

Albumin Administration in Patients with Severe Sepsis Due to Secondary Peritonitis

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Background: To determine whether or not intravenous administration of human albumin can reduce mortality in patients with severe sepsis due to secondary peritonitis.

Methods: Adult patients who were admitted to the surgical intensive care unit (SICU) who fulfilled the criteria of severe sepsis due to secondary peritonitis were consecutively included in this retrospective study. Patients who received and those who did not receive at least a daily minimum of 25 g intravenous human albumin for 3 days during their first 7 days of SICU admission were classified as the study group and control group, respectively.

Results: A total of 133 patients were included in this study. For patients with baseline serum albumin ≤ 20 g/L, 28-day mortality was significantly lower in the study group. For patients with baseline serum albumin > 20 g/L, albumin administration had no significant effects on 28-day mortality.

Conclusion: For patients with severe sepsis due to secondary peritonitis, albumin administration may reduce 28-day mortality in patients whose baseline serum albumin is ≤ 20 g/L, but no such effect was found in patients whose baseline serum albumin was > 20 g/L. [*J Chin Med Assoc* 2009;72(5):243–250]

Key Words: albumin, hypoalbuminemia, mortality, secondary peritonitis, severe sepsis

Introduction

Severe sepsis defined as sepsis with acute organ dysfunction^{1,2} is associated with high morbidity and mortality rates despite advances in critical care management.^{3,4} In the United States, the mortality rate of severe sepsis was 30–50%, which increased to 80–90% for septic shock with multiple organ dysfunction.⁵ In European countries, the mortality rate of patients with severe sepsis and septic shock in the intensive care unit (ICU) was 32.2–54.1%.^{6,7} In China, 28-day mortality for patients with severe sepsis in the surgical ICU (SICU) was 44.7%.⁸

Secondary peritonitis is a common problem in SICU practice and is mostly caused by intra-abdominal visceral perforation, acute infection of intra-abdominal

viscera, bowel wall necrosis, post-trauma and post-operation.⁹ In most patients, secondary peritonitis resolves following prompt operative intervention and appropriate antimicrobial therapy.¹⁰ However, elderly patients are more likely to develop severe sepsis, hence prolonged ICU stay and increased mortality.^{11–13}

Albumin is the main determinant of plasma oncotic pressure. It plays a pivotal role in modulating the distribution of fluid between compartments. Moreover, it has many biological properties that may be important not only for its physiologic actions but also for its therapeutic effects. The non-oncotic properties of albumin include molecular transportation, free radical scavenging, modulation of capillary permeability, neutrophil adhesion and activation, and hemostatic effects.¹⁴ The rate of albumin synthesis is affected by both nutrition



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and inflammation.¹⁵ Patients with severe sepsis and secondary peritonitis usually suffer from severe hypoalbuminemia and inflammatory process.

There is controversy regarding albumin administration among meta-analyses. The meta-analysis performed by the *Cochrane Injuries Group Albumin Reviewers* found no evidence to support the notion that albumin administration reduces mortality in critically ill patients with hypovolemia, burns or hypoalbuminemia; in contrast, they found that albumin might increase mortality.¹⁶ Choi et al found no difference in mortality and pulmonary edema between crystalloid and colloid resuscitation.¹⁷ The meta-analysis performed by Wilkes and Navickis¹⁸ showed no effect of albumin on mortality. Two studies have reported the benefit of albumin administration. Rackow et al¹⁹ showed that resuscitation of hypovolemic and septic shock patients with either 6% hetastarch or 5% albumin was associated with a lower incidence of pulmonary edema than was resuscitation with 0.9% saline. Sort et al²⁰ showed that albumin given to patients with cirrhosis and spontaneous bacterial peritonitis in addition to antibiotics reduced the incidence of renal impairment and death compared to treatment with antibiotics alone. In addition, albumin has been shown to be effective in preventing renal failure in patients with cirrhosis and ascites, and in reducing mortality in patients with spontaneous bacterial peritonitis.^{21,22}

The *Saline vs. Albumin Fluid Evaluation* (SAFE) trial, looking to settle the disputes through randomized controlled trials for mortality in ICU patients, has shown that the use of albumin for fluid resuscitation resulted in similar outcomes at 28 days.²³ In the SAFE trial, albumin seemed to improve survival in patients with severe sepsis despite statistical insignificance (relative risk of death [RR], 0.87; 95% confidence interval [CI], 0.74–1.02; $p=0.09$). One meta-analysis performed by Vincent et al²⁴ reported that albumin significantly reduced overall morbidity (RR, 0.92; 95% CI, 0.86–0.98; $p=0.002$).

Although the SAFE study revealed no significant difference in all-cause 28-day mortality between the albumin group and non-albumin group irrespective of their baseline albumin concentration, the Bureau of National Health Insurance in Taiwan has set a more restrictive policy on albumin administration as many surgeons continue to recommend albumin use in patients with severe sepsis due to secondary peritonitis in their daily practice. Based on the above reasons, we speculated that these small subsets of ICU patients with severe sepsis and hypoalbuminemia due to secondary peritonitis might benefit from albumin administration. Therefore, we conducted this retrospective study to

investigate whether albumin administration could reduce mortality in patients with severe sepsis and hypoalbuminemia due to secondary peritonitis.

Methods

Patients

This was a retrospective study conducted in the SICU of a tertiary care hospital. Patients who were diagnosed with severe sepsis associated with secondary peritonitis from March 2003 to March 2008 were consecutively enrolled. The criteria for severe sepsis were those defined by the International Sepsis Definitions Conference.² In brief, severe sepsis was defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Organ dysfunction variables included arterial hypoxemia ($\text{PaO}_2/\text{F}_{\text{IO}_2} < 300$), acute oliguria (urine output $< 0.5 \text{ mL/kg/hr}$ for at least 2 hours), creatinine increase $> 0.5 \text{ mg/dL}$, coagulation abnormalities (international normalized ratio > 1.5 or activated partial thromboplastin time > 60 seconds), ileus (absent bowel sounds), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$), and hyperbilirubinemia (plasma total bilirubin $> 4 \text{ mg/dL}$). Tissue perfusion variables included hyperlactatemia ($> 2 \text{ mmol/L}$), and decreased capillary refilling or mottling. Septic shock was defined as acute circulatory failure unexplained by other causes, and acute circulatory failure was defined as persistent arterial hypotension (systolic blood pressure $< 90 \text{ mmHg}$, mean arterial pressure $< 60 \text{ mmHg}$, or a reduction in systolic blood pressure $> 40 \text{ mmHg}$ from baseline despite adequate volume resuscitation).² Secondary peritonitis was diagnosed by either abdominal ultrasonography or abdominal computed tomography and confirmed intraoperatively.

Patients who received a daily minimum of 25 g intravenous human albumin for at least 3 days within the first week of SICU stay were classified into the study group. Patients who received the daily dosage of human albumin but who died within 3 days of SICU admission were also classified into the study group. Patients who did not receive intravenous human albumin or whose daily albumin dosage was $< 25 \text{ g}$ were classified into the control group. All septic patients received aggressive fluid resuscitation in addition to albumin administration. Patients were excluded if they were pregnant, younger than 18 years, or died within 24 hours after admission to the SICU. The study protocol was approved by the institutional review board of the hospital, and written informed consent was waived because this was a retrospective study.

Data collection

The demographic data of the patients on their admission to the SICU were collected. The status of acute organ dysfunction due to severe sepsis was recorded and compared. The presence of comorbidities and transfusion of fresh frozen plasma (FFP) were recorded. Admission severity of illness was estimated by using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, and Multiple Organ Dysfunction Score (MODS). The patients in each group were further stratified into 2 strata: baseline serum albumin concentration ≤ 20 g/L and baseline serum albumin concentration > 20 g/L. The 28-day mortality rate was compared.

Statistical analysis

Categorical variables were expressed as absolute number and relative frequencies, and were compared using χ^2 or Fisher's exact test when appropriate. Continuous variables with normal distribution were expressed as mean \pm standard deviation and compared using Student's *t* test. Univariate analysis was performed for the comparison of the risk of death for all baseline characteristics between the study and control groups in different strata according to their baseline serum albumin concentration. Multivariate logistic regression analysis was performed if the *p* value of the variable was < 0.1 on univariate analysis. Survival times were compared with the use of the log rank test and were presented as Kaplan–Meier curves.

Results

Patient characteristics

Within the study period, 133 patients were diagnosed with secondary peritonitis and severe sepsis, and were admitted to the SICU. There were 52 patients in the study group and 81 patients in the control group. Table 1 summarizes the patients' clinical characteristics. There were no significant differences in any of the baseline characteristics between the study and control groups except for the total amount of albumin administered in the first 7 days.

Comparison of mortality

Table 2 compares the 28-day mortality rates of the study and control groups. Among the patients with baseline serum albumin ≤ 20 g/L, there were 10 (45%) patients in the study group and 28 (76%) in the control group who died within 28 days (RR, 0.27; 95% CI, 0.09–0.83; *p*=0.03). Albumin significantly reduced

the 28-day mortality rate in patients with secondary peritonitis and severe sepsis whose baseline serum albumin was ≤ 20 g/L. For patients with baseline serum albumin > 20 g/L, there were 15 (50%) study group patients and 14 (32%) control group patients who died within 28 days (RR, 2.14; 95% CI, 0.82–5.58; *p*=0.18). Albumin administration resulted in no significant difference in the 28-day mortality rate in patients with baseline albumin concentration > 20 g/L.

Univariate analysis showed that variables such as diagnosis (infection site or source), operation (type of surgery) and type of cultured bacteria had *p* > 0.10 on the risk of 28-day mortality. These variables were not analyzed further using multivariate analysis. In the group of patients with baseline serum albumin ≤ 20 g/L, univariate analysis showed that the variables of age, APACHE II, SOFA, MODS and frequency of septic shock had *p* < 0.1 . In the group of patients with baseline serum albumin > 20 g/L, univariate analysis showed that APACHE II, SOFA, MODS and frequency of septic shock, respiratory dysfunction and renal dysfunction had *p* < 0.1 . These variables were further analyzed using multivariate analysis. Table 3 shows the results of univariate analysis of all the baseline characteristics that might affect the risk of 28-day mortality in the 2 groups of patients.

Table 4 shows the results of multivariate analysis of the variables that might affect 28-day mortality after univariate regression with *p* < 0.10 in the 2 groups of patients. We found that albumin administration reduced 28-day mortality in patients whose baseline serum albumin was ≤ 20 g/L (odds ratio, 0.203; 95% CI, 0.049–0.844; *p*=0.028); but no such effect was found in patients whose baseline serum albumin was > 20 g/L (OR, 1.995; 95% CI, 0.607–6.555; *p*=0.255).

The probability of survival in the study and control groups with baseline albumin concentration ≤ 20 g/L is shown in the Kaplan–Meier curves (Figure 1). The study group was associated with a significantly higher probability of survival (*p*=0.002, log-rank test). The probabilities of survival in the study and control groups with baseline albumin concentration > 20 g/L are shown in Figure 2. No significant difference in probability of survival was found between the study and control groups (*p*=0.08, log-rank test).

Discussion

In this study, we found no significant difference in the 28-day and hospital mortalities between the study and control groups (*p*=1.00 and *p*=0.96, respectively) if the patients were not stratified according to their

Table 1. Clinical characteristics of the patients*

	Control group	Study group
Baseline serum albumin concentration ≤ 20 g/L		
Patients (n)	37	22
Plasma albumin at admission (g/L)	16.9 \pm 2.8	16.7 \pm 2.3
Total albumin in first 7 d (g)	15 \pm 18 [†]	90 \pm 22
Fresh frozen plasma transfusion	30 (81)	19 (86)
Age (yr)	70.9 \pm 14.6	71.8 \pm 14.4
Male	22 (60)	16 (73)
Admission APACHE II	22.7 \pm 5.8	21.6 \pm 5.7
Admission SOFA	9.9 \pm 2.9	9.1 \pm 3.2
Admission MODS	7.0 \pm 2.8	6.6 \pm 2.8
Comorbidity	33 (89)	20 (91)
Cardiovascular disease	11 (30)	9 (41)
Chronic respiratory disease	6 (16)	5 (23)
Chronic hepatic disease	8 (22)	6 (27)
Chronic renal failure	7 (19)	6 (27)
Diabetes mellitus	14 (38)	8 (36)
Organs with acute dysfunction		
Shock	32 (87)	15 (68)
Respiratory dysfunction	34 (92)	21 (96)
Renal dysfunction	18 (49)	13 (59)
Hematologic dysfunction	16 (43)	8 (36)
Hepatic dysfunction	8 (22)	3 (14)
Referred from		
ER	15 (41)	8 (36)
Ward	16 (43)	9 (41)
MICU	6 (16)	5 (23)
Baseline serum albumin concentration > 20 g/L		
Patients (n)	44	30
Plasma albumin at admission (g/L)	25.7 \pm 4.3	25.1 \pm 3.8
Total albumin in first 7 d (g)	6.5 \pm 13 [†]	111 \pm 54
Age (yr)	78.9 \pm 12.4	76.5 \pm 13.2
Male	23 (52)	15 (50)
Admission APACHE II	22.2 \pm 7.2	21.0 \pm 7.0
Admission SOFA	8.5 \pm 2.7	9.3 \pm 3.0
Admission MODS	5.9 \pm 2.2	6.5 \pm 2.1
Comorbidity	42 (96)	28 (93)
Cardiovascular disease	32 (73)	20 (67)
Chronic respiratory disease	7 (16)	7 (23)
Chronic hepatic disease	5 (11)	7 (23)
Chronic renal failure	8 (18)	6 (20)
Diabetes mellitus	14 (32)	12 (40)
Organs with acute dysfunction		
Shock	27 (61)	22 (73)
Respiratory dysfunction	32 (73)	28 (93)
Renal dysfunction	26 (59)	23 (77)
Hematologic dysfunction	10 (23)	13 (43)
Hepatic dysfunction	6 (14)	5 (17)
Referred from		
ER	8 (18)	4 (13)
Ward	29 (66)	15 (50)
MICU	7 (16)	11 (37)

*Data presented as mean \pm standard deviation or n (%); [†] $p < 0.05$. APACHE II = Acute Physiology and Chronic Health Evaluation II score; SOFA = Sequential Organ Failure Assessment score; MODS = Multiple Organ Dysfunction Score; ER = emergency room; MICU = medical intensive care unit.

Table 2. The 28-day mortality of the patients

Control group	Study group	RR (95% CI)	<i>p</i>
All patients 42 (50%)	25 (51%)	1.04 (0.52–2.11)	1.00
Baseline serum albumin concentration ≤ 20 g/L 28 (76%)	10 (45%)	0.27 (0.09–0.83)	0.03
Baseline serum albumin concentration > 20 g/L 14 (32%)	15 (50%)	2.14 (0.82–5.58)	0.18

RR = relative risk; CI = confidence interval.

baseline albumin concentration on admission (Table 2). Follow-up analysis of the SAFE study²⁵ gave us the idea to further stratify our patients in each group into 2 subgroups: baseline serum albumin concentration ≤ 20 g/L and baseline serum albumin concentration > 20 g/L. The result of this stratification showed that albumin could reduce 28-day mortality in patients with secondary peritonitis and severe sepsis whose baseline serum albumin concentration was ≤ 20 g/L, and that no difference was found in the 28-day mortality rate between the study and control groups in patients with baseline serum albumin concentration > 20 g/L. Using multivariate analysis, we found that septic shock was more important than other confounding factors in the determination of 28-day mortality no matter which baseline albumin group the patient belonged to. In the SAFE study, no significant difference in all-cause mortality at 28 days was found between the albumin group and non-albumin group irrespective of their baseline albumin concentration. Our result was inconsistent with the SAFE study for 28-day survival in patients whose baseline serum albumin concentration was ≤ 20 g/L. The different patient entity and different baseline albumin cut-off point might partly explain this discrepancy.

Why would albumin administration only benefit patients with extremely low baseline serum albumin concentration? The reason might be that plasma oncotic pressure should be maintained at a suitable level so as to maintain homeostasis. If the patient's plasma albumin concentration has declined below that level, then the administration of exogenous albumin might have positive effects on the restoration of homeostasis. However, if the patient's plasma albumin concentration is already beyond that level, then it is possible that exogenous albumin may cause detrimental effects. Several reasons might account for why albumin supplementation could make things worse for critically ill patients. First, cardiac decompensation might occur after rapid volume expansion with 20% albumin, which might lead to an increase in volume retention up to four-fold.²⁶

Indeed, a previous study in baboons found that interstitial pulmonary edema developed after albumin infusion in hemorrhagic shock.²⁷ Second, in patients with increased capillary permeability or capillary leak syndrome, albumin administration may become detrimental when albumin and water cross the capillary membrane and cause or worsen pulmonary edema, compromising tissue oxygenation and leading to multiorgan failure. Third, the anti-hemostatic and platelet-lowering properties of albumin may increase blood loss in post-surgical or trauma patients.²⁸ Finally, albumin administration during resuscitation of hypovolemic shock may impair sodium and water excretion and worsen renal function.²⁹

Although FFP has an oncotic effect and most surgeons prefer using FFP in patients with secondary peritonitis, our study did not find any significant difference in mortality rate due to FFP infusion. Our result was in accordance with the systematic review of Stanworth et al.³⁰ Transfusion of FFP was even said to be associated with an increased risk of infection in critically ill patients.³¹ Thus, it is not surprising that we found no significant difference in mortality rate after FFP infusion.

Elderly patients are at risk of developing severe sepsis after contraction of secondary peritonitis. Anaya and Nathens¹³ showed that patients with severe sepsis due to secondary peritonitis were significantly older (68 ± 19 years *vs.* 46 ± 25 years; $p < 0.001$) and more likely to have pre-existing illnesses than those without severe sepsis. Our results were consistent with their's because patients with both secondary peritonitis and severe sepsis in this study had higher 28-day and hospital mortality rates (50% and 58%, respectively) than those with either severe sepsis alone^{5–8} or secondary peritonitis alone.

It has been shown that the most common cause of peritonitis is a perforated appendix; however, most cases of peritonitis due to perforated appendix is localized and rarely develops into severe sepsis.¹³ Similarly, we found that no patient with severe sepsis due to secondary

Table 3. Univariate analysis of baseline characteristics for the risk of 28-day mortality

	RR (95% CI)	p
Baseline serum albumin concentration \leq 20 g/L		
Plasma albumin at admission (g/L)	0.508 (0.059–4.377)	0.537
Fresh frozen plasma transfusion	1.354 (0.311–5.901)	0.686
Age (yr)	1.041 (1.000–1.083)	0.051*
Male	1.167 (0.380–3.580)	0.788
Admission APACHE II	1.097 (0.993–1.211)	0.069*
Admission SOFA	1.551 (1.204–1.998)	0.001*
Admission MODS	1.533 (1.169–2.010)	0.002*
Comorbidity		
Cardiovascular disease	1.040 (0.337–3.213)	0.946
Chronic respiratory disease	1.600 (0.375–6.820)	0.525
Chronic hepatic disease	1.518 (0.411–5.607)	0.531
Chronic renal failure	0.565 (0.161–1.976)	0.371
Diabetes mellitus	0.508 (0.170–1.519)	0.225
Organs with acute dysfunction		
Shock	8.750 (2.028–37.749)	0.004*
Respiratory dysfunction	6.167 (0.599–63.520)	0.126
Renal dysfunction	2.492 (0.834–7.447)	0.102
Hematologic dysfunction	1.619 (0.534–4.913)	0.395
Hepatic dysfunction	2.948 (0.573–15.163)	0.196
Baseline serum albumin concentration $>$ 20 g/L		
Plasma albumin at admission (g/L)	0.301 (0.083–1.088)	0.067*
Fresh frozen plasma transfusion	0.781 (0.191–3.189)	0.731
Age (yr)	1.025 (0.984–1.067)	0.239
Male	0.618 (0.214–1.586)	0.317
Admission APACHE II	1.086 (1.010–1.107)	0.025*
Admission SOFA	1.203 (1.007–1.437)	0.042*
Admission MODS	1.285 (1.020–1.619)	0.033*
Comorbidity		
Cardiovascular disease	2.155 (0.714–6.267)	0.177
Chronic respiratory disease	0.833 (0.249–2.392)	0.768
Chronic hepatic disease	0.740 (0.201–2.704)	0.651
Chronic renal failure	2.476 (0.738–8.090)	0.133
Diabetes mellitus	0.954 (0.358–2.540)	0.925
Organs with acute dysfunction		
Shock	3.840 (1.242–11.872)	0.019*
Respiratory dysfunction	3.000 (1.100–8.180)	0.032*
Renal dysfunction	2.801 (0.955–8.214)	0.061*
Hematologic dysfunction	1.296 (0.476–3.525)	0.612
Hepatic dysfunction	0.869 (0.230–3.278)	0.835

* $p < 0.1$. RR = relative risk; CI = confidence interval; APACHE II = Acute Physiology and Chronic Health Evaluation II score; SOFA = Sequential Organ Failure Assessment score; MODS = Multiple Organ Dysfunction Score.

peritonitis had appendiceal perforation. It has also been shown that the 3 most common presenting symptoms of severe sepsis are respiratory system dysfunction, shock and renal system dysfunction.^{6,8} Our findings were consistent with these reports.

The potential weaknesses of this study were the limited case number and retrospective methodology. Moreover, although the Bureau of National Health Insurance of Taiwan had established the criteria for

albumin administration, in most circumstances, the patient's condition did not meet the criteria for albumin administration when the physician in charge felt that albumin administration was necessary for the patient's good. In that case, albumin administration could be at the patient's own expense. The reasons for why some patients who had secondary peritonitis and severe sepsis did not receive albumin administration might include the financial consideration of the family, the hopeless

Table 4. Multivariate analysis of assigned group and baseline characteristics with risk of 28-day mortality

	RR (95% CI)	<i>p</i>
Baseline serum albumin concentration ≤ 20 g/L		
Study vs. control group	0.203 (0.049–0.844)	0.028*
Age	1.051 (1.004–1.101)	0.034*
APACHE II	0.958 (0.821–1.117)	0.584
SOFA	1.495 (1.131–1.975)	0.005*
MODS	1.602 (0.767–3.346)	0.210
Shock	7.965 (1.467–43.254)	0.016*
Baseline serum albumin concentration > 20 g/L		
Study vs. control group	1.995 (0.607–6.555)	0.255
Albumin at admission	0.296 (0.064–1.365)	0.119
APACHE II	1.079 (1.003–1.162)	0.042*
SOFA	0.836 (0.560–1.246)	0.378
MODS	1.269 (0.753–2.139)	0.371
Shock	3.572 (1.122–11.373)	0.031*
Respiratory dysfunction	0.827 (0.195–3.497)	0.796
Renal dysfunction	2.662 (0.765–9.264)	0.124

* $p < 0.05$. RR = relative risk; CI = confidence interval; APACHE II = Acute Physiology and Chronic Health Evaluation II score; SOFA = Sequential Organ Failure Assessment score; MODS = Multiple Organ Dysfunction Score.

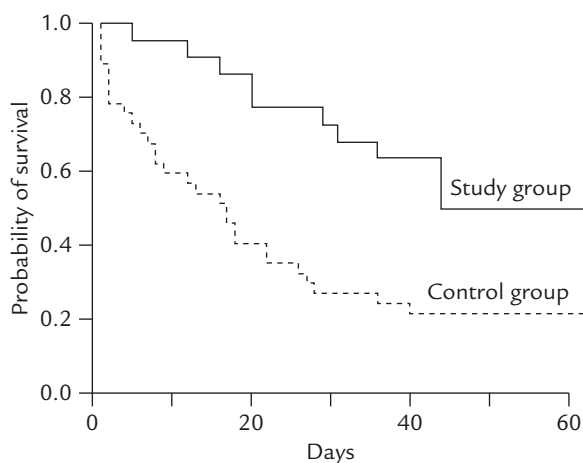


Figure 1. Kaplan–Meier estimates of the probability of survival for baseline albumin concentration of ≤ 20 g/L. The figure shows the probability of survival in the study and control groups with baseline albumin concentration of ≤ 20 g/L within 60 days. The study group was associated with a significantly higher probability of survival ($p = 0.002$, log rank test).

prognosis of the patient's disease, and the personal preference of the physician in charge. These factors might influence the mortality rate of the patients. Nevertheless, our findings suggest that intravenous human albumin could be administered with possible benefit to patients with severe sepsis and secondary peritonitis whose plasma albumin concentration is extremely low.

In conclusion, intravenous administration of human albumin may reduce 28-day mortality in the small subset of ICU patients who contract secondary peritonitis and severe sepsis, with an extremely low baseline serum

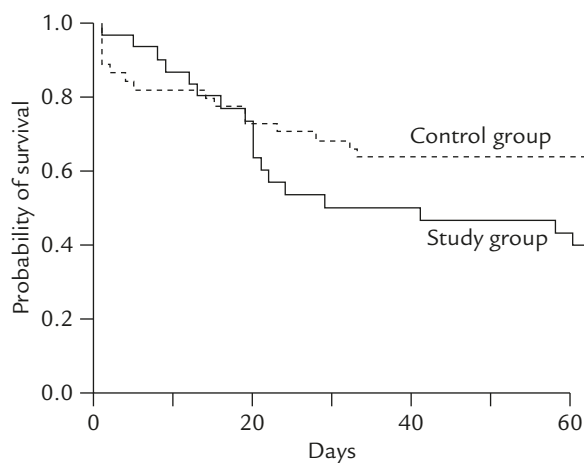


Figure 2. Kaplan–Meier estimates of the probability of survival for baseline albumin concentration > 20 g/L. The figure shows the probability of survival in the study and control groups with baseline albumin concentration > 20 g/L within 60 days. There was no significant difference in probability of survival between the study and control groups ($p = 0.08$, log rank test).

albumin concentration. However, in patients with secondary peritonitis and severe sepsis whose baseline serum albumin is > 20 g/L, albumin administration is not recommended, as indicated in previous studies.

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References

- Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, Schein RM, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis: the ACCP/SCCM Consensus Conference Committee: American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992;101:1644–55.
- Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, et al. SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003;31:1250–6.
- Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, et al. Surviving Sepsis Campaign Guidelines for management of severe sepsis/septic shock. *Crit Care Med* 2004;32:858–73.
- Russell JA. Management of sepsis. *N Engl J Med* 2006;355:1699–713.
- Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med* 2001;29:1303–10.
- Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, Moreno R, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006;34:344–53.
- Adrie C, Alberti C, Chaix-Couturier C, Azoulay E, De Lassence A, Cohen Y, Meshaka P, et al. Epidemiology and economic evaluation of severe sepsis in France: age, severity, infection site, and place of acquisition (community, hospital, or intensive care unit) as determinants of workload and cost. *J Crit Care* 2005;20:46–58.
- Cheng B, Xie G, Yao SL, Wu X, Guo Q, Gu M, Fang Q, et al. Epidemiology of severe sepsis in critical ill surgical patients in ten university hospitals in China. *Crit Care Med* 2007;35:2538–46.
- Borgonovo G, Amato A, Varaldo E, Mattioli FP. Definition and classification of peritonitis. *Méd Mal Infect* 1995;25:7–12.
- Borgonovo G, Amato A, Varaldo E, Mattioli FP. Epidemiology of peritonitis. *Méd Mal Infect* 1995;25:13–9.
- Merlani P, Chenaud C, Mariotti N, Ricou B. Long-term outcome of elderly patients requiring intensive care admission for abdominal pathologies: survival and quality of life. *Acta Anaesthesiol Scand* 2007;51:530–7.
- Hall JC, Hall JL. ASA status and age predict adverse events after abdominal surgery. *J Qual Clin Pract* 1996;16:103–8.
- Anaya DA, Nathens AB. Risk factors for severe sepsis in secondary peritonitis. *Surg Infect* 2003;4:355–62.
- Evans TW. Albumin as a drug—biological effects of albumin unrelated to oncotic pressure. *Aliment Pharmacol Ther* 2002;16(Suppl):6–11.
- Don BR, Kaysent G. Serum albumin: relationship to inflammation and nutrition. *Semin Dial* 2004;17:432–7.
- Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. *BMJ* 1998;317:235–40.
- Choi PT, Yip G, Quinonez LG, Cook DJ. Crystalloids vs. colloids in fluid resuscitation: systematic review. *Crit Care Med* 1999;27:200–10.
- Wilkes MM, Navickis RJ. Patient survival after human albumin administration: meta-anal randomized, controlled trials. *Ann Intern Med* 2001;135:149–64.
- Rackow EC, Falk JL, Fein IA, Siegel JS, Packman MI, Haupt MT, Kaufman BS, et al. Fluid resuscitation in circulatory shock: a comparison of the cardiorespiratory effects of albumin, hetastarch, and saline solutions in patients with hypovolemic and septic shock. *Crit Care Med* 1983;11:839–50.
- Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L, Castells L, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* 1999;341:403–9.
- Xue HP, Lin B, Zhong J, Ji Q. Effect of albumin infusion on preventing the deterioration of renal function in patients with spontaneous bacterial peritonitis. *Chin J Dig Dis* 2002;3:32–4.
- Gines P, Guevara M, De Las Heras D, Arroyo V. Albumin for circulatory support in patients with cirrhosis. *Aliment Pharmacol Ther* 2002;16(Suppl):24–31.
- The SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004;350:2247–56.
- Vincent JL, Navickis RJ, Wilkes MM. Morbidity in hospitalized patients receiving human albumin: a meta-analysis of randomized, controlled trials. *Crit Care Med* 2004;32:2029–38.
- Saline versus Albumin Fluid Evaluation (SAFE) Investigators. Effect of baseline serum albumin concentration on outcome of resuscitation with albumin or saline in patients in intensive care units: analysis of data from the saline versus albumin fluid evaluation (SAFE) study. *BMJ* 2006;333:1044–6.
- Ferreira da Cunha D, Santana FAH, Guiães Tachotti FJ, Freire de Carvalho da Cunha S. Intravenous albumin administration and body water balance in critically ill patients. *Nutrition* 2003;19:157–8.
- Moss GS, Das Gupta TK, Brinkman R, Sehgal L, Newsom B. Changes in lung ultrastructure following heterologous and homologous serum albumin infusion in the treatment of hemorrhagic shock. *Ann Surg* 1979;189:236–42.
- Johnson SD, Lucas CE, Gerrick SJ, Ledgerwood AM, Higgins RF. Altered coagulation after albumin supplements for treatment of oligemic shock. *Arch Surg* 1979;114:379–83.
- Moon MR, Lucas CE, Ledgerwood AM, Kosinski JP. Free water clearance after supplemental albumin resuscitation for shock. *Circ Shock* 1989;28:1–8.
- Stanworth SJ, Brunskill SJ, Hyde CJ, McClelland DB, Murphy MF. Is fresh frozen plasma clinically effective? *Br J Haematol* 2004;126:139–52.
- Sarani B, Dunkman WJ, Dean L, Sonnad S, Rohrbach JI, Gracias VH. Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection. *Crit Care Med* 2008;36:1114–8.