Albumin: does it make a difference? Prognostic maker?

Pusan National University

Jae Hun Kim

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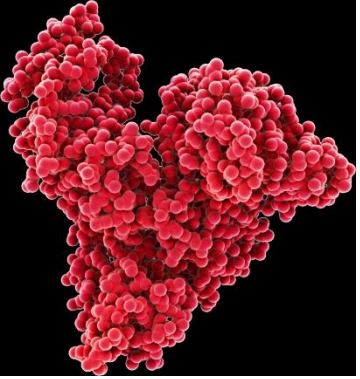


Introduction

- Most abundant circulating protein
- 66.5 kDa
- Negative net charge

➡ *Oncotic properties*

Main modulator of fluid distribution

- Plasma oncotic pressure: 70~80 %

HEPATOCYTE

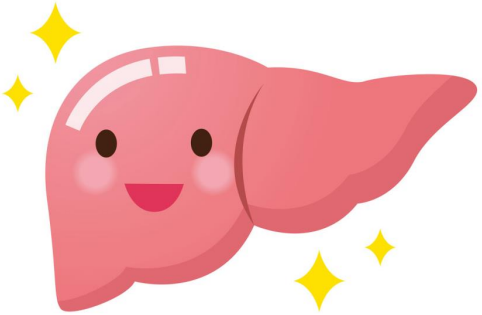
PRE-PROALBUMIN

↓ Signal Peptidase

PROALBUMIN

↓ Furin

ALBUMIN



13.6 g/day

↓

INTRAVASCULAR SPACE (~40%) → EXTRAVASCULAR SPACE (~60%)

118 g

242 g

LYMPHATIC SYSTEM

↓

DEGRADATION / ELIMINATION

- Muscles → 40~60 %
- Kidneys → 10 %
- Liver → 15 %
- Gastrointestinal system → 10 %

13.6 g/day = 3.7 %/day

Half life – 19days

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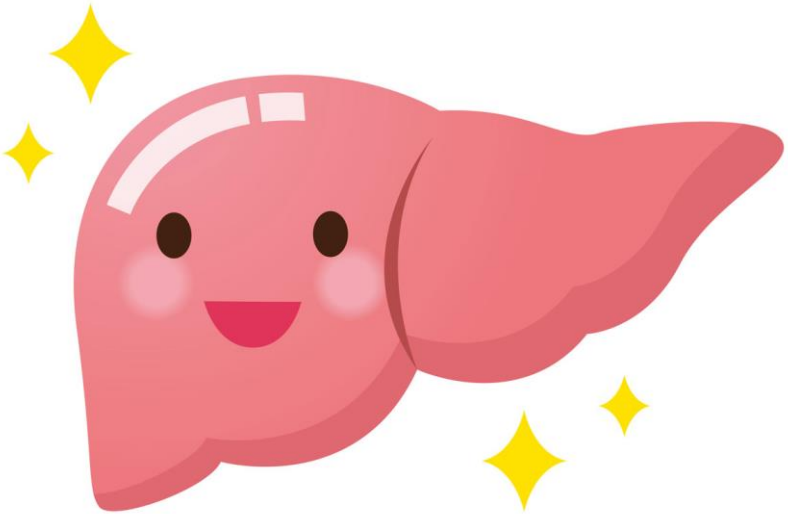
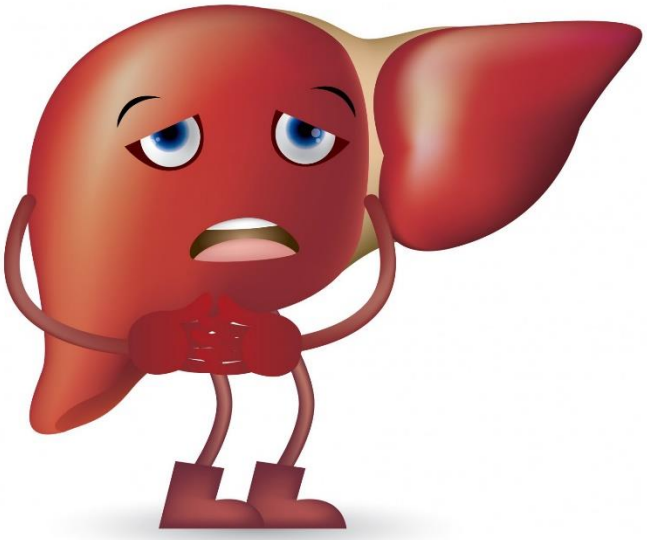




Synthesis

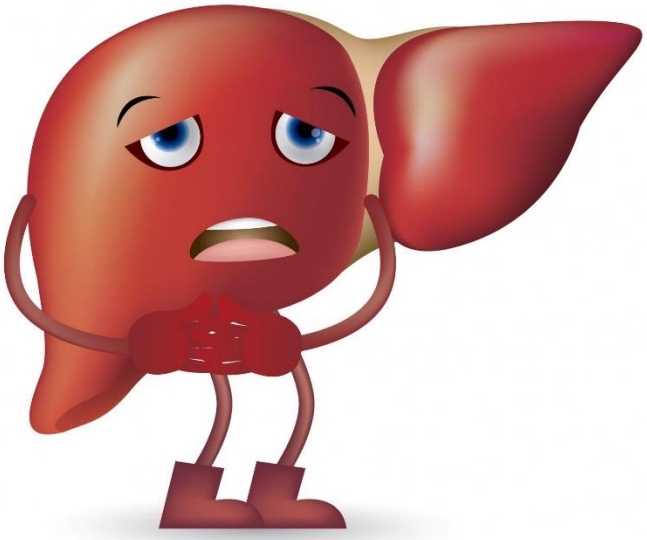
- *Nutrition* → Protein
- *Hormon* → Insulin, Corticosteroid, Growth hormon
- *Osmotic environment* → Colloid osmotic pressure
- *Cytokines* → IL-6, TNF-a

Distribution

- *Dysfuntion of Endotheilal barrier -> capillary leakage*

- *Endotoxin – G(-) bacteria*
- *Cytokines – TNF-a, IL-6*
- *Arachidonic acid metabolites – Leukotrienes and Prostaglandins*
- *Complements components – C3a, C5a*
- *Vasoactive peptides – Bradykinin, Histamine*
- *Chemokines – Macrophage inflammatory protein 1a*

300% ↑



Synthesis

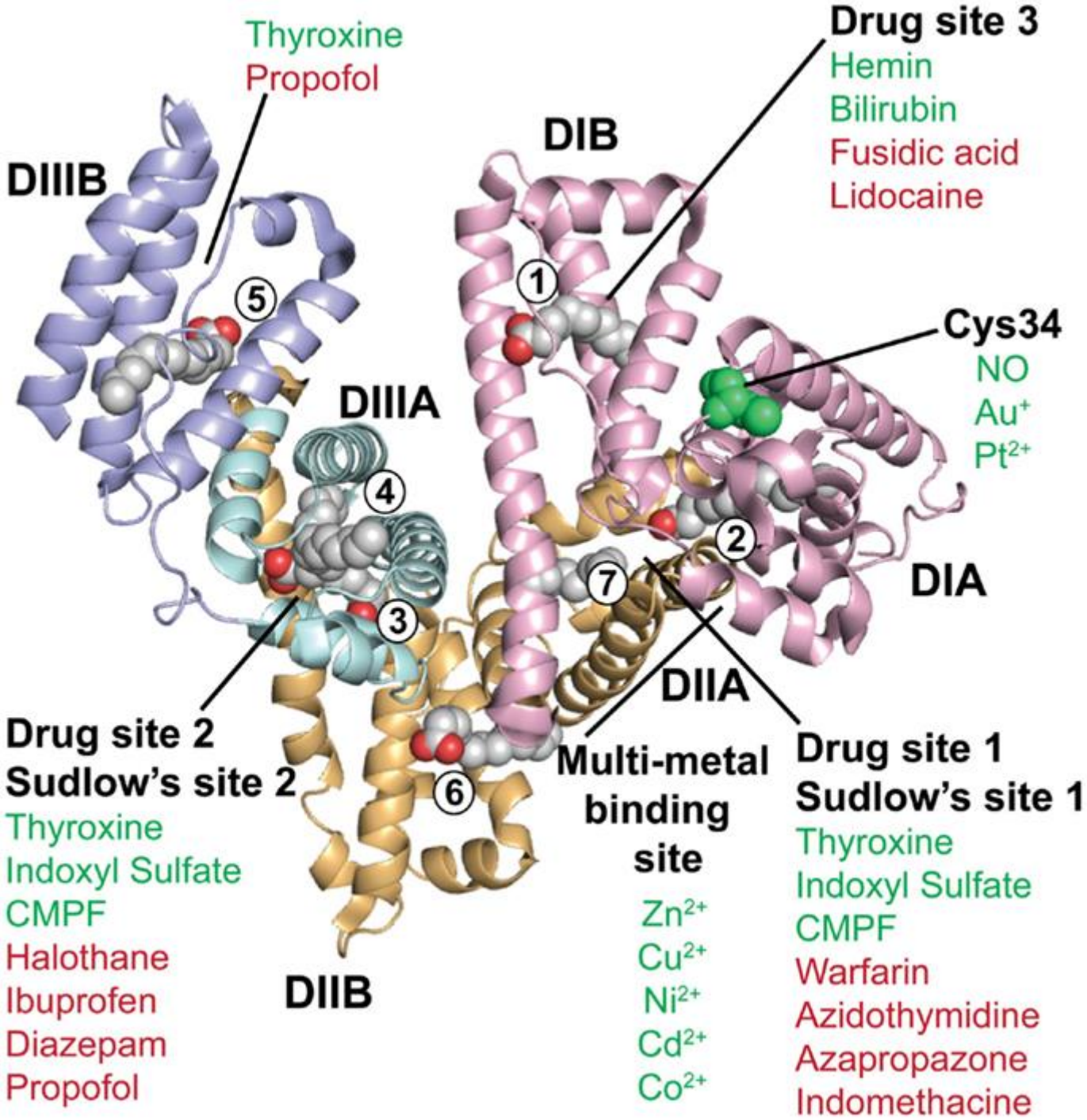
- ***Gene Transcription Rate*** ↓

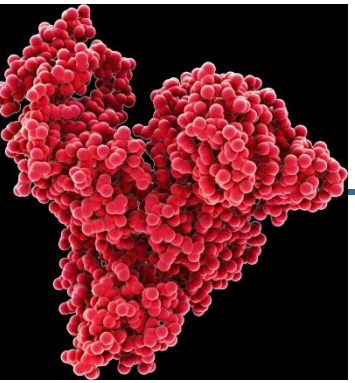
- *Protein depletion*
- *TNF-a, IL-6*

Catabolism

- ***Increase Transcapillary Flux -> Degradation in vascular endothelium*** ↑

TPN : Half life = 9 days


Thyroxine
Propofol
DIIIB
DIB
Drug site 3
Hemin
Bilirubin
Fusidic acid
Lidocaine
1
5
Cys34
NO
Au+
Pt2+
DIIIA
4
2
7
DIA
3
DIIA
Drug site 2
Sudlow's site 2
Thyroxine
Indoxyl Sulfate
CMPF
Halothane
Ibuprofen
Diazepam
Propofol
6
Multi-metal
binding
site
Zn2+
Cu2+
Ni2+
Cd2+
Co2+
Drug site 1
Sudlow's site 1
Thyroxine
Indoxyl Sulfate
CMPF
Warfarin
Azidothymidine
Azapropazone
Indomethacine
DIIB
CENTER



Oncotic Pressure	60% oncotic pressure 40% negative charge	Pulmonary Edema Circulatory Dysfunction
Binding and Transport	Endogenous compounds, Drugs, Trace elements	Endotoxemia Drug toxicity
Acid-base Function	Effective plasma buffer	Acid-base imbalance
Antioxidant Function	Scavenger of oxygen free radicals	Systemic inflammation
Microvascular integrity	Capillary permeability Protective function	Transcapillary leakage Vasodilation
Anticoagulant effects	Heparin like action Platelet aggregation inhibitor	Thrombosis

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Association of Serum Albumin and Mortality Risk

Philip Goldwasser[1,*] *and Joseph Feldman*[2]

[1]Department of Medicine, Brooklyn Veterans Affairs Medical Center, Brooklyn, New York and [2]Department of Preventive Medicine and Community Health, State University of New York-Health Sciences Center-Brooklyn, Brooklyn, New York

ABSTRACT. Reduced levels of serum albumin concentration, a routine blood test, within the "normal" range have been reported to be associated with mortality risk. The literature is reviewed, with a focus on cohort studies meeting specified criteria, and findings are summarized. In studies of many populations, comprising healthy subjects and patients with acute or chronic illness, serum albumin concentration is inversely related to mortality risk in a graded manner over its entire range; the estimated increase in the odds of death ranges from 24% to 56% for each 2.5 g/l decrement in serum albumin concentration. The association predicts overall and cause-specific mortality including cardiovascular mortality. It is likely that albumin concentration is a highly sensitive indicator of preclinical disease and disease severity. A direct protective effect of the albumin molecule is suggested by the persistence of the association after adjustment for other known risk factors and preexisting illness, and after exclusion of early mortality. Although biologically plausible, there is no direct evidence for this hypothesis. Serum albumin concentration is an independent predictor of mortality risk and could be useful in the quantification of risk in a broad range of clinical and research settings. J CLIN EPIDEMIOL 50;6:693–703, 1997. © 1997 Elsevier Science Inc.

KEY WORDS. Serum albumin, mortality, prognosis

Reference	Population (study[a])	*n*	Mean age	Design	Maximum follow-up	Model	Covariates
[2]	Hemodialysis, prevalent cases	12,099	58	Cohort	1 year	LR	D, C, B
[3]	Hemodialysis, incident cases (USRDS)	3,399	59	Cohort	4½ years	Cox	D, C, B, BP, S, F, W
[4]	Renal transplant	706	41	Cohort	19 years	Cox	D, C, B, R
[5]	Critical care admissions (APACHE III)	17,440	59	Cohort	Hospital discharge	LR	D, C, BP, B, F
[6]	Middle-aged men (British Regional Heart Study)	7,735	40–59	Cohort	10 years	LR	D, C, B, BP, S
[7]	National sample, aged 45–74 at entry into NHANES I	5,765	45–74	Cohort	16 years	Cox	D, C, B, BP, S
[8]	Community (Rancho Bernardo)	2,342	50–89	Cohort	3 years	LR	D, C, A, S, F
[9]	Community elderly (EPESE)	4,116	79	Cohort	5 years	Cox	Age, C, S, F, W
[10]	Professional and businessman (BUPA)	1,754	54	Nested case-control	10 years		Age
[11]	Middle-aged men with increased cardiac risk (MRFIT)	609	47	Nested case-control	10½ years	LR	Age, BP, B, S

Each 25g/L -> Odds of death : 24-56% ⬆

Serum albumin concentration is an independent predictor of mortality risk and could be useful in the quantification of risk in a broad range of clinical and research settings.

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Lack of Predictive Value of the APACHE II Score in Hypoalbuminemic Patients

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ABSTRACT. The APACHE II score predicts mortality in severely ill patients. This score does not account for the serum albumin level. Ninety-three patients (28 with serum albumin levels <2.5 g/dL [group I] and 65 with serum albumin levels ≥2.5 [group II]) were retrospectively reviewed. Patients were comparable in age, APACHE II score, and compliance with required protein needs. Patients with severe hypoalbuminemia had nearly double the death rate of patients with mildly low or normal albumin concentrations (54% compared with 29%). The death rate in the severely hypoalbuminemic patients was 5.1-fold higher than would be predicted by their APACHE II score. The death rate in those patients with mildly low or normal albumin levels had only a 1.9-fold higher rate than would be predicted by their APACHE II score. It is concluded that severe hypoalbuminemia increases the risk of death significantly higher than would be predicted by the APACHE II score. APACHE II score is not as accurate in a severely hypoalbuminemic population. (*Journal of Parenteral and Enteral Nutrition* **15**:313–315, 1991)

Variables	Group I	Group II
Age	65.9 ± 3.45	63.4 ± 7.69
Medical service	13	22
Surgical service	15	43
Albumin*	2.08 ± 0.100	3.35 ± 0.14
% Sugg kcal†	82.3 ± 4.37	1.02 ± 5.01
% Sugg protein	91.4 ± 4.47	99.6 ± 4.37
APACHE II	9.46 ± 1.35	9.81 ± 1.33
CHP	0.93 ± 1.94	0.86 ± 1.83
Creatinine	1.33 ± 1.22	1.50 ± 0.74
No. (%) central TPN‡	21/28 (75.0 ± 16.03)	27/63 (42.9 ± 12.22)
No. (%) required vent§	16/28 (57.1 ± 18.33)	20/63 (31.7 ± 11.49)
Vent LOS		
ALL	12.6 ± 3.47 [16]	19.2 ± 8.2 [20]
LIVED	9.67 ± 3.67 [6]	7.25 ± 0.9 [12]
No. of patients	28	63

Variable	Group I	Group II
Hospital LOS, d	35.9 ± 7.53	32.5 ± 13.2
LIVED	39.0 ± 11.63 [13]	27.4 ± 5.86 [15]
No. (%) required ICU	25/28 (89.3 ± 11.45)	44/63 (69.8 ± 11.34)
ICU LOS, d		
ALL	14.4 ± 4.20 [25]	15.5 ± 7.04 [44]
LIVED	7.50 ± 3.03 [10]	9.17 ± 3.07 [30]
No. (%) death rate*	15/28 (53.6 ± 18.47)	18/63 (28.6 ± 11.16)
No. (%) complication rate	11/28 (39.3 ± 18.09)	32/63 (50.8 ± 12.35)

This supports the view that ***serum albumin*** is an ***independent variable*** not accounted for in the *APACHE II score*.

Anaesthesia, 1996, Volume 51, pages 724–727

The prognostic value of serial measurements of serum albumin concentration in patients admitted to an intensive care unit

A. McCLUSKEY, A. N. THOMAS, B. J. M. BOWLES AND R. KISHEN

Summary

The prognostic value of serial measurements of serum albumin concentration during the first 72 h after admission to a general adult intensive care unit was retrospectively reviewed in 348 consecutive critically ill patients over a one year period. The accuracy of the admission APACHE II (Acute Physiology And Chronic Health Evaluation) score in correctly predicting patient outcome was compared with the serum albumin concentration measured at different times after intensive care unit admission. Multiple logistical regression analyses were performed to evaluate whether combining APACHE II and serum albumin into a unified risk index improved prognostic accuracy. Serum albumin concentration on admission was lower in non-survivors than in survivors and decreased more rapidly in non-survivors ($p < 0.001$). The admission serum albumin concentration was found to be an insensitive prognostic indicator. However, serum albumin measured after 24 h was as accurate as the admission APACHE II score in correctly classifying patients according to outcome. There was a good correlation between the admission APACHE II score and serum albumin measured after 24 h but not between the admission APACHE II and the admission serum albumin. Combining the APACHE II score and serial albumin concentrations into a unified risk of death equation did not improve the accuracy of outcome prediction.

Parameter(s)	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
APACHE II	48.9	90.4	78.1	68.6	80.6
Admission albumin	16.7	94.3	69.9	57.1	71.2
Albumin 12–24 h	39.7	92.1	77.6	65.9	79.9
Albumin 24–48 h	49.2	92.4	80.4	71.4	82.5
Albumin 48–72 h	53.7	84.8	74.2	64.4	78.1
APACHE II Admission albumin	54.3	90.3	78.5	73.1	80.2
APACHE II Albumin 24–48 h	63.3	90.6	82.8	73.1	86.0

The serum *albumin* concentration measured *24–48 h* following ICU admission was a better prognostic indicator than that measured on admission and was itself as accurate as the admission *APACHE II score*

Journal of
Clinical Medicine

MDPI

Article

The C-Reactive Protein/Albumin Ratio as a Predictor of Mortality in Critically Ill Patients

Ji Eun Park [1,2], Kyung Soo Chung [3], Joo Han Song [3], Song Yee Kim [3], Eun Young Kim [3], Ji Ye Jung [3], Young Ae Kang [3], Moo Suk Park [3], Young Sam Kim [3,*,†], Joon Chang [3] and Ah Young Leem [3,*,†]

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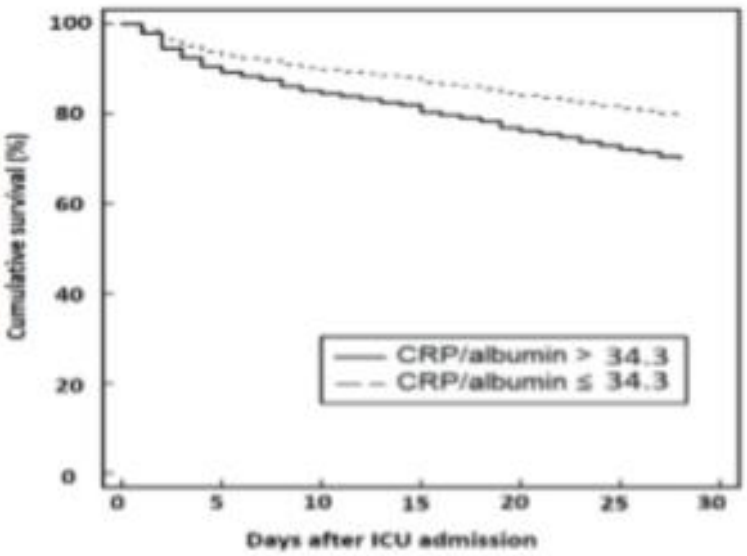
† These two authors contributed equally to this work.

Variables	OR	95% CI	*p*-Value
Age	1.00	0.99–1.02	0.601
Sex, F/M (%)			
Male	Reference	Reference	Reference
Female	1.18	0.83–1.66	0.358
BMI	0.99	0.96–1.01	0.254
APACHE II score	1.06	1.04–1.08	<0.001
Underlying diseases			
Cancer	1.59	1.11–2.30	0.012
CRP/Albumin	1.01	1.00–1.02	0.001



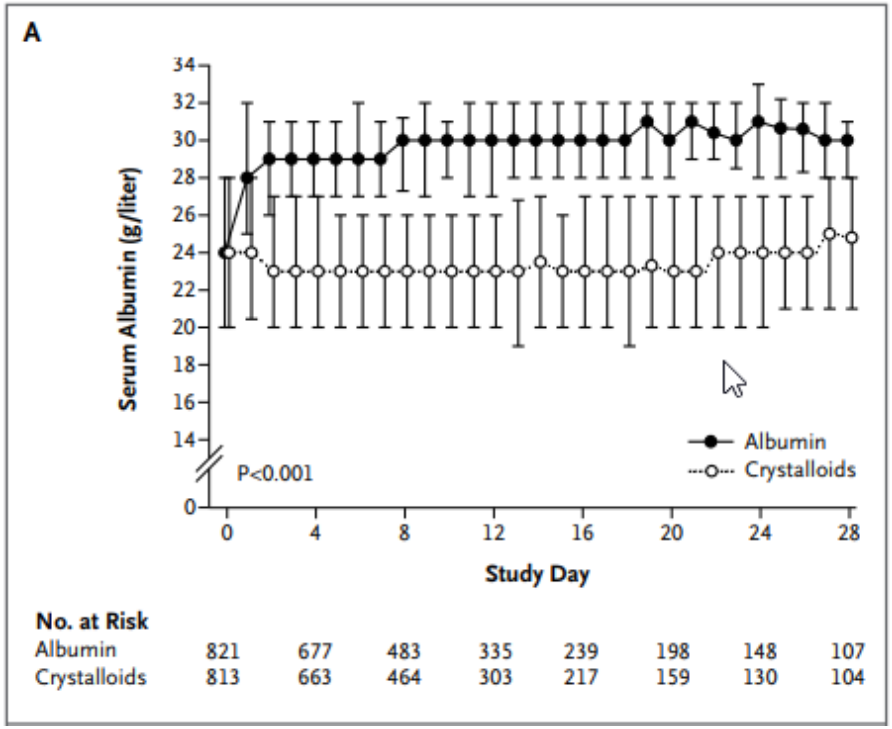
This study showed that a *higher CRP/albumin ratio* is associated with increased mortality in ICU patients. However, the sensitivity and specificity of CRP/albumin ratio for prediction of mortality were not so high in this single center study

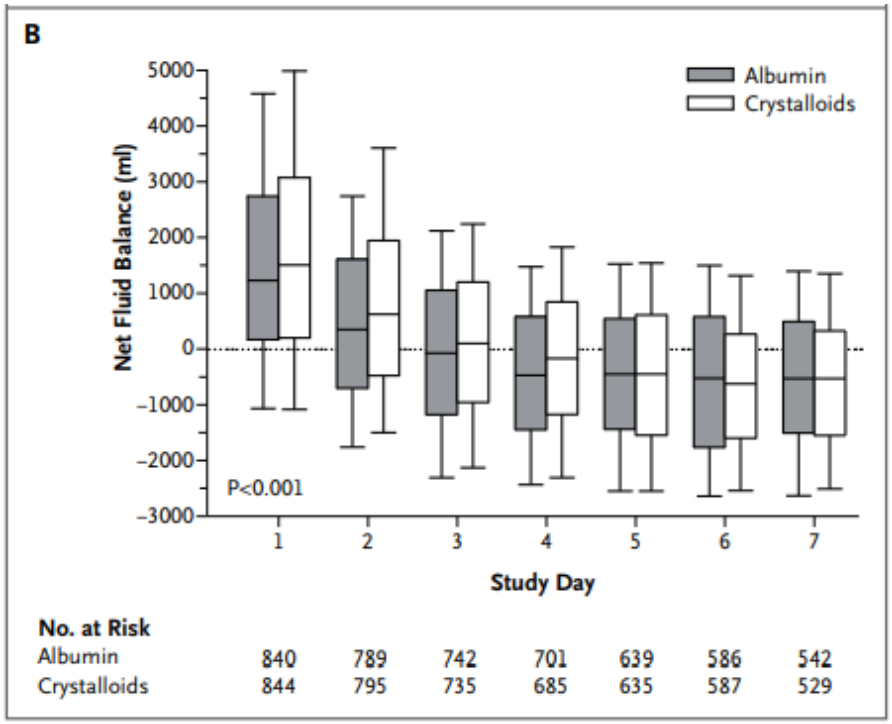
The NEW ENGLAND JOURNAL of MEDICINE

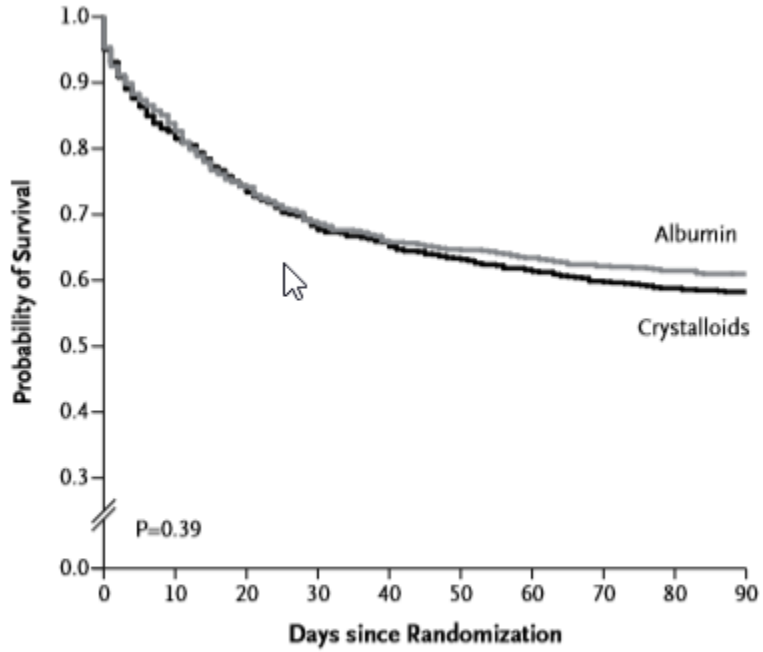
ORIGINAL ARTICLE

Albumin Replacement in Patients with Severe Sepsis or Septic Shock

Pietro Caironi, M.D., Gianni Tognoni, M.D., Serge Masson, Ph.D., Roberto Fumagalli, M.D., Antonio Pesenti, M.D., Marilena Romero, Ph.D., Caterina Fanizza, M.Stat., Luisa Caspani, M.D., Stefano Faenza, M.D., Giacomo Grasselli, M.D., Gaetano Iapichino, M.D., Massimo Antonelli, M.D., Vieri Parrini, M.D., Gilberto Fiore, M.D., Roberto Latini, M.D., and Luciano Gattinoni, M.D., for the ALBIOS Study Investigators*







No. at Risk										
Albumin	903	733	647	597	567	556	545	535	529	523
Crystalloids	907	729	652	598	676	551	538	521	511	504

In conclusion, the use of albumin in addition to crystalloids to correct hypoalbuminemia, as compared with the use of crystalloids alone, in patients with severe sepsis during their stay in the ICU did not provide a survival benefit at 28 or 90 days, despite improvements in hemodynamic variables.

1. López-Martín JM, Salviati L, Trevisson E, et al. Missense mutation of the COQ2 gene causes defects of bioenergetics and de novo pyrimidine synthesis. Hum Mol Genet 2007;16:2091-7.

Albumin Replacement in Severe Sepsis or Septic Shock

TO THE EDITOR: The Albumin Italian Outcome Sepsis study conducted by Caironi et al. (April 10 issue)[1] is the third large-scale, randomized trial to compare albumin with crystalloids in adult patients with severe sepsis. The first such trial was the Saline versus Albumin Fluid Evaluation study.[2] In addition, the Early Albumin Resuscitation during Septic Shock study has been completed and its mortality results published.[3]

In all three trials, mortality was lower among patients receiving albumin, and the respective relative risks coincided closely, ranging from 0.87 to 0.94 (Fig. 1). Although the effect did not attain statistical significance in any of the individual trials, the pooled relative risk in all three trials is 0.92 (95% confidence interval [CI], 0.84 to 1.00; P=0.046), indicating a significant reduction in mortality associated with albumin use among adults with severe sepsis. This result portant pathophysiological features with severe sepsis.[5]

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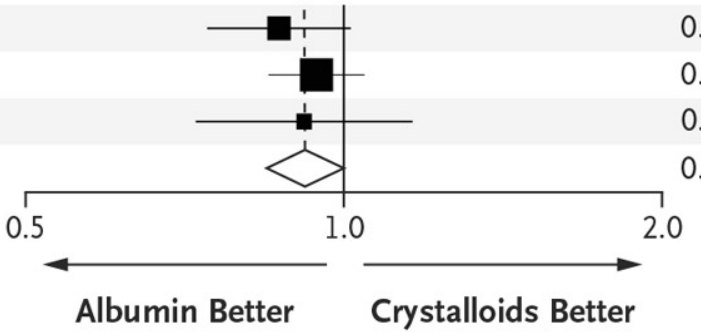
Dr. Wiedermann reports receiving lecture fees from CSL Behring, Baxter, and the Plasma Protein Therapeutics Association; and Dr. Joannidis, lecture fees from Baxter, Fresenius, Gambro, Orion Pharma, CLS Behring, and B. Braun Melsungen. No other potential conflict of interest relevant to this letter was reported.

1. Caironi P, Tognoni G, Masson S, et al. Albumin replacement in patients with severe sepsis or septic shock. N Engl J Med 2014;370:1412-21.
2. The SAFE Study Investigators. Impact of albumin compared to saline on organ function and mortality of patients with severe sepsis. Intensive Care Med 2011;37:86-96.
3. Charpentier J, Mira J-P. Efficacy and tolerance of hyperoncotic albumin administration in septic shock patients: the EARSS

Trial	Albumin	Crystalloids	Relative Weight	Relative Risk (95% CI)	P Value
	no. of patients who died/total no.		%		
SAFE[2]	185/603	217/615	30.41	0.87 (0.74–1.02)	
ALBIOS[1]	365/888	389/893	54.90	0.94 (0.85–1.05)	
EARSS[3]	96/399	103/393	14.69	0.92 (0.72–1.17)	
All trials	646/1890	709/1901	100.00	0.92 (0.84–1.00)	0.046



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Conclusion

- *Important prognostic marker in ICU*

  But sensitivity and specificity ⬇

  -> Future Research (CRP, Lactic acid)

- *Not harmful but not necessary*

  in all critically ill patients

- *Maybe useful*

  -> Future Research (Patients Selection, Timing, Dosage…)

Thank you !

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