

Critical Review Form

Meta-analysis

PGY-3

[Albumin infusion improves outcomes of patients with spontaneous bacterial peritonitis: a meta-analysis of randomized trials. Clin Gastroenterol Hepatol. 2013 Feb;11\(2\):123-30.](#)

Objectives: To quantitatively combine "the results of all currently available RCTs evaluating the effects of albumin infusion on renal impairment and mortality in patients with SBP [spontaneous bacterial peritonitis]." (p. 124)

Methods: For this systematic review and meta-analysis, randomized controlled trials assessing the effect of albumin in patients with SBP were included. Studies in which different albumin doses were compared were not eligible for inclusion. A search was performed of MEDLINE, EMBASE, the Cochrane Library, ClinicalTrials.gov, abstract databases from major meetings in hepatology and gastroenterology, and sources indexed by Google Search. The authors also examined reference lists of articles about cirrhosis and the online tables of contents for major hepatology and gastroenterology journals. Three investigators independently determined trial eligibility.

Out of 64 studies screened, 4 trials meeting eligibility requirements were identified comprising a total of 288 patients and were included in the meta-analysis using a [fixed-effects model](#). The endpoints being evaluated were renal impairment and mortality. The authors evaluated study quality by assessing randomization method, allocation concealment, and blinding. All studies defined SBP by the presence of > 250 or ≥ 250 polymorphonuclear cells (PMNs) per mm^3 . All studies limited enrollment to adults, and all excluded patients who had received antibiotics in the previous week, patients with cardiac or renal disease, patients with HIV, patients with grade 3-4 hepatic encephalopathy, those with GI bleeding, or those of "advanced age." The length of follow-up was 90 days in one study, and was not specified in the other 3 studies.

In 3 trials, for patients without preexisting kidney disease renal impairment was defined as an increase in serum creatinine to > 1.5 mg/dL, or alternatively an increase in BUN to > 30 mg/dL in 2 of the trials. For patients with preexisting renal insufficiency in 2 of these 3 trials, renal impairment was defined as a relative increase in creatinine or BUN or $> 50\%$. In the fourth trial, renal impairment was defined solely as a serum creatinine > 1.5 mg/dL or BUN > 25 mg/dL.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. Patients with cirrhosis and SBP are at risk of developing renal failure and mortality. 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 hence restore arterial blood volume, and to minimize the body's inflammatory response could reduce adverse events.
2.	Was the search for relevant studies details and exhaustive?	Yes. The authors searched all of the major databases. They also searched clinicaltrials.gov for possible unpublished studies registered there, conference abstracts, and tables of content from appropriate journals.
3.	Were the primary studies of high methodological quality?	No. Quality among the studies ranged from high to low. Three of the trials used appropriate computer-generated randomization sequences with sealed envelopes to conceal allocation. The fourth article used coin toss to randomize patients. Only one of the trials was blinded
4.	Were the assessments of the included studies reproducible?	Yes. The authors assessed study quality by looking at three criteria: randomization method, allocation concealment, and blinding. They did not assess for selective outcome reporting or incomplete outcome data .
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<p><u>Renal impairment</u></p> <ul style="list-style-type: none"> For all trials, 12 of 144 patients receiving albumin (8.3%) developed renal impairment compared to 44 of 144 patients not receiving albumin (30.6%). The pooled OR was 0.21 (95% CI 0.11-0.42, $I^2 = 0\%$). This correlates to an approximate NNT of 4[†]. <p><u>Mortality</u></p> <ul style="list-style-type: none"> Total mortality in all 4 trials was 23 of 144 patients receiving albumin (16.0%) compared to 51 of 144 patients not receiving albumin (35.4%) The pooled OR was 0.34 (95% CI 0.19-0.60, $I^2 = 0\%$). This correlates to an approximate NNT of 5[†]. <p>† Calculated using http://ktclearinghouse.ca/cebm/practise/ca/calculators/ortonnt</p>
2.	How precise are the results?	See above. The 95% CIs are relatively narrow and do not cross 1.0 for either of the outcomes.
3.	Were the results similar from study to study?	Yes. By visual analysis of the Forest plots the 95% CI's off all 4 studies overlap for both outcomes. Additionally the I^2 statistic was 0% for both outcomes.

III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	This well-done meta-analysis suggests that administration of albumin in patients with SBP reduces the risk of renal impairment and mortality. These results are based on one high quality blinded RCT, two non-blinded studies of moderate quality, and one low quality trial in which a coin toss was used to assign patients.
2.	Were all patient important outcomes considered?	No. The authors considered the most important outcomes (mortality and renal impairment), but did not assess hemodynamic decompensation, need for fluid administration or pressors, or incidence of volume overload/respiratory compromise.
3.	Are the benefits worth the costs and potential risks?	Likely yes. The use of albumin in patients with cirrhosis, are typically quite hypoalbuminemic, can restore circulatory volume and reduce inflammation. There are few adverse effects associated with albumin administration in such patients as long as volume overload is avoided. To mitigate this, all studies in this analysis excluded patients with prior cardiac disease.

Limitations:

- 1. The authors do not provide the date on which the search was performed.**
- 2. The assessment of the quality of the included studies was somewhat limited, as the authors did not assess for [selective outcome reporting](#) or [incomplete outcome data](#).**
- 3. There was a good deal of methodological heterogeneity between studies, and one incidence of significant clinical heterogeneity. One of the included studies compared albumin to hydroxyethyl starch, probably should not have been included in the meta-analysis, though this would not have had a large impact on the results.**
- 4. The relatively small number of studies pooled for each outcome makes an assessment of [publication bias](#) very limited.**

Bottom Line:

This well-done meta-analysis suggests that administration of albumin in patients with SBP reduces the risk of renal impairment and mortality, with approximate NNTs of 4 and 5, respectively. These results are based on one high quality blinded

RCT, two non-blinded studies of moderate quality, and one low quality trial in which a coin toss was used to assign patients.