Apports Liquidiens en Période Postopératoire

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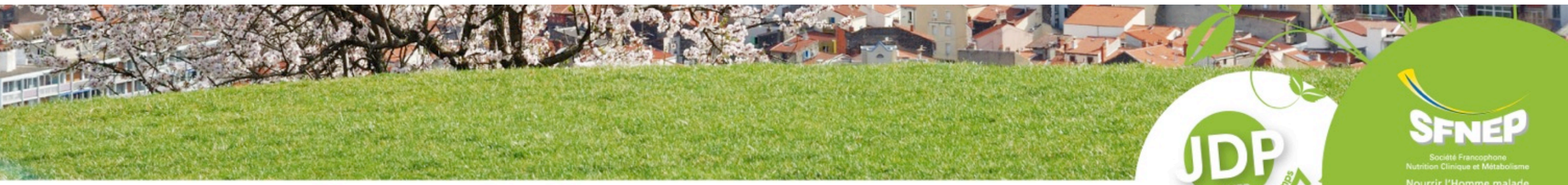


Information / <u>Conflits d'intérêts</u>

Je déclare ne pas avoir de lien d'intérêts (autres que scientifiques) en relation avec le contenu de cette présentation

THERE'S ONLY ONE RULE,

NO FOOD, NO DRINK, JUST FLUIDS !

Mais ça c’était avant …

ERAS

Early Rehabilitation After Surgery

Avoid opiates

Patient Education

Carbo hydrate loading

No MBP

No Premed

2-4 hours fasting

Active Warming

Short-acting drugs

Epidural

Minimal invasive incision

No routine NGT

Active rewarming

No routine Abdominal drainage

Routine PONV

No routine Abdominal drainage

Early oral fluids

Early oral Mobilization

Early oral diet

Early oral Mobilization

Fearon KCH et al. Clin Nutr 2005
Kehlet H et al. lancet 2005

Early oral diet

ERAS

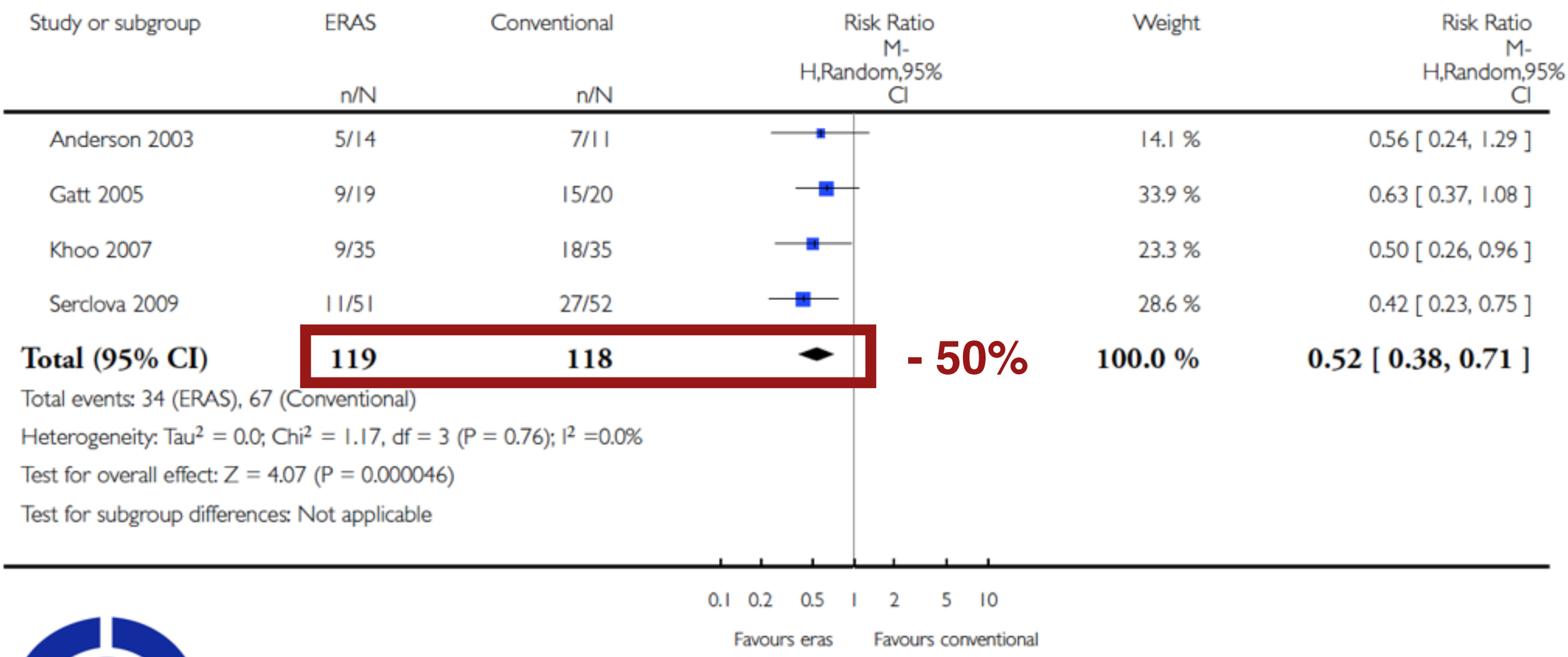
Early Rehabilitation After Surgery

Early oral fluids

Fearon KCH et al. Clin Nutr 2005
Kehlet H et al. lancet 2005

Réhabilitation Améliorée Après Chirurgie

Analysis 1.2. **ERAS versus conventional**, **Outcome: All Complications**



THE COCHRANE COLLABORATION®

Spanjersberg WR et al. **Cochrane Database Syst Rev**. 2011

Réhabilitation Améliorée Après Chirurgie

Analysis 1.7. **ERAS versus conventional, Outcome: Hospital Stay**

Study or subgroup	ERAS N	Mean(SD)[days]	Conventional N	Mean(SD)[days]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Anderson 2003	14	4 (1.8)	11	7 (2.1)		23.4 %	-3.00 [-4.56, -1.44]
Gatt 2005	19	6.6 (4.4)	20	9 (4.6)		7.1 %	-2.40 [-5.22, 0.42]
Khoo 2007	35	5 (8.5)	35	7 (14.75)		1.8 %	-2.00 [-7.64, 3.64]
Serclova 2009	51	7.4 (1.3)	52	10.4 (3.1)		67.8 %	-3.00 [-3.92, -2.08]
Total (95% CI)	**119**		**118**			**100.0 %**	**-2.94 [-3.69, -2.19]**

Heterogeneity: $Chi^2 = 0.27$, $df = 3$ ($P = 0.97$); $I^2 = 0.0\%$

Test for overall effect: $Z = 7.65$ ($P < 0.00001$)

Test for subgroup differences: Not applicable

- 2 jours

-4 -2 0 2 4

ERAS Conventional

THE COCHRANE COLLABORATION®

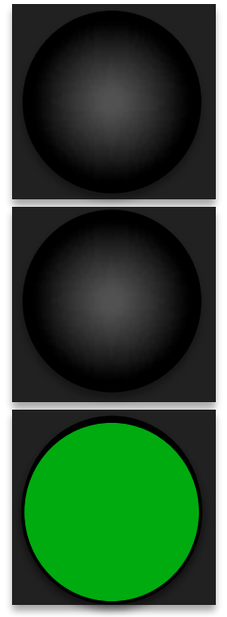
Spanjersberg WR et al. **Cochrane Database Syst Rev**. 2011

TAKE HOME MESSAGE

Réhabilitation Améliorée Après Chirurgie

ERAS

Early Rehabilitation After Surgery



Ça marche !

Laparoscopy in Combination with Fast Track Multimodal Management is the Best Perioperative Strategy in Patients Undergoing Colonic Surgery

LAFA trial

N=427

The essence of the fast track care program

DAY OF SURGERY Early post-operative management	- First oral drinks at 2 h post-surgery, supplemented with CHL liquids - First semi-solid food intake in the evening
DAY 1 AFTER SURGERY Postoperative Management	- Oral intake > 2 l (including 4 units CHL liquids) - Normal diet - Stop IV fluid administration (leave canulla)
DAY 2 AFTER SURGERY Postoperative Management	- Remove IV cannula - Normal diet
DAY 3 AFTER SURGERY	Continue as on day 2 untill discharge criteria are fulfilled

Malaika S. Vlug et al. on behalf of the collaborative LAFA study group Ann Surg 2011;254:868–875

Laparoscopy in Combination with Fast Track Multimodal Management is the Best Perioperative Strategy in Patients Undergoing Colonic Surgery

LAFA trial

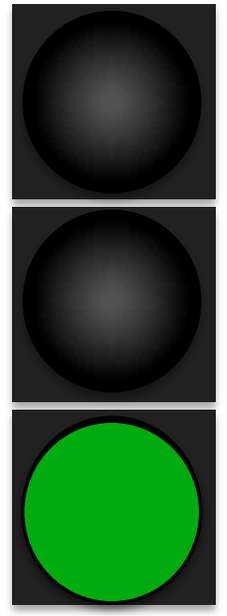
N=427

Protocol Compliance

	Laparoscopy and Fast Track (n = 100)	Open and Fast Track (n = 93)
DAY OF SURGERY		
Early post-operative management		
Total oral intake – after surgery, median (IQR), liter	0.5 (0.1–0.8)	0.3 (0–0.8)
Intake of CHL, median (IQR, L)		
POD 1	0.2 (0–0.4)	0.2 (0–0.4)
POD 2	0.2 (0–0.4)	0.2 (0–0.4)
POD 3	0.2 (0–0.4)	0.0 (0–0.4)
Total oral intake, median (IQR, L)		
POD 1	1.5 (0.9–1.9)	1.1 (0.7–1.6)
POD 2	1.1 (0.7–1.6)	1.4 (0.8–2.0)
POD 3	1.8 (1.2–2.0)	1.8 (1.0–2.0)

TAKE HOME MESSAGE

Ré-alimenter Précocement Après Chirurgie



Ç’est possible !

Early Enteral Nutrition Within 24 h of Intestinal Surgery Versus Later Commencement of Feeding

A Systematic Review and Metaanalysis

Study	Treatment n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
Anastomotic dehiscence					
Sagar 1979	0/15	1/15		1.61	0.33 [0.01, 7.58]
Reissman 1995	0/80	1/81		1.60	0.34 [0.01, 8.16]
Beier-Holgersen 1996	2/30	4/30		4.30	0.50 [0.10, 2.53]
Ortiz 1996	2/95	4/95		4.30	0.50 [0.09, 2.67]
Hartsell 1997	0/29	1/29		1.61	0.33 [0.01, 7.86]
Heslin 1997	3/97	4/98		4.28	0.76 [0.17, 3.30]
Watters 1997	1/13	4/15		4.00	0.29 [0.04, 2.27]
Stewart 1998	1/40	0/40		0.54	3.00 [0.13, 71.51]
Mulrooney 2004	3/36	0/37		0.53	7.19 [0.38, 134.42]
Subtotal (95% CI)	435	440		22.79	0.69 [0.36, 1.32]
Total events: 12 (Treatment), 19 (Control)					
Test for heterogeneity: Chi² = 4.89, df = 8 (P = 0.77), I² = 0%, p=0.769					
Test for overall effect: Z = 1.11 (P = 0.27)					
Pneumonia					
Schroeder 1991	1/16	0/16		0.54	3.00 [0.13, 68.57]
Reissman 1995	0/80	1/81		1.60	0.34 [0.01, 8.16]
Beier-Holgersen 1996	1/30	2/30		2.15	0.50 [0.05, 5.22]
Ortiz 1996	2/95	2/95		2.15	1.00 [0.14, 6.95]
Hartsell 1997	0/29	1/29		1.61	0.33 [0.01, 7.86]
Heslin 1997	3/97	7/98		7.49	0.43 [0.12, 1.63]
Stewart 1998	1/40	1/40		1.08	1.00 [0.06, 15.44]
Mulrooney 2004	2/36	0/37		0.53	5.14 [0.26, 103.39]
Subtotal (95% CI)	423	426		17.16	0.76 [0.36, 1.58]
Total events: 10 (Treatment), 14 (Control)					
Test for heterogeneity: Chi² = 3.73, df = 7 (P = 0.81), I² = 0%, p=0.810					
Test for overall effect: Z = 0.75 (P = 0.46)					
Mortality					
Beier-Holgersen 1996	2/30	4/30		4.30	0.50 [0.10, 2.53]
Carr 1996	0/14	1/14		1.61	0.33 [0.01, 7.55]
Hartsell 1997	0/29	1/29		1.61	0.33 [0.01, 7.86]
Heslin 1997	2/97	3/98		3.21	0.67 [0.12, 3.94]
Stewart 1998	0/40	1/40		1.61	0.33 [0.01, 7.95]
Mulrooney 2004	2/36	7/37		7.43	0.29 [0.07, 1.32]
Subtotal (95% CI)	246	248		19.79	0.41 [0.18, 0.93]
Total events: 6 (Treatment), 17 (Control)					
Test for heterogeneity: Chi² = 0.60, df = 5 (P = 0.99), I² = 0%, p=0.988					

Lewis SJ. J Gastrointest Surg (2009) 13:569–575

Early enteral nutrition versus later commencement after gastrointestinal surgery

Andersen HK, Lewis SJ, Thomas S

Outcome: 4 **mortality**

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI	**Route of feeding**
Beier-Holgersen 1996	2/30	4/30		0.50 [0.10, 2.53]	Nasoduodenal
Carr 1996	0/14	1/14		0.33 [0.01, 7.55]	Nasojejunal
Hartsell 1997	0/29	1/29		0.33 [0.01, 7.86]	Oral
Heslin 1997	2/97	3/98		0.67 [0.12, 3.94]	Jejunostomy
Mulrooney 2004	2/36	7/37		0.29 [0.07, 1.32]	NR
Ortiz 1996	0/95	0/95		0.0 [0.0, 0.0]	Oral
Reissman 1995	0/80	0/81		0.0 [0.0, 0.0]	Oral
Sagar 1979	0/15	0/15		0.0 [0.0, 0.0]	Nasojejunal
Schroeder 1991	0/16	0/16		0.0 [0.0, 0.0]	Nasojejunal
Stewart 1998	0/40	1/40		0.33 [0.01, 7.95]	Oral
Total (95% CI)	**452**	**455**		**0.41 [0.18, 0.93]**	

Total events: 6 (Treatment), 17 (Control)

Heterogeneity: $Chi^2 = 0.60$, df = 5 (P = 0.99); $I^2 = 0.0\%$

Test for overall effect: Z = 2.13 (P = 0.033)

0.1 0.2 0.5 1 2 5 10

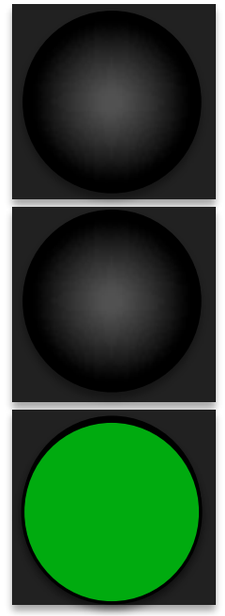
Favours treatment Favours control

THE COCHRANE COLLABORATION®

Cochrane Database Syst Rev 2006, Issue 4. Art. No.: CD004080

TAKE HOME MESSAGE

Ré-alimenter Précocement Après Chirurgie



Safe !

SFAR
Société Française d'Anesthésie et de Réanimation

2010

SFNEP
Société Francophone
Nutrition Clinique et Métabolisme

Recommandations de bonnes pratiques cliniques sur la nutrition périopératoire

3. Nutrition dans la période postopératoire (dont urgence)

R27 : Il **est recommandé** de reprendre le plus rapidement possible, au cours des 24 premières heures postopératoires, une alimentation orale, selon la tolérance du patient, sauf contre indication chirurgicale.

3.1. Patients non dénutris (GN1 et GN 2)

R28 : Chez les patients non dénutris (GN1 et 2), la durée d'une assistance nutritionnelle postopératoire, quand elle est requise, **ne doit pas** être inférieure à 7 jours.

3.2. Patients dénutris (GN 3 et GN 4)

R31 : Il **faut** instaurer, dès les 24 premières heures postopératoires, un support nutritionnel chez les patients dénutris (GN 3 et 4) qu'ils aient reçu ou non un support nutritionnel préopératoire.

3.3. Patients admis en urgence

R32 : La prise en charge nutritionnelle postopératoire d'un patient opéré en urgence n'est pas différente de celle recommandée pour la chirurgie programmée.

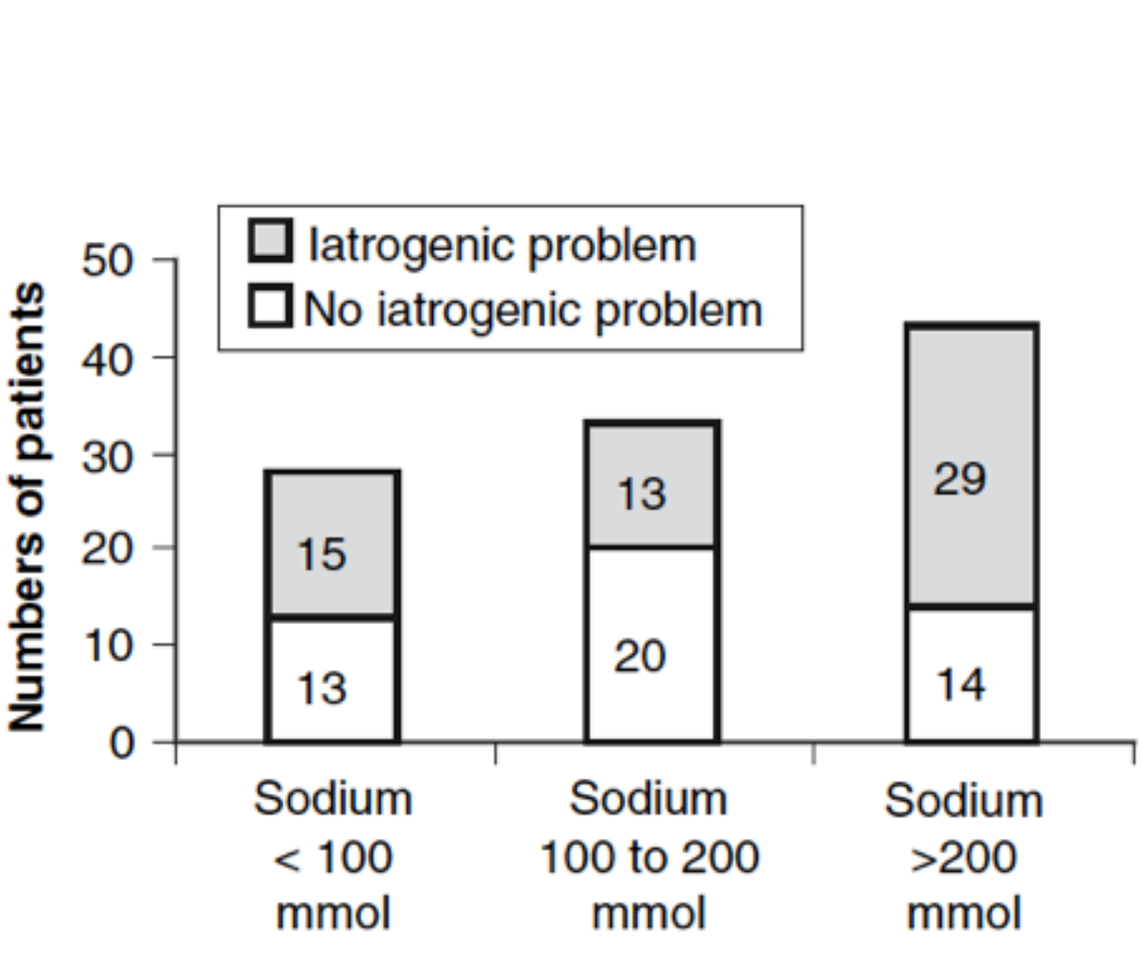

What is the sense
of using iv fluids ?

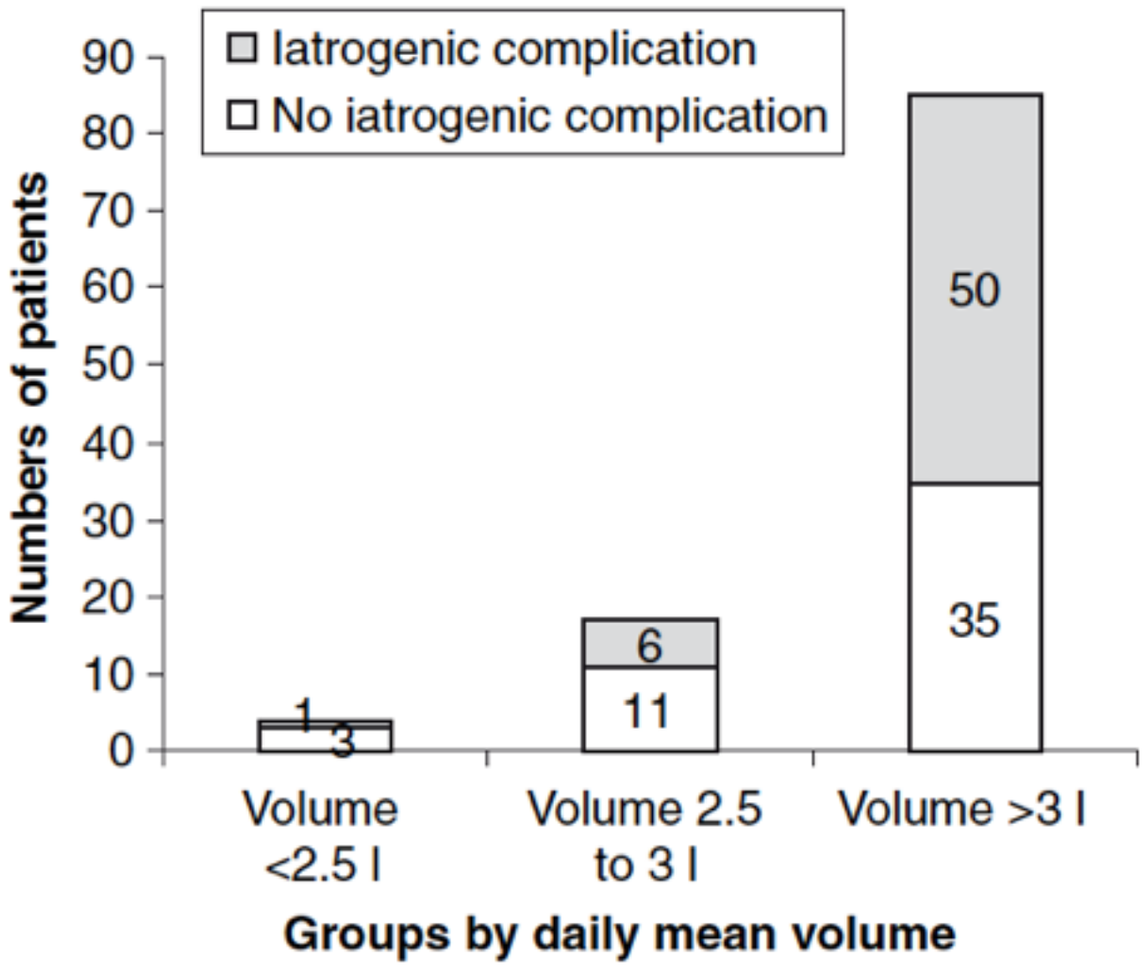
AUDIT

Perioperative fluid management: prospective audit

S. R. Walsh,[1,2] E. J. Cook,[1] R. Bentley,[1] N. Farooq,[1] J. Gardner-Thorpe,[1] T. Tang,[2] M. E. Gaunt,[2] E. C. Coveney[1]

- A prospective audit (6-month period) in a UK district general hospital to assess current fluid management practice in patients following laparotomy and to determine the incidence of iatrogenic fluid-related complications
- 574 patient-days of intravenous hydration were available for analysis

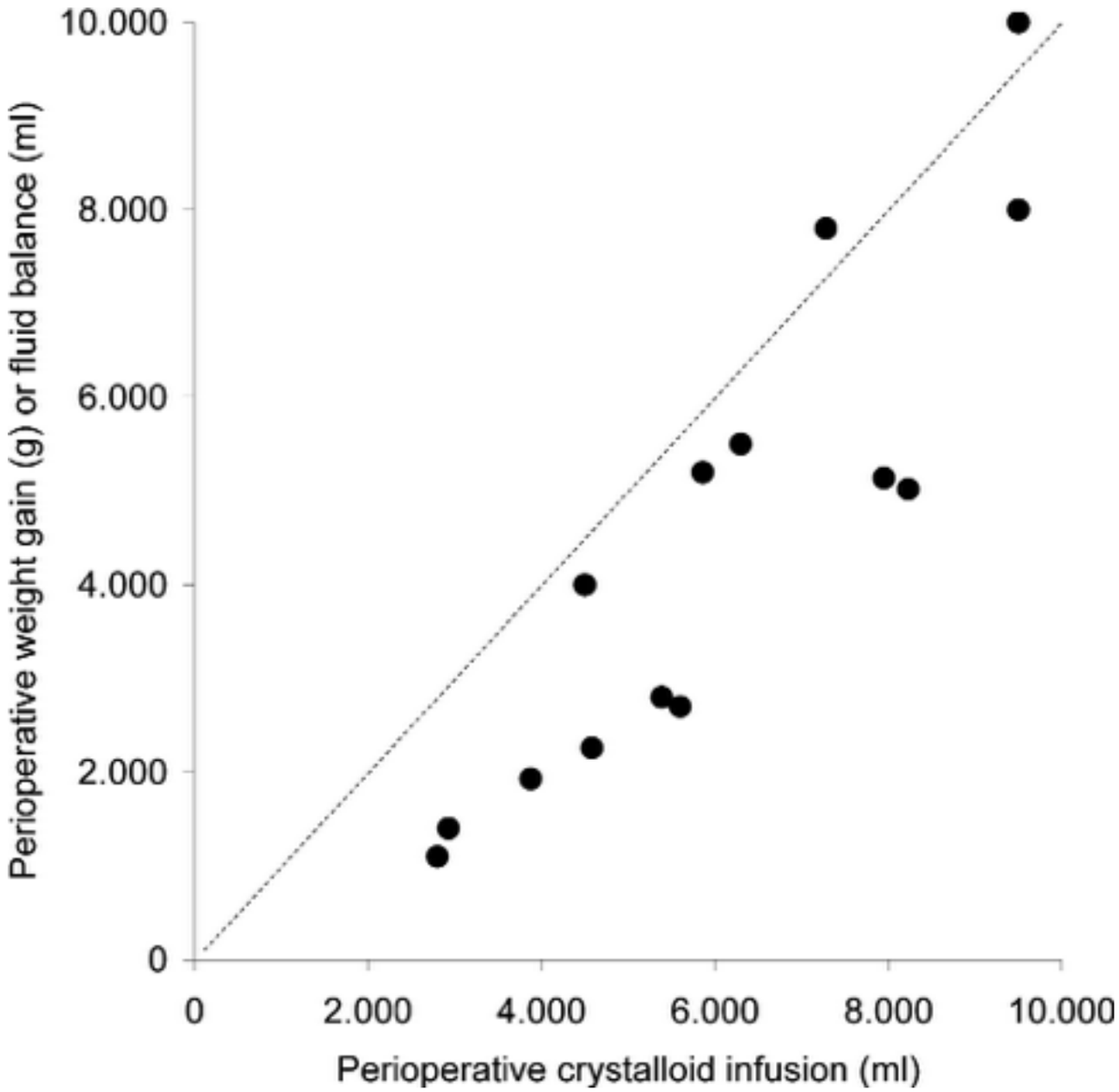


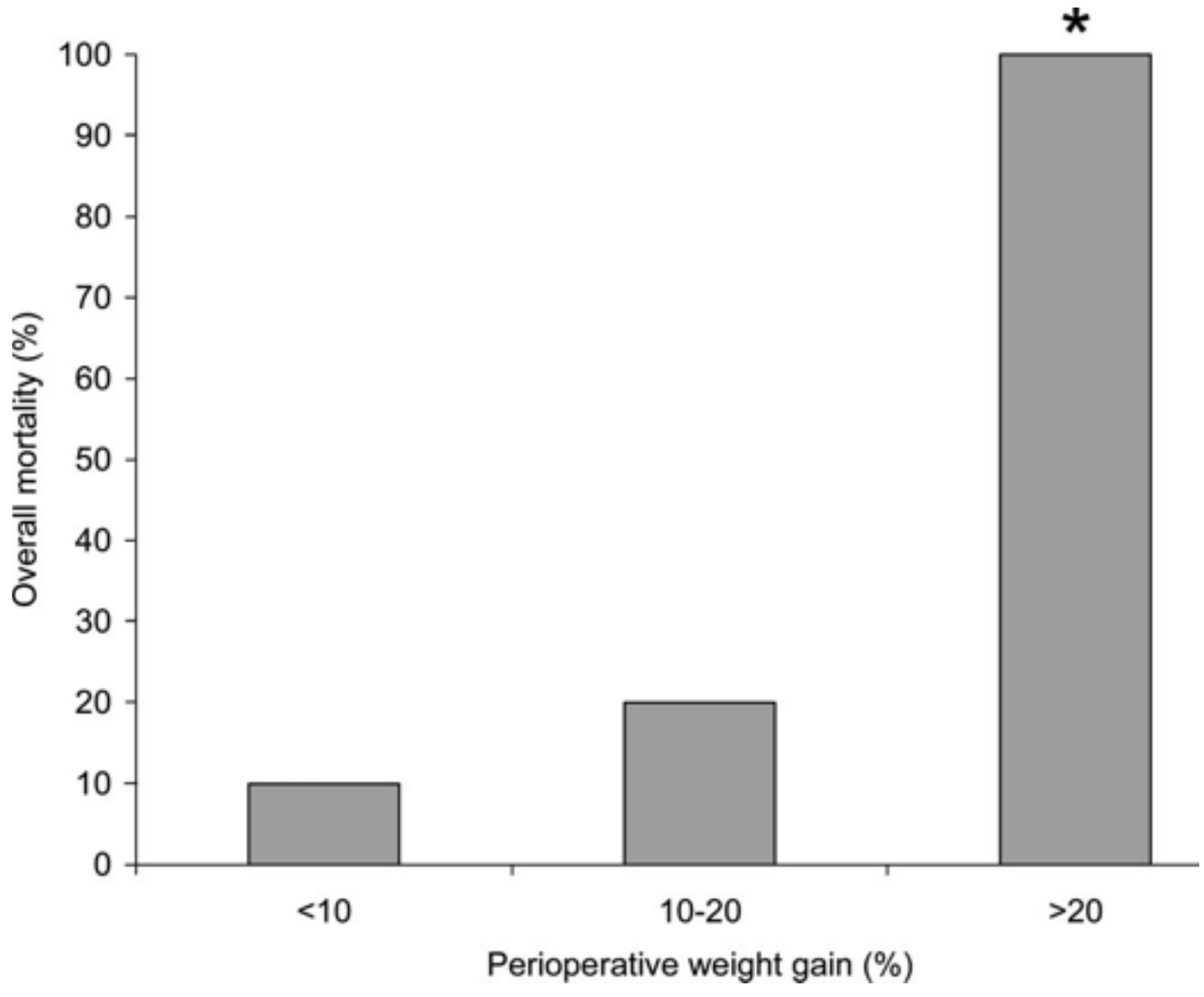


Int J Clin Pract 2008; 62: 498–9

A Rational Approach to Perioperative Fluid Management

Daniel Chappell, M.D.,* Matthias Jacob, M.D.,* Klaus Hofmann-Kiefer, M.D.,* Peter Conzen, M.D.,† Markus Rehm, M.D.‡



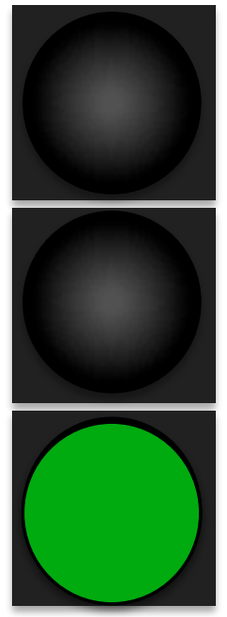


Anesthesiology 2008; 109:723–40

THERE'S ONLY ONE RULE,

There is NO FIXED RULE!

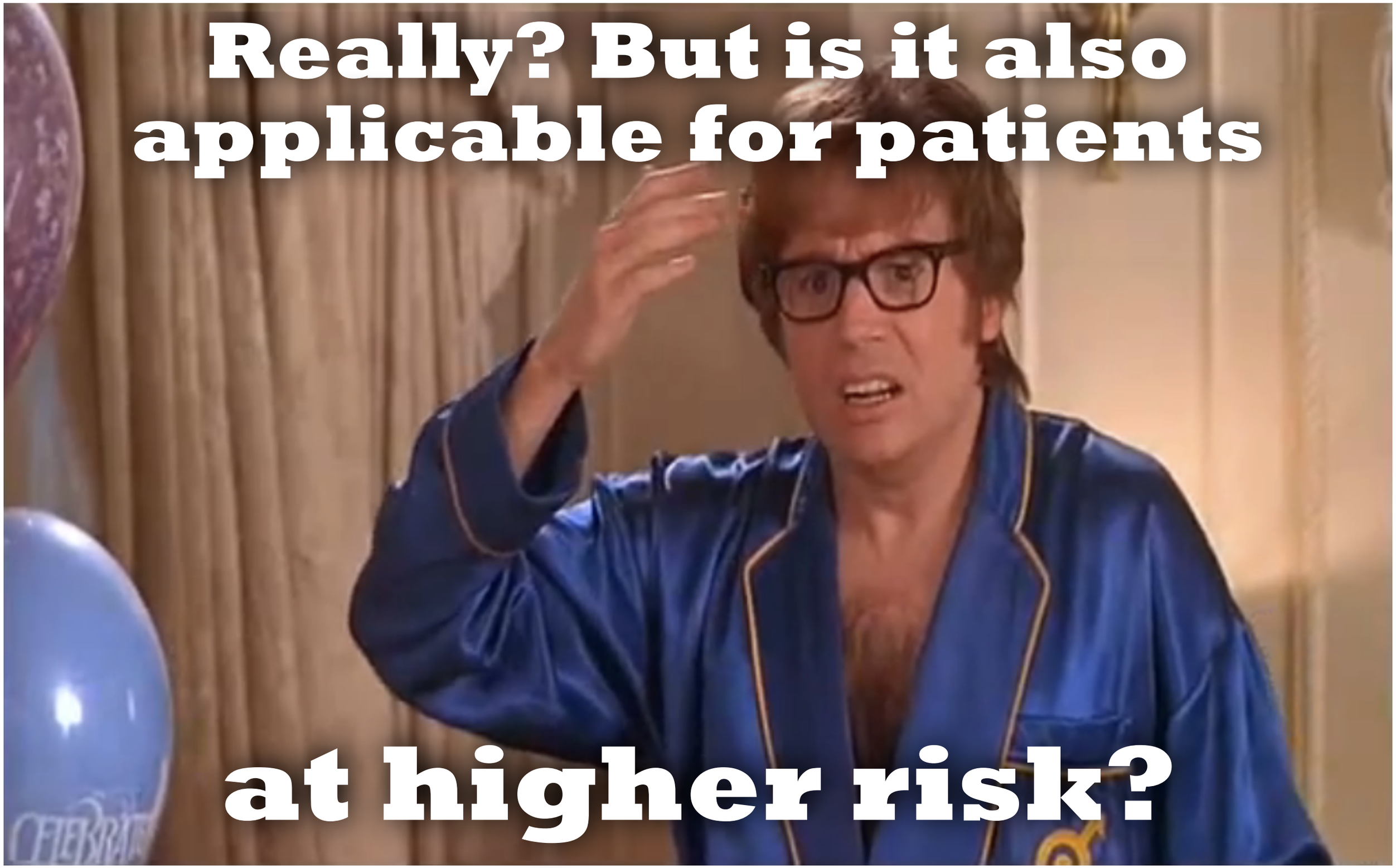
TAKE HOME MESSAGE



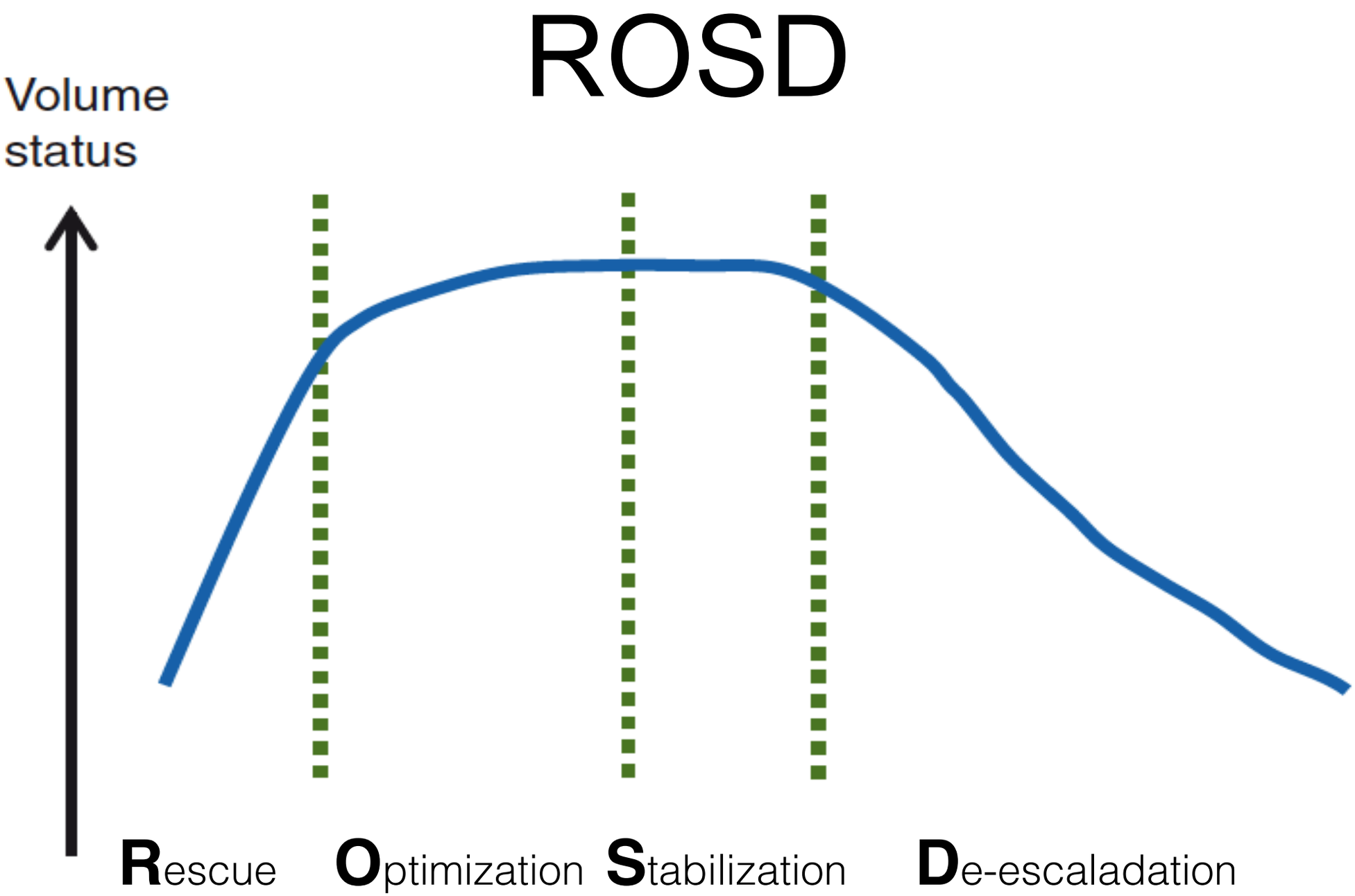
Pour l’essentiel des patients,

aucun apport de liquide intraveineux n’est nécessaire en postopératoire !

Pour les patients normovolémique et hémodynamiquement stable, une reprise des apports oraux doit être envisagée précocement


Really? But is it also applicable for patients
at higher risk?

Four phases of intravenous fluid therapy



Fluid Maintenance ≠ Fluid optimization

Br J Anaesth 2014,113 (5): 740–7

Silva et al. *Critical Care* 2013, 17:R288
http://ccforum.com/content/17/6/R288

The effect of excess fluid balance on the mortality rate of surgical patients: a multicenter prospective study

João M Silva Jr[1,2,4*], Amanda Maria Ribas Rosa de Oliveira[2,3], Fernando Augusto Mendes Nogueira[1], Pedro Monferrari Monteiro Vianna[1], Marcos Cruz Pereira Filho[1], Leandro Ferreira Dias[1], Vivian Paz Leão Maia[1], Cesar de Souza Neucamp[1], Cristina Prata Amendola[3], Maria José Carvalho Carmona[2] and Luiz M Sá Malbouisson[2]

N=479 patients aged ≥18 years that have undergone surgery that required postoperative ICU

Variables	Fluid balance NOT excessive	Fluid balance excessive	P Value
Postoperative organ dysfunction (%)	57.1	77.4	<0.001
Respiratory (%)	11.6	34.3	<0.001
Cardiovascular (%)	39.6	63.2	<0.001
Renal (%)	19.9	20.0	0.99
Infection (%)	25.9	41.6	0.001
ICU stay (days)	3.0 (2.0-6.0)	4.0 (3.0-8.0)	<0.001

CRITICAL CARE

The effect of excess fluid balance on the mortality rate of surgical patients: a multicenter prospective study

João M Silva Jr[1,2,4*], Amanda Maria Ribas Rosa de Oliveira[2,3], Fernando Augusto Mendes Nogueira[1], Pedro Monferrari Monteiro Vianna[1], Marcos Cruz Pereira Filho[1], Leandro Ferreira Dias[1], Vivian Paz Leão Maia[1], Cesar de Souza Neucamp[1], Cristina Prata Amendola[3], Maria José Carvalho Carmona[2] and Luiz M Sá Malbouisson[2]

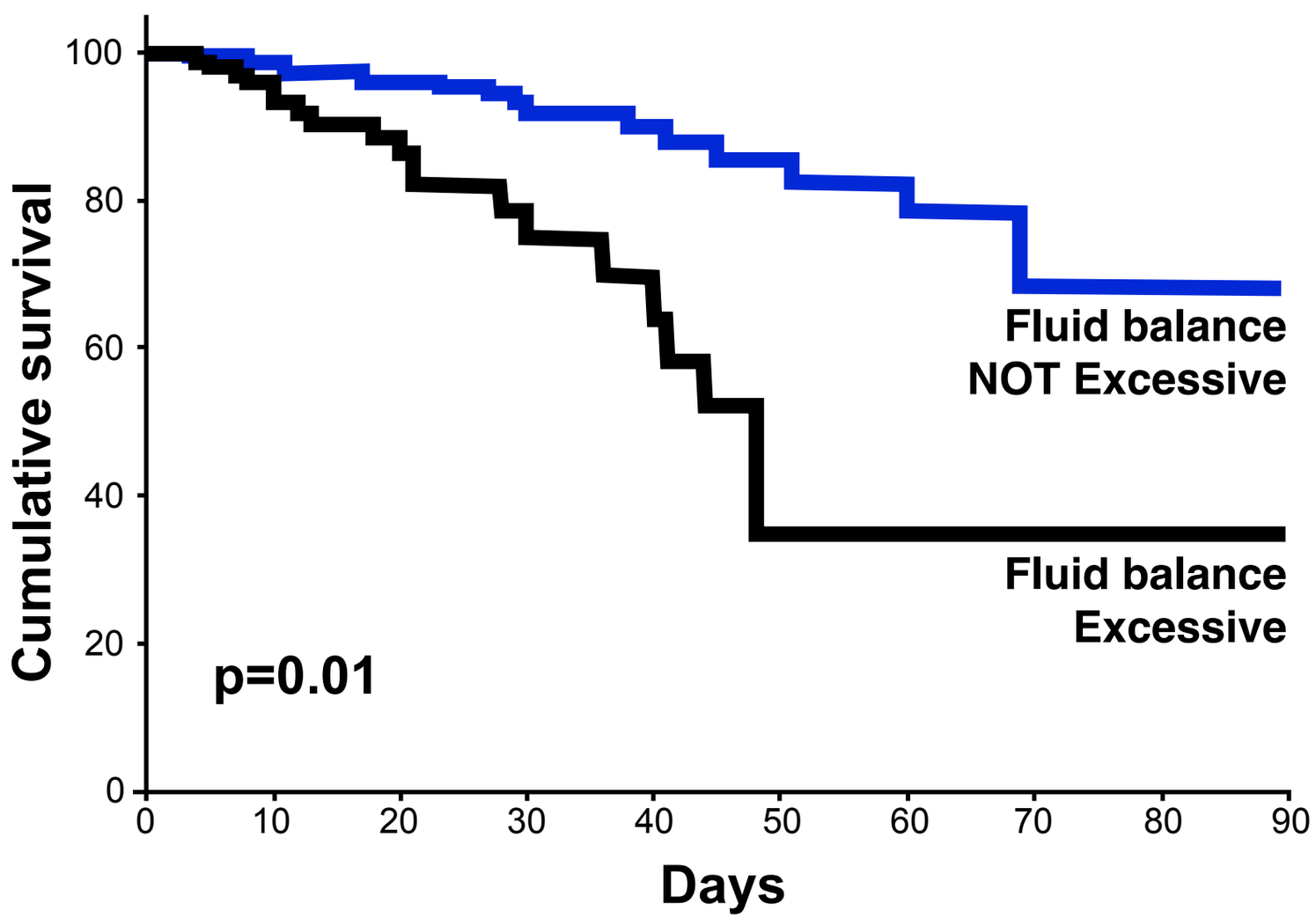


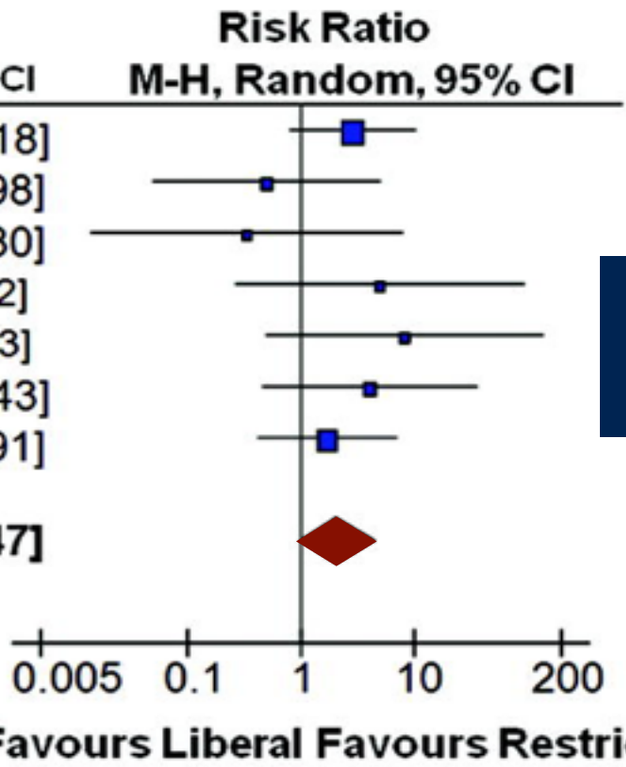
Figure 2 Kaplan-Meier curve among patients with or without excessive fluid balance up to 90 days.

Restrictive *versus* Liberal

Study	Liberal Events	Liberal Total	Restrictive Events	Restrictive Total	Weight	Risk Ratio M-H, Random, 95% CI
Brandstrup [7]	9	72	3	69	33.2%	2.88 [0.81, 10.18]
Holte [53]	1	16	2	16	10.0%	0.50 [0.05, 4.98]
Holte [54]	0	24	1	24	5.3%	0.33 [0.01, 7.80]
Lobo [56]	2	10	0	10	6.2%	5.00 [0.27, 92.62]
McArdle [58]	4	11	0	10	6.7%	8.25 [0.50, 136.33]
Muller [59]	4	75	1	76	11.3%	4.05 [0.46, 35.43]
Nisanevich [60]	5	75	3	77	27.2%	1.71 [0.42, 6.91]
Total (95% CI)		**283**		**282**	**100.0%**	**2.16 [1.04, 4.47]**
Total events	25		10			

Heterogeneity: Tau² = 0.00; Chi² = 4.75, df = 6 (P = 0.58); I² = 0%

Test for overall effect: Z = 2.07 (P = 0.04)

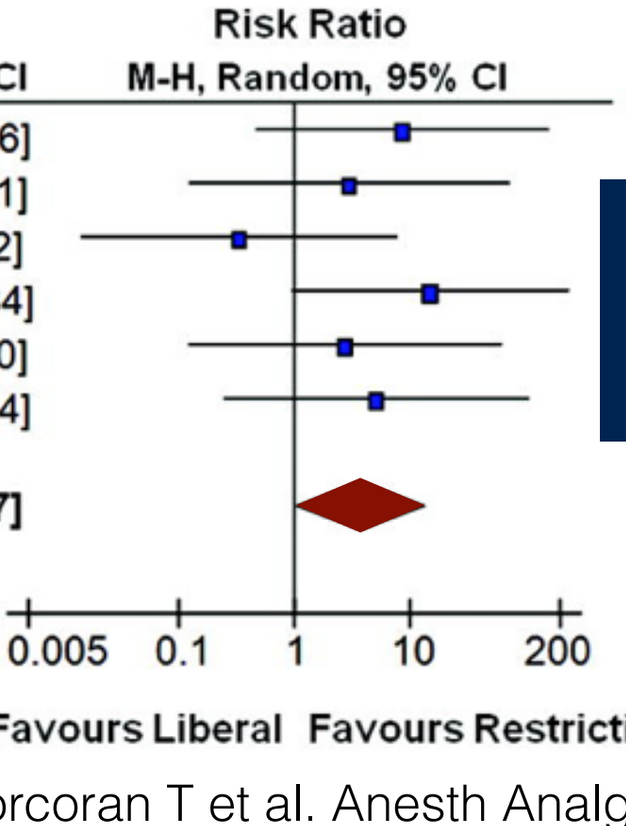


Risk of pneumonia

Study	Liberal Events	Liberal Total	Restrictive Events	Restrictive Total	Weight	Risk Ratio M-H, Random, 95% CI
Brandstrup [7]	4	72	0	69	17.8%	8.63 [0.47, 157.36]
Gonzalez-Fajardo [52]	1	40	0	40	14.9%	3.00 [0.13, 71.51]
Holte [53]	0	16	1	16	15.3%	0.33 [0.01, 7.62]
Lobo [56]	7	10	0	10	20.0%	15.00 [0.97, 231.84]
McArdle [58]	1	11	0	10	15.6%	2.75 [0.12, 60.70]
Nisanevich 60	2	75	0	77	16.4%	5.13 [0.25, 105.14]
Total (95% CI)		**224**		**222**	**100.0%**	**3.84 [1.13, 13.07]**
Total events	15		1			

Heterogeneity: Tau² = 0.00; Chi² = 3.75, df = 5 (P = 0.59); I² = 0%

Test for overall effect: Z = 2.16 (P = 0.03)



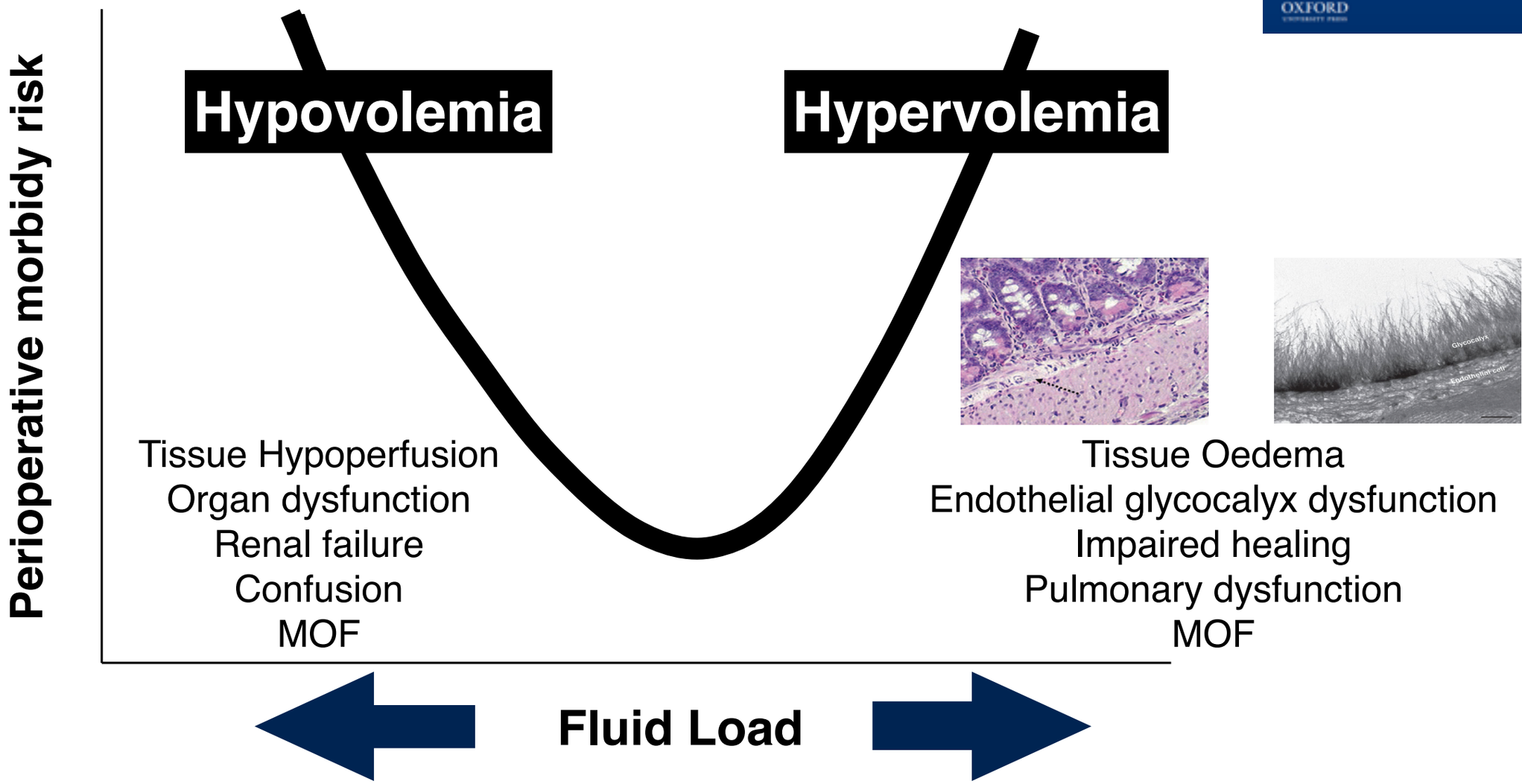
Risk of pulmonary edema

D

Corcoran T et al. Anesth Analg 2012;114(3):640-51

Intraoperative fluids: how much is too MUCH?

M. Doherty[1*] and D.J. Buggy[1,2]



Doherty M et al. Br J Anaesth 2012; 109(1):69-79

A Systematic Review and Meta-Analysis on the Use of Preemptive Hemodynamic Intervention to Improve Postoperative Outcomes in Moderate and High-Risk Surgical Patients

Mark A. Hamilton, MRCP, FRCA, Maurizio Cecconi, MD, and Andrew Rhodes, FRCP, FRCA

N= 29 RCTs
(4805 patients)

Study or Subgroup	Protocol Events	Protocol Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Bender 1997 (32)	1	51	1	53	1.7%	1.04 [0.06, 17.08]
Berlauk 1991 (31)	1	68	2	21	2.1%	0.14 [0.01, 1.65]
Bishop 1995 (30)	9	50	24	65	8.5%	0.38 [0.16, 0.90]
Bonazzi 2002 (29)	0	50	0	50		Not estimable
Boyd 1993 (28)	3	53	12	54	5.4%	0.21 [0.06, 0.79]
Buettner 2008 (27)	0	40	1	40	1.3%	0.33 [0.01, 8.22]
Chytra 2007 (26)	13	80	18	82	9.3%	0.69 [0.31, 1.52]
Conway 2002 (25)	0	29	1	28	1.3%	0.31 [0.01, 7.95]
Donati 2007 (24)	2	68	2	67	3.0%	0.98 [0.13, 7.20]
Gan 2002 (23)	0	50	0	50		Not estimable
Kapoor 2008 (19)	0	15	0	15		Not estimable
Lobo 2000 (22)	3	19	9	18	4.4%	0.19 [0.04, 0.88]
Lobo 2006 (21)	2	25	7	25	3.9%	0.22 [0.04, 1.21]
Lopes 2007 (20)	2	17	5	16	3.5%	0.29 [0.05, 1.80]
Mckendry 2004 (18)	4	89	2	90	3.7%	2.07 [0.37, 11.60]
Mythen 1995 (17)	0	30	1	30	1.3%	0.32 [0.01, 8.24]
Noblett 2006 (16)	0	51	1	52	1.3%	0.33 [0.01, 8.37]
Pearse 2005 (15)	7	62	9	60	7.1%	0.72 [0.25, 2.08]
Polonen 2000 (14)	2	196	6	197	4.1%	0.33 [0.07, 1.65]
Sandham 2003 (13)	78	997	77	997	13.9%	1.01 [0.73, 1.41]
Schultz 1985 (12)	1	35	10	35	2.7%	0.07 [0.01, 0.61]
Shoemaker 1988 (11)	1	28	18	60	2.8%	0.09 [0.01, 0.69]
Sinclair 1997 (10)	1	20	2	20	2.1%	0.47 [0.04, 5.69]
Ueno 1998 (9)	0	16	2	18	1.4%	0.20 [0.01, 4.49]
Valentine 1998 (8)	3	60	1	60	2.4%	3.11 [0.31, 30.73]
Venn 2002 (7)	3	30	2	29	3.3%	1.50 [0.23, 9.70]
Wakeling 2005 (6)	0	67	1	67	1.3%	0.33 [0.01, 8.21]
Wilson 1999 (5)	3	92	8	46	5.1%	0.16 [0.04, 0.64]
Ziegler 1997 (4)	3	32	2	40	3.3%	1.97 [0.31, 12.54]
Total (95% CI)		**2420**		**2385**	**100.0%**	**0.48 [0.33, 0.70]**
Total events	142		224			

Heterogeneity: $Tau^2 = 0.25$; $Chi^2 = 37.72$, df = 25 (P = 0.05); $I^2 = 34\%$
Test for overall effect: Z = 3.77 (P = 0.0002)

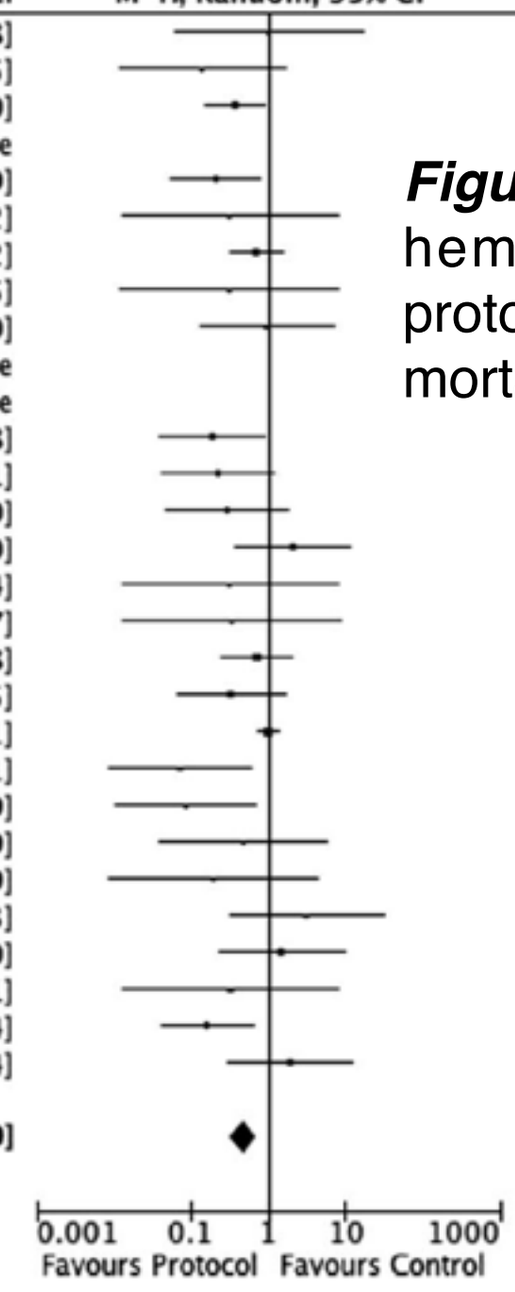
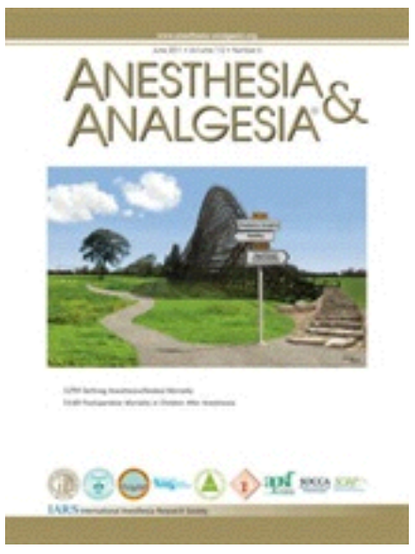


Figure 2. Effects of preemptive hemodynamic intervention in protocol group versus control on mortality rate.



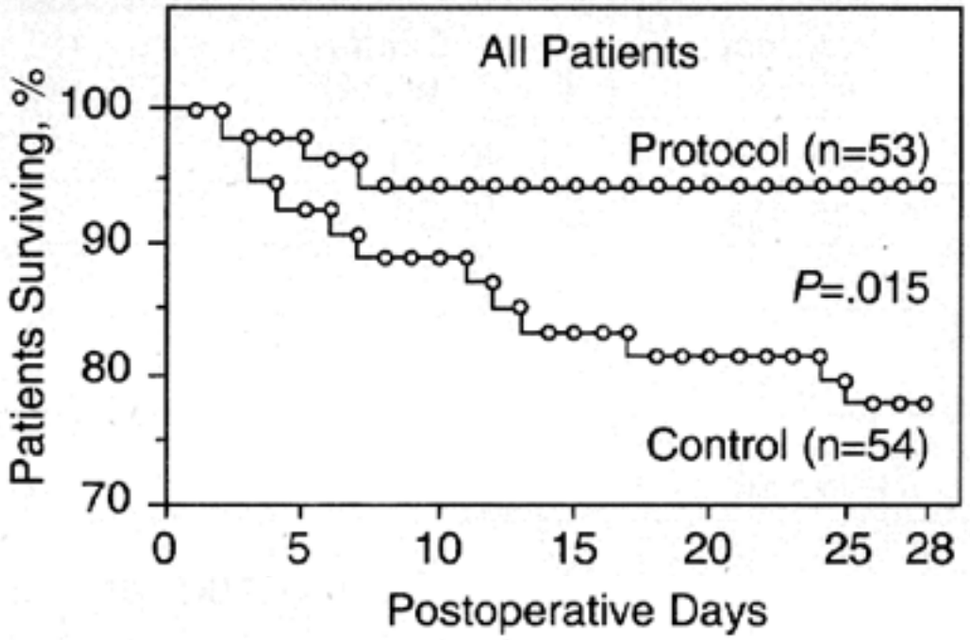
Anesth Analg. 2011;112:1392-402

Intensive Care Med
DOI 10.1007/s00134-010-1869-6

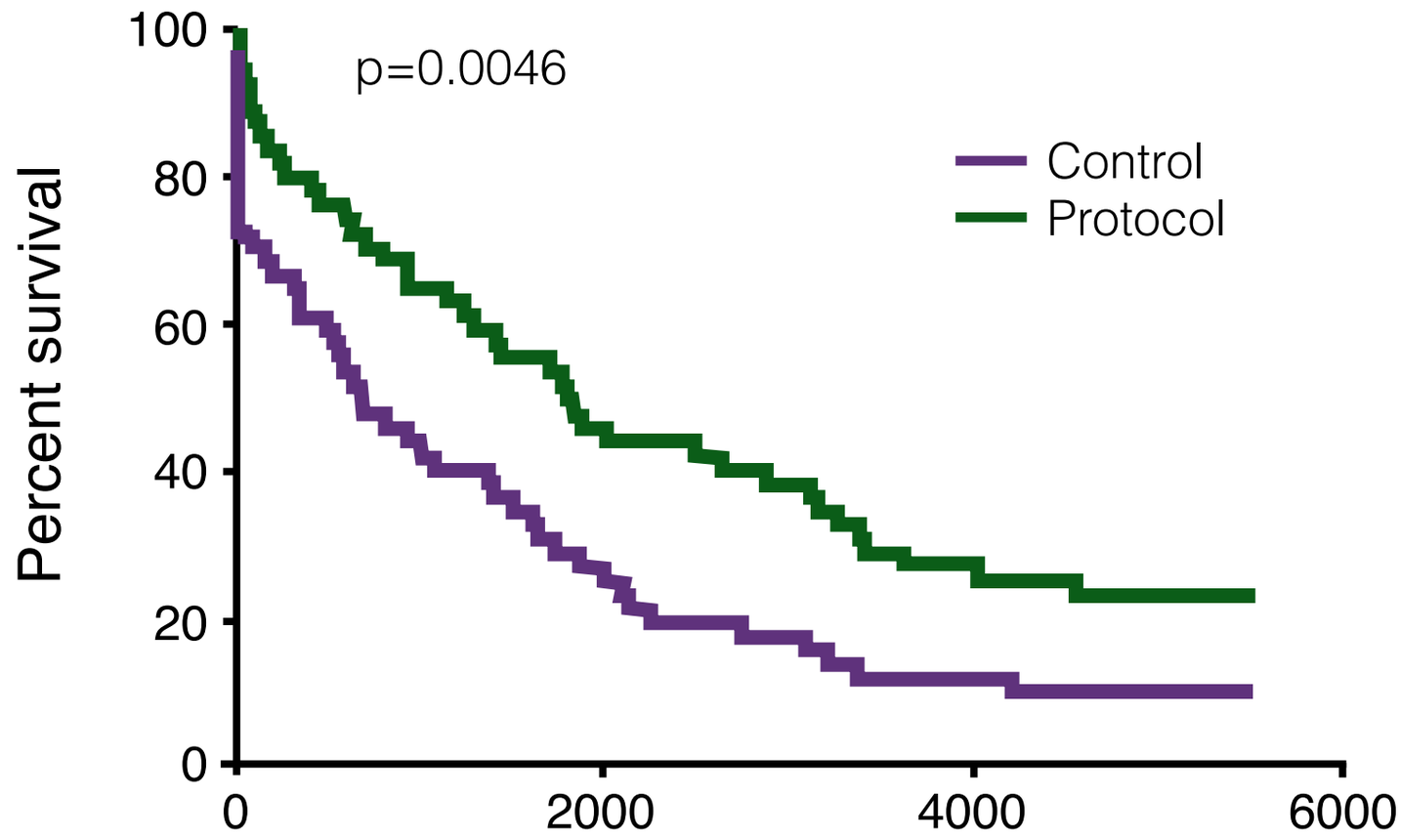
ORIGINAL

Andrew Rhodes
Maurizio Cecconi
Mark Hamilton
Jan Poloniecki
Justin Woods
Owen Boyd
David Bennett
R. Michael Grounds

Goal-directed therapy in high-risk surgical patients: a 15-year follow-up study



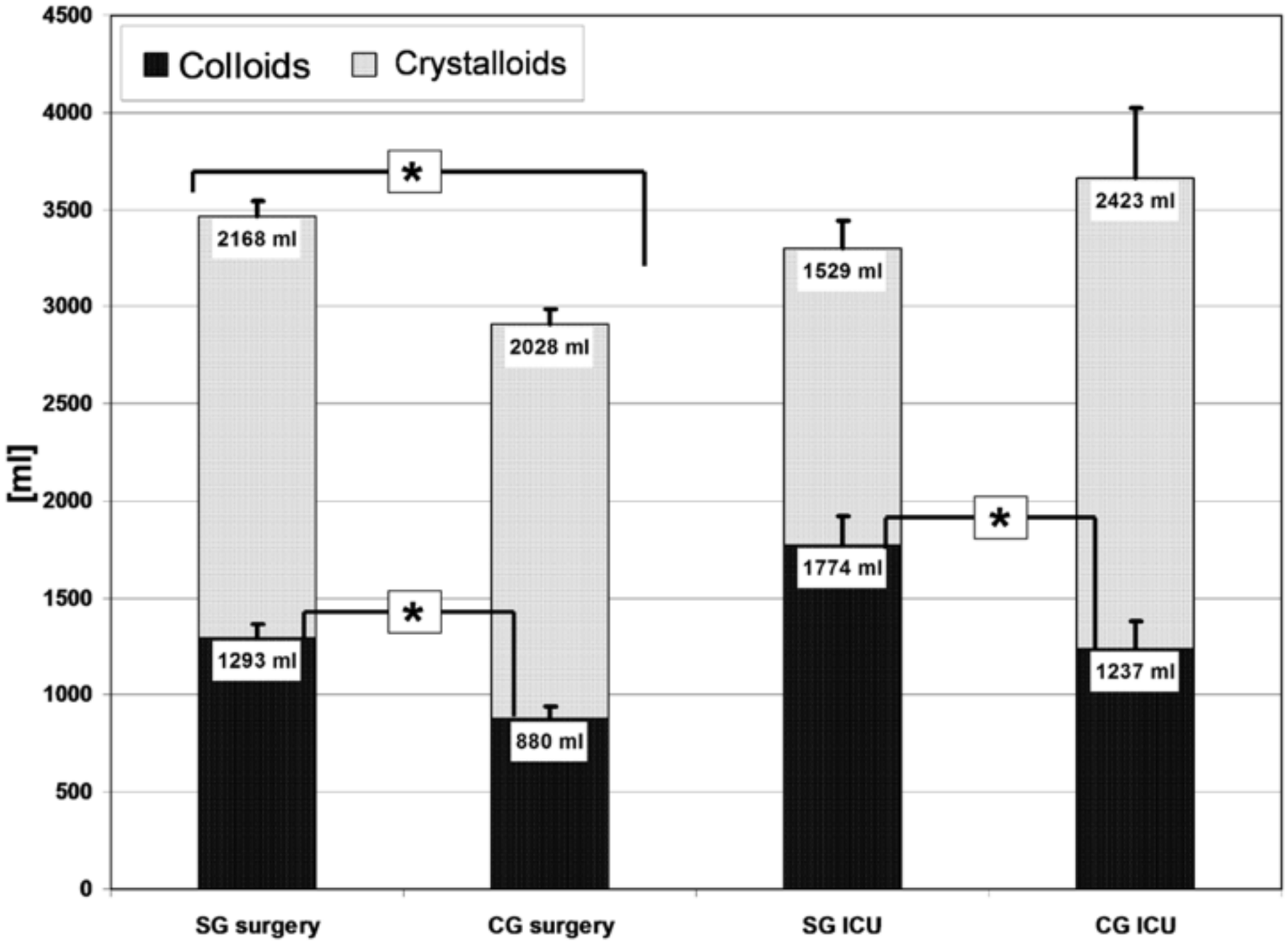
Boyd O et al. JAMA 1993;270:2699-707



Intensive Care Med. 2010;36:1327-32

Individually Optimized Hemodynamic Therapy Reduces Complications and Length of Stay in the Intensive Care Unit

A Prospective, Randomized Controlled Trial



Goepfert MS et al. Anesthesiology. 2013 Oct;119(4):824-36

VISEP

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D., Andreas Meier-Hellmann, M.D., Max Ragaller, M.D., Norbert Weiler, M.D., Onnen Moerer, M.D., Matthias Gruendling, M.D., Michael Oppert, M.D., Stefan Grond, M.D., Derk Olthoff, M.D., Ulrich Jaschinski, M.D., Stefan John, M.D., Rolf Rossaint, M.D., Tobias Welte, M.D., Martin Schaefer, M.D., Peter Kern, M.D., Evelyn Kuhnt, M.Sc., Michael Kiehntopf, M.D., Christiane Hartog, M.D., Charles Natanson, M.D., Markus Loeffler, M.D., Ph.D., and Konrad Reinhart, M.D., for the German Competence Network Sepsis (SepNet)

ABSTRACT

BACKGROUND
The role of intensive insulin therapy in patients with severe sepsis is uncertain. Fluid resuscitation improves survival among patients with septic shock, but evidence is lacking to support the choice of either crystalloids or colloids.

METHODS
In a multicenter, two-by-two factorial trial, we randomly assigned patients with severe sepsis to receive either intensive insulin therapy to maintain euglycemia or conventional insulin therapy and either 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES 200/0.5), or modified Ringer's lactate for fluid resuscitation. The rate of death at 28 days and the mean score for organ failure were coprimary end points.

RESULTS
The trial was stopped early for safety reasons. Among 537 patients who could be evaluated, the mean morning blood glucose level was lower in the intensive-therapy group (112 mg per deciliter [6.2 mmol per liter]) than in the conventional-therapy group (151 mg per deciliter [8.4 mmol per liter], P<0.001). However, at 28 days, there was no significant difference between the two groups in the rate of death or the mean score for organ failure. The rate of severe hypoglycemia (glucose level, ≤40 mg per deciliter [2.2 mmol per liter]) was higher in the intensive-therapy group than in the conventional-therapy group (17.0% vs. 4.1%, P<0.001), as was the rate of serious adverse events (10.9% vs. 5.2%, P=0.01). HES therapy was associated with higher rates of acute renal failure and renal-replacement therapy than was Ringer's lactate.

CONCLUSIONS
The use of intensive insulin therapy placed critically ill patients with sepsis at increased risk for serious adverse events related to hypoglycemia. As used in this study, HES was harmful, and its toxicity increased with accumulating doses. (ClinicalTrials.gov number, NCT00135473.)

2008

6S

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D., Anne B. Guttormsen, M.D., Ph.D., Jyrki Tenhunen, M.D., Ph.D., Gudmundur Klemenzson, M.D., Anders Åneman, M.D., Ph.D., Kristian R. Madsen, M.D., Morten H. Møller, M.D., Ph.D., Jeanie M. Elkjær, M.D., Lone M. Poulsen, M.D., Asger Bendtsen, M.D., M.P.H., Robert Winding, M.D., Morten Steensen, M.D., Pawel Berezowicz, M.D., Ph.D., Peter Søe-Jensen, M.D., Morten Bestle, M.D., Ph.D., Kristian Strand, M.D., Ph.D., Jørgen Wiis, M.D., Jonathan O. White, M.D., Klaus J. Thornberg, M.D., Lars Quist, M.D., Jonas Nielsen, M.D., Ph.D., Lasse H. Andersen, M.D., Lars B. Holst, M.D., Katrin Thormar, M.D., Anne-Lene Kjældgaard, M.D., Maria L. Fabritius, M.D., Frederik Mondrup, M.D., Frank C. Pott, M.D., D.M.Sci., Thea P. Møller, M.D., Per Winkel, M.D., D.M.Sci., and Jørn Wetterslev, M.D., Ph.D., for the 6S Trial Group and the Scandinavian Critical Care Trials Group*

ABSTRACT

BACKGROUND
Hydroxyethyl starch (HES) 130/0.4 is widely used for fluid resuscitation in intensive care units (ICUs), but its safety and efficacy have not been established in patients with severe sepsis.

METHODS
In this multicenter, parallel-group, blinded trial, we randomly assigned patients with severe sepsis to fluid resuscitation in the ICU with either 6% HES 130/0.4 or Ringer's acetate at a dose of up to 33 ml per kilogram of ideal body weight per day. The primary outcome measure was either death or end-stage kidney failure (dependence on dialysis) at 90 days after randomization.

RESULTS
Of the 804 patients who underwent randomization, 798 were included in the modified intention-to-treat population. The two intervention groups had similar baseline characteristics. At 90 days after randomization, 201 of 398 patients (51%) assigned to HES 130/0.4 had died, as compared with 172 of 400 patients (43%) assigned to Ringer's acetate (relative risk, 1.17; 95% confidence interval [CI], 1.01 to 1.36; P=0.03); 1 patient in each group had end-stage kidney failure. In the 90-day period, 87 patients (22%) assigned to HES 130/0.4 were treated with renal-replacement therapy versus 65 patients (16%) assigned to Ringer's acetate (relative risk, 1.35; 95% CI, 1.01 to 1.80; P=0.04), and 38 patients (10%) and 25 patients (6%), respectively, had severe bleeding (relative risk, 1.52; 95% CI, 0.94 to 2.48; P=0.09). The results were supported by multivariate analyses, with adjustment for known risk factors for death or acute kidney injury at baseline.

CONCLUSIONS
Patients with severe sepsis assigned to fluid resuscitation with HES 130/0.4 had an increased risk of death at day 90 and were more likely to require renal-replacement therapy, as compared with those receiving Ringer's acetate. (Funded by the Danish Research Council and others; 6S ClinicalTrials.gov number, NCT00962156.)

2012

CHEST

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

ABSTRACT

BACKGROUND
The safety and efficacy of hydroxyethyl starch (HES) for fluid resuscitation have not been fully evaluated, and adverse effects of HES on survival and renal function have been reported.

METHODS
We randomly assigned 7000 patients who had been admitted to an intensive care unit (ICU) in a 1:1 ratio to receive either 6% HES with a molecular weight of 130 kD and a molar substitution ratio of 0.4 (130/0.4, Voluven) in 0.9% sodium chloride or 0.9% sodium chloride (saline) for all fluid resuscitation until ICU discharge, death, or 90 days after randomization. The primary outcome was death within 90 days. Secondary outcomes included acute kidney injury and failure and treatment with renal-replacement therapy.

RESULTS
A total of 597 of 3315 patients (18.0%) in the HES group and 566 of 3336 (17.0%) in the saline group died (relative risk in the HES group, 1.06; 95% confidence interval [CI], 0.96 to 1.18; P=0.26). There was no significant difference in mortality in six predefined subgroups. Renal-replacement therapy was used in 235 of 3352 patients (7.0%) in the HES group and 196 of 3375 (5.8%) in the saline group (relative risk, 1.21; 95% CI, 1.00 to 1.45; P=0.04). In the HES and saline groups, renal injury occurred in 34.6% and 38.0% of patients, respectively (P=0.005), and renal failure occurred in 10.4% and 9.2% of patients, respectively (P=0.12). HES was associated with significantly more adverse events (5.3% vs. 2.8%, P<0.001).

CONCLUSIONS
In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. (Funded by the National Health and Medical Research Council of Australia and others; CHEST ClinicalTrials.gov number, NCT00935168.)

2012

Human medicines
- European public assessment reports
- Patient safety
- Pending EC decisions
- Withdrawn applications
- Paediatrics
- Rare disease designations
- Medicines under evaluation
- Medicines for use outside the EU

Hydroxyethyl starch solutions for infusion

Hydroxyethyl-starch solutions (HES) should no longer be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

On 23 October 2013, the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)*, endorsed by majority the recommendations of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that **HES solutions must no longer be used to treat patients with sepsis** (bacterial infection in the blood) **or burn injuries or critically ill patients because of an increased risk of kidney injury and mortality**.

HES solutions may continue to be used in patients to treat hypovolaemia (low blood volume) caused by acute (sudden) blood loss, where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient. In order to minimise potential risks in these patients, HES solutions should not be used for e than 24 hours and patients' kidney function should be monitored after HES nistration. In addition to updating the product information, further studies should ied out on the use of these medicines in elective surgery and trauma patients.

ew of HES solutions was carried out by the PRAC following the publication of ies showing an increased risk of mortality in patients with sepsis[1,2] and an increased risk of kidney injury requiring dialysis in critically ill patients[1,2,3] following treatment with HES solutions.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and, on 19 December 2013, adopted a final legally binding decision valid throughout the European Union (EU).

Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

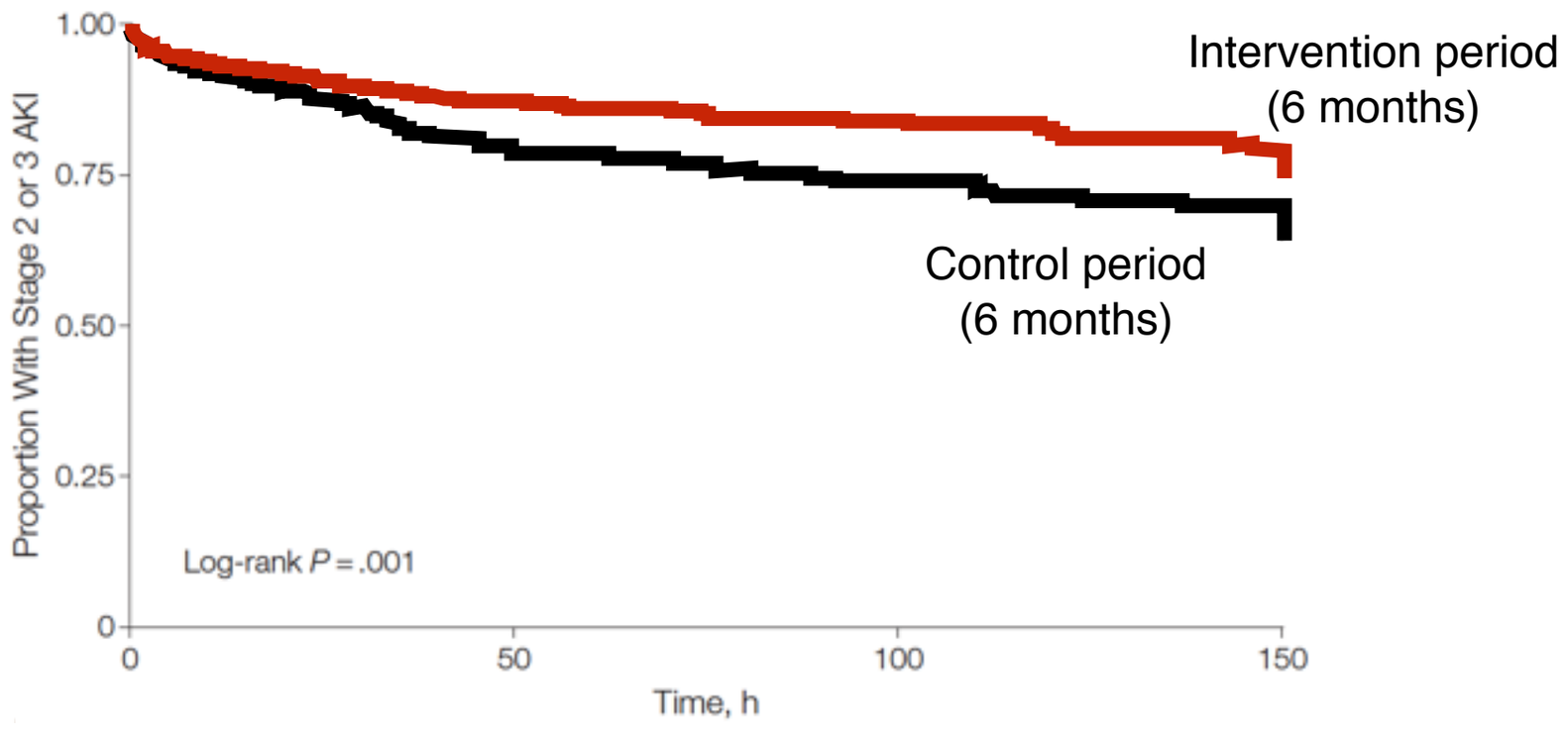
JAMA
The Journal of the American Medical Association

JAMA 2012;308(15):1566-1572

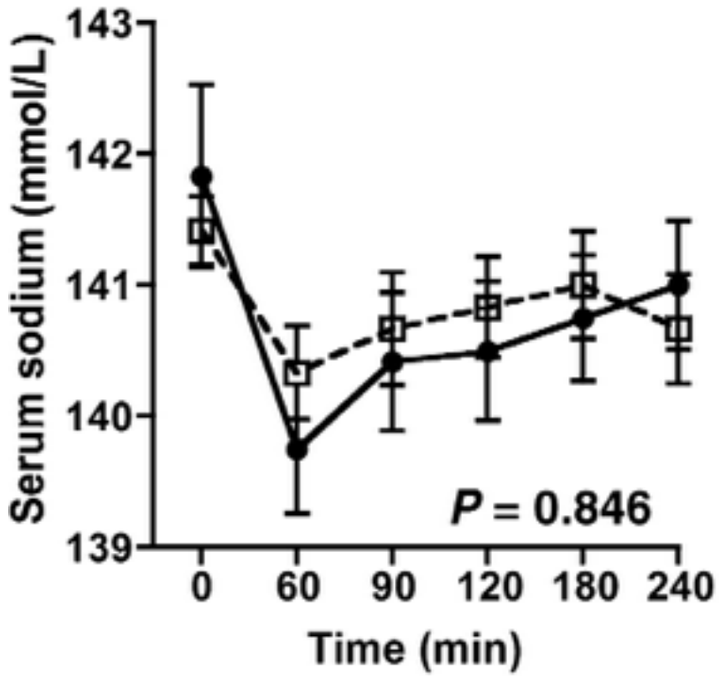
Nor'azim Mohd Yunos, MD
Rinaldo Bellomo, MD, FCICM
Colin Hegarty, BSc
David Story, MD
Lisa Ho, MClinPharm
Michael Bailey, PhD

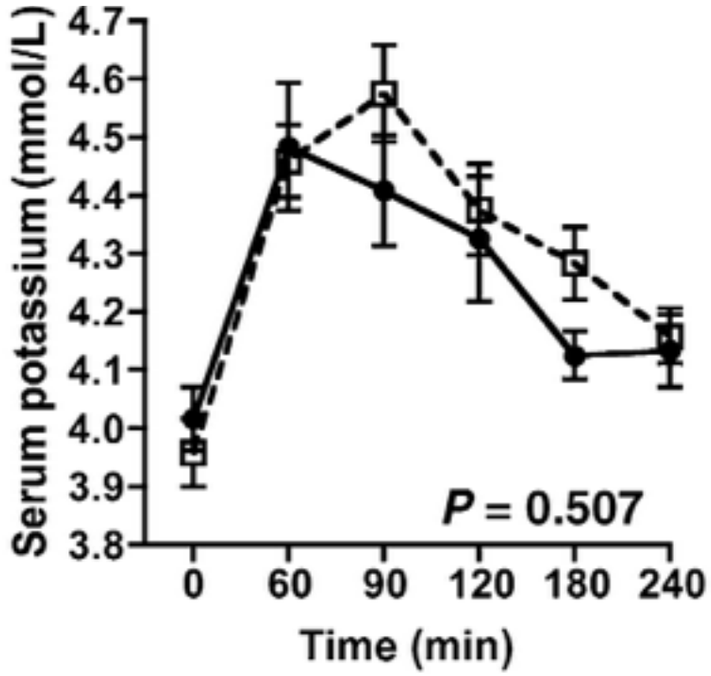
- A prospective, open label, before-and-after pilot study
- **Control 'Chloride-liberal' period** (N=760 patients) with free use of chloride-rich fluids
- **Intervention 'Chloride-restrictive' period** (N=773 patients) with use of balanced fluids and chloride-rich fluids made available only for specific conditions

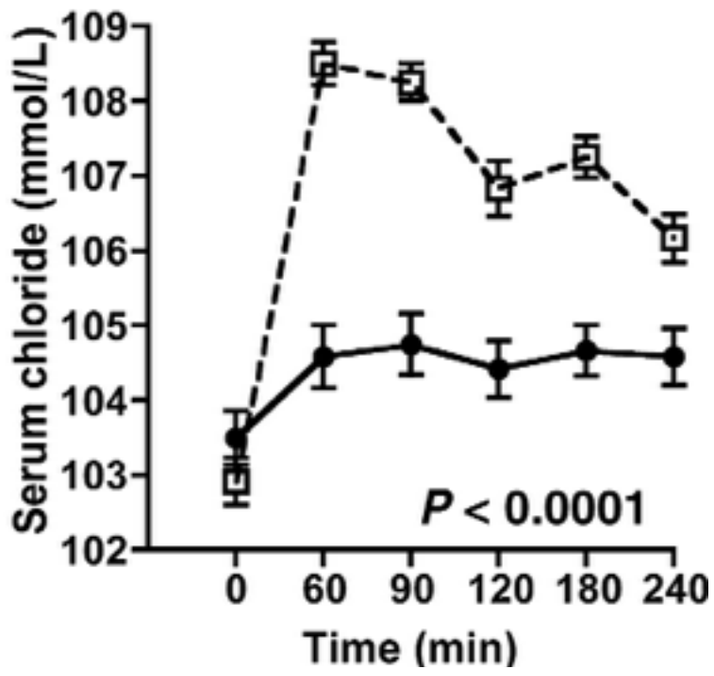
	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class			
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65 (8.4) [6.4-10.0]	<.001

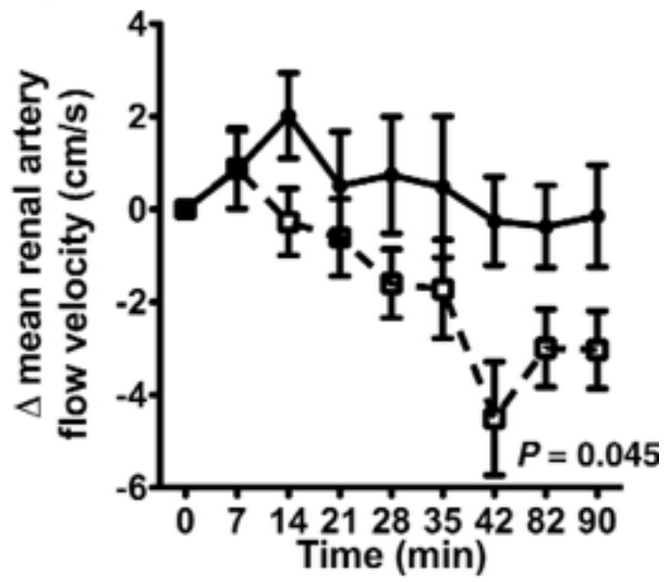


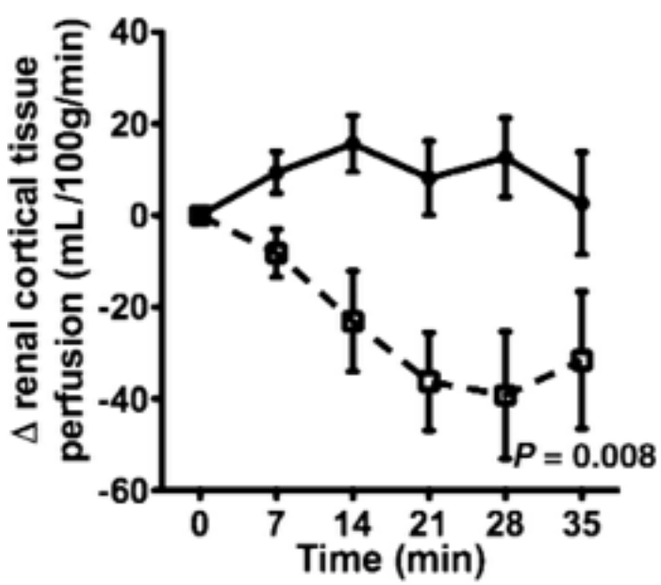
A Randomized, Controlled, Double-Blind Crossover Study on the Effects of 2-L Infusions of 0.9% Saline and Plasma-Lyte 148 on Renal Blood Flow Velocity and Renal Cortical Tissue Perfusion in Healthy Volunteers











Plasma-Lyte 148
0.9% Saline

FEATURE

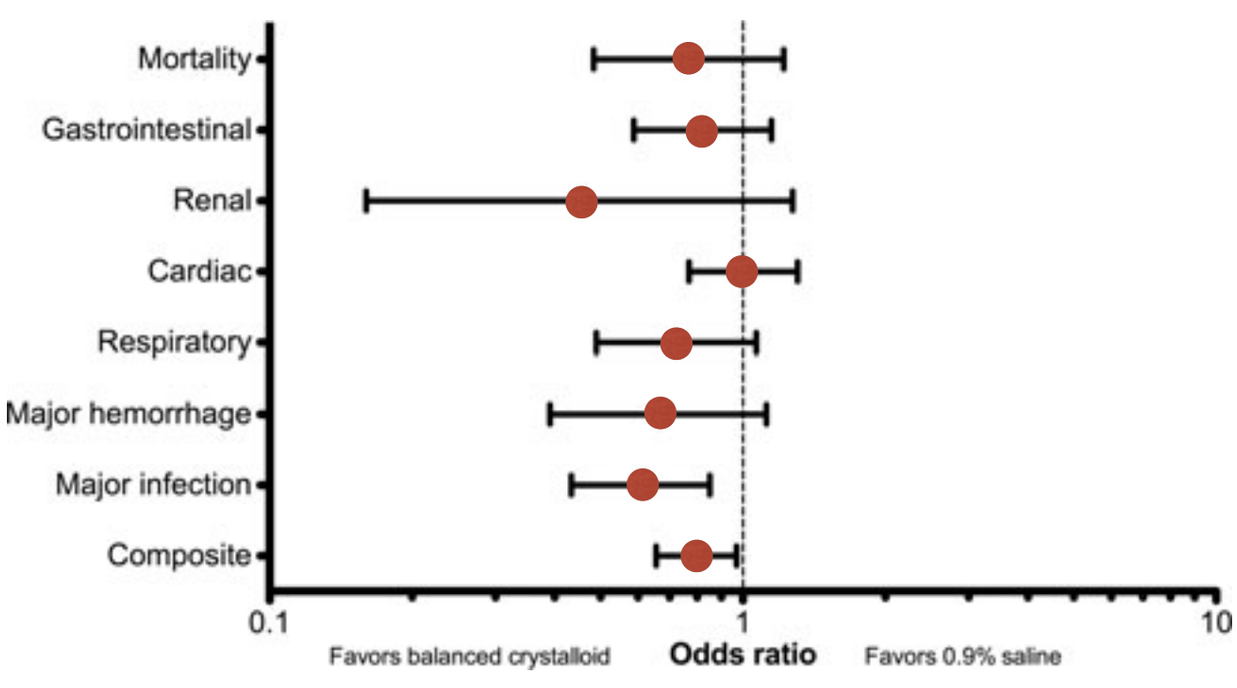
Ann Surg 2012;255:821–829

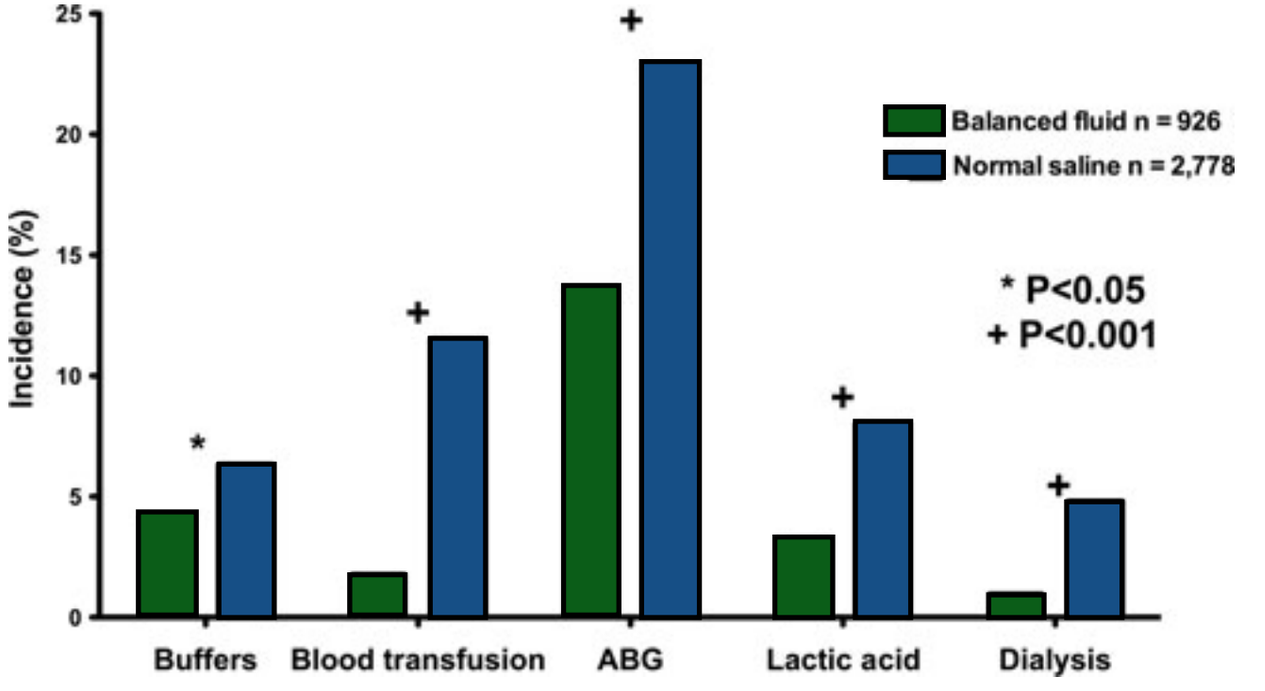
Major Complications, Mortality, and Resource Utilization After Open Abdominal Surgery

0.9% Saline Compared to Plasma-Lyte

Andrew D. Shaw, MB, FRCA, FCCM, Sean M. Bagshaw, MD,† Stuart L. Goldstein, MD,‡ Lynette A. Scherer, MD,§ Michael Duan, MS,‖ Carol R. Schermer, MD,¶ and John A. Kellum, MD#*

- A retrospective observational study of adult patients who received intravenous crystalloid replacement therapy during an elective or emergency open general surgical operation and received exclusively 0.9% saline (N=30994) or Plasma-Lyte 148 (N=926) on the day of surgery





Conclusions: Among hospitals in the Premier Perspective Database, the use of a calcium-free balanced crystalloid for replacement of fluid losses on the day of major surgery was associated with less postoperative morbidity than 0.9% saline.

Conclusion

Apports Liquidiens en Période Postopératoire

- Iatrogénie postopératoire importante : Éviter les apports systématiques et non raisonnés (Éducation +++)

- Limiter les apports riches en chlore (NaCl 0.9%)

- Maintien postopératoire de liquides intraveineux :
  - Nausées, vomissements (NVPO)
  - Troubles de la déglutition
  - Compensation pertes liquidiennes (drains)

Vomiting and nasogastric tube loss

Gastric fluid contains:
- 20–60 mmol Na^+/l
- 14 mmol K^+/l
- 140 mmol/l Cl^-/l
- 60–80 mmol H^+/l.

Excessive loss causes a hypochloraemic (hypokalaemic), metabolic alkalosis. Correction requires supplemental K^+ and Cl^-.

'Pure' water loss (eg fever, dehydration, hyperventilation)

Mainly insensible water loss (ie relatively low electrolyte content); results in potential hypernatraemia.

Biliary drainage loss

- 145 mmol Na^+/l
- 5 mmol K^+/l
- 105 mmol Cl^-/l
- 30 mmol HCO_3^-/l

Pancreatic drain or fistula

- 125–138 mmol Na^+/l
- 8 mmol K^+/l
- 56 mmol Cl^-/l
- 85 mmol HCO_3/l

Diarrhoea or excess colostomy loss

- 30–140 mmol Na^+/l
- 30–70 mmol K^+/l
- 20–80 mmol HCO_3^-/l

Jejunal loss via stoma or fistula

- 140 mmol Na^+/l
- 5 mmol K^+/l
- 135 mmol Cl^-/l
- 8 mmol HCO_3/l

High volume ileal loss via new stoma, high stoma or fistula

100–140 mmol Na^+/l
4–5 mmol K^+/l
75–125 mmol Cl^-/l
0–30 mmol HCO_3/l

Lower volume ileal loss via established stoma or low fistula

50–100 mmol Na^+/l
4–5 mmol K^+/l
25–75 mmol Cl^-/l
0–30 mmol HCO_3/l

Inappropriate urinary loss (eg polyuria)

Na^+/l and K^+/l very variable, so monitor serum electrolytes closely. Match hourly urine output (minus 50 ml) to avoid intravascular depletion.

Ongoing blood loss

(eg melaena)

Apports Liquidiens en Période Postopératoire

- Iatrogénie postopératoire importante : Éviter les apports systématiques et non raisonnés (Éducation +++)

- Limiter les apports riches en chlore (NaCl 0.9%)

- Maintien postopératoire de liquides intraveineux :
  - Nausées, vomissements (NVPO)
  - Troubles de la déglutition
  - Compensation pertes liquidiennes (drains)

- Apports oraux (boissons, nutrition) dès que possible

NICE National Institute for Health and Care Excellence

Intravenous fluid therapy in adults in hospital

Issued: December 2013

NICE clinical guideline 174

guidance.nice.org.uk/cg174

Principles and protocols for intravenous fluid therapy

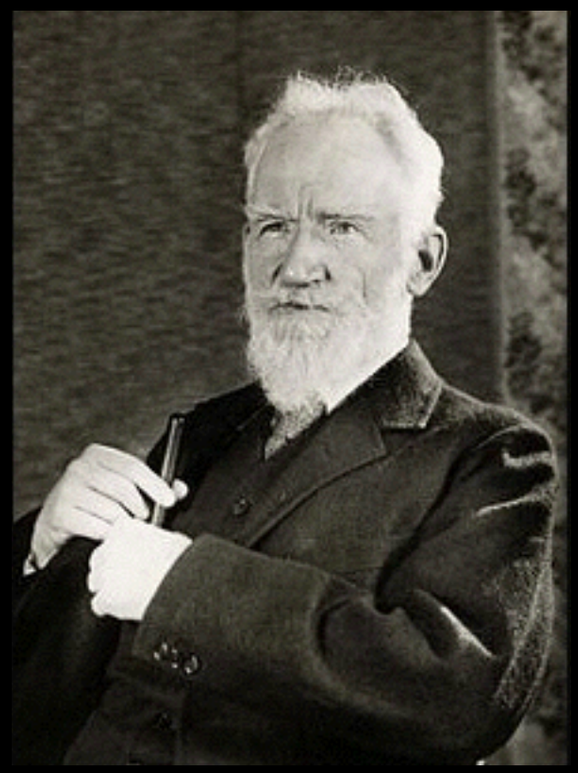
When prescribing IV fluids, remember the 5 Rs

Resuscitation (= Fluid optimization)

Routine maintenance (= Fluid maintenance)

Replacement and **R**edistribution

Reassessment of patient's fluid and electrolytes need



La règle d’or, c’est qu’il n’y a pas de règle d’or

(George Bernard Shaw)