 16 studies had adequate sequence generation but only 2 had adequate allocation concealment. Blinding was unclear in the majority of studies. Most studies did not have any evidence of selective reporting or baseline differences in study groups.
4.	Were the assessments of the included studies reproducible?	Yes. The authors used criteria set forth in the <a href="#">Cochrane Handbook (Chapter 8)</a> , a widely used tool to evaluate study quality in systematic reviews.
<b>II.</b>	<b><i>What are the results?</i></b>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> <li>• 3 studies evaluating albumin in large volume paracentesis in patients without infection were included with a total population of 228. These demonstrated a significant reduction in paracentesis-induced circulatory dysfunction: OR 0.26, 95% CI 0.08-0.93. No significant difference was observed for other outcomes, including death (OR 1.36, 95% CI 0.61-3.04).</li> <li>• 8 studies compared albumin to other volume expanders in patients without infection. There was no statistically significant difference between albumin and other expanders for any of the outcomes, including death (OR 0.63, 95% CI 0.38-1.03) and renal impairment (OR 1.09, 95% CI 0.51-2.34). Results were not provided for circulatory dysfunction.</li> <li>• 5 studies included patients with any infection. The use of albumin was associated with a reduced risk of death (OR 0.46, 95% CI 0.25-0.86, <math>I^2 = 24\%</math>) and renal impairment (OR 0.34, 95% CI 0.15-0.75, <math>I^2 = 34\%</math>).</li> <li>• 3 studies included participants with SBP. The use of albumin was associated with a reduced risk of death (OR 0.39, 95% CI 0.18-0.84) with a trend towards reduced risk of renal impairment (OR 0.32, 95% CI 0.10-1.04).</li> </ul>
2.	How precise are the results?	See 95% confidence intervals above. The included studies were primarily small, and the resulting confidence intervals in the meta-analysis remain fairly wide, though some do achieve statistical significance.
3.	Were the results similar from study to study?	Uncertain. The authors failed to provide forest plots or $I^2$ statistics for the majority of the analyses. They provide these only for the analyses in studies comparing albumin vs. no albumin in patients with infection. For these analyses, the results were similar from study to study based on visual analysis and based on $I^2$ statistics (all $< 50\%$ ).
<b>III.</b>	<b><i>Will the results help me in caring for my patients?</i></b>	

1.	How can I best interpret the results to apply them to the care of my patients?	<p>The administration of albumin in patients undergoing large volume paracentesis resulted in a significant reduction in the incidence of postparacentesis circulatory dysfunction, with no significant differences in any of the other outcomes, including death and renal impairment. The importance of this reduction in circulatory dysfunction is uncertain, as the authors were unable to assess the interventions required.</p> <p>In patients with SBP, albumin administration was associated with a significant reduction in the risk of death, with a trend towards reduced risk of renal impairment. Based on these results, albumin administration should be strongly considered in patients with SBP without significant contraindication (i.e. CHF).</p>
2.	Were all patient important outcomes considered?	Yes. The meta-analysis considered a wide range of outcomes, including the most clinically relevant outcomes of death, circulatory dysfunction, and renal impairment. The authors were unable to assess outcomes such as cost or hospital length of stay.
3.	Are the benefits worth the costs and potential risks?	<ul style="list-style-type: none"> <li>• In patients with SBP, the evidence for the use of albumin is fairly compelling, as it seems to prevent death with a significant trend towards reduction in renal impairment.</li> <li>• In patients undergoing large-volume paracentesis, the evidence is less compelling; albumin in such cases seems to prevent circulatory dysfunction, but does not prevent death. Given the low risk associated with albumin administration and relatively low cost, it seems reasonable to administer albumin in such cases.</li> </ul>

**Limitations:**

1. **The search strategy was not very comprehensive. The authors did not search CINAHL, the Cochrane database, clinicaltrials.gov, or conference abstracts.**
2. **The included studies were of only moderate quality; the majority was not blinded and had poor allocation concealment. They were also relatively small studies, the largest of which comprised only 135 patients.**
3. **The relatively small number of studies pooled for each outcome makes an assessment of [publication bias](#) very limited. This is particularly true in light of the lack of effort to obtain any possible unpublished studies to include in the meta-analyses.**

4. Assessment of [heterogeneity](#) is difficult for most of the pooled results as the authors failed to provide [forest plots](#) or  $I^2$  statistics for the majority of the analyses.

**Bottom Line:**

The administration of albumin in patients undergoing large volume paracentesis resulted in a significant reduction in the incidence of postparacentesis circulatory dysfunction (OR 0.26, 95% CI 0.08 to 0.93), with no significant differences in any of the other outcomes, including death and renal impairment. The importance of this reduction in circulatory dysfunction is uncertain, as the authors were unable to assess the interventions required. In patients with SBP, albumin administration was associated with a significant reduction in the risk of death (OR 0.39, 95% CI 0.18 to 0.84), with a trend towards reduced risk of renal impairment. Based on these results, albumin administration is reasonable in patients undergoing large volume paracentesis and should be strongly considered in patients with SBP without significant contraindication (i.e. CHF).