

Fluid – up(dead)



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Medizinische Universität Innsbruck



Krankenhaus
St. Vinzenz
Zams

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Astra Zeneca, Baxter, BBraun, Cytosorb, CSL Behring, Ethypharm,
IL-Werfen, LFB-France, Mitsubishi Pharma und Octapharma.



THE CONVERSION

He's had 220 papers retracted so far

How scientific misconduct is becoming increasingly common worldwide

VERY FAKE NEWS

Trauma und Sepsis: Volumen und Flüssigkeitsmanagement

Hypovolämie
Blutdruckabfall
► Organschäden

Volumentherapie

Kristalloide Kolloide Blutprodukte

Stabilisierung Kreislauf

Gewebeperfusion verbessern



1997: 8l colloids & crystalloids (= 4,8l volume effect)

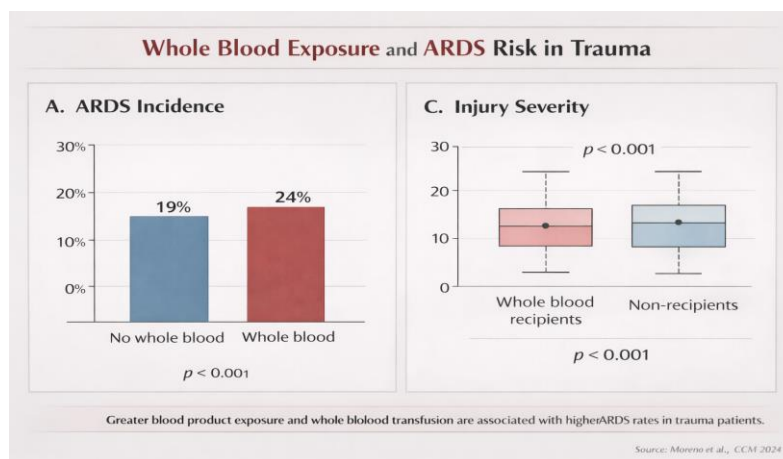
2004: 4l colloids & crystalloids (= 2,4l volume effect)

2013: 2l crystalloids (= 400 ml volume effect)

2019: 1l crystalloids (= 200 ml volume effect)

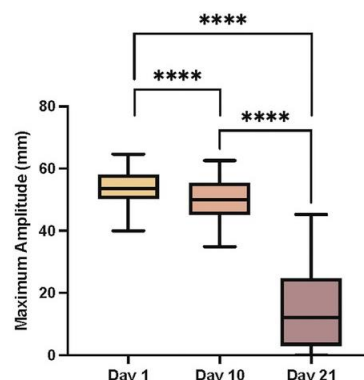
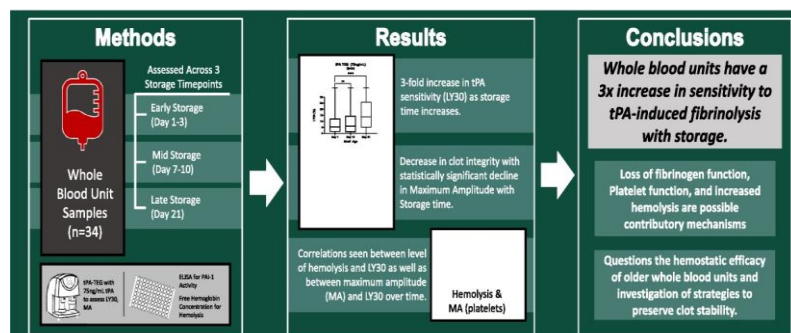
2025: „crystalloids as a bridging fluid for blood products (LTOWB)“
Ramasamy A. Advanced trauma life support 2025: A brief review of updates. Injury. 2026 Apr;57(4):113079

An Analysis of the Association of Whole Blood Transfusion With the Development of **Acute Respiratory Distress Syndrome**



Moreno AR, Fisher AD, Long BJ, Douin DJ, Wright FL, Rizzo JA, April MD, Cohen MJ, Getz TM, Schauer SG. Crit Care Med. 2025 Jan 1;53(1):e109-e116.

Whole blood becomes increasingly susceptible to **tPA-mediated fibrinolysis** with storage



Maginot ER, Barmettler NK, Moore EE, Moore HB, Gawargi FI, White CM, Hiser DC, Sextro KS, Clegg AA, Moody TB, Volk GE, Goodman N, Bobr A, Henry R, Barrett CD. J Trauma Acute Care Surg. 2025 Dec 17.

Four-factor prothrombin complex concentrate in adjunct to whole blood in trauma-related hemorrhage: Does whole blood replace the need for factors?

Outcome	WB Alone (n=168)	4-PCC + WB (n=84)	P Value
24-h Transfusion			
pRBC, median (IQR)	10 (6-18)	8 (5-14)	0.04
FFP, median (IQR)	8 (4-12)	6 (4-10)	0.01
Platelets, median (IQR)	2 (1-4)	2 (1-3)	0.19
Cryoprecipitate, median (IQR)	2 (1-5)	2 (1-4)	0.37
Mortality, n (%)			
ED mortality	10 (6%)	3 (4%)	0.42
Overall in-hospital mortality	74 (44%)	39 (46%)	0.72

Approximate Mortality vs ISS: Germany (TR-DGU) vs US Trauma Registries



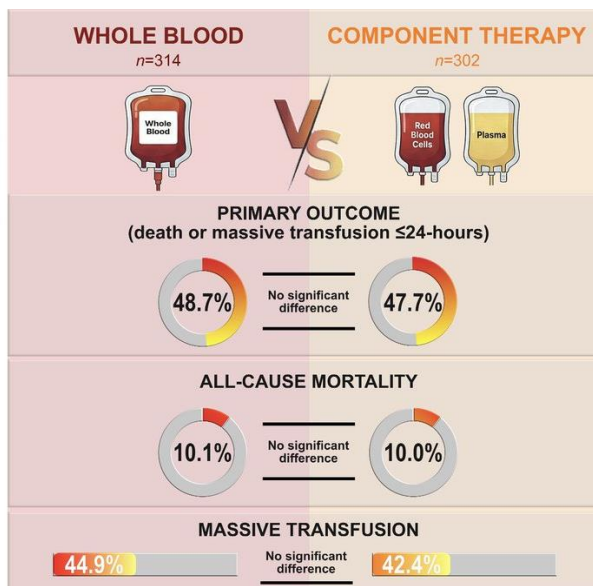
Khurrum M, et al. Four-factor prothrombin complex concentrate in adjunct to whole blood in trauma-related hemorrhage: Does whole blood replace the need for factors? *J Trauma Acute Care Surg.* 2021 Jul 1;91(1):34-39.

Whole Blood vs Comp: SWiFT Trial Results

Smith JE, Cardigan R, Sanderson E, et al.



10 AIR AMBULANCE SERVICES



Smith JE, et al; SWiFT Trial Group. Prehospital Whole Blood in Traumatic Hemorrhage - a Randomized Controlled Trial. *N Engl J Med.* 2026 Mar 17.

The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

Recommendation 15 We recommend that fluid therapy using a **0.9% sodium chloride** or **balanced crystalloid** solution be initiated in the hypotensive bleeding trauma patient (Grade 1B).

*“The concept of a restricted volume replacement and permissive hypotension. This **strategy was mainly triggered by a RCT published in the 1990s demonstrating increased survival in penetrating trauma ...**”*

(Bickell WH et al. 1994)

Rossaint R et al. Critical Care 2023; 27:80

Re-calculation of the Bickel trial: Statistics: Fisher Exact Test

	Survivor	Non Survivor
immediate fluid replacement	193	116
delayed fluid replacement	1 patient 203	86

p=0.04



Re-calculation of the Bickel trial: Statistics: Fisher Exact Test

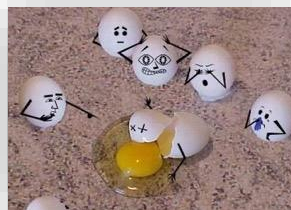
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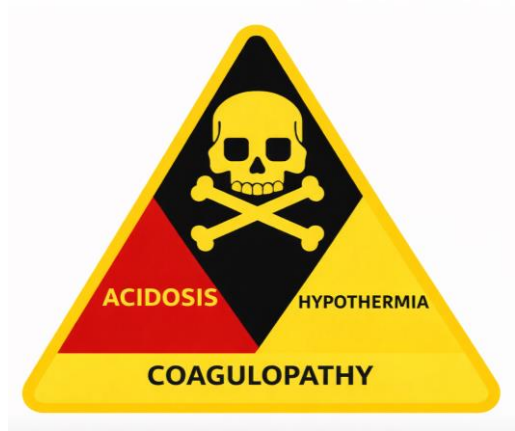
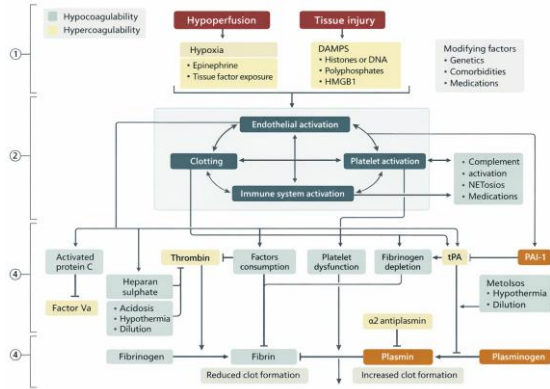
$p=0.057$



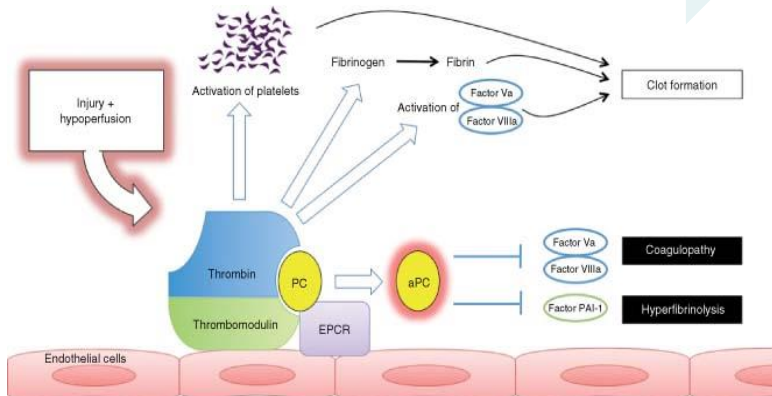
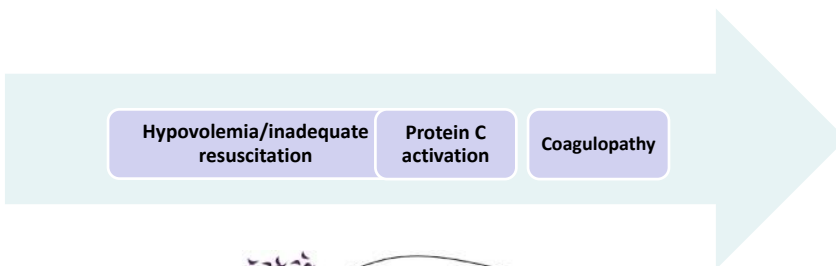
Side effects of fluid replacement therapy in trauma hemorrhage

- Dilution
- Coagulopathy
- Volume overload
- Pulmonary dysfunction
- (Abdominal compartment) syndrome
- Increase in blood pressure → increases blood loss
- Hypothermia due to cold infusion solutions





Moore EE et al. Trauma-induced coagulopathy. Nat Rev Dis Primers. 2021 Apr 29;7(1)



Thorsen K et al. 2011; British J of Surgery 98(7):894-907



S3-Leitlinie Intravasale Volumentherapie bei Erwachsenen AWMF

- Der Volumenersatz beim Intensivpatienten sollte mit **kristalloiden Lösungen** erfolgen.
- **HES** soll bei Intensivpatienten nicht verwendet werden.
- Wenn eine akute Hypovolämie allein mit Kristalloiden nicht ausreichend therapiert werden kann, können darüber hinaus **Gelatine und Humanalbumin** zum Einsatz kommen.

OUTDATED

The Surviving Sepsis Campaign Guidelines 2026:

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- **suggest** administering at least **30 mL/kg** of IV crystalloid in the first 3 h. (strong recommendation, moderate certainty evidence)
- **suggest** using **balanced crystalloids** over 0.9% saline. (strong recommendation, moderate certainty evidence)
- **suggest** supplemental **albumin** for fluid resuscitation. (conditional recommendation; moderate certainty evidence)
- **recommend against** using **starches** for resuscitation. (strong recommendation, high-certainty evidence)
- **suggest against** using **gelatin** for resuscitation. (conditional recommendation, moderate certainty evidence)
- **Fluid administration** should be individualized after initial fluid bolus and **monitoring of lactate** decrement achieved. (conditional recommendation; moderate certainty evidence)

Prescott HC, Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026. *Intensive Care Med.* 2026 Mar 23.

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Fact check (1)...

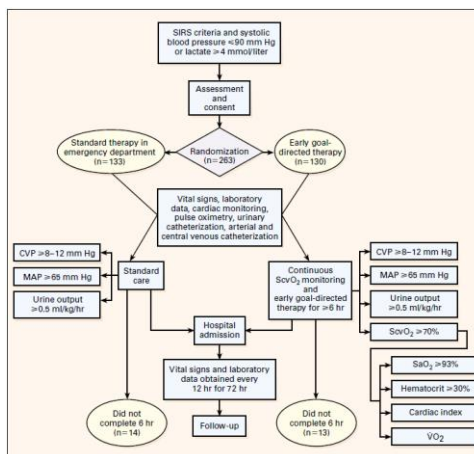


The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S.,
ALEXANDRIA MUZZINI, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D.,
FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

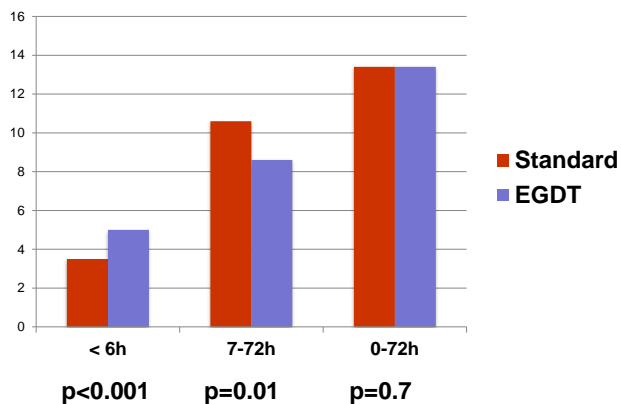
- MAP** > 65 mmHg
- CVP** > 8-10 mmHg
- Urin** > 0,5 ml/kg/h
- ScvO₂** > 70%
- Hct** > 30%



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MAP > 65 mmHg ?????

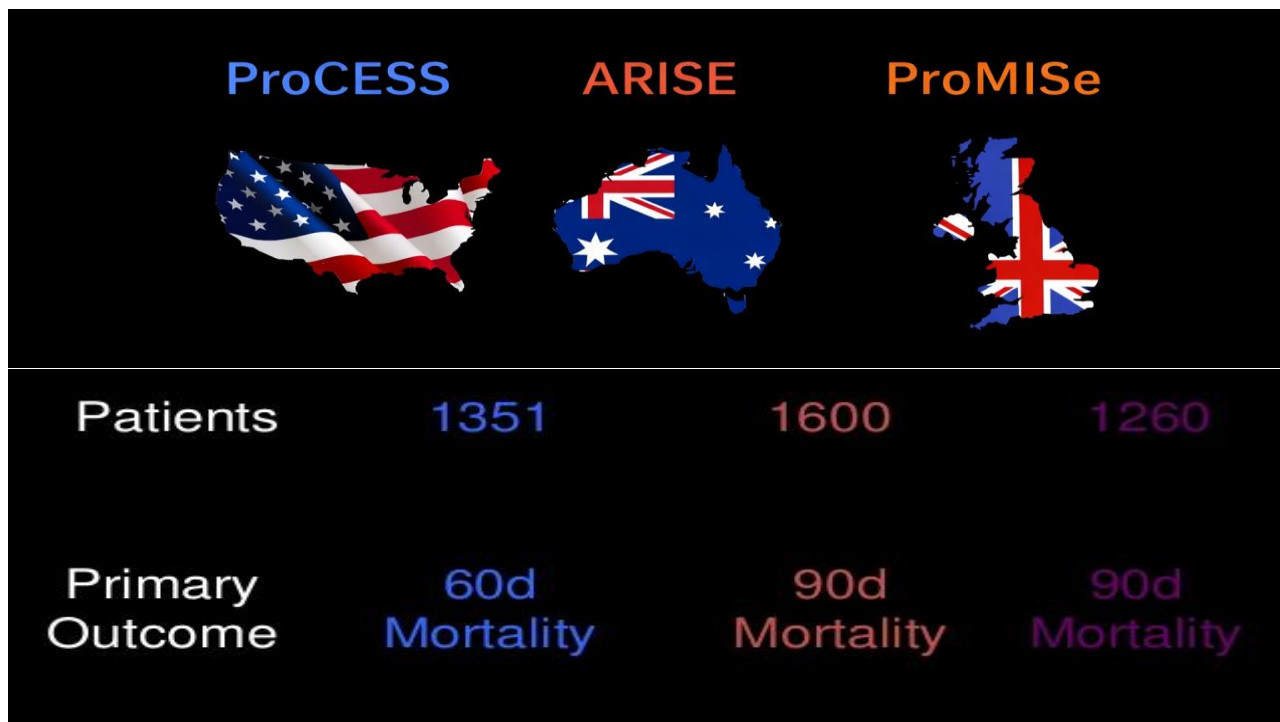
CVP > 8-10 mmHg ??????

Urin > 0,5 ml/kg/h ?????

ScVO2 > 70% ?????

Hct > 30% ?????





The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 1, 2014

VOL. 370 NO. 18

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

Outcome	Protocol-based EGDT (N = 439)	Protocol-based Standard Therapy (N = 446)	Usual Care (N = 456)	P Value [†]
Death — no./total no. (%)				
In-hospital death by 60 days: primary outcome	92/439 (21.0)	81/446 (18.2)	86/456 (18.9)	0.83 [‡]
Death by 90 days	129/405 (31.9)	128/415 (30.8)	139/412 (33.7)	0.66

PROCESS Investigators; *N Engl J Med* 370;18:1683-1693

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

Table 2. Study Outcomes.

Variable	EGDT (N=793)	Usual Care (N=798)	Relative Risk (95% CI)	Risk Difference (95% CI) ^a percentage points	P Value
Primary outcome: death by day 90 — no./total no. (%)	147/792 (18.6)	150/796 (18.8)	0.98 (0.80 to 1.21)	-0.3 (-4.1 to 3.6)	0.90
Secondary outcomes					
Median duration of stay (IQR) †					
Emergency department — hr	1.4 (0.5–2.7)	2.0 (1.0–3.8)			-0.001
ICU — days	2.8 (1.4–5.1)	2.8 (1.5–5.7)			0.81
Hospital — days	8.2 (4.9–16.7)	8.5 (4.9–16.5)			0.89
Use and duration of organ support‡					
Invasive mechanical ventilation — no./total no. (%)	238/793 (30.0)	251/798 (31.5)	0.95 (0.82 to 1.11)	-1.4 (-6.0 to 3.1)	0.52
Median duration of invasive mechanical ventilation (IQR) — hr	62.2 (23.5–181.8)	65.5 (23.0–157.9)			0.28
Vasopressor support — no./total no. (%)	605/793 (76.3)	525/798 (65.8)	1.16 (1.09 to 1.24)	10.5 (6.1 to 14.9)	<0.001
Median duration of vasopressor support (IQR) — hr	29.4 (12.9–61.0)	34.2 (14.0–67.0)			0.24
Renal-replacement therapy — no./total no. (%)	106/793 (13.4)	108/798 (13.5)	0.99 (0.77 to 1.27)	-0.2 (-3.5 to 3.2)	0.94
Median duration of renal-replacement therapy (IQR) — hr§	57.8 (25.3–175.0)	85.9 (29.3–182.9)			0.40
Tertiary outcomes — no./total no. (%)					
Death by day 28	117/792 (14.8)	127/797 (15.9)	0.93 (0.73 to 1.17)	-1.2 (-4.7 to 2.4)	0.53
Death by the time of discharge from ICU	79/725 (10.9)	85/661 (12.9)	0.85 (0.64 to 1.13)	-2.0 (-5.4 to 1.5)	0.28
Death by the time of discharge from hospital¶	115/793 (14.5)	125/797 (15.7)	0.92 (0.73 to 1.17)	-1.2 (-4.7 to 2.3)	0.53

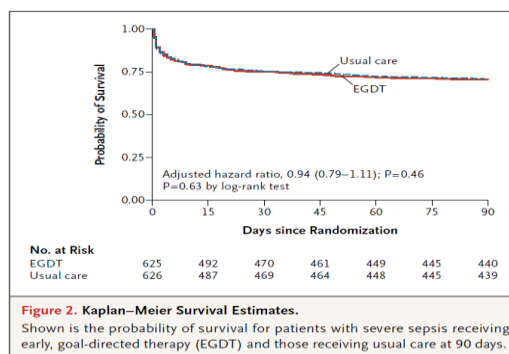
ARISE Investigators; *N Engl J Med* 371;16:1496-1506

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc.,



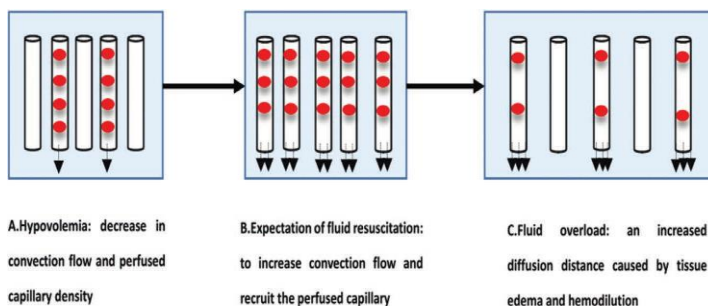
ProMISE Investigators; *N Engl J Med* 2015;372,14:1311-14

2001 Rivers Study → Mortality
47 → 31% (NNT = 6)

Sepsis Trilogy → Mortality
18.2 – 29.5%

Compartment	Glucose 5%	Crystalloid	Colloid
intravascular	↑	↑	↑↑↑
interstitial	↑↑	↑↑↑	—
intracellular	↑↑↑	—	—

Fluids and the Microcirculation

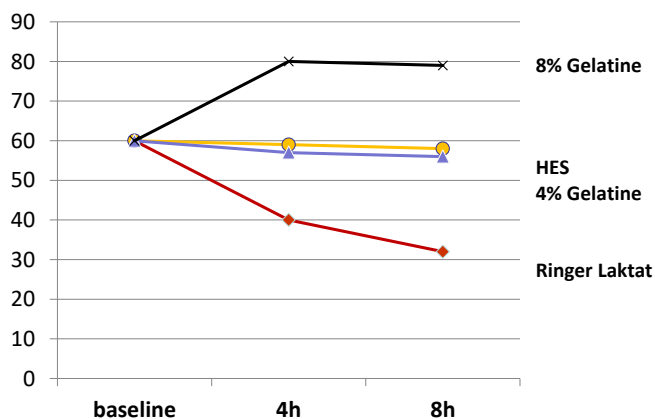


Colloids and the Microcirculation, Huaiwu H, Can Ince. Anesth&Analg 2018; 126,5:1747-1754.

The intravascular volume effect of Ringer's lactate is below 20%: a prospective study in humans. Jacob M et al. Crit Care 2012.

Exact Measurement of volume effect of 6% HES 130/0.4 during acute normovolemic hemodilution. Jacob M et al. Anaesthesist 2012.

Hydroxyethyl starch and modified fluid gelatin maintain plasma volume in a porcine model of **septic shock with capillary leakage**



Marx G, et al. Intensive Care Med (2002) 28:629-635

Different effects of fluid loading with saline, gelatine, hydroxyethyl starch or albumin solutions on acid-base status in the critically ill

	NaCl 0.9% n = 28	Gelatine 4% n = 28	HES 6% n = 29	Albumin 5% n = 30
Age, years	61 (12)	61 (13)	60 (13)	60 (9)
Sex, female	5 (18%)	3 (11%)	10 (34%)	8 (27%)
Weight, kg	78 (12)	82 (13)	75 (11)	79 (16)
Height, m	1.75 (0.08)	1.77 (0.07)	1.72 (0.09)	1.71 (0.20)
APACHE II	10 (5)	11 (5)	11 (4)	11 (4)
Fluid infused, mL	1723 (209)	1509 (328)	1441 (295)	1553 (258)
Hb, mmol/L				
T = 0	6.2 (1.2)	5.7 (0.9)	5.7 (1.1)	5.9 (1.2)
T = 90*, **	6.1 (0.9)	5.0 (0.7) ^A	5.0 (0.8) ^A	5.2 (0.9) ^A
Change in PV, %**	5 [18-24]	18 [-8-49] ^A	21 [-11-50] ^A	16 [2-61] ^A

Values are mean (SD) or number (percentage), where appropriate. Abbreviations: PV, plasma volume; HES, hydroxyethyl starch.

* P<0.001 for decrease in whole group;

** P<0.001 between fluids;

^A P<0.001 for change vs saline.

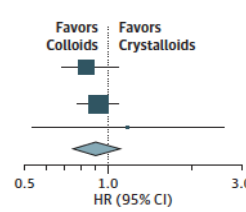
A. Spoelstrade Man et al. PLoS ONE 2017 12(4): e0174507

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock The CRISTAL Randomized Trial

Djillali Annane, MD, PhD; Shidadsp Siami, MD; Samir Jaber, MD, PhD; Claude Martin, MD, PhD; Souheil Elatrous, MD; Adrien Descorps Declère, MD;

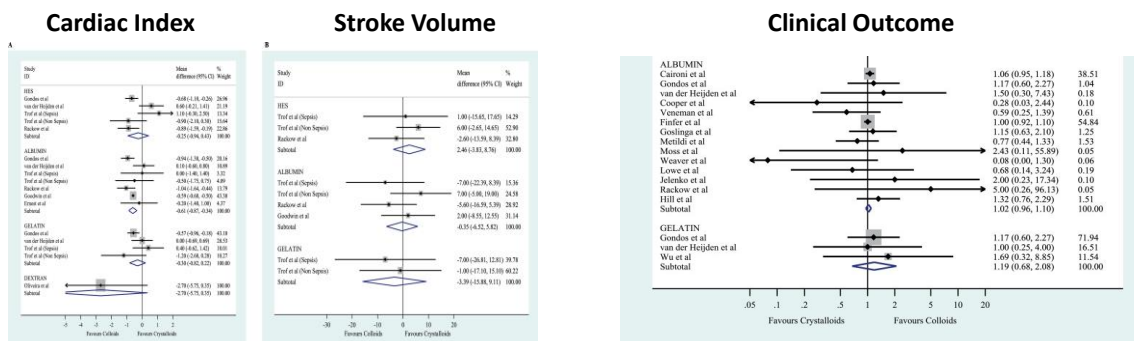
Reason for ICU Admission	Colloids Group (n = 1414)		Crystalloids Group (n = 1443)		HR (95% CI)
	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	
Other causes of hypovolemic shock	555	131	572	152	0.87 (0.69-1.10)
Sepsis	774	215	779	226	0.95 (0.78-1.10)
Trauma	85	13	92	12	1.19 (0.54-2.60)
All patients	1414	359	1443	390	0.93 (0.80-1.10)



	Colloids (n = 1414)	Crystalloids (n = 1443)	RR (95% CI)	P Value ^a
Death				
Within 28 d	359 (25.4)	390 (27.0)	0.96 (0.88 to 1.04)	.26
Within 90 d	434 (30.7)	493 (34.2)	0.92 (0.86 to 0.99)	.03

Annane D et al; JAMA 2013 Nov 6;310(17):1809-17

Crystalloids vs. colloids for fluid resuscitation in the Intensive Care Unit: a systematic review and meta-analysis



**Crystalloids were less efficient than colloids at stabilizing resuscitation endpoints;
„guidance on when to switch is urgently required“**

Martin & Besset. *Journal of Critical Care* 50 (2019) 144–154

Surviving Sepsis Campaign

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Prescott HC, *Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026. Intensive Care Med.* 2026 Mar 23.

Die Anaesthesiologie
Journal der Anaesthesiologie

Leitlinien und Empfehlungen

Anaesthesiologie 2025 · 78:827–838
<https://doi.org/10.1007/s00101-025-01629-3>
 Eingegangen: 11. August 2025
 Angenommen: 14. Oktober 2025
 Online publiziert: 28. Oktober 2025
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**Update 2025 der S3-Leitlinie:
 „Sepsis – Prävention, Diagnose,
 Therapie und Nachsorge“**

Was ist neu?

Caroline Neumann¹ · Daniel Ebert¹ · Michael Bucher¹ · Michael Bauer¹
¹Klinik für Anaesthesiologie und Intensivmedizin, Universitätsklinikum Jena, Jena, Deutschland
²Klinik für Anaesthesiologie und operative Intensivmedizin, Universitätsklinikum Halle, Halle (Saale), Deutschland



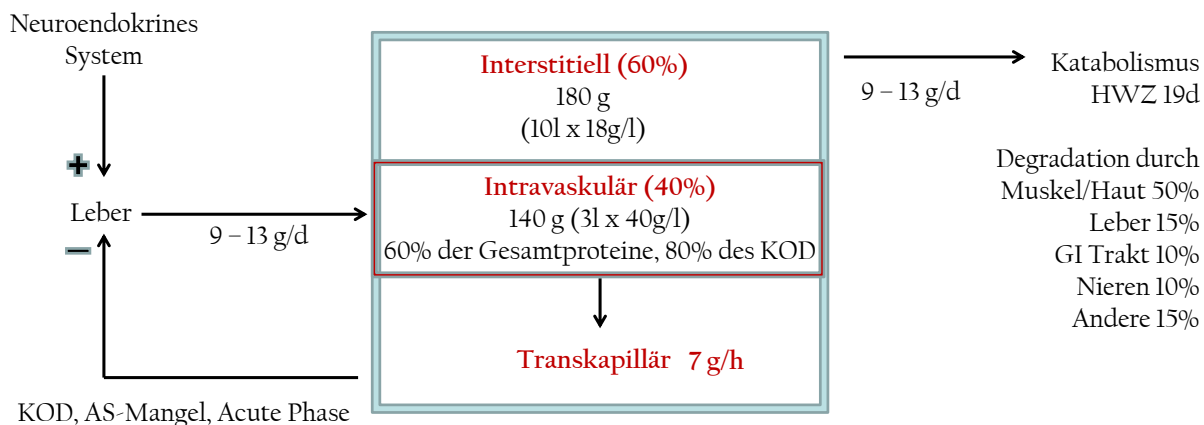
- **DSG 2018:** Wir schlagen vor, dass von einer Verwendung von **Albumin oder Gelatine** bei der Behandlung von Patienten mit septischem Schock abgesehen wird, sofern eine adäquate Flüssigkeitstherapie mit Kristalloiden in der Lage ist, die hämodynamische Stabilität zu erreichen. Für den Fall, dass dies nicht möglich sein sollte, schlagen wir den ergänzenden Einsatz von **Albumin oder Gelatine** vor (*Empfehlungsgrad: schwach*).
- **DSG 2025 (NEU):** Wir schlagen vor, bei Patienten mit Sepsis und septischem Schock **Gelatine NICHT** anzuwenden. (*Empfehlungsgrad: schwach*).
- **DSG 2025 (Änderung):** Wir schlagen vor, bei Patienten mit Sepsis oder septischem Schock **Albumin additiv** zu balancierten Kristalloiden zu verabreichen, wenn große Mengen an Flüssigkeit benötigt werden, um eine hämodynamische Stabilität zu erreichen.¹ (*Empfehlungsgrad: schwach*).

Brunkhorst FM, et al. S3-Leitlinie Sepsis – Prävention, Diagnose, Therapie und Nachsorge – Update 2025. *Med Klin Intensivmed Notfmed.* 2025 Aug 18.

Fact check (2)...



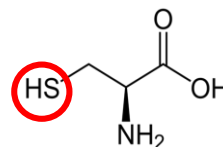
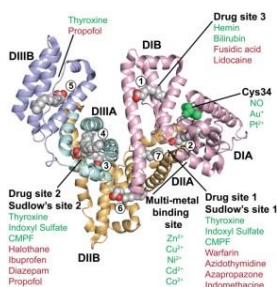
Was ist Albumin - Metabolismus



... nach Gattinoni et al. Albumin administration: volume replacement or pharmacological treatment? Minerva Anestesiol 2005

Was kann Albumin ... ?

- Bindung und Transport (toxischer) endogener und exogener Verbindungen
- Radikalfänger / NO Modulation (Thiolgruppe)
- Antiinflammatorische Aktivität / Inhibition von Apoptose

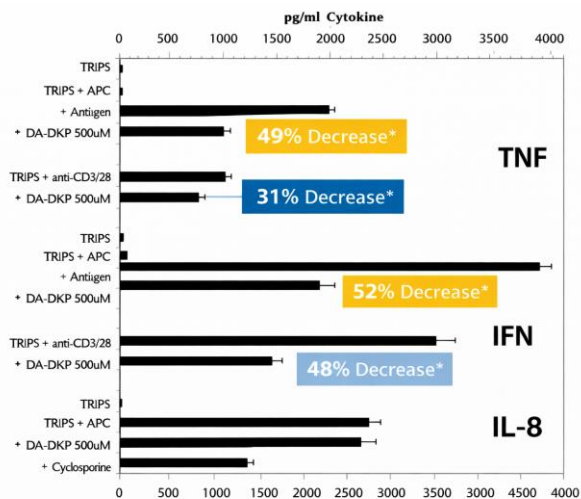


Thiolgruppe (R-SH) → ROS → Disulfidbrücke R-SS-R'
 → Thionitrit R-SN=O= reversibel mittels NADP/NADPH
 → Sulfonsäure R-SO₂-OH = irreversibel

ROS: Hydroxyl Radikal
 Superoxid Radikal
 Wasserstoffperoxid

Antiinflammatorische, antioxidative und NO Modulierende Wirkung des Albumins

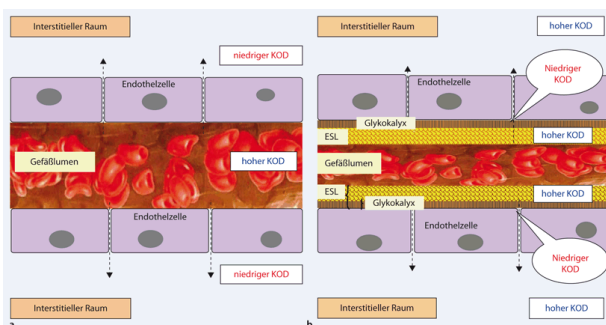
→ **CAVE: Reduziertes Antioxidatives Potential von handelsfertigen Albumin**



Bar-Or D et al. Heterogeneity and oxidation status of commercial human albumin preparations in clinical use. Crit Care Med. 2005

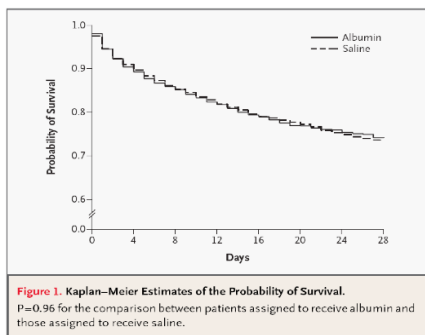
Was kann Albumin ... ?

- Bindung und Transport (toxischer) endogener und exogener Verbindungen
- Radikalfänger / NO Modulation (Thiolgruppe)
- Antiinflammatorische Aktivität / Inhibition von Apoptose
- **Aufrechterhaltung des KOD und der Kapillarpermeabilität**



Chappell D. et al. Expedition Glykokalyx: Ein neu entdecktes „Great Barrier Reef“. Der Anästhesist. 2008

A comparison of albumin and saline for fluid resuscitation in the intensive care unit



Patients	Albumin Group	Saline Group	Relative Risk (95% CI)	
	no. of deaths/total no.			
Overall	726/3473	729/3460	0.99	(0.91–1.09)
Trauma				
Yes	81/596	59/590	1.36	(0.99–1.86)
No	641/2831	666/2830	0.96	(0.88–1.06)
Severe sepsis				
Yes	185/603	217/615	0.87	(0.74–1.02)
No	518/2734	492/2720	1.05	(0.94–1.17)
ARDS				
Yes	24/61	28/66	0.93	(0.61–1.41)
No	697/3365	697/3354	1.00	(0.91–1.09)

In ICU patients, the use of 4 % albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.

Finfer S, et al. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med.* 2004 May 27;350(22):2247-56. doi: 10.1056/NEJMoa040232. PMID: 15163774.

The EARSS Study:

- Prospective randomized controlled double blinded multicentric study including **792 patients with septic shock**
- **100ml 3x20% Albumin vs. saline in the ICU for 3 days**
- No effect on kidney function
- No difference in mortality
- + **Less catecholamines in the Albumin group (p < 0,05)**

EARSS Study Group: Efficacy and tolerance of hyperoncotic albumin administration in septic shock patients: the EARSS study. *Intensive Care Med* 2011, 37(Suppl 2):S115–0438

SAFE-Studie (BMJ 2006) – Subgruppenanalyse Albumin –



Einfluss des **Serumalbumins** auf das Outcome bei Volumentherapie mit:
Albumin vs. NaCl (Saline)



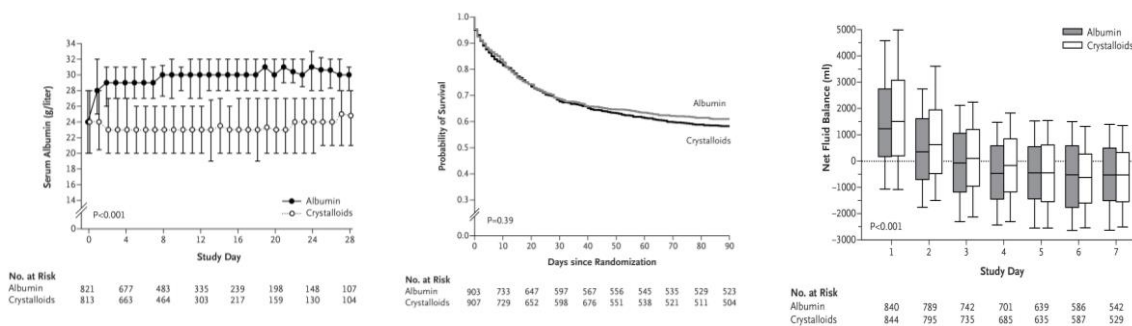
	Mortalität		Odds Ratio (95% CI)	Odds Ratio (95% CI)
	Albumin	Saline		
Gesamtpopulation	644/3012	655/3028	OR: 0.99 (0.87-1.11)	0.99 (0,87-1,11)
Albumin ≤ 25 g/L	291/1228	321/1223	0.87 (0,73-1,05)	0.87 (0,73-1,05)
Albumin > 25 g/L	353/1784	334/1805	1,09 (0,92-1,28)	1,09 (0,92-1,28)

Kein Unterschied
→ Trend zugunsten Albumin
Heterogenität: P=0,08

0.5 0.9 1.0 1 1,2 1.6
Bevorzugung Albumin → Bevorzugung NaCl

SAFE Study Investigators; BMJ. 2006; 333:7577-1044

**Albion Study:
Albumin Replacement in Severe Sepsis or Septic Shock**



Serum albumin kept to a level of 30 g/L (n = 1.810 patients):

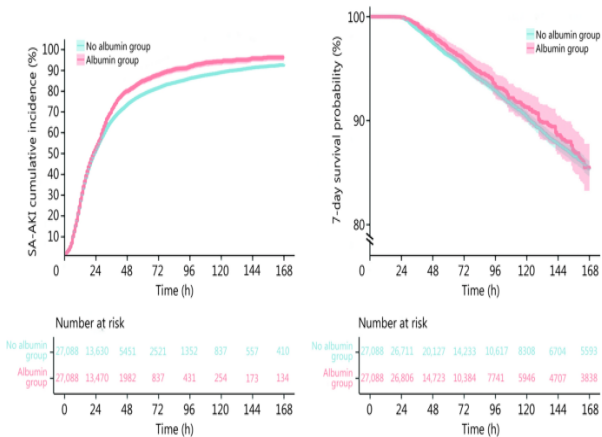
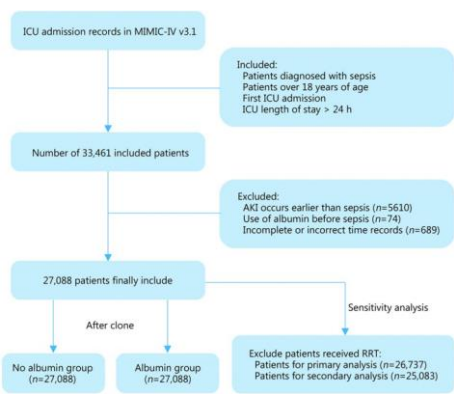
- No effect on outcome

+ Time to suspension of vasopressor: 3d (Albumin) vs 4 d (Crystalloid)

+ Lower net fluid balance (Albumin group)

Caironi P et al; ALBION Study Investigators. Albumin replacement in patients with severe sepsis or septic shock. *N Engl J Med.* 2014 Apr 10;370(15):1412-21.

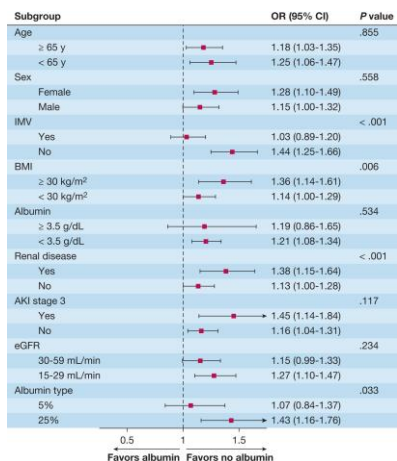
Early use of albumin may increase the risk of sepsis-associated acute kidney injury in sepsis patients: a target trial emulation



➡ significantly higher SA-AKI risk (relative difference = 3.47%, 95% CI 1.76-5.23)

Li XY, et al. Early use of albumin may increase the risk of sepsis-associated acute kidney injury in sepsis patients: a target trial emulation. *Mil Med Res.* 2025 Aug 21;12(1):51. [PMCID:471236924](https://pubmed.ncbi.nlm.nih.gov/471236924/).

Comparative effectiveness of albumin versus no albumin on renal replacement therapy and mortality in patients with septic shock and renal impairment



Outcomes	No albumin n = 7980	Albumin n = 2020	OR / Coefficient (95% CI)	P value
Primary				
RRT or death – n (%)	2694 (33.8)	803 (39.7)	1.29 (1.14 – 1.47) [†]	<0.001
Secondary				
RRT – n (%)	154 (1.9)	90 (4.5)	2.37 (1.77 – 3.18) [†]	<0.001
Death – n (%)	2605 (32.6)	747 (37.0)	1.21 (1.07 – 1.37) [†]	0.003
MAKE – n (%)	3283 (41.1)	961 (47.6)	1.30 (1.15 – 1.47) [†]	<0.001
Stage 3 AKI – n (%)	1965 (24.6)	584 (28.9)	1.25 (1.09 – 1.42) [†]	0.001
Maximum SCR [mg/dL] – median (IQR)	2.3 (1.7 – 3.3)	2.4 (1.7 – 3.2)	0.18 (-0.20 – 0.57) [‡]	0.347
SCR increase [mg/dL] – median (IQR)	1.1 (0.6 – 2.0)	1.1 (0.7 – 2.0)	0.22 (-0.16 – 0.60) [‡]	0.263
Duration of IMV [days] – median (IQR)	0 (0 – 3)	1 (0 – 4)	1.17 (0.87 – 1.48) [‡]	<0.001
Hospital LOS [days] – median (IQR)	6 (2 – 11)	7 (3 – 13)	1.92 (1.41 – 2.42) [‡]	<0.001

RRT = renal replacement therapy; MAKE = major adverse kidney event (decrease in eGFR >25% or CRRT [or other dialysis] or death); SCR = serum creatinine; AKI = acute kidney injury (Kidney Disease: Improving Global Outcomes definition); IMV = invasive mechanical ventilation; LOS = length of stay; [†]odds ratio; [‡]coefficient.

Albumin was associated with an increased risk of RRT or in-hospital mortality, which was most associated with hyperoncotic (25%) rather than iso-oncotic albumin.

Patanwala AE, et al. Comparative Effectiveness of Albumin vs No Albumin on Renal Replacement Therapy and Mortality in Patients With Septic Shock and Renal Impairment. *Chest.* 2025 Apr;167(4):1090-1098.

FRISC-Studie (2021): 5% Humanalbumin vs. NaCl

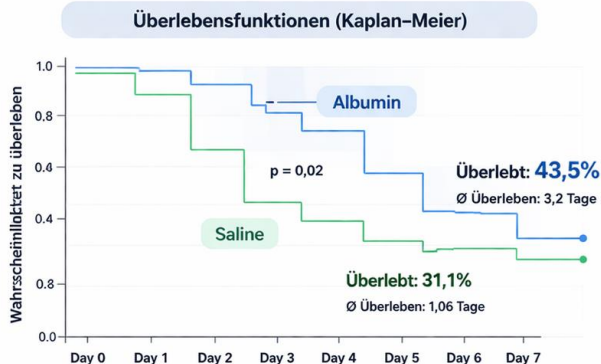
Flüssigkeitsresuscitation bei **Sepsis-bedingter Hypotonie unter Zirrhose**

Design
Randomisierte kontrollierte Studie

Population
Patient:innen mit Zirrhose + Sepsis + Hypotonie

Intervention
5% Albumin vs. NaCl (Saline)

Endpunkt
Überleben (7 Tage)



Tag	0	1	2	3	4	5	6	7	Gesamt
Albumin	154	149	161	132	123	101	84	67	154
Saline	95	94	113	85	76	68	64	59	95

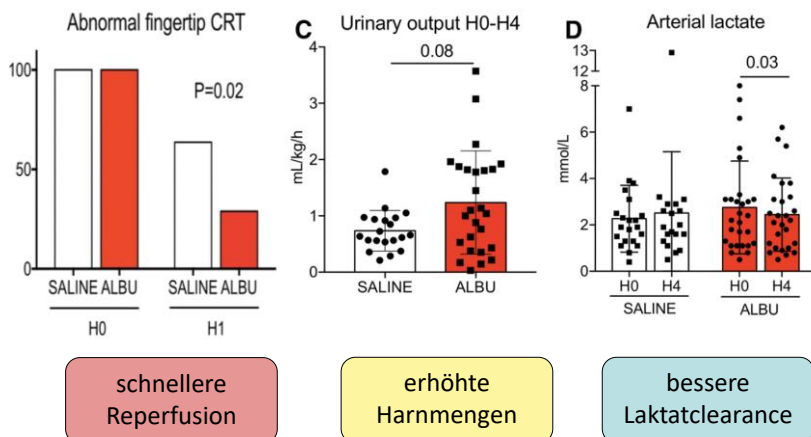
Kernergebnisse

- Höhere Überlebensrate**
• 43,5% vs. 31,1%
- Längeres Überleben**
• 3,2 Tage vs. 1,06 Tage
- Statistisch signifikant**
• p = 0,02

Albumin verbessert das 7-Tage-Überleben signifikant bei Sepsis & Zirrhose.

Philips CA, et al. *Hepatal Int.* 2021 Aug;15(4):983-994.

Albumin versus saline infusion for sepsis-related peripheral tissue hypoperfusion: a proof-of-concept prospective study



Proof-Of-Concept-Studie (2024)

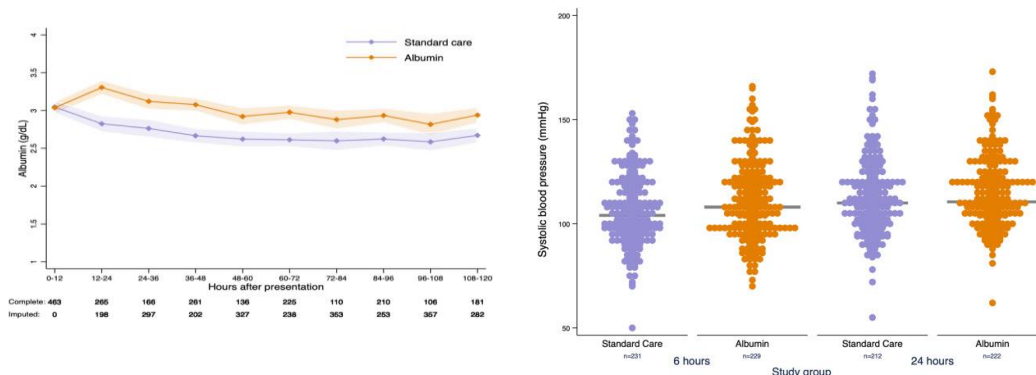
50 Patient:innen
21 NaCl, 29 Albumin

SOFA-Score: 8 (5-11)
SAPS I: 53 (45-70)

= 0,02
Schnellere Normalisierung mit Albumin

Gabarre P, et al. *Albumin versus saline infusion for sepsis-related peripheral tissue hypoperfusion: a proof-of-concept prospective study.* *Crit Care.* 2024 Feb 7;28(1):43.

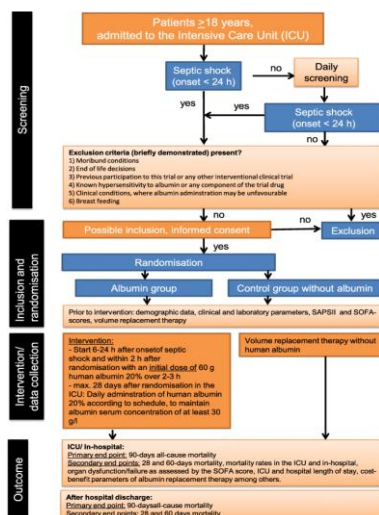
Intervention With Concentrated Albumin for Undifferentiated Sepsis in the Emergency Department (ICARUS-ED): A Pilot Randomized Controlled Trial



SBP higher at 6 hours, less total fluid at 72 hours, fewer patients required vasopressor at 24 and 72 hour

Williams JM, et al. Intervention With Concentrated Albumin for Undifferentiated Sepsis in the Emergency Department (ICARUS-ED): A Pilot Randomized Controlled Trial. *Ann Emerg Med.* 2025 Jul;86(1):59-69.

Randomized controlled multicentre study of albumin replacement therapy in septic shock (ARISS): protocol for a randomized controlled trial



Sakr Y, et al. and SepNet - Critical Care Trials Group. Randomized controlled multicentre study of albumin replacement therapy in septic shock (ARISS): protocol for a randomized controlled trial. *Trials.* 2020 Dec 7;21(1):1002.

Sepsis: an **inadequate response of the immune system** to an infection



Yes, Albumin has:

anti-inflammatory, antioxidant, and NO-modulating effects.



But commercial Albumin:

Reduced antioxidant potential of commercially prepared albumin

Bar-Or D et al. Heterogeneity and oxidation status of commercial human albumin preparations in clinical use. Crit Care Med. 2005

What can **Albumin do...** and what can it (absolutely) not do?

Yes, it can:



+ improve **micro- and macocirculation**, less catecholamines and less fluid overload.

+ Keep your **endothelial surface layer (ESL) happy and tight** — even at levels down to **1 g/dL**.
Protect the ESL by avoiding intravascular overfilling and calming inflammation.

(+) **anti-inflammatory, antioxidant, and NO-modulating** effects, but reduced antioxidant potential of commercially prepared albumin.

No, it definitely can't:



- Improve survival in septic shock

- Create a strong intravascular **oncotic "pull."** (Starling 1.0 is dead — albumin is a barrier-buddy, not a vacuum pump.)

Maybe:



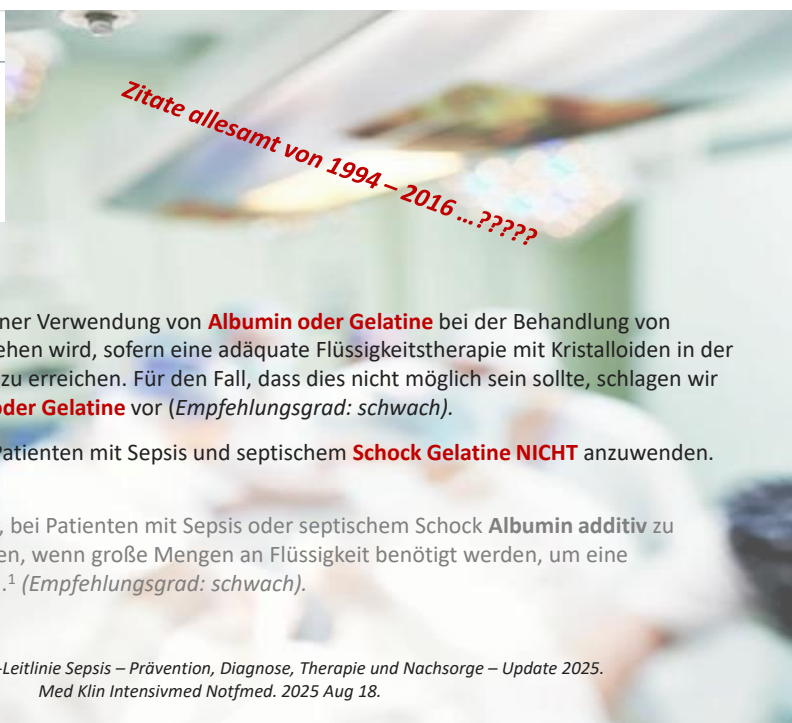
+/- Effect on kidney function especially in pre-existing disease unclear.

Jacob M et al. Reappraising Starling: the physiology of the microcirculation. Curr Opin Crit Care. 2013



FAZIT FÜR ALBUMIN IN DER SEPSIS

- Albumin: **nephrotoxizität** nicht vollständig ausgeschlossen.
- Albumin zur **HDS tendenziell besser als Kristalloide** alleine - Albumin vs. Gelatine?
- Als **Basiskolloid** zum Flüssigkeitsersatz derzeit nicht zu empfehlen (teuer, lange HWZ, Akkumulation, Benefit?) – preiswertere Alternative.
- Abgesehen von kolloid-onkotischen Eigenschaften aber **andere Effekte möglicherweise vorteilhaft** (NO Modulation, Antioxidant, Antiinflammatorisch, Anti-Immunsuppressive, Medikamenten-Nephrotoxizität).
- Exogen **zugeführtes Albumin ≠ endogenes Albumin**
- Bei **starker Hypoalbuminämie (<1-2g/dl) in jedem Fall Ersatz sinnvoll**



- **DSG 2018:** Wir schlagen vor, dass von einer Verwendung von **Albumin oder Gelatine** bei der Behandlung von Patienten mit septischem Schock abgesehen wird, sofern eine adäquate Flüssigkeitstherapie mit Kristalloiden in der Lage ist, die hämodynamische Stabilität zu erreichen. Für den Fall, dass dies nicht möglich sein sollte, schlagen wir den ergänzenden Einsatz von **Albumin oder Gelatine** vor (*Empfehlungsgrad: schwach*).
- **DSG 2025 (NEU):** Wir schlagen vor, bei Patienten mit Sepsis und septischem **Schock Gelatine NICHT** anzuwenden. (*Empfehlungsgrad: schwach*).
- **DSG 2025 (Änderung):** Wir schlagen vor, bei Patienten mit Sepsis oder septischem Schock **Albumin additiv** zu balancierten Kristalloiden zu verabreichen, wenn große Mengen an Flüssigkeit benötigt werden, um eine hämodynamische Stabilität zu erreichen.¹ (*Empfehlungsgrad: schwach*).

Brunkhorst FM, et al. S3-Leitlinie Sepsis – Prävention, Diagnose, Therapie und Nachsorge – Update 2025. Med Klin Intensivmed Notfmed. 2025 Aug 18.

The Surviving Sepsis Campaign Guidelines 2026:

➤ **suggest against using gelatin for resuscitation.** (weak recommendation, moderate certainty evidence)

Rochberg B, et al; Fluids in Sepsis and Septic Shock Group: Fluid resuscitation in sepsis: A systematic review and network meta-analysis. *Ann Intern Med* 2014; 161:347–355.

Keine verlässliche Aussage zur Sicherheit oder Überlegenheit von Gelatine.

Annane D, et al; CRISTAL Investigators: Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients. *Critical Care Medicine* 2013; 310:1809–1817

Vorteile für Kolloide per se.

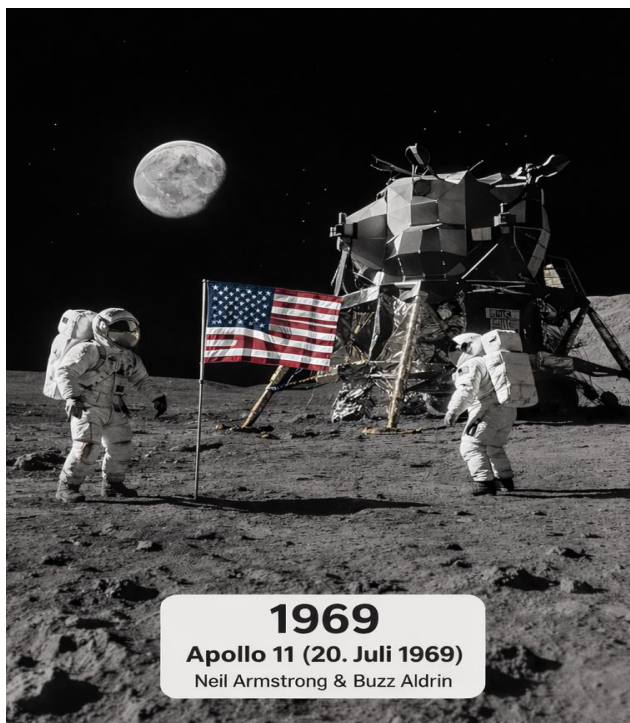
Rochberg B et al; FISSH Group (Fluids in Sepsis and Septic Shock): Fluid type and the use of renal replacement therapy in sepsis: A systematic review and network meta-analysis. *Intensive Care Med* 2015; 41:1561–1571

Keine Aussage bzgl. Gelatine möglich

Moeller C, et al; How safe is gelatin? A systematic review and meta-analysis of gelatin-containing plasma expanders vs crystalloids and albumin. *J Crit Care* 2016; 35:75–83.

Kein signifikanter Unterschied zu Kristalloiden und Albumin.

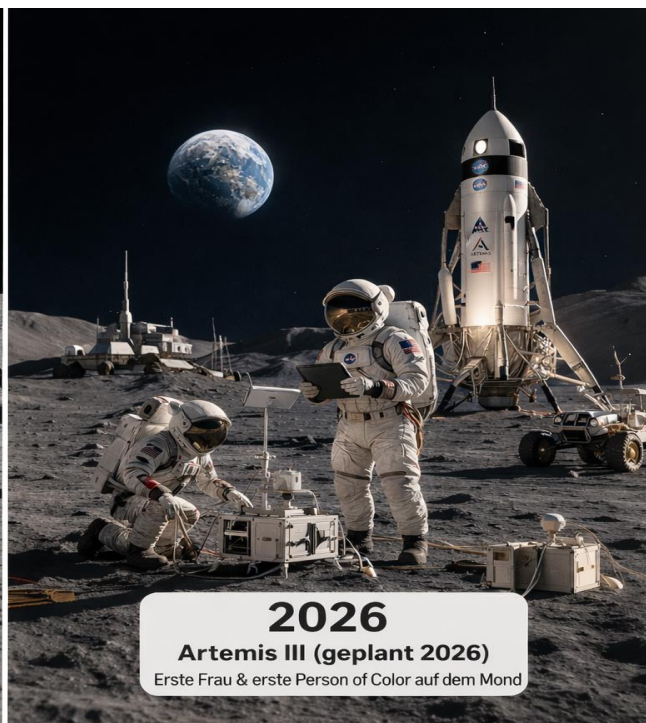
Prescott HC, *Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026. Intensive Care Med.* 2026 Mar 23.



1969

Apollo 11 (20. Juli 1969)

Neil Armstrong & Buzz Aldrin



2026

Artemis III (geplant 2026)

Erste Frau & erste Person of Color auf dem Mond

Succinylated gelatin vs. urea-cross linked gelatin



Schlechter Volumeneffekt
Jakob Creutzfeldt Disease
Hohe Anaphylaxierate
Nephrotoxisch

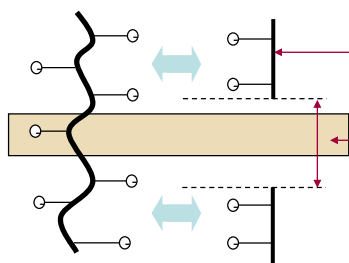


Characteristics	Gelofusine	Gelofusin Iso/Gelaspan	Haemacel
Type of gelatin	Succinylated	Succinylated	Urea-linked
Gelatin concentration	4%	4%	3.5%
Osmolarity [mOsm/l]	274	284	293
Mean Mw	30 Kd	30 Kd	35 Kd
Volume Effect	100%, 3-4 h	100%, 3-4 h	~70%, 1-2 h
Na ⁺ [mmol/l]	154	151	145
Cl ⁻ [mmol/l]	120	103	145
K ⁺ [mmol/l]	0	4	5.1
Ca ²⁺ [mmol/l]	0	1	6.25
Mg ²⁺ [mmol/l]	0	1	0
Acetate [mmol/l]	0	24	0

Influences on passage through membrane pores



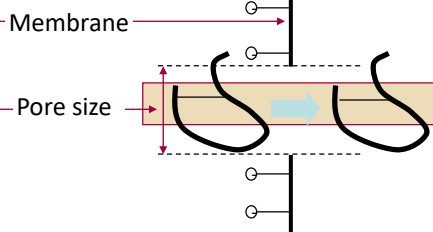
Stretched molecule,
strong negative charge



Succinylated gelatin

- Elimination through kidneys is slower
- Duration of volume effect prolonged

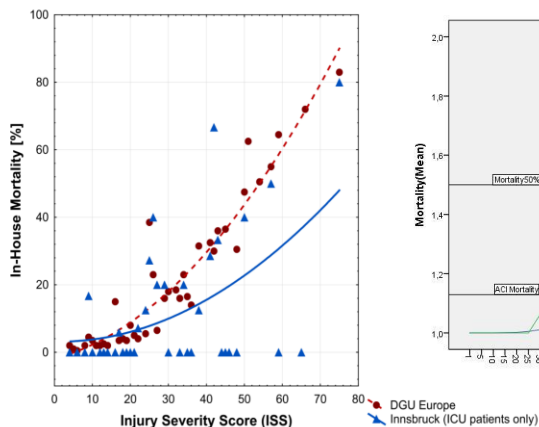
Globular molecule,
little negative charge



Urea-cross linked gelatin

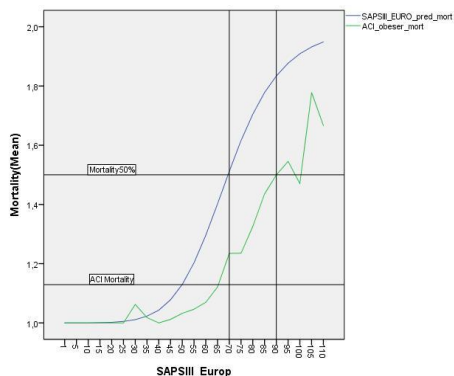
Webb A R et al. *Intensive Care Med* 15 (1989) 116-120

Trauma



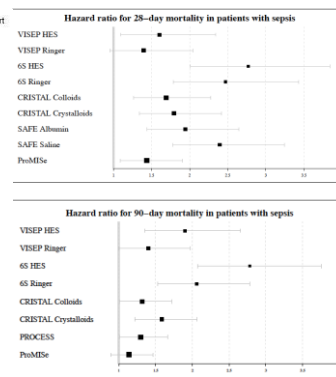
retrospective cohort study of 220 adult trauma patients treated in the ICU at Innsbruck University Hospital. Prehospital phase, emergency room, operating room, and ICU days 1–7 were analyzed.

Sepsis



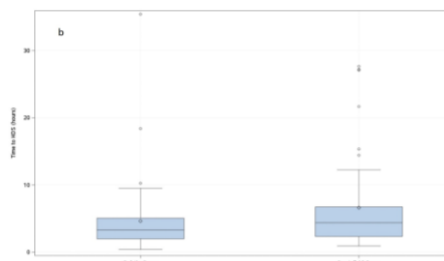
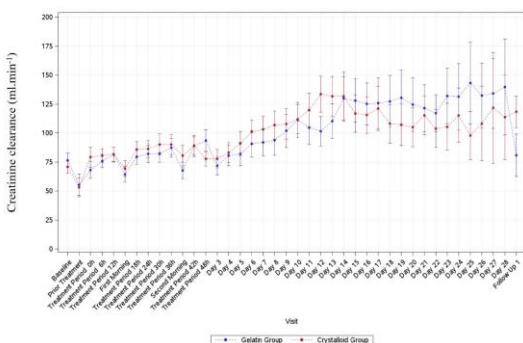
Sepsis mortality of gelatin treated ICU patients (n=1.259) in Innsbruck. Bei einer zu erwartenden Mortalität von 50% (zentraleuropäisch korrigierter SAPS3) Mortalität von 22%.

ICU mortality



ICU mortality of gelatin treated ICU patients (n=1.600) in Innsbruck compared to mortality from other RCTs.

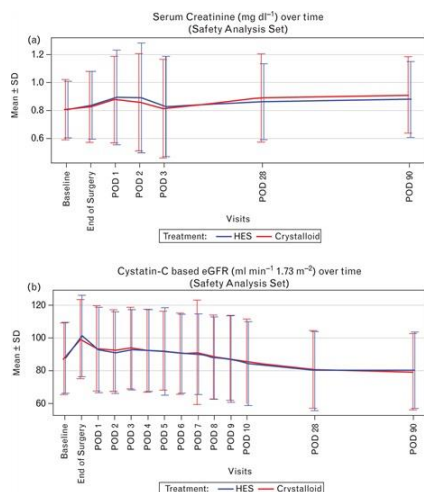
Efficacy and Safety of a Balanced Gelatine Solution for Fluid Resuscitation in Sepsis: A Prospective, Randomised, Controlled, Double-Blind Trial - **GENIUS Trial**



- ✓ **HDS** mit Gelifusin effektiver bei chirurgischen septischen Patient:Innen 4,7h (Gelifusin) vs 5,8h (Kristalloid)
- ✓ Weniger **fluid overload** in der Gelifusingruppe
- ✓ **CrCl** 76,5 mL/min (Gelifusin) vs 70,8 mL/min (Kristalloid)
- ✓ **Keine anaphylaktische Reaktion**

Marx G, et al. Efficacy and Safety of a Balanced Gelatine Solution for Fluid Resuscitation in Sepsis: A Prospective, Randomised, Controlled, Double-Blind Trial-GENIUS Trial. J Clin Med. 2025 Jul 28;14(15):5323.

Safety and efficacy of 6% hydroxyethyl starch in patients undergoing major surgery: The randomised controlled **PHOENICS** trial



of 4.8 ± 2.6 l of fluids, and patients assigned to the crystalloid-only group received 5.1 ± 2.7 l, respectively.

In a post hoc analysis, the proportion of patients who required **vasoactive/inotropic drugs** was significantly lower in the HES group compared to the crystalloid-only group (26 vs. 35%, $P < 0.0001$).

Buhre W, et al. Safety and efficacy of 6% hydroxyethyl starch in patients undergoing major surgery: The randomised controlled PHOENICS trial. *Eur J Anaesthesiol.* 2025 Oct 23

	CON	PRO
Saline	<ul style="list-style-type: none"> Azidose Schlechter Volumeneffekt 	
Balancierte Kristalloide	<ul style="list-style-type: none"> Schlechter Volumeneffekt 	<ul style="list-style-type: none"> Keine Azidose im Vgl. zu Saline „sog. balancierte“ E-lyte
Albumin	<ul style="list-style-type: none"> Lange Verweildauer Interstitium Niereneffekt unklar Preis 	<ul style="list-style-type: none"> Guter Volumeneffekt Mikrozirkulation Endotheleffekt
HES	<ul style="list-style-type: none"> Nierenfunktion Kumulation Gewebe und RES Gerinnungsstörungen 	<ul style="list-style-type: none"> Guter Volumeneffekt
Gelatine	<ul style="list-style-type: none"> Fibrinpolymerationsstörung (Anaphylaxie) 	<ul style="list-style-type: none"> Keine Akkumulation/Speicherung Guter Volumeneffekt

Fluid is a drug ...!

