Albumin Versus Gelatin Solution for the Treatment of Refractory Septic Shock: A Patient Baseline-Matched-Cohort Study

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ABSTRACT

Objective: Although albumin solution is the colloid of choice to resuscitate septic shock patients who do not respond to crystalloid solutions, its usage is limited by its cost. Gelatin solution, is less expensive, but its efficacy has not yet been identified. This study aimed to compare the outcomes of gelatin and albumin solutions for septic shock resuscitation.

Methods: This baseline-matched-cohort study, enrolled septic shock patients who had a mean arterial blood pressure (MAP) below 65 mmHg after receiving at least 30 mL per kilogram of crystalloid resuscitation fluid, and who required either an albumin or gelatin solution as fluid therapy. The primary outcome was the 28-day mortality.

Results: In all, 224 patients who were administered either an albumin or gelatin solution were examined. After adjusting for differences in their baseline characteristics, 206 patients were included (104 receiving albumin, and 102 given gelatin). A comparison of the albumin and gelatin groups revealed no significant baseline differences in their respective mean APACHE II scores (22.8±8.5 vs. 23.2±8.1), MAPs (55.1±8.0 vs. 54.6±9.1 mmHg), and lactate levels (5.6±4.7 vs. 6.3±4.9 mmol/L). The 28-day mortality rates were 27.9% and 38.2% for the albumin and gelatin groups, respectively, with adjusted p=0.02. Moreover, the accumulation of fluid intake over output at 72 hours was significantly lower for the albumin than the gelatin group (5,964.5±4,959.7 vs. 8,133.2±3,743.2 ml; p=0.01). The RRT rate was higher for the albumin group (30.8% vs. 15.7%; p=0.01).

Conclusion: Albumin resuscitation associated with lower 28-day mortality than gelatin resuscitation. The patients in the albumin group had a higher RRT rate and a lower fluid accumulation as at 72 hours.

Keywords: Septic shock; colloid solution; albumin solution; gelatin solution; crystalloid solution; fluid resuscitation (Siriraj Med J 2020; 72: 451-461)

INTRODUCTION

According to the Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2016, crystalloid solutions are the fluid of choice for the initial resuscitation of septic shock patients.[1] In the case of patients who do not respond to a certain volume of crystalloid resuscitation (usually at least 30 mL per kilogram of body weight), colloid solutions should be used. Albumin is recommended as the first-choice colloid, based on the evidence of two large randomized controlled trials[2,3] and two meta-analyses.[4,5] Unfortunately, albumin usage in resource-limited countries

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is restricted by its cost, with many patients unable to afford albumin-based resuscitation. In our hospital, when the cost of albumin therapy would prove to be prohibitive for a patient, the alternative colloid utilized for the resuscitation of refractory septic shock is gelatin solution. Gelatin is a small fragment of collagen, and it is one of a number of synthetic colloids that have long been used for volume expansion in certain situations.[6] A previous study demonstrated that resuscitation with a gelatin solution expanded the intravascular volume by about 1.4 times that gained through resuscitation with a crystalloid solution.[7] A similar ratio was achieved with a 5% albumin solution. In addition, data from a meta-analysis showed that resuscitation with a gelatin solution was not only associated with better hemodynamic stabilization than resuscitation with a crystalloid alone, but may also be associated with lower mortality.[8] Although there has been evidence from a few randomized controlled trials relating to the efficacy of gelatin solution relative to that of other colloid solutions, those clinical trials employed small sample sizes and were not performed on septic shock patients.[9,10] Moreover, there is limited information concerning the comparative outcomes of albumin versus (vs.) gelatin solutions for septic shock patient resuscitation.[11]

Septic shock resuscitation typically requires a high fluid volume.[12,13] This raises concerns about the extravasation of colloid molecules, which may be associated with organ dysfunction. Acute kidney injury is associated with hydroxyethyl starch administration among critically ill patients.[14] Although data in a meta-analysis suggested that gelatin solution resuscitation might be associated with subsequent acute kidney injury, the findings were not statistically significant.[7] Even though the lower-priced gelatin solution is used as an alternative colloid to albumin for septic shock resuscitation, its efficacy and safety outcomes have not yet been identified. The aims of this study were to compare the efficacies and safety outcomes of gelatin and albumin solution usage for septic shock resuscitation.

MATERIALS AND METHODS

Study design and ethical considerations

This patient baseline-matched-cohort, retrospective study enrolled septic shock patients who had been admitted to the Internal Medicine Ward, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, 15 December 2014 - 31 October 2018. We used database of a study protocol number: 100/2018(EC1), which was approved by the Siriraj Institutional Review Board (Si 421/2018).

Participants

We screened for patients who were aged over 18 years and had been diagnosed with septic shock, as defined in the Surviving Sepsis Campaign guidelines of 2012.[15] The septic shock patients had been diagnosed and treated by attending physicians at the emergency room, internal medicine ward, or the medical intensive care unit. The treatments followed the Surviving Sepsis Campaign guidelines of 2012 and 2016, which required the initiation of antibiotics coupled with the administration of fluid resuscitation with a crystalloid solution (30 mL/kg) and norepinephrine to reach a target mean arterial blood pressure (MAP) ≥ 65 mmHg.[1] In the event that a patient's hemodynamic state subsequently remained unstable, the use of a colloid solution was considered. The decision to initiate the colloid infusion as well as the type and dose to be used were dependent on each attending physician's clinical judgment. We enrolled those patients who, despite having received at least 30 mL/kg of crystalloid solution resuscitation, still had either a MAP < lower than 65 mmHg or evidence of inadequate tissue perfusion requiring additional fluid resuscitation. The inadequate tissue perfusion was defined as a urine output of < 0.5 mL/kg of body weight or a serum lactate concentration of ≥ 4 mmol/dL.[16] The requirement for additional fluid resuscitation was indicated by the following criteria: a central venous pressure of < 12 mmHg or 15 cmH_2O; a pulmonary wedge pressure of < 18 mmHg; or evidence of fluid responsiveness from one or more non-invasive tests, specifically, an inferior vena cava diameter variation of > 15%, a pulse pressure variation of > 15%, or a positive passive-leg-raising test. Patients receiving a 5% albumin solution but no gelatin solution were classified as members of the albumin group, while those administered a gelatin solution without an albumin solution were enrolled in the gelatin group. We excluded all patients who received both the albumin and gelatin solutions for septic shock resuscitation, as well as any patient who was given a colloid other than an albumin or gelatin solution. Also excluded were patients who had prolonged shock exceeding 24 hours; were pregnant; had suspected cardiogenic shock (demonstrated by an echocardiogram showing a left ventricular ejection fraction of < 35%); had a chest X-ray revealing cardiogenic pulmonary edema; or had a history of an allergy to colloid solutions causing anaphylaxis.

We performed the patient-matching process following the STROBE recommendations.[17] The patients who received albumin were matched with those administered gelatin in a 1:1 ratio. The matchings were based on each patient's age (± 5 years), Acute Physiology and Chronic

Health Evaluation (APACHE) II severity score (± 3 score), MAP (± 5 mmHg), and baseline lactate level (± 1 mmol/L).

Data collections and outcomes

We compiled the patients' baseline information and hemodynamic parameters (age, gender, APACHE II score, comorbidities, baseline serum albumin, source of infection, pathogenic details, MAP, and initial serum lactate). In addition, details of the treatment strategies employed (fluid resuscitation volume, and vasopressor type and dosage) were collected. Also recorded was information on the crystalloid and colloid solution volumes received during the first 3 days after each septic shock diagnosis, and the fluid balance volumes on Days 1, 2 and 3. The fluid balance was determined from the difference between the fluid resuscitation volume (consisting of the crystalloid and colloid solutions) that a patient received minus all fluid output, which was comprised of the urine output and, in cases where a patient underwent renal replacement therapy, the ultrafiltration volume.

The primary outcome of this study was the all-cause mortality at 28 days. The secondary outcomes were the hospital mortality; the cumulative fluid balance 72 hours after the septic shock diagnosis; and the days alive and free of organ support, ventilator support, vasopressor usage, and renal replacement therapy to Day 28 after the diagnosis.[18]

Statistical analyses

The categorical variables were expressed as number and percentage per group, and the group results were compared using Fisher's exact test or Chi-squared test, as appropriate. The continuous variables were described as mean ± standard deviation and compared using Student's t-test. A Kaplan–Meier curve analysis was performed to reveal the 28-day mortality differences between the albumin- and gelatin-receiving groups. We used PASW Statistics for Windows, version 18 (SPSS Inc., Chicago, Ill., USA) to analyze the data.

RESULTS

In all, 555 patients were diagnosed with septic shock and screened during the study period. Of those, 219 saw their hemodynamic state restored after receiving a crystalloid solution and vasopressor, and they were thus excluded from the study. Another 112 patients were not enrolled as they were given a mix of colloid solutions. The remaining 224 patients received either the albumin solution or the gelatin solution; after their baseline ages, severity scores, MAPs, and lactate levels were matched, 18 of those patients were eliminated from the study. That left a total of 206 enrolled patients: 104 in the albumin group, and 102 in the gelatin group (Fig 1).

The patients' baseline characteristics are summarized in Table 1. There were no significant differences in the mean ages, gender profiles, APACHE II scores, sites

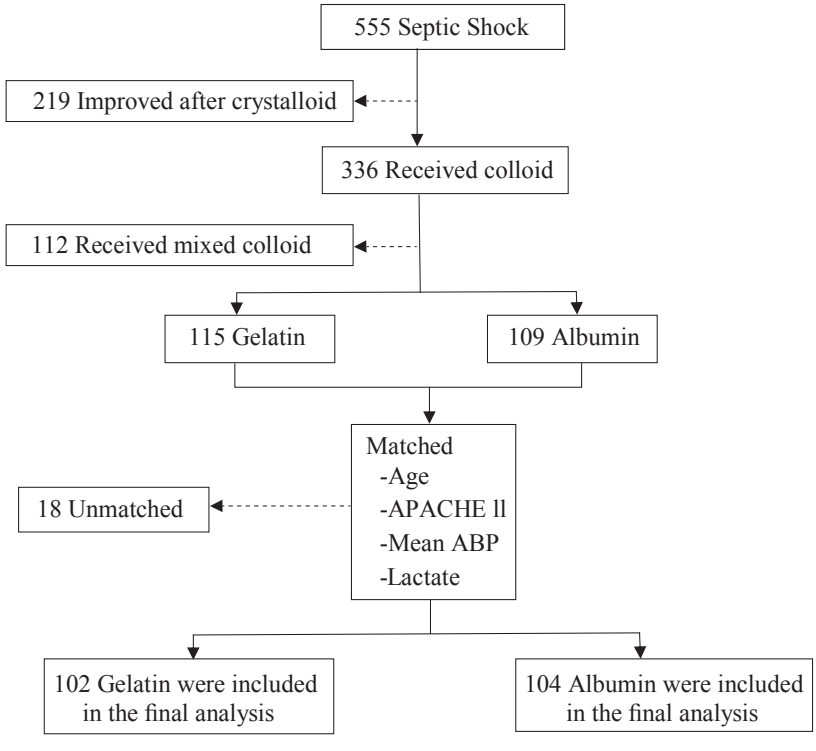

Fig 1. Flow diagram illustrating screening, enrollment, and baseline matching of patients

of infection, and hemodynamic parameters of the 2 groups. However, the patients in the albumin group had a higher proportion of the underlying conditions of hypertension and diabetes mellitus than the patients in the gelatin group. The most common infection source was pneumonia, followed by intra-abdominal and urinary tract infections. As to the respective degrees of septic shock severity at baseline enrollment of the albumin- and gelatin-receiving groups, there were no significant differences between the data of the 2 groups. The mean APACHE II scores were 22.8 ± 8.5 vs. 23.2 ± 8.1; the mean Sequential Organ Failure Assessment scores were 9.7 ± 3.4 vs. 9.7 ± 3.8; the average MAPs were 55.1 ± 8.0 mmHg vs. 54.6 ± 9.1 mmHg; and the average initial serum lactate levels were 5.6 ± 4.7 mmol/L vs. 6.3 ± 4.9 mmol/L. Finally, the average initial serum albumin levels were not statistically different (2.5 ± 0.6 g/dl vs. 2.4 ± 0.7 g/dl; $p = 0.16$).

The septic shock treatments that the patients were provided are detailed in Table 2. The total fluid volume and total crystalloid volume received on the first, second, and third days of resuscitation did not differ. However, the albumin group was given a significantly lower colloid volume on the first day than the gelatin group (1,068 ± 1,002 mL vs. 1,366 ± 1,020 mL; $p = 0.04$). The cumulative fluid balance at 72 hours was also significantly lower for the albumin group than the gelatin group (5,964 ± 4,960 mL vs. 8,133 ± 3,743 mL; $p = 0.01$). On the other hand, there were no significant differences in the two groups' vasopressor requirements, maximum vasopressor doses, hydrocortisone doses, or levels of mechanical ventilator support. The most common vasopressor used in this study was norepinephrine. In addition, a higher proportion of patients in the albumin group received renal replacement therapy than in the gelatin group (30.8% vs. 15.7%; $p = 0.01$).

The 28-day mortality was 27.9% for the albumin group, compared with 38.2% for the gelatin group; nevertheless, the difference was not statistically significant ($p = 0.11$; Table 3). The Kaplan–Meier curves for 28-day mortality are illustrated in Fig 2. The hospital mortalities (39.4% vs. 44.1%; $p = 0.50$) was were also not significantly different. The days alive and free of organ support to Day 28 were not different (11.2 ± 12.0 days vs. 11.9 ± 12.0 days; $p = 0.56$). There was also no significant difference in the rates of long-term renal replacement therapy for the septic shock patients who survived until hospital discharge (14.3% vs. 7.0%; $p = 0.2$).

To identify conditions that may be beneficially associated with the use of the albumin solution over the gelatin solution for septic shock resuscitation, a subgroup analysis was performed based on the patients' baseline APACHE II scores, serum albumin and serum lactate levels, epinephrine requirements, maximum vasopressor doses, need for ventilator support, and requirements for renal replacement therapy. The septic shock patients in the albumin group who had a baseline APACHE II score ≥ 20 or had a baseline serum albumin < 3 g/dL were associated with a significantly lower 28-day mortality rate than the patients in the gelatin group (Table 4).

DISCUSSION

In this retrospective, baseline-matched-cohort study, the resuscitation with an albumin solution for septic shock patients who were refractory to crystalloid solution was not statistically associated with a difference in the 28-day mortality rate, compared with the patients who were resuscitated with a gelatin solution. Nonetheless, among the patients who had either a baseline APACHE II score of ≥ 20 or a baseline serum albumin level of < 3 g/dL, resuscitation with the albumin solution was associated with a lower 28-day mortality than that for the gelatin solution. The occurrence of renal failure requiring renal replacement therapy was higher among patients who received the albumin than the gelatin solution. Still, there was no significant difference in the long-term renal replacement therapy requirements of the two groups of septic shock hospital survivors.

To date, no study has directly compared the efficacies of albumin and gelatin solutions for septic shock resuscitation. One meta-analysis, which compared albumin with other fluids for the treatment of sepsis patients, revealed that there was no mortality benefit in using albumin in preference to a hydroxyethyl starch and gelatin solution.[5] That result corresponds with the finding of our study. Moreover, the 28-day mortality for the albumin therapy of the septic shock patients in the current study was 27.9%, which was similar to the rate of 31.8% for the albumin-treated group reported by the Albumin Italian Outcome Sepsis (ALBIOS) trial. Furthermore, patients in the present study who received albumin resuscitation were associated with acute kidney injury, for which 30.8% of cases required renal replacement therapy; this is comparable with the corresponding figure of 24.6% determined by the ALBIOS trial.[3] In terms of the hospital mortality of the gelatin-solution users, a previous prospective study on shock patients revealed that the mortality rate of patients who received gelatin solutions was 30%[11], which was lower than the proportion of 44.1% found by our study.

TABLE 1. Patients' baseline characteristics.

Patient characteristic	Albumin (n = 104)	Gelatin (n = 102)	*P*-value
Age (years)	67.9 ± 14.8	64.9 ± 14.9	0.15
Male gender, n (%)	47 (45.2)	54 (52.9)	0.27
Body weight (kilogram)	61.0 ± 14.2	59.3 ± 13.6	0.38
APACHE II score†	22.8 ± 8.5	23.2 ± 8.1	0.73
SOFA score*	9.7 ± 3.4	9.7 ± 3.8	0.87
Underlying conditions, n (%)			
Hypertension	74 (71.2)	37 (36.3)	0.002
Diabetes mellitus	53 (51.0)	37 (36.3)	0.03
Chronic kidney disease	32 (30.8)	22 (22.6)	0.13
Cirrhosis	25 (24.0)	19 (18.6)	0.34
Malignancy	18 (17.3)	23 (22.5)	0.35
Ischemic heart disease	24 (23.1)	15 (14.7)	0.13
Site of infection, n (%)			
Pneumonia	37 (35.6)	36 (35.3)	0.97
Intra-abdominal infection	28 (26.9)	17 (16.7)	0.08
Urinary tract infection	18 (17.3)	29 (28.4)	0.06
Skin and soft tissue infection	7 (6.7)	7 (6.9)	0.97
Primary bacteremia	15 (14.4)	13 (12.7)	073
Other	2 (1.9)	8 (7.8)	0.05
Initial vital signs and investigations			
Temperature (°C)	37.4 ± 3.6	37.6 ± 1.4	0.57
Heart rate (per minute)	103.3 ± 23.0	108.0 ± 24.2	0.15
Respiratory rate (per minute)	27.9 ± 7.7	29.4 ± 7.1	0.16
Mean arterial blood pressure (mmHg)	55.1 ± 8.0	54.6 ± 9.1	0.72
Serum lactate (mmol/L)	5.6 ± 4.7	6.3 ± 4.9	0.26
Serum albumin (g/dL)	2.5 ± 0.6	2.4 ± 0.7	0.16
Fluid responsive test			
Central venous pressure guide	58 (55.8)	43 (42.2)	0.07
Inferior vena cava diameter variation	37 (35.6)	37 (36.3)	0.92
Pulse pressure variation	9 (8.7)	22 (21.6)	0.16
Fluid responsiveness	91 (87.5)	95 (93.1)	0.26

†The APACHE II (Acute Physiology and Chronic Health Evaluation) score, a severity-determining score, ranges from 0 to 71. Higher scores indicate a more severe disease.

*The SOFA (Sequential Organ Failure Assessment) score, a severity-determining score, ranges from 0–24. Higher scores indicate greater organ failure and disease severity.

TABLE 2. Detailed treatment strategies.

Clinical parameters	Albumin (n = 104)	Gelatin (n = 102)	*P*-value
Total fluid resuscitation (mL)			
Total fluid received on the first day	6,375 ± 2,227	6,203 ± 2,040	0.63
Total fluid received on the second day	3,037 ± 1,470	2,944 ± 2,056	0.71
Total fluid received on the third day	2,228 ± 1,637	2,232 ± 1,890	0.99
Crystalloid resuscitation (mL)*			
Total crystalloid received before colloid administration	3,067 ± 2,935	2,967 ± 3,701	0.69
Total crystalloid received on the first day	4,969 ± 1,898	4,662 ± 1,867	0.24
Total crystalloid received on the second day	1,783 ± 1,346	2,030 ± 1,764	0.27
Total crystalloid received on the third day	1,243 ± 1,224	1,969 ± 1,349	0.34
Colloid resuscitation (mL)†			
Total colloid received on the first day	1,068 ± 1,002	1,366 ± 1,020	0.04
Total colloid received on the second day	512 ± 667	559 ± 768	0.65
Total colloid received on the third day	305 ± 608	402 ± 794	0.34
Fluid balance at 72 hours (mL)	5,964 ± 4,960	8,133 ± 3,743	0.01
Vasopressors, n (%)			
Norepinephrine	98 (94.2)	97 (95.1)	0.78
Epinephrine	33 (31.7)	39 (38.2)	0.33
Dopamine	2 (1.9)	1 (1)	0.57
Dobutamine	8 (7.7)	3 (2.9)	0.13
Maximum vasopressor dose (mcg/kg/min)	0.38 ± 0.55	0.38 ± 0.45	0.93
Hydrocortisone, n (%)	72 (69.2)	68 (62.3)	0.77
Mechanical ventilator, n (%)	74 (71.2)	67 (65.7)	0.40
Renal replacement therapy, n (%)	32 (30.8)	16 (15.7)	0.01

* Crystalloid solution that was administration for septic shock resuscitation was 0.9% sodium chloride solution

†For patients in albumin group, all of them received 5% albumin solution

TABLE 3. Patient outcomes.

Clinical outcome	Albumin (n = 104)	Gelatin (n = 102)	Unadjusted Odds Ratio (95% confidence interval)	*P*-value	Adjusted Odds Ratio (95% confidence interval)†	*P*-value†
28-day mortality, n (%)	29 (27.9)	39 (38.2)	0.63 (0.35–1.12)	0.11	0.46 (0.24-0.89)	0.02
Hospital mortality, n (%)	41 (39.4)	45 (44.1)	0.82 (0.47–1.44)	0.50	0.60 (0.32-1.12)	0.11
Days alive and free of ventilator support to Day 28	13.5 ± 12.6	13.5 ± 12.8		0.98		
Days alive and free of vasopressor usage to Day 28	15.7 ± 12.0	14.2 ± 12.2		0.35		
Days alive and free of renal replacement therapy to Day 28	13.9 ± 13.3	14.3 ± 13.0		0.83		
Days alive and free of organ support to Day 28	11.2 ± 12.0	11.9 ± 12.0		0.56		
Long term renal replacement therapy requirement after discharge, n renal replacement/n survivors (%)	9/63 (14.3)	4/57 (7.0)	2.21 (0.64-7.61)	0.20	1.80 (0.47-6.95)	0.40

†Performed by Logistic regression analysis adjusted for baseline underlying conditions (hypertension and diabetes mellitus) and site of infection (intra-abdominal infection, urinary tract infection and other sites of infection)

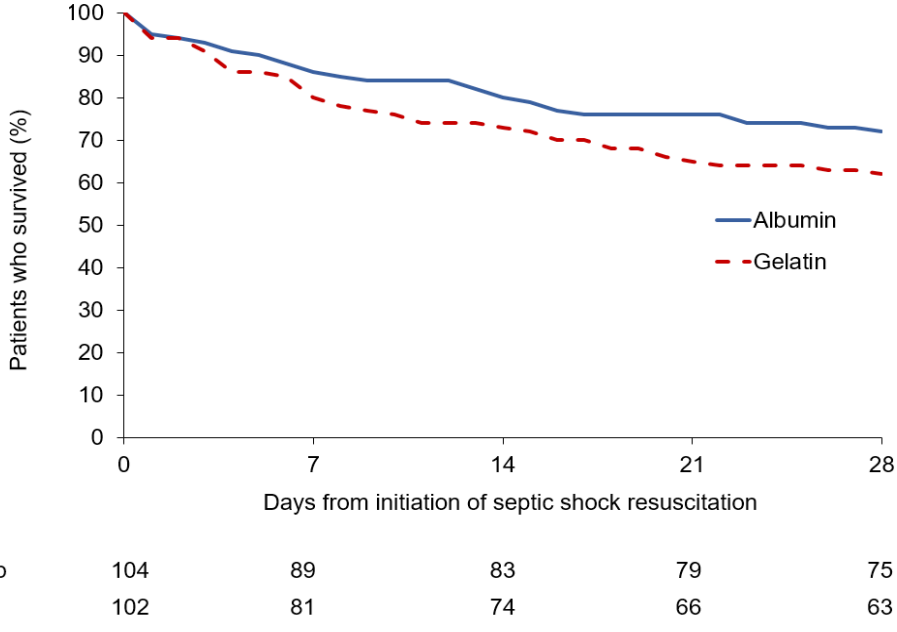

Fig 2. Kaplan–Meier curve of 28-day survival. The hazard ratio for death in patients who received albumin solution (albumin group) compared with patients who received gelatin solution (gelatin group) during septic shock resuscitation was 0.69 (95% confidence interval, 0.42–1.11; $p = 0.12$).

TABLE 4. Subgroup analysis of 28-day mortalities according to clinical parameters.

Clinical parameter	Albumin n deaths/ n per group (%)	Gelatin n deaths/ n per group (%)	Adjusted Odds Ratio (95% confidence interval)†	*P*-value†
APACHE II score*				
< 20	10/46 (21.7)	9/45 (19.6)	1.09 (0.33–3.66)	0.88
≥ 20	19/58 (32.8)	30/57 (53.6)	0.28 (0.12–0.68)	0.005
Baseline serum albumin				
< 3 g/dL	21/81 (25.9)	34/74 (45.9)	0.29 (0.14–0.63)	0.002
≥ 3 g/dL	8/23 (34.8)	5/28 (17.9)	2.87 (0.62–13.31)	0.18
Baseline serum lactate				
< 4 mmol/L	9/55 (16.4)	12/43 (27.9)	0.34 (0.11–1.07)	0.06
≥ 4 mmol/L	20/49 (40.8)	27/59 (45.8)	0.61 (0.27–1.39)	0.24
Epinephrine				
Not receiving	12/71 (16.9)	14/63 (22.2)	0.51 (0.19–4.36)	0.18
Receiving	17/33 (51.5)	25/39 (64.1)	0.56 (0.20–1.57)	0.27
Maximum dose of vasopressors				
< 0.2 mcg/kg/min	12/68 (17.6)	12/56 (21.4)	0.64 (0.23–1.75)	0.39
≥ 0.2 mcg/kg/min	17/36 (47.2)	27/46 (58.7)	0.44(0.17–1.16)	0.10
Ventilator support				
Not receiving	2/30 (6.7)	6/35 (17.1)	0.35 (0.05–2.22)	0.26
Receiving	27/74 (36.5)	33/67 (49.3)	0.46 (0.22–0.96)	0.04
Renal replacement therapy				
Not receiving	13/72 (18.1)	28/86 (32.6)	0.37 (0.16–0.85)	0.02
Receiving	16/32 (50)	11/16 (68.8)	0.49 (0.09–2.53)	0.39

†Performed by Logistic regression analysis adjusted for baseline underlying conditions (hypertension and diabetes mellitus) and site of infection (intra-abdominal infection, urinary tract infection and other sites of infection)

*The APACHE II score, a severity-determining score, ranges from 0 to 71. Higher scores indicate a more severe disease.

Interestingly, the results of our study demonstrated the benefits of using an albumin solution over a gelatin solution for the resuscitation of the more severely ill patients whose baseline APACHE II scores were ≥ 20 and of patients who had a baseline serum albumin level of < 3 g/dL. As to the more severe patients, a subgroup analysis conducted by the ALBIOS study identified that septic shock patients who were resuscitated with albumin were associated with a lower mortality rate than those who were resuscitated with a crystalloid solution.[3] This benefit of albumin was not evident among the severe sepsis patients participating in the ALBIOS trial. In the case of our cohort, all of the enrolled patients had been diagnosed with septic shock, and their hemodynamics had not properly responded to crystalloid resuscitation; it was therefore not possible for our study to compare the efficacies of the use of the albumin and gelatin solutions with the severe sepsis patients. Nonetheless, there were no differences in the efficacies of the two solutions among the patients who received or did not received epinephrine, nor among the patients who required maximum doses of vasopressor of < 0.2 mcg/kg/min or ≥ 0.2 mcg/kg/min (Table 4).

With regard to the influence of the serum albumin level and the benefits of albumin over gelatin solution for septic shock resuscitation, albumin is considered to be the most important plasma protein to maintain oncotic pressure.[19] Septic shock patients with a low baseline serum albumin level and a low oncotic-pressure are at risk of fluid extravasation from the blood vessels into the interstitial tissue (especially the lung parenchyma), which causes hypoxemia due to non-cardiogenic pulmonary edema. The clinical findings from our cohort showed that among the subgroup of septic shock patients who had a baseline serum albumin level of < 3.0 g/dL, the resuscitation with the albumin solution was associated with a lower 28-day mortality than the rate achieved with the gelatin solution. This finding correlates well with information from a prospective randomized controlled study that enrolled critically ill patients with an average baseline serum albumin level of 2.3 g/dL. The results of that research demonstrated that hypoalbuminemia patients who received albumin administration were associated with significantly better Sequential Organ Failure Assessment scores, especially improved PaO_2/FiO_2 ratios, cardiovascular scores, and Glasgow Coma Scale scores.[20] The target serum albumin level of 3 g/dL was also the same as that employed by the ALBIOS trial.

On the other hand, our study demonstrated that there was a trend toward a higher 28-day mortality among septic shock patients with a baseline serum albumin level of ≥ 3 g/dL who received albumin than those who received gelatin, although the difference did not reach statistical significance. This can be partly explained in two possible ways. The first is that cardiac decompensation might occur after rapid volume expansion with exogenous albumin in patients with a high baseline serum albumin, which might lead to an abrupt increase in the venous return and hydrostatic pressure. The second explanation is that in the case of septic shock patients with increased capillary permeability or capillary leak syndrome, albumin administration may become detrimental when albumin and water cross the capillary membrane and aggravate severe hypoxemia due to acute pulmonary edema.[21]

The strength of our study is that it is the first to compare the efficacies of albumin and gelatin solutions for septic shock resuscitation. Given the finding that there was no significant difference in the 28-day mortality rates of the gelatin and albumin groups, gelatin solution could be used as an alternative to colloid fluid for septic shock resuscitation, especially with patients whose baseline serum albumin is ≥ 3.0 g/dL or whose APACHE II score is < 20. As to the cost of each solution, albumin currently costs 7,672 Thai Baht/liter whereas gelatin is priced at 430 Thai Baht/liter. In view of the marked price differential, gelatin solution could be used as an alternative colloid for septic shock patients who cannot afford the cost of albumin resuscitation. On the other hand, albumin should be recommended for patients whose baseline serum albumin is < 3.0 g/dL or APACHE II score is ≥ 20.

There are certain limitations to our study. For one thing, we did not calculate the number of patients who needed to be enrolled to ensure that the study power was adequate. This is because-to our knowledge-no information was available from any previous study directly comparing the efficacies of albumin and gelatin solutions for septic shock resuscitation. Given our research result that the 28-day mortality of the patients in the gelatin group was 38.2%, then 200 patients per group would have needed to be recruited to detect a 10% absolute mortality difference with a power of 20%. Our study may therefore have inadequate power to detect the precise differences between albumin and gelatin resuscitation. Secondly, as this was a retrospective observational study in which the decisions to use particular colloid solutions were made by the individual attending physicians, a selection bias might have occurred. However, after adjusting the patients' baseline data (age, APACHE II scores, MAPs, and baseline serum lactate levels), the baseline characteristics of the two enrolled groups were well-matched. In addition, as this was a single center study, generalization of the results

could be limited. Physicians who would like to apply the results could adjust the context of the study population to better match their own situation. To confirm the benefits of using an albumin solution for septic shock resuscitation and broaden the applicability of the results, a large multicenter randomized study with adequate power to evaluate the mortality differences between albumin and gelatin (and possibly other colloid solutions) could be conducted.

CONCLUSION

For septic shock resuscitation, the albumin and gelatin solutions did not have any differences in their 28-day mortality rates or organ support-free survival days in the overall populations. However, resuscitation with albumin was associated with better outcomes among patients who had hypoalbuminemia or high APACHE II scores. Further study is required to confirm these benefits.

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Abbreviations: MAP: mean arterial blood pressure; RRT: renal replacement therapy; APACHE II score: Acute Physiology and Chronic Health Evaluation II score; SOFA score: Sequential Organ Failure Assessment score

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