Choc

Définition

Le choc est une altération de la circulation (déficit hémodynamique) où la perfusion tissulaire est insuffisante pour assurer le métabolisme cellulaire

Sémiologie

- hypotension artérielle
- tachycardie (pouls filant)
- lipothymie, apathie, agitation
- pâleur, froideur, moiteur
- marbrures cutanées, cyanose
- oligurie, anurie
- hyperventilation (acidose métabolique)
- « choc chaud »: extrémités vasodilatées, rouges, chaudes, sèches

Evaluation des signes vitaux (paramètres cliniques)

- Respiration : FR, VT, couleur peau
- Cerveau : pupilles (taille, L+), sensibilité, conscience
- Reins : diurèse normale = 6-15 ml/ 10 min
- Température
- Cardiovasculaire : TA, pouls, FC, RC, turgescence jugulaire, pouls capillaire (front: N < 1,5 sec), sudations, vasoconstriction, marbrures, monitoring cardiaque et hémodynamique

Bilan paraclinique

- Biologie : EHC, urée, créatinine, glycémie, iono, Ca, coagulation, gazométrie, groupe + compat, enzymes, CRP
- RX thorax
- ECG
- Centre antipoison
- Aspiration gastrique (hématest)
- Gastroscopie
- Abdomen : RX à blanc, échographie, TDM
- Bactériologie : HC, EMU + culture, expectorations, PL, FG, FV

Classification

- choc hypovolémique
- choc cardiogénique
- choc obstructif
- choc distributif

Choc hypovolémique

= le volume contenu dans le compartiment intravasculaire n'assure pas une perfusion tissulaire adéquate

- par pertes externes de liquide: sang, plasma, hydroélectrolytiques, digestives, cutanées, rénales
- par séquestration interne de liquide: hémorragies internes, 3è espace, choc anaphylactique, phéochromocytome

Principales étiologies

A. Par pertes externes de liquide

- pertes de sang : hémorragies externes
- pertes de plasma : brûlures, lésions exsudatives
- pertes hydro-électrolytiques:

- pertes digestives : vomissements, diarrhées
- pertes cutanées : déshydratation (fièvre)
- pertes rénales : diabète sucré, diabète insipide, diurétiques, crise addisonienne, hypercalcémie

B. Par séquestration interne du liquide

- hémorragies internes :
  - fractures
  - digestives (ulcus, varices œsophagiennes,...)
  - hémothorax
  - hémopéritoine
  - hématome retropéritonéal
  - anévrisme disséquant de l'aorte
  - pancréatite hémorragique
  - infarctus intestinal,...
- 3e espace :
  - ascite
  - obstruction intestinale
  - épanchement pleural
- choc anaphylactique
- phéochromocytome

Choc cardiogénique

= la pompe cardiaque est incapable d 'assurer un volume circulant suffisant

- altérations myocardiques: infarctus, cardiomyopathies
- lésions valvulaires et septales
- tachycardies (remplissage diastolique inadéquat)

Principales étiologies

1. **Altérations myocardiques**
- infarctus du myocarde
- myocardite aiguë
- cardiomyopathies au stade terminal

2. **Lésions valvulaires et septales**
- rupture de pilier ou de cordage tendineux
- rupture ou perforation valvulaire
- perforation du septum interventriculaire

3. **Tachycardies** (remplissage diastolique inadéquat)

Choc obstructif

= obstruction à la circulation du sang au niveau des grosses veines, du cœur, des artères pulmonaires, de l'aorte

Principales étiologies

- compression des veines caves
- tamponnade péricardique
- ball-valve thrombus, myxome de l'oreillette
- embolie pulmonaire
- anévrysme disséquant de l'aorte
- pneumothorax
- épanchements pleuraux massifs
- VA à pression positive élevée

Choc distributif

= déficit majeur de la résistance artérielle et/ou de la capacité veineuse responsable d'une perturbation de la distribution de la masse sanguine

- choc septique
- intoxication barbiturique
- blocage ganglionnaire (anesthésie)
- choc spinal (section cervicale moelle épinière)

Traitement du choc

Principes

- Traitement étiologique
- Augmenter le transport de l'oxygène

  $DO_2 = Ca\ O_2 \times DC$
- Diminuer la demande en oxygène

  $VO_2 = Ca\text{-}v\ O_2 \times DC$
- Divers: combattre l'acidose

  combattre l'anurie

Augmenter le transport en oxygène

A. le débit cardiaque

- expanseurs: sang, colloïdes, cristalloïdes
- sympathomimétiques: dopamine, dobutamine, isoprotérénol, noradrénaline

B. la concentration en hémoglobine (!anémie)

C. Fi O_2 (oxygénothérapie)

Les expanseurs

Bénéfices attendus du remplissage

régression des signes cliniques d'hypovolémie

- augmentation de la délivrance en oxygène aux tissus: correction acidose lactique et hypotension artérielle
- redistribution favorable des débits régionaux : reprise de la diurèse et réduction de la fréquence cardiaque

Table 1. Types and Compositions of Resuscitation Fluids.*

Variable	Human Plasma	Colloids									Crystalloids		
		4% Albumin	Hydroxyethyl Starch						4% Succinylated Modified Fluid Gelatin	3.5% Urea-Linked Gelatin	0.9% Saline	Compounded Sodium Lactate	Balanced Salt Solution
			10% (200/0.5)	6% (450/0.7)	6% (130/0.4)		6% (130/0.42)						
Trade name		Albumex	Hemohes	Hextend	Voluven	Volulyte	Venofundin	Tetraspan	Gelofusine	Haemaccel	Normal saline	Hartmann's or Ringer's lactate	PlasmaLyte
Colloid source		Human donor	Potato starch	Maize starch	Maize starch	Maize starch	Potato starch	Potato starch	Bovine gelatin	Bovine gelatin			
Osmolarity (mOsm/liter)	291	250	308	304	308	286	308	296	274	301	308	280.6	294
Sodium (mmol/liter)	135–145	148	154	143	154	137	154	140	154	145	154	131	140
Potassium (mmol/liter)	4.5–5.0			3.0		4.0		4.0		5.1		5.4	5.0
Calcium (mmol/liter)	2.2–2.6			5.0				2.5		6.25		2.0	
Magnesium (mmol/liter)	0.8–1.0			0.9		1.5		1.0					3.0
Chloride (mmol/liter)	94–111	128	154	124	154	110	154	118	120	145	154	111	98
Acetate (mmol/liter)						34		24					27
Lactate (mmol/liter)	1–2			28								29	
Malate (mmol/liter)								5					
Gluconate (mmol/liter)													23
Bicarbonate (mmol/liter)	23–27												
Octanoate (mmol/liter)		6.4											

* To convert the values for potassium to milligrams per deciliter, divide by 0.2558. To convert the values for calcium to milligrams per deciliter, divide by 0.250. To convert the values for magnesium to milligrams per deciliter, divide by 0.4114.

Cristalloïdes

Sérum physiologique

- 9 g de NaCl/L d'eau
- 154 mmol/L sodium
- 154 mmol/L chlorure
- Osmolalité = 308 mosm/L
- pH = 5,0

Solution de Ringer

- Sodium: 147 mmol/l
- Potassium: 4 mmol/l
- Calcium: 2,25 mmol
- Chlorures: 155,5 mmol/l
- Osmolarité approximative: 309 mOsm/L
- pH: 5 – 7,5

Solution de Lactate Ringer

Un litre de liquide de Ringer contient :

- 130 mEq d'ion sodium = 130 mmol/l
- 109 mEq d'ion chlorure = 109 mmol/l
- 28 mEq de lactate = 28 mmol/l
- 4 mEq d'ion potassium = 4 mmol/l
- 3 mEq d'ion calcium = 1,5 mmol/l
- pH = 5,0

Solution de Hartmann

- Un litre de liquide de Hartmann contient:
- 131 mEq d'ion sodium = 131 mmol/L.
- 111 mEq d'ion chlorure = 111 mmol/L.
- 29 mEq de lactate = 29 mmol/L.
- 5 mEq d'ion potassium = 5 mmol/L.
- 4 mEq d'ion calcium = 2 mmol/L.
- pH = 6,5
- Osmolarité = 279 mosm/L

Plasmalyte A

- Composition (en mmole/l) :
  - sodium 140
  - chlore 98
  - lactate 28
  - potassium 5
  - magnésium 1,5
  - acétate 27
  - gluconate 23
- pH 7,4

Colloïdes

- Gélatines
- Amidons

Gélatines

- Gélofusine^{R} : flacon de 500 ml à 4 %, contenant 154 mEq Na/l et de PM moyen de 30000
- autre spécialité : Geloplasma^{R}, Plasmion^{R}
- expansion volémique = volume perfusé
- effets secondaires : rarement réaction allergique

Hydroxyéthylamidons (HEA)

- Haes-steril^{R}, Plasmasteril^{R}, Voluven^{R}: solution à 6 % en NaCl isotonique
- expansion volémique supérieure au volume perfusé (550 à 750 ml pour 500 ml perfusé)
- effets secondaires : rarement réaction allergique et surtout troubles de l'hémostase à doses totales élevées ou si forme à longue durée d'action (Elohès); risque accru d'insuffisance rénale; prurit au long terme

Dérivés plasmatiques

- *Plasma frais congelé*
  risque de transmission de maladies virales (hépatite, SIDA) : à ne plus utiliser comme expanseur
- *SSPP* (solution stable de protéines plasmatiques): Albumine à 4%
  - 40 g protéines/l en solution isotonique et avec > 95 % d'albumine (correspond en fait à de l'albumine à 4%); flacon de 400 ml
  - volume injecté = expansion volumique
  - très peu de risque
  - *! critères restreints de remboursement en Belgique !* prescription limitée au choc distributif et anaphylactique et au choc associé à pancréatite; ascite réfractaire du cirrhotique avec hypoprotéinémie et ponctions itératives; syndrome néphrotique avec hypoprotéinémie; plasmaphérèse itérative; cirrhose décompensée avec ponction d'ascite de > 5l ou péritonite bactérienne spontanée
- *Albumine humaine à 20%*
  - flacon de 100 ml à 20 % (=20 g d'albumine)
  - expansion volumique importante (400 ml pour un flacon)
  - intérêt : œdème interstitiel important (notamment pulmonaire)

Que prescrire?

Fraudes aux données

The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis*

Anthony P. Delaney, MD, FCICM; Arina Dan, MD, FCICM; John McCaffrey, MD, FCICM; Simon Finfer, MD, FCICM

(Crit Care Med 2011; 39:386–391)

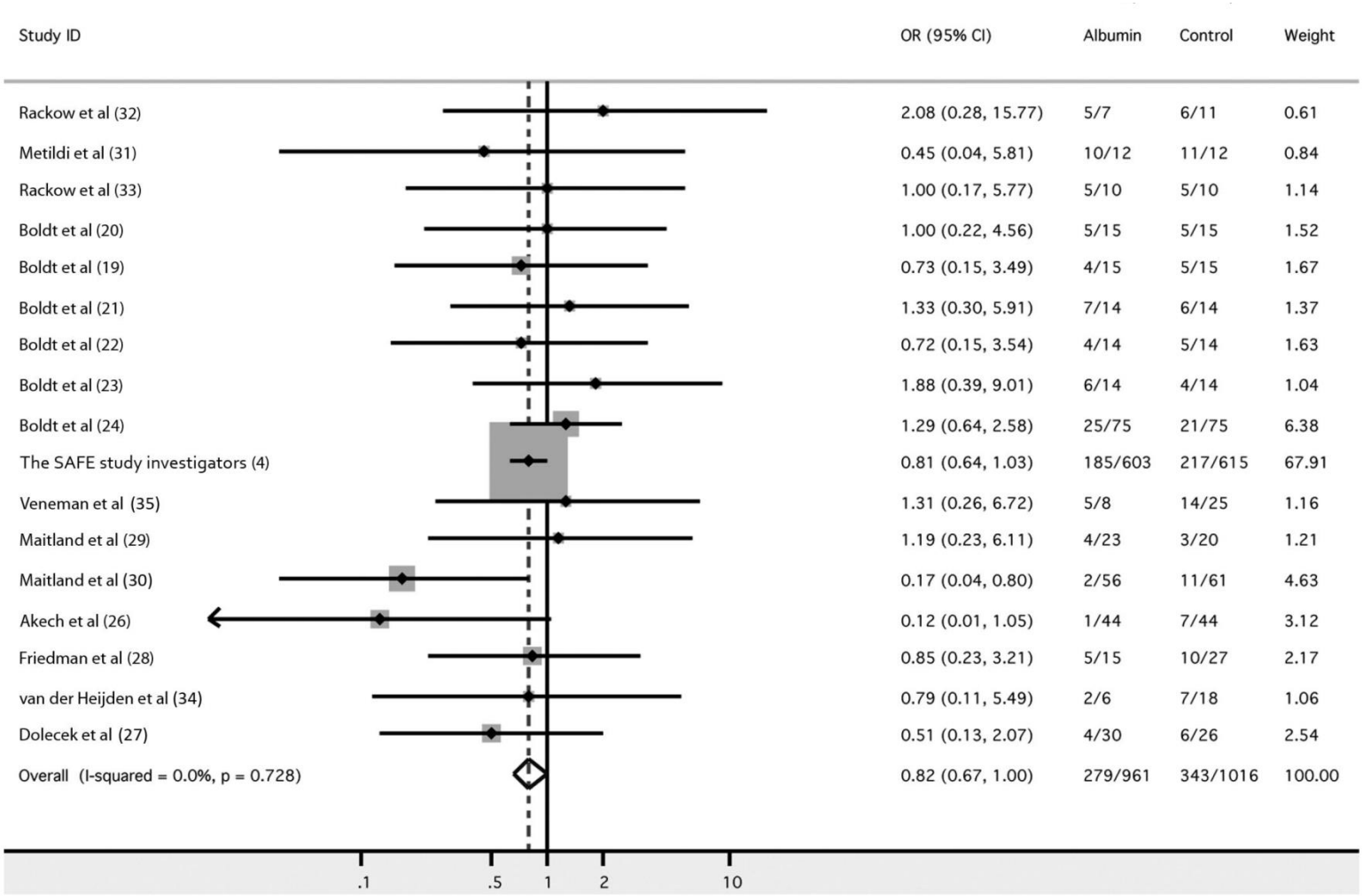

Figure 2. Forrest plot showing the pooled estimate of the effect of resuscitation with albumin-containing solutions on mortality for patients with sepsis. *OR*, odds ratio; *CI*, confidence limit.

Cardiopulmonary Bypass Priming Using a High Dose of a Balanced Hydroxyethyl Starch Versus an Albumin-Based Priming Strategy

Joachim Boldt, MD

Stephan Suttner, MD

Christian Brosch, MD

Andreas Lehmann, MD

Kerstin Röhm, MD

Andinet Mengistu, MD

BACKGROUND: The optimal priming solution for cardiopulmonary bypass (CPB) is unclear. In this study, we evaluated the influence of high-volume priming with a modern balanced hydroxyethyl starch (HES) preparation on coagulation, inflammation, and organ function compared with an albumin-based CPB priming regimen.

METHODS: In 50 patients undergoing coronary artery bypass grafting, the CPB circuit was prospectively and randomly primed with either 1500 mL of 6% HES 130/0.42 in a balanced electrolyte solution (Na^+ 140 mmol/L, Cl^- 118 mmol/L, K^+ 4 mmol/L, Ca^{2+} 2.5 mmol/L, Mg^{++} 1 mmol/L, $acetate^-$ 24 mmol/L, $malate^-$ 5 mmol/L) (n = 25) or with 500 mL of 5% human albumin plus 1000 mL 0.9% saline solution (n = 25). Inflammation (interleukins [IL]-6, -10), endothelial damage (soluble intercellular adhesion molecule-1), kidney function (kidney-specific proteins α-glutathione *S*-transferase, neutrophil gelatinase-associated lipocalin), coagulation (measured by thrombelastometry [ROTEM®, Pentapharm, Munich, Germany]), and platelet function (measured by whole blood aggregometry [Multiplate® analyzer, Dynabyte Medical, Munich, Germany]) were assessed after induction of anesthesia, immediately after surgery, 5 h after surgery, and on the morning of first and second postoperative days.

RESULTS: Total volume given during and after CPB was 3090 ± 540 mL of balanced HES and 3110 ± 450 mL of albumin. Base excess after surgery was lower in the albumin-based priming group than in the balanced HES priming group (−5.9 ± 1.2 mmol/L vs +0.2 ± 0.2 mmol/L, P = 0.0003). Plasma levels of IL-6, IL-10, and intercellular adhesion molecule-1 were higher after CPB in the albumin-based priming group compared with the HES priming group at all time periods (P = 0.0002). Urinary concentrations of α-glutathione *S*-transferase and neutrophil gelatinase-associated lipocalin were higher after CPB through the end of the study in the albumin group compared with the balanced HES group (P = 0.00004). After surgery through the first postoperative day, thrombelastometry data (clotting time and clot formation time) revealed more impaired coagulation in the albumin-based priming group compared with the HES priming group (P = 0.004). Compared with baseline, platelet function was unchanged in the high-dose balanced HES priming group after CPB and 5 h after surgery, but it was significantly reduced in the albumin-based priming group.

CONCLUSION: High-volume priming of the CPB circuit with a modern balanced HES solution resulted in reduced inflammation, less endothelial damage, and fewer alterations in renal tubular integrity compared with an albumin-based priming. Coagulation including platelet function was better preserved with high-dose balanced HES CPB priming compared with albumin-based CPB priming.

(Anesth Analg 2009;109:1752–62)

Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically Ill Patients Requiring Volume Resuscitation

A Systematic Review and Meta-analysis

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Alexis F. Turgeon, MD, MSc
Brett L. Houston, BSc
Lauralyn McIntyre, MD, MSc
John C. Marshall, MD
Dean A. Fergusson, PhD, MHA

Importance Hydroxyethyl starch is commonly used for volume resuscitation yet has been associated with serious adverse events, including acute kidney injury and death. Clinical trials of hydroxyethyl starch are conflicting. Moreover, multiple trials from one investigator have been retracted because of scientific misconduct.

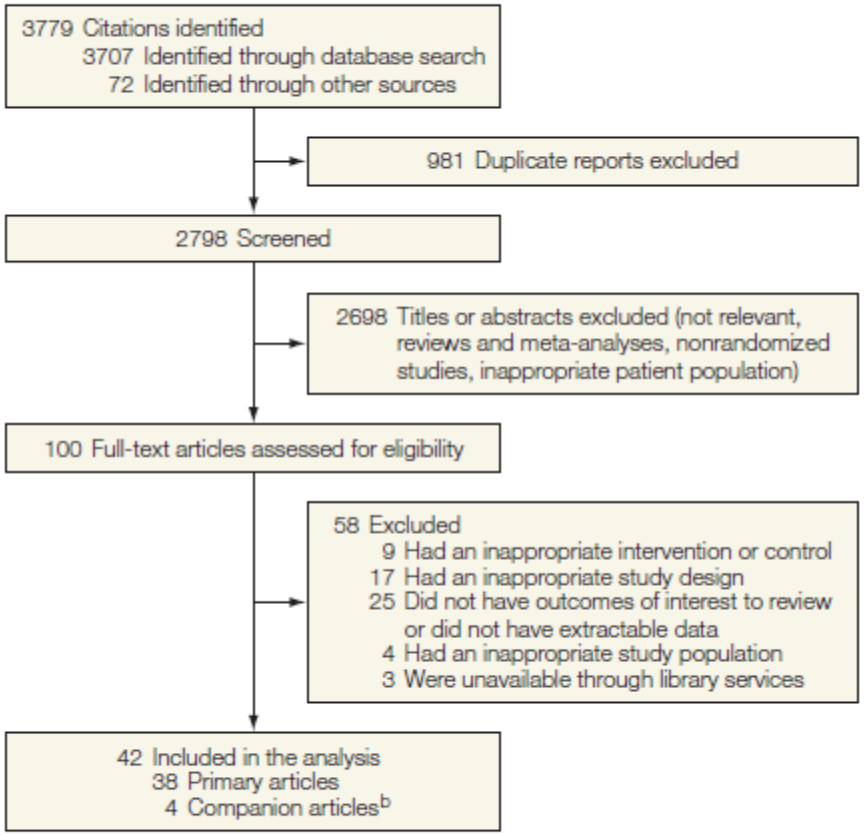
Objectives To evaluate the association of hydroxyethyl starch use with mortality and acute kidney injury.

Data Sources Randomized controlled trials from MEDLINE, EMBASE, CENTRAL, Global Health, HealthStar, Scopus, Web of Science, the International Clinical Trials Registry Platform (inception to October 2012), reference lists of relevant articles, and gray literature.

FLUIDS ARE A CORE ELEMENT IN

JAMA. 2013;309(7):678-688

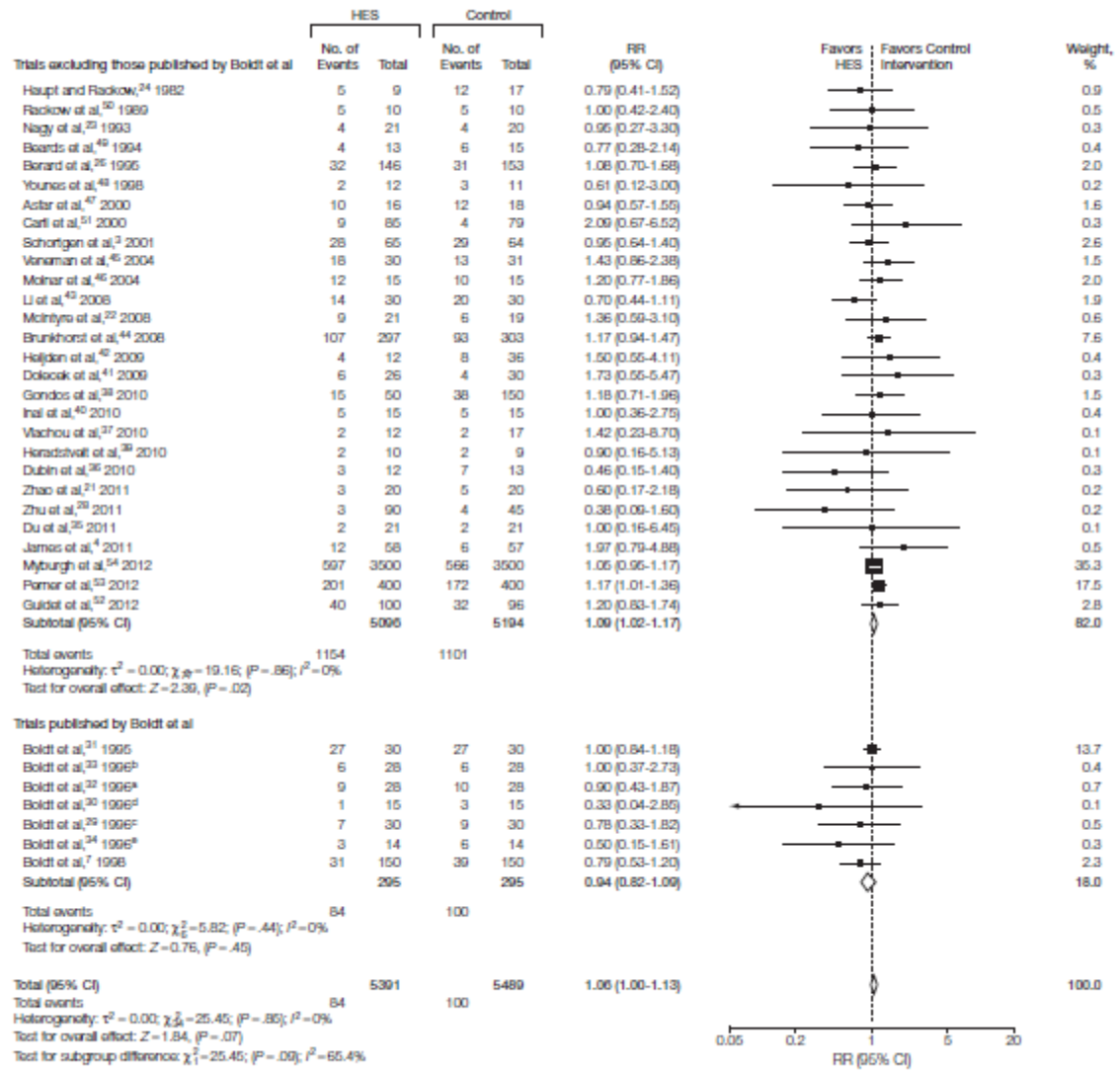
Figure 1. Study Flow Diagram[a]



[a] This flow diagram follows the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA)[14] with modifications.

[b] Companion articles represent reports of previously published analyses involving the same study population.

Figure 2. Mortality and Hydroxyethyl Starch



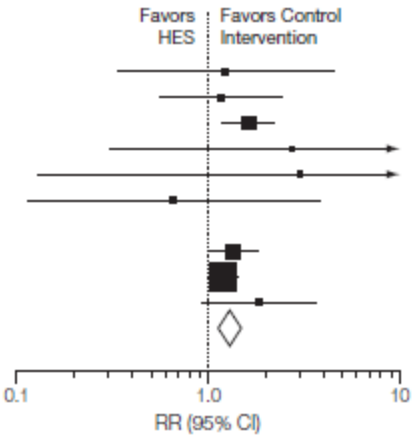
The varying sizes of the boxes represent the weight in the analysis. HES indicates hydroxyethyl starch. Risk ratios (RRs) are derived by a random-effects model using Mantel-Haenszel tests.

Figure 3. Renal Replacement Therapy and Hydroxyethyl Starch

Source	HES No. of Events	HES Total	Control No. of Events	Control Total	RR (95% CI)	Weight, %
Berard et al,[26] 1995	5	155	4	152	1.23 (0.34-4.48)	1.0
Schortgen et al,[3] 2001	13	65	11	64	1.16 (0.56-2.40)	3.3
Brunkhorst et al,[44] 2008	81	297	51	303	1.62 (1.19-2.21)	18.0
McIntyre et al,[22] 2008	3	21	1	19	2.71 (0.31-23.93)	0.4
Du et al,[35] 2011	1	21	0	21	3.00 (0.13-69.70)	0.2
James et al,[4] 2011	2	58	3	57	0.66 (0.11-3.78)	0.6
Viachou et al,[37] 2010	0	12	0	17	Not estimable	
Perner al,[53] 2012	87	400	65	400	1.34 (1.00-1.79)	20.8
Myburgh et al,[54] 2012	235	3500	196	3500	1.20 (1.00-1.44)	51.8
Guidet et al,[52] 2012	21	100	11	96	1.83 (0.93-3.59)	3.9
Total (95% CI)		**4629**		**4629**	**1.32 (1.15-1.50)**	**100.00**
Total events	448		342			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_8 = 5.07$; ($P = .75$); $I^2 = 0\%$

Test for overall effect: $Z = 4.08$, ($P < .001$)



The varying sizes of the boxes represent the weight in the analysis. HES indicates hydroxyethyl starch. Risk ratios (RRs) are derived by a random-effects model using Mantel-Haenszel tests.

EDITORIAL

Hydroxyethyl Starch for Intravenous Volume Replacement

More Harm Than Benefit

Massimo Antonelli, MD

Claudio Sandroni, MD

In addition, this meta-analysis[4] included 3 additional randomized trials published in 2012—the Crystalloid Versus Hydroxyethyl Starch Trials (CHEST),[2] the Scandinavian

Intensive Care Med (2012) 38:1258–1271
DOI 10.1007/s00134-012-2614-0

SYSTEMATIC REVIEW

Christiane S. Hartog
Helga Skupin
Charles Natanson
Junfeng Sun
Konrad Reinhart

Systematic analysis of hydroxyethyl starch (HES) reviews: proliferation of low-quality reviews overwhelms the results of well-performed meta-analyses

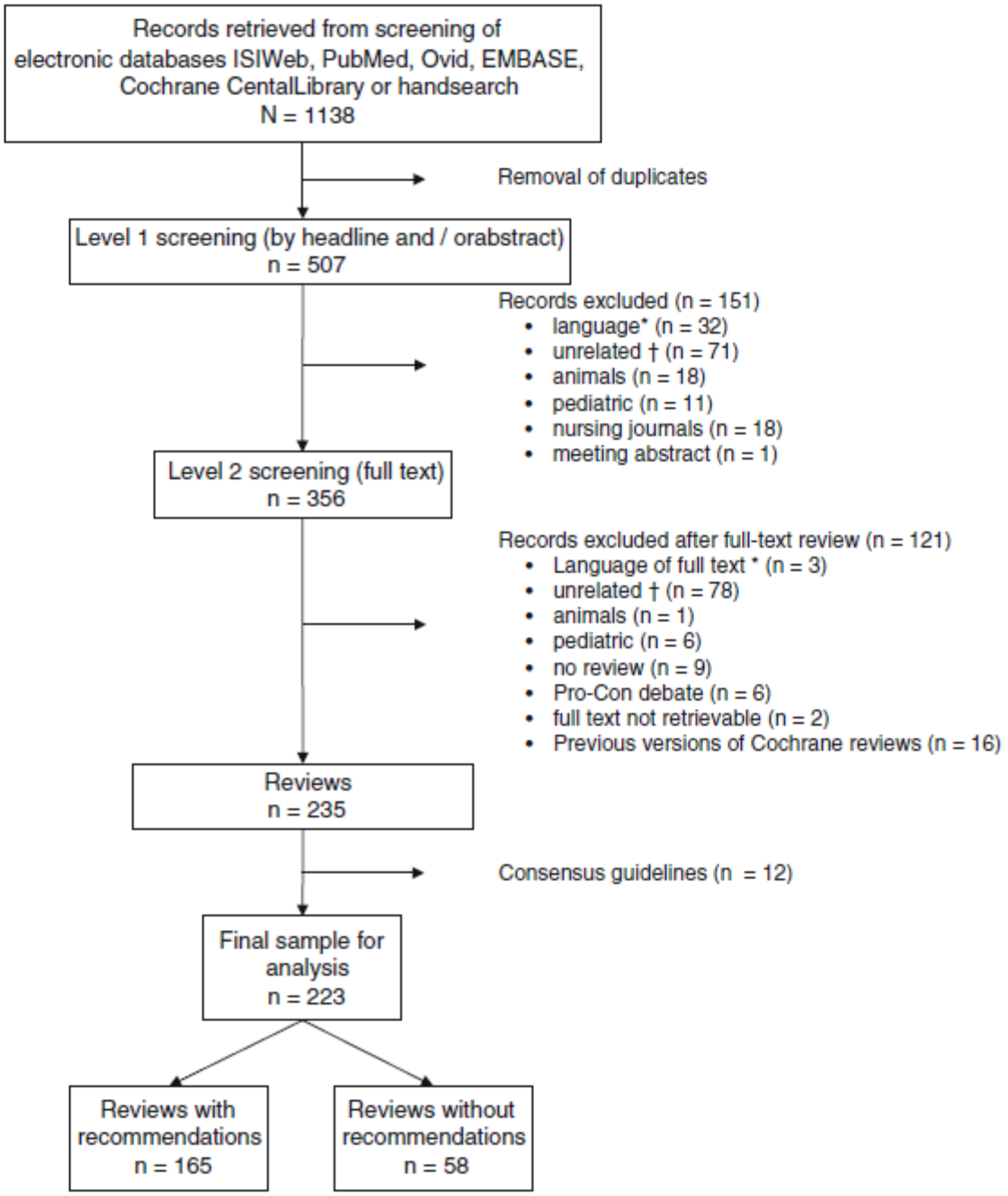


Fig. 1 Study flow. *Excluded languages: Japanese, Russian, Serbocroatian, Polish, Danish, Swedish, Spanish, Portuguese, Chinese, Lithuanian, Czech, Italian. †Unrelated conditions: ovarian hyperstimulation syndrome, retinal vein occlusion, small-volume resuscitation, idiopathic sensorineural hearing loss, eclampsia, diabetic ketoacidosis, chronic obstructive lung disease, polymer science, pharmacokinetics, apheresis, cell harvest, blood component harvest and organ preservation

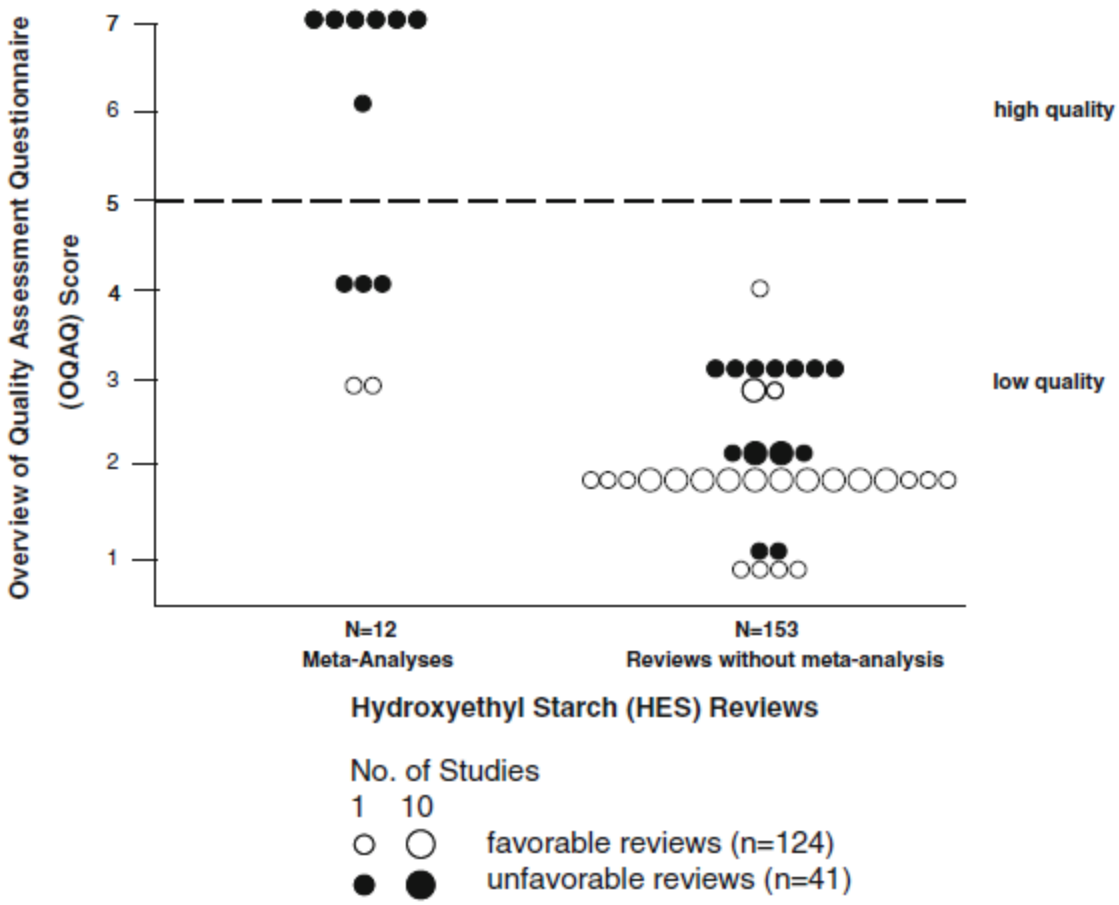


Fig. 2 Quality assessment of hydroxyethyl starch (*HES*) reviews by *OQAQ* score. Reviews with an overall Overview of Quality Assessment Questionnaire (OQAQ) score of ≥5 are regarded as having minor or minimal flaws, i.e., being of high quality. HES meta-analyses achieved significantly higher OQAQ scores [$n = 12$; median (range) 6.5 (3–7)] than HES reviews without a meta-analysis [$n = 153$; 2 (1–4); $p < 0.0001$]. Meta-analyses that were not in favor of HES use achieved significantly higher OQAQ scores [$n = 10$, 7 (4–7)] than favorable meta-analyses [$n = 2$, 3 (3–3); $p = 0.02$]

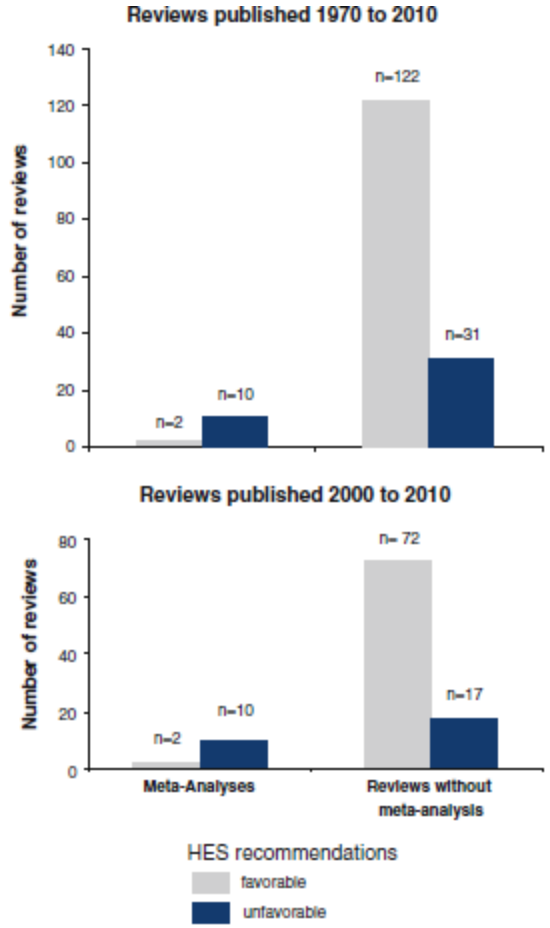


Fig. 3 Hydroxyethyl starch recommendation in the meta-analyses and reviews without a meta-analysis. If a recommendation was made in a review with a meta-analysis, 83 % of the recommendations were unfavorable. In contrast, only 20 % of reviews without a meta-analysis made an unfavorable recommendation (83 vs. 20 %, respectively; $p < 0.0001$, Fisher's exact test). The results are virtually identical if only studies from 2000 to 2010 are included (*lower panel*), the years in which HES meta-analyses began to be published

Table 1 Clinical condition focused on by the HES reviews

Clinical condition	Meta-analyses			Reviews without a meta-analysis		
	Unfavorable ($n = 10$)	Favorable ($n = 2$)	Total ($n = 12$)	Unfavorable ($n = 31$)	Favorable ($n = 122$)	Total ($n = 153$)
Hypovolemia not specified	3	0	3	12	51	63
Shock, major bleeding, trauma, burns, pre-clinical fluid therapy	1	0	1	11	19	30
Critically ill and septic patients	3	0	3	5	22	27
Peri-operative volume therapy and ANH prior to surgery, fluid therapy to prevent hypotension following neural block	2	2	4	2	25	27
Fluid therapy for brain injury, including stroke, intracerebral hemorrhage or neurosurgery	1	0	1	1	5	6

ANH Acute normovolemic hemodilution
Data are presented as the number of studies

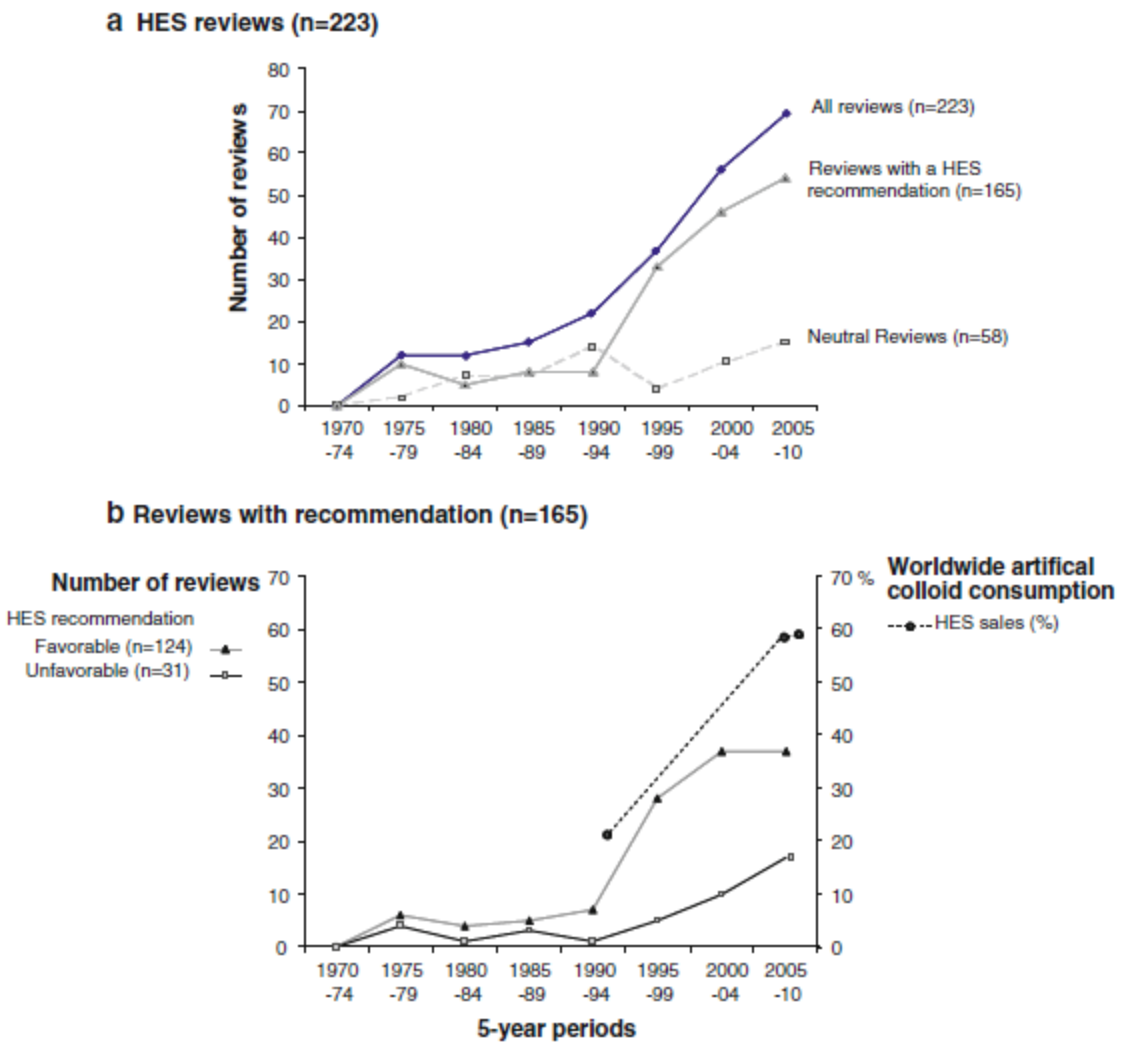


Fig. 4 Hydroxyethyl starch reviews and HES consumption. The number of HES reviews increased after 1990, and most of these contained a recommendation (**a**). Favorable reviews in particular increased dramatically during this period in which the HES market share of worldwide artificial colloid consumption tripled from approx. 20 % [43] to approx. 60 % [44] (**b**)

Table 2 The 14 most prolific authors of 124 favorable HES reviews and their potential conflict of interest with fluid manufacturers

Author	pCOI declared/ HES reviews by this author (*n*)	Years in which HES reviews were published	Years in which a pCOI related to a fluid manufacturer was declared by the author
1	1/21	1998–2009	2009 ("past research activities were funded by…") [19]
2	1/5	2005, 2007–2009	2008 (lead author of a meta-analysis funded by and co-authored by a salaried employee of a fluid manufacturer) [70]; 2010 ("has received honoraria as a speaker and research support from…") [86]
3	0/5	1997–2000	2003 ("unrestricted grant by fluid manufacturer") [87]
4	0/4	1998, 2001, 2003	2006 ("received honoraria from …") [88]
5	1/4	2007–2009	2008 ("recipient of travel grants" and an "unrestricted educational grant") [89]
6	0/4	1993, 2003–2005	2008 ("honoraria and unrestricted grants from… ") [54]
7	0/4	1991, 2000, 2004	2006 ("has received unrestricted grants") [90]; see correction published [Br Med J 2006; 333 doi:10.1136/bmj.39041.739479.68]
8	0/3	1998, 2000, 2002	2002 (recipient of salary from fluid manufacturer) [91]
9	0/3	2008, 2009	2011 (recipient of salary from fluid manufacturer) [92]
10	3/3	2005, 2007–2008	2002–2008 (recipient of salary from fluid manufacturer) [70, 92]
11	0/4	1993, 1998, 2007, 2009	No pCOI identified
12	0/4	1982, 1986, 1996, 2002	No pCOI identified
13	0/3	1986, 1996, 2007	No pCOI identified
14	0/3	2004–2006	No pCOI identified

A potential conflict of interest (pCOI) was declared by four authors in six of these reviews. A pCOI with a fluid manufacturer was declared by additional six authors in other publications at the time or up to 3 years after their last HES review was published. Three authors (9/124 reviews) served as salaried Medical Officers for a fluid manufacturing company at the time of writing or soon thereafter

Fourteen authors wrote 56 % (70/124) of all favorable reviews. The three most prolific authors (authors 1, 2 and 3) wrote 25 % (31/124) of these reviews; the remaining 11 authors wrote 31 % (39/124)

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*

From Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Ca' Granda–Ospedale Maggiore Policlinico, Università degli Studi

ABSTRACT

BACKGROUND

Although previous studies have suggested the potential advantages of albumin administration in patients with severe sepsis, its efficacy has not been fully established.

N Engl J Med 2014;370:1412-21.
DOI: 10.1056/NEJMoa1305727

Table 1. Characteristics of the Patients at Baseline.*

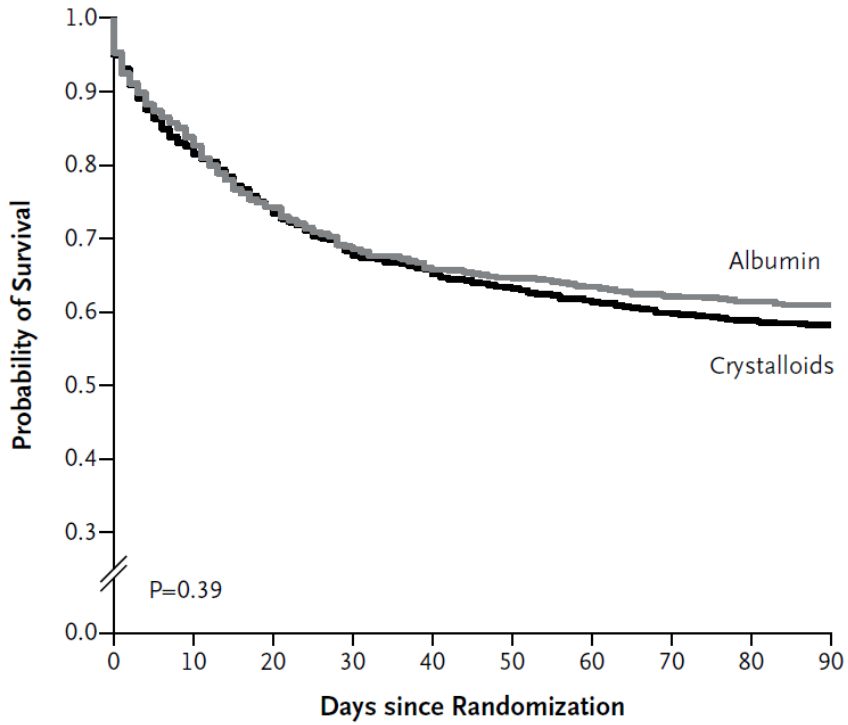
Characteristic	Albumin Group (N = 903)	Crystalloid Group (N = 907)
Age — yr		
Median	70	69
Interquartile range	57–77	59–77
Female sex — no. (%)	360 (39.9)	357 (39.4)
Body-mass index†	27±6	27±6
Reason for ICU admission — no. (%)		
Medical	511 (56.6)	518 (57.1)
Elective surgery	69 (7.6)	58 (6.4)
Emergency surgery	323 (35.8)	331 (36.5)
Preexisting condition — no. (%)‡		
Liver disease	13 (1.4)	14 (1.5)
COPD	113 (12.5)	108 (11.9)
Chronic renal failure	44 (4.9)	32 (3.5)
Immunodeficiency	115 (12.7)	128 (14.1)
Congestive or ischemic heart disease	149 (16.5)	165 (18.2)
SAPS II score§		
Median	48	48
Interquartile range	37–59	37–60

Table 2. Outcomes.

Outcome	Albumin Group	Crystalloid Group	Relative Risk (95% CI)	P Value
Primary outcome: death at 28 days — no./total no. (%)	285/895 (31.8)	288/900 (32.0)	1.00 (0.87–1.14)	0.94
Secondary outcomes				
Death at 90 days — no./total no. (%)	365/888 (41.1)	389/893 (43.6)	0.94 (0.85–1.05)	0.29
New organ failures — no./total no. (%)*				0.99
None	372/836 (44.5)	383/841 (45.5)		
1 organ	283/836 (33.9)	287/841 (34.1)		
2 organs	130/836 (15.6)	123/841 (14.6)		
3 organs	40/836 (4.8)	36/841 (4.3)		
4 organs	10/836 (1.2)	11/841 (1.3)		
5 organs	1/836 (0.1)	1/841 (0.1)		
SOFA score†			—	0.23
Median	6.00	5.62		
Interquartile range	4.00–8.50	3.92–8.28		
SOFA subscore†				
Cardiovascular			—	0.03
Median	1.20	1.42		
Interquartile range	0.46–2.31	0.60–2.50		
Respiratory			—	0.63
Median	2.00	2.00		
Interquartile range	1.56–2.48	1.57–2.50		
Renal			—	0.15
Median	0.83	0.75		
Interquartile range	0.14–2.14	0.07–2.00		
Coagulation			—	0.04
Median	0.64	0.50		
Interquartile range	0.00–1.62	0.00–1.59		
Liver			—	0.02
Median	0.28	0.20		
Interquartile range	0.00–1.00	0.00–0.92		
Length of stay — days				
In ICU			—	0.42
Median	9	9		
Interquartile range	4–18	4–17		
In hospital‡			—	0.65
Median	20	20		
Interquartile range	10–36	9–38		

Table 2. (Continued.)

Outcome	Albumin Group	Crystalloid Group	Relative Risk (95% CI)	P Value
Tertiary outcomes§				
Renal-replacement therapy — no./total no. (%)¶	222/903 (24.6)	194/907 (21.4)		0.11
Acute kidney injury — no./total no. (%)‖	183/834 (21.9)	190/837 (22.7)		0.71
Duration of mechanical ventilation — days**			—	0.50
Median	6	6		
Interquartile range	2–14	2–13		
Time to suspension of vasopressor or inotropic agents — days††			—	0.007
Median	3	4		
Interquartile range	1–6	2–7		



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

Figure 2. Probability of Survival from Randomization through Day 90.

The graph shows the Kaplan–Meier estimates for the probability of survival among patients receiving albumin and crystalloids and among those receiving crystalloids alone. The P value was calculated with the use of the log-rank test.

Conclusions

Les solutions recommandées sont:

- Cristalloïdes
- Gélatines (à éviter en cas de risque ou présence d'insuffisance rénale)

Les amidons ne doivent plus être utilisés.

Les catécholamines

TABLEAU 5

Principales catécholamines adrénergiques actuellement utilisées au cours du choc

Récepteur adrénergique	Site anatomique principal	Effet physiologique de la stimulation	Effets cliniques favorables (bénéfices)	Effets cliniques péjoratifs (risques)	Catécholamine agoniste
Alpha	▮ Vaisseaux	▮ Vasoconstriction	▮ ↗ RVS et PA	▮ Ischémie viscérale ou périphérique	▮ Noradrénaline ▮ Adrénaline
Bêta	▮ Cœur	▮ Inotrope (contractilité) ▮ Chronotrope (fréquence) ▮ Dromotrope (conduction) ▮ Bathmotrope (excitabilité) ▮ Lusitrope (relaxation)	▮ ↗ DC ± PA	▮ Ischémie myocardique	▮ Dobutamine ▮ Adrénaline

RVS : résistances vasculaires systémiques ; PA : pression artérielle ; DC : débit cardiaque.

Les agents sympathomimétiques

récepteur	***α***	***β1***	***β2***	***δ***
effet	vasoconstricteur	inotrope	vasodilatateur	splanchnique
dopamine ***µg/kg/min***	++ (>15)	+++ (2,5 à 10)	++ (id)	+++ (< 5)
dobutamine ***µg/kg/min***	+/-	+++ (5 à 10)	+	-
adrénaline ***µg/min***	++ (>20)	++ (1-4)	++ (id)	
noradrénaline ***µg/kg/min***	+++ (0,02 à 0,1)	+		

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Comparison of Dopamine and Norepinephrine in the Treatment of Shock

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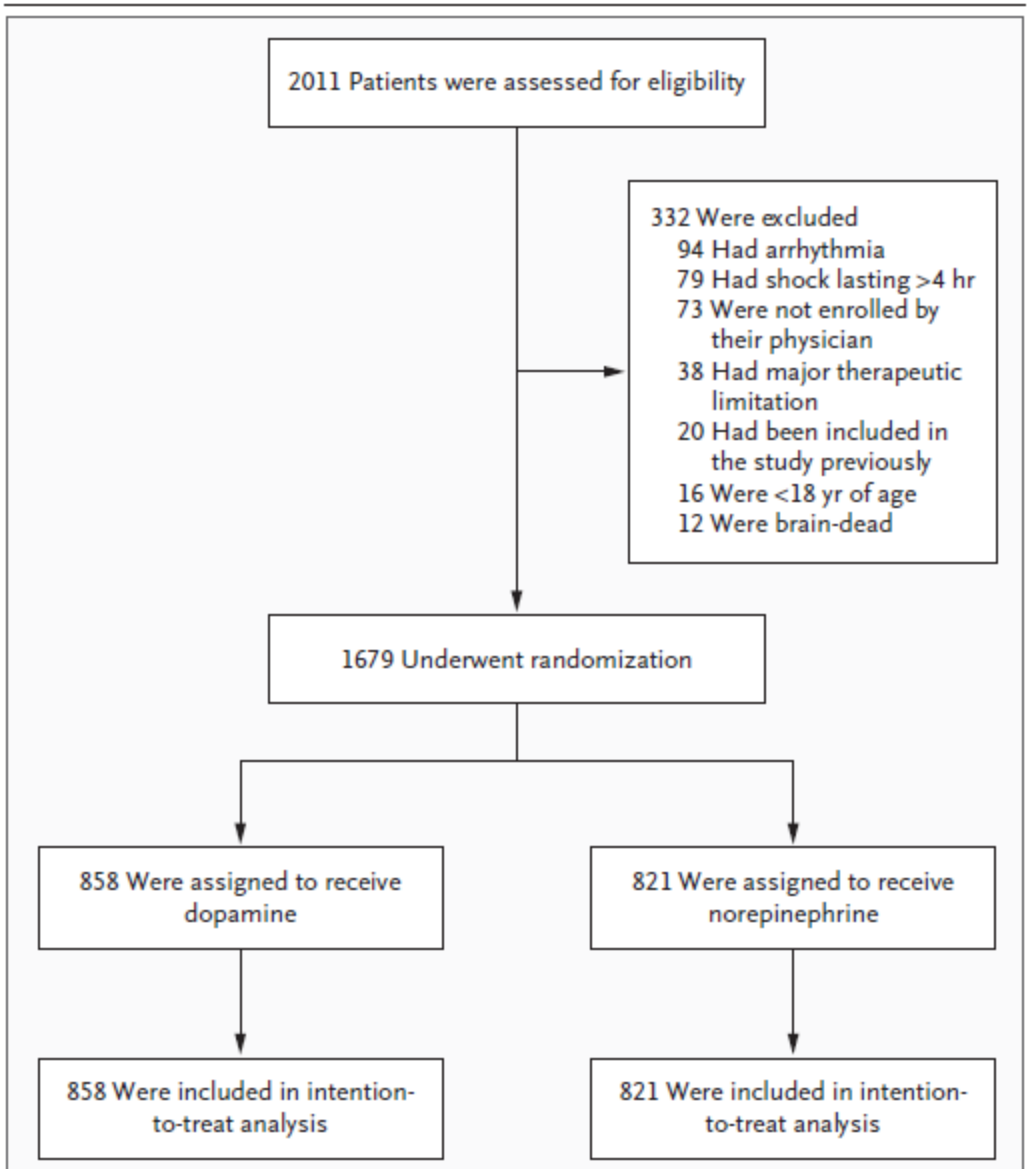
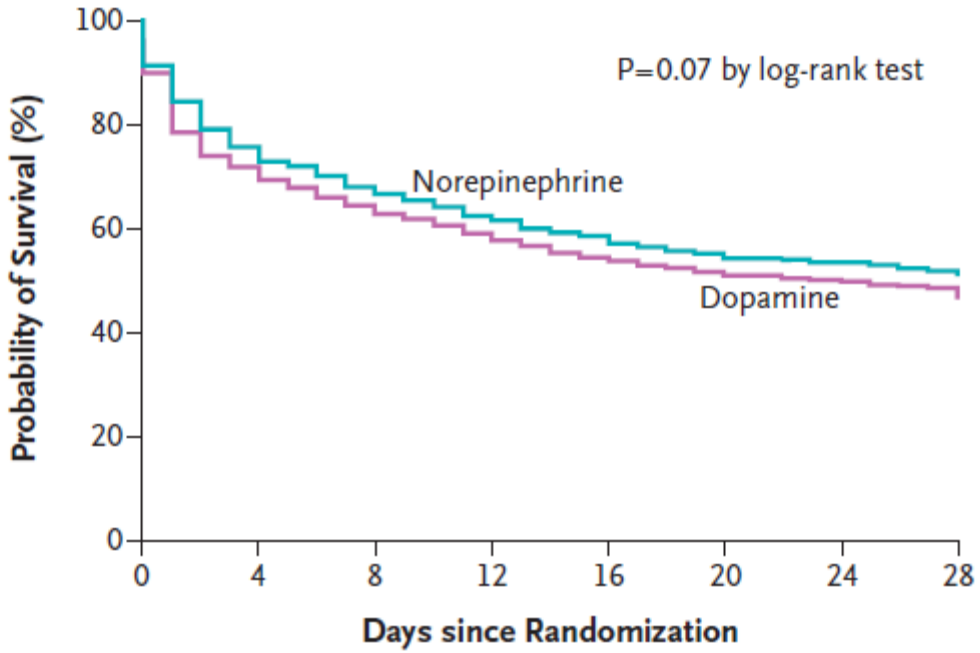


Figure 1. Screening and Enrollment.

Table 2. Mortality Rates.*

Time Period	Dopamine	Norepinephrine	Odds Ratio (95% CI)†	P Value
	percent mortality			
During stay in intensive care unit	50.2	45.9	1.19 (0.98–1.44)	0.07
During hospital stay	59.4	56.6	1.12 (0.92–1.37)	0.24
At 28 days	52.5	48.5	1.17 (0.97–1.42)	0.10
At 6 mo	63.8	62.9	1.06 (0.86–1.31)	0.71
At 12 mo	65.9	63.0	1.15 (0.91–1.46)	0.34

* Data were available for 1656 patients in the intensive care unit, in the hospital, and at 28 days; for 1443 patients at 6 months; and for 1036 patients at 12 months.
† Odds ratios for death are for the comparison of the dopamine group with the norepinephrine group.



No. at Risk								
Norepinephrine	821	617	553	504	467	432	412	394
Dopamine	858	611	546	494	452	426	407	386

Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

Table 1. Baseline Characteristics of the Patients and Major Therapeutic Interventions at Baseline.*

Variable	Dopamine (N = 858)	Norepinephrine (N = 821)
Age — yr		
Median	68	67
Interquartile range	55–76	56–76
Male sex — no. (%)	507 (59.1)	449 (54.7)
APACHE II score†		
Median	20	20
Interquartile range	15–28	14–27
SOFA score‡		
Median	9	9
Interquartile range	7–12	6–12
Reason for admission — no. (%)		
Medical	565 (65.9)	532 (64.8)
Scheduled surgery	168 (19.6)	161 (19.6)
Emergency surgery	125 (14.6)	128 (15.6)
Cause of shock — no. (%)		
Sepsis	542 (63.2)	502 (61.1)
Lungs	278 (32.4)	246 (30.0)
Abdomen	138 (16.1)	135 (16.4)
Urine	51 (5.9)	42 (5.1)
Catheter	14 (1.6)	10 (1.2)
Endocardium	9 (1.0)	11 (1.3)
Mediastinum	10 (1.2)	15 (1.8)
Soft tissues	11 (1.3)	13 (1.6)
Other	15 (1.7)	20 (2.4)
Cardiogenic source	135 (15.7)	145 (17.6)
Myocardial infarction	75 (8.7)	86 (10.5)
Dilated cardiomyopathy	25 (2.9)	19 (2.3)
Tamponade	2 (0.2)	7 (0.9)
Pulmonary embolism	10 (1.2)	8 (1.0)
Valvular disease	4 (0.5)	5 (0.6)
After cardiopulmonary bypass	19 (2.2)	20 (2.4)
Other		
Hypovolemia	138 (16.1)	125 (15.2)
Hemorrhage	130 (15.2)	116 (14.1)
Trauma	17 (2.0)	23 (2.8)
Gastrointestinal bleeding	31 (3.6)	22 (2.7)
Bleeding at surgical site	64 (7.5)	57 (6.9)
Other	18 (2.1)	14 (1.7)
Dehydration	8 (0.9)	9 (1.1)
Other	48 (5.9)	44 (5.0)
Spinal	6 (0.7)	8 (1.0)
Peridural§	13 (1.5)	4 (0.5)
Intoxication-related¶	7 (0.8)	4 (0.5)
Anaphylactic	3 (0.3)	4 (0.5)
Miscellaneous	13 (1.5)	29 (3.5)
Hemodynamic, respiratory, and biologic variables		

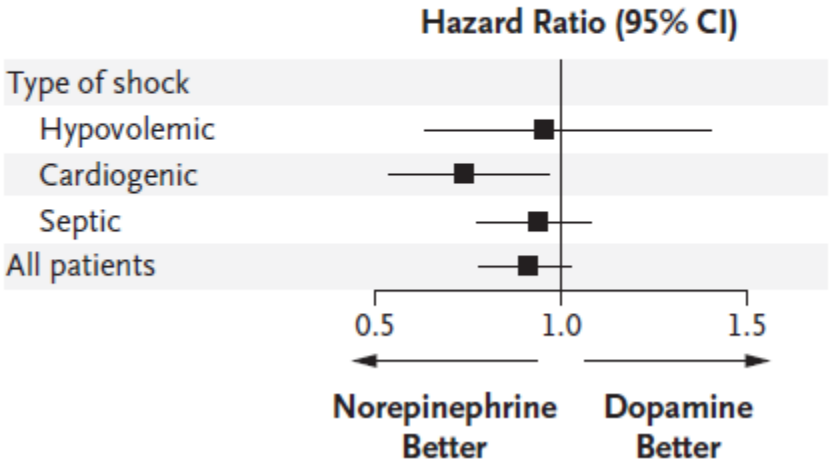


Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.

Dopamine versus norepinephrine in the treatment of septic shock: A meta-analysis*

Daniel De Backer, MD, PhD; Cesar Aldecoa, MD; Hassane Njimi, MSc, PhD; Jean-Louis Vincent, MD, PhD, FCCM

Objectives: There has long-been controversy about the possible superiority of norepinephrine compared to dopamine in the treatment of shock. The objective was to evaluate the effects of norepinephrine and dopamine on outcome and adverse events in patients with septic shock.

Data Sources: A systematic search of the MEDLINE, Embase, Scopus, and CENTRAL databases, and of Google Scholar, up to June 30, 2011.

Study Selection and Data Extraction: All studies providing information on the outcome of patients with septic shock treated with dopamine compared to norepinephrine were included. Observational and randomized trials were analyzed separately. Because time of outcome assessment varied among trials, we evaluated 28-day mortality or closest estimate. Heterogeneity among trials was assessed using the Cochrane Q homogeneity test. A Forest plot was constructed and the aggregate relative risk of death was computed. Potential publication bias was evaluated using funnel plots.

Methods and Main Results: We retrieved five observational (1,360 patients) and six randomized (1,408 patients) trials, totaling 2,768 patients (1,474 who received norepinephrine and 1,294 who received dopamine). In observational studies, among which there was significant heterogeneity ($p < .001$), there was no difference in mortality (relative risk, 1.09; confidence interval, 0.84–1.41; $p = .72$). A sensitivity analysis identified one trial as being responsible for the heterogeneity; after exclusion of that trial, no heterogeneity was observed and dopamine administration was associated with an increased risk of death (relative risk, 1.23; confidence interval, 1.05–1.43; $p < .01$). In randomized trials, for which no heterogeneity or publication bias was detected ($p = .77$), dopamine was associated with an increased risk of death (relative risk, 1.12; confidence interval, 1.01–1.20; $p = .035$). In the two trials that reported arrhythmias, these were more frequent with dopamine than with norepinephrine (relative risk, 2.34; confidence interval, 1.46–3.77; $p = .001$).

Conclusions: In patients with septic shock, dopamine administration is associated with greater mortality and a higher incidence of arrhythmic events compared to norepinephrine administration. (Crit Care Med 2012; 40:725–730)

KEY WORDS: adrenergic agents; adverse effects; mortality; outcome; vasopressor

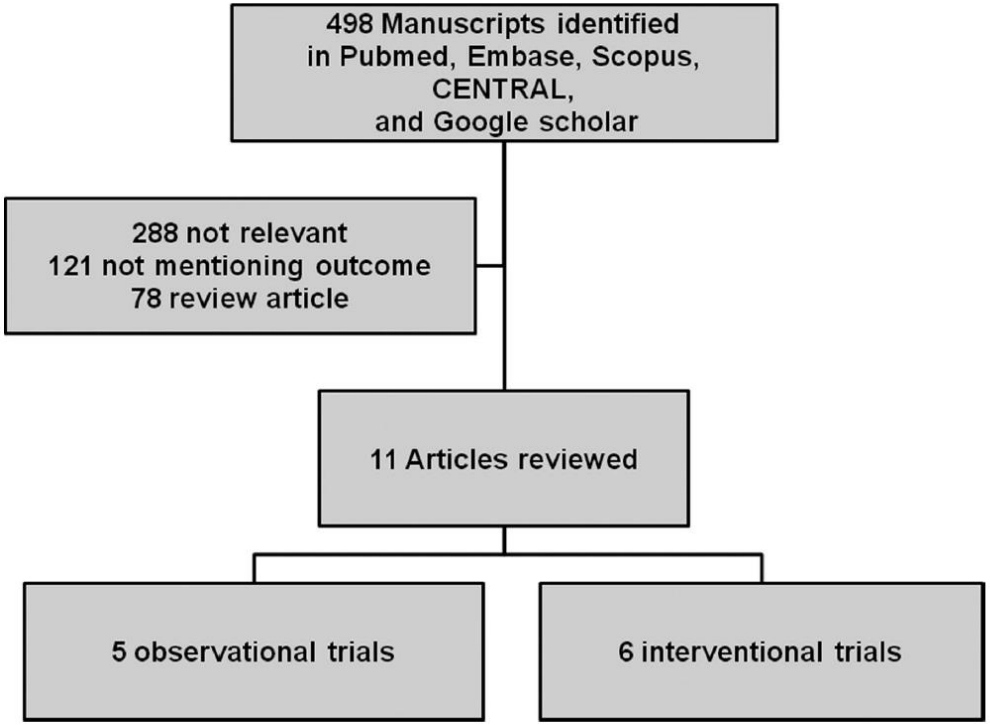


Figure 1. Flow chart of systematic search.

Table 2. Characteristics of interventional studies

	Martin (1993) (27)	Marik (1994) (30)	Ruokonen (2003) (29)	Mathur (2007) (25)	De Backer (2010) (15)	Patel (2010) (16)
Dopamine, n	16	10	5	25	542	134
Norepinephrine, n	16	10	5	25	502	118
Exposure time	Weaning or dead	3 hrs	3 hrs	6 hrs	Maximum 28 days	Maximum 28 days
Type of patients	Sepsis	Sepsis	Sepsis	Sepsis	Sepsis[a]	Sepsis
Mortality rate	Hospital	Not defined	Not defined	Not defined	28 day[b]	28 day
Cochrane risk of bias in included studies						
Concealment on allocation	No	Yes	No	No	Yes	Yes (odd or even)
Inclusion/exclusion	Yes	Yes	Yes	Yes	Yes	Yes
Patient description	No	No	No	No	Yes	Yes
Similar care	Yes	Yes	No	Yes	Yes	Yes
Blinding of caregivers	No	No	No	No	Yes	No
Blinding of assessors	No	No	No	No	Yes	No
Intention to treat	Yes	Yes	Yes	Yes	Yes	Yes
Free from selective reporting	Yes				Yes	Yes
Risk of bias for secondary outcomes assessment in included studies						
Adverse events						
Defined	No	No	No	No	No	Yes
Assessed	No	No	No	No	No	Yes
Time of assessment	No	No	No	No	No	Yes
Organ function						
Defined	No	No	No	No	Yes	Yes
Assessed	No	No	No	No	Yes	Yes
Time of assessment	No	No	No	No	Yes	Yes

[a]In this trial, patients with other sources of shock were also included. The intention-to-treat analysis covers the whole population of 1679 patients included in the trial. The authors extracted data of patients with sepsis only for this analysis. Other trials only included patients with sepsis; [b]in this trial, 28-day mortality was the primary outcome, intensive care unit, hospital, and 6-month and 12-month mortality were also provided.

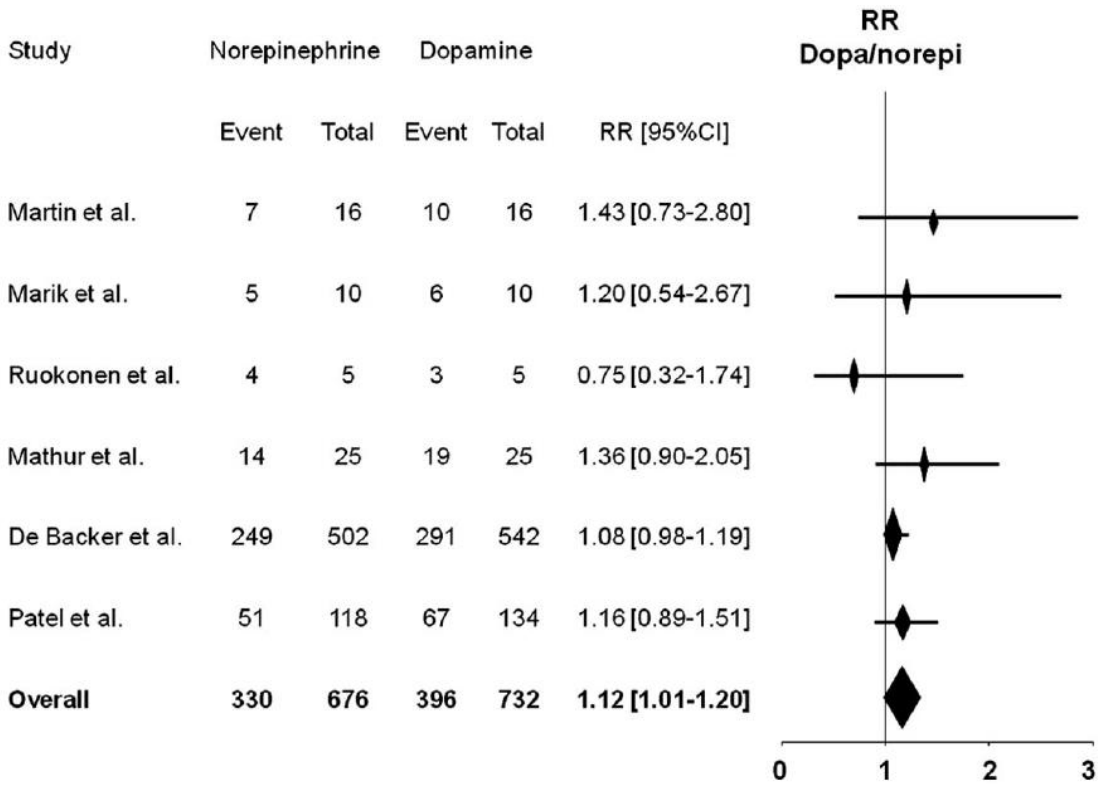


Figure 3. Forest plot of risk ratio (*RR*) of death (28 days or nearest estimate) in interventional trials. The *p* value for aggregate RR of dopamine (*dopa*) compared to norepinephrine (*norepi*) in interventional studies was .035. Relative weights of the different trials in the analysis: Martin et al (27) 2%; Marik et al (30) 1%; Ruokonen et al (29) 1%; Mathur et al (25) 4%; De Backer et al (15) 81%; and Patel et al (16) 10%. No heterogeneity was observed ($p = .77$; $I^2 = 0$; confidence interval, 0%–25%).

Diminuer la demande en oxygène

A. Ventilation artificielle (travail respiratoire)

B. Sédatifs et narcotiques

C. Réduire les stimulations adrénergiques

Combattre l'anurie

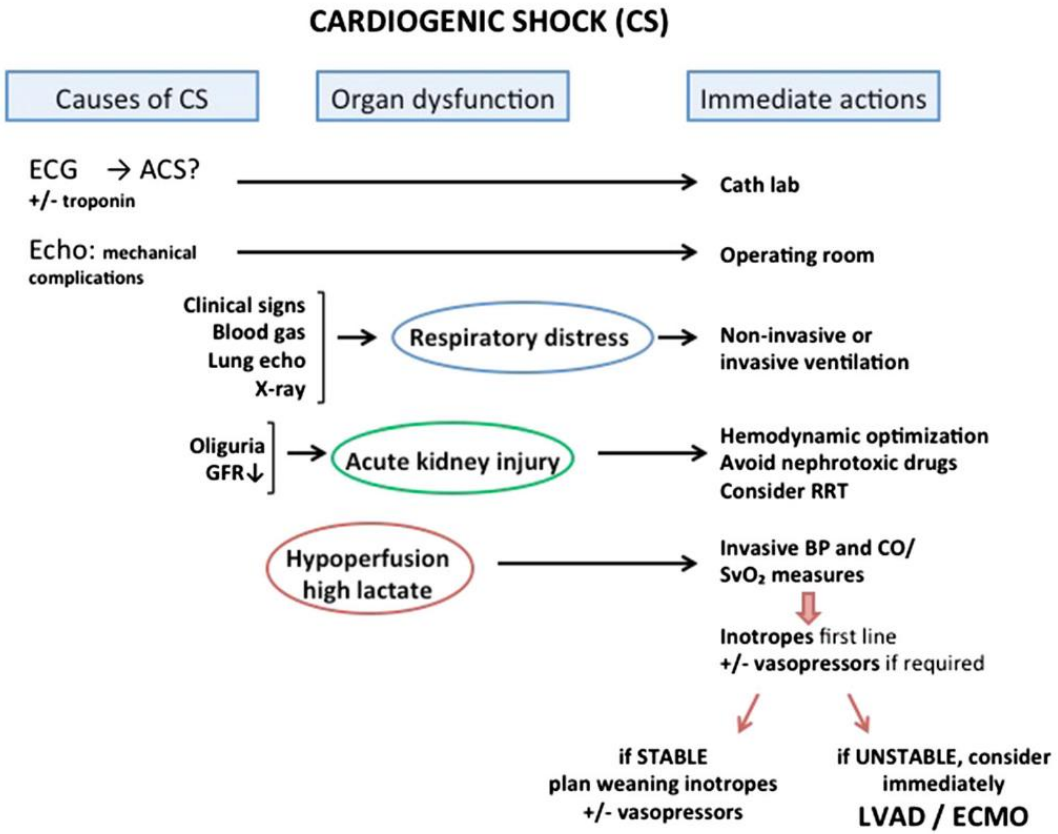
- remplissage vasculaire : en évitant l'Elohes^{R} (Lancet 2001)
- dopamine à dose rénale: abandonné (Lancet 2000)
- furosémide pour relancer diurèse : à éviter (JAMA 2002)

Traitement étiologique: exemples

- Choc septique : antibiothérapie empirique
- Tamponnade péricardique
- Choc hémorragique
  - Corriger troubles de coagulation
- Choc anaphylactique
- Choc cardiogénique
  - Reperfusion coronaire
- Tachyarythmies

Choc cardiogénique

Fig. 2 Treatment schema for patients with cardiogenic shock. *ECG* electrocardiogram, *echo* echocardiography, *ACS* acute coronary syndrome, *cath lab* cardiac catheterization laboratory, *BP* blood pressure, *CO* cardiac output, SvO_2 mixed venous oxygen saturation, *LVAD* left ventricular assist device, *ECMO* extracorporeal membrane oxygenation



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