Central Manchester and Manchester Children's University Hospitals NHS Trust

NHS

North West & North Wales Paediatric Transport Service

27 September 2016

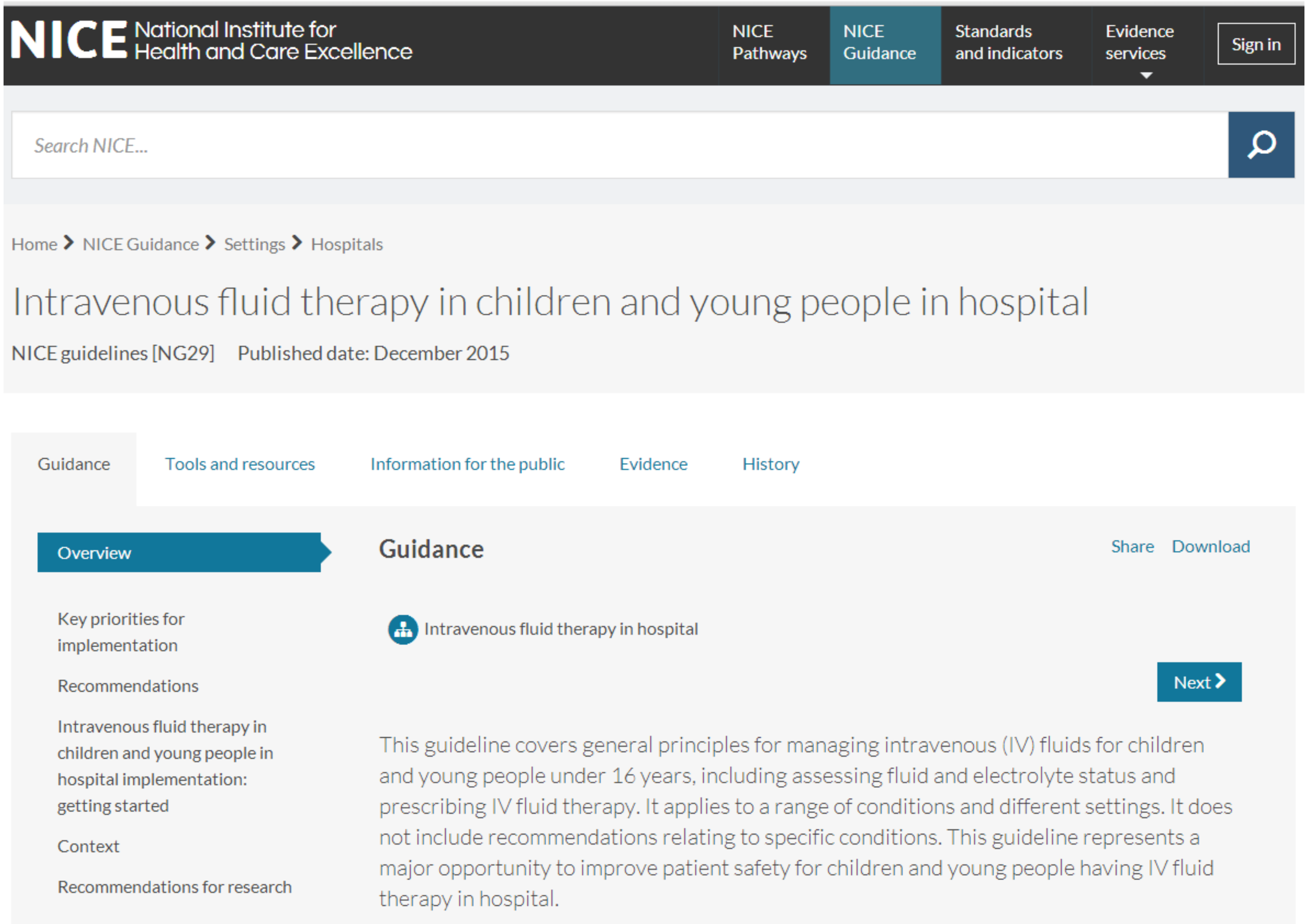
An Update on IV Fluids for Children

Stephen Playfor
Consultant in PICU

An update on IV fluids for children

- NICE guidance; December 2015
- Choice of isotonic crystalloids;
  - 0.9% sodium chloride solution
  - Balanced electrolyte solution
    - Plasma-Lyte 148
    - Hartmann’s solution
- Review of latest research

NICE guidance December 2015



NICE National Institute for Health and Care Excellence

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Intravenous fluid therapy in children and young people in hospital

NICE guidelines [NG29] Published date: December 2015

Guidance | Tools and resources | Information for the public | Evidence | History

- Overview
- Key priorities for implementation
- Recommendations
- Intravenous fluid therapy in children and young people in hospital implementation: getting started
- Context
- Recommendations for research

Guidance

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Intravenous fluid therapy in hospital

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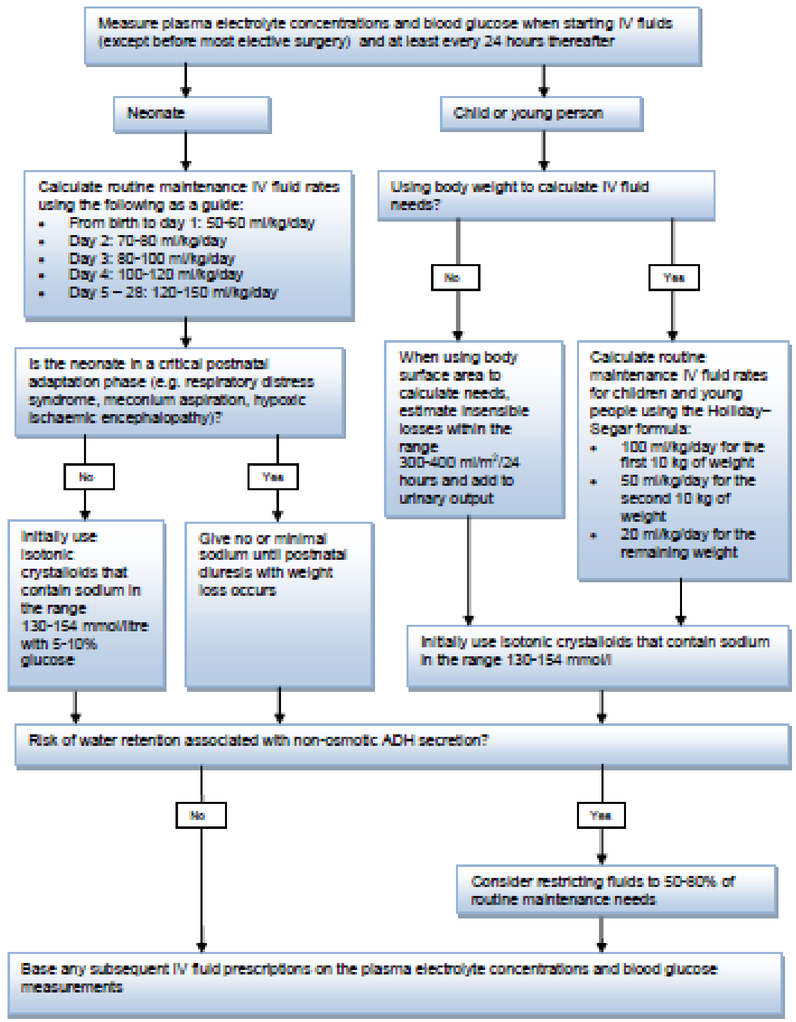
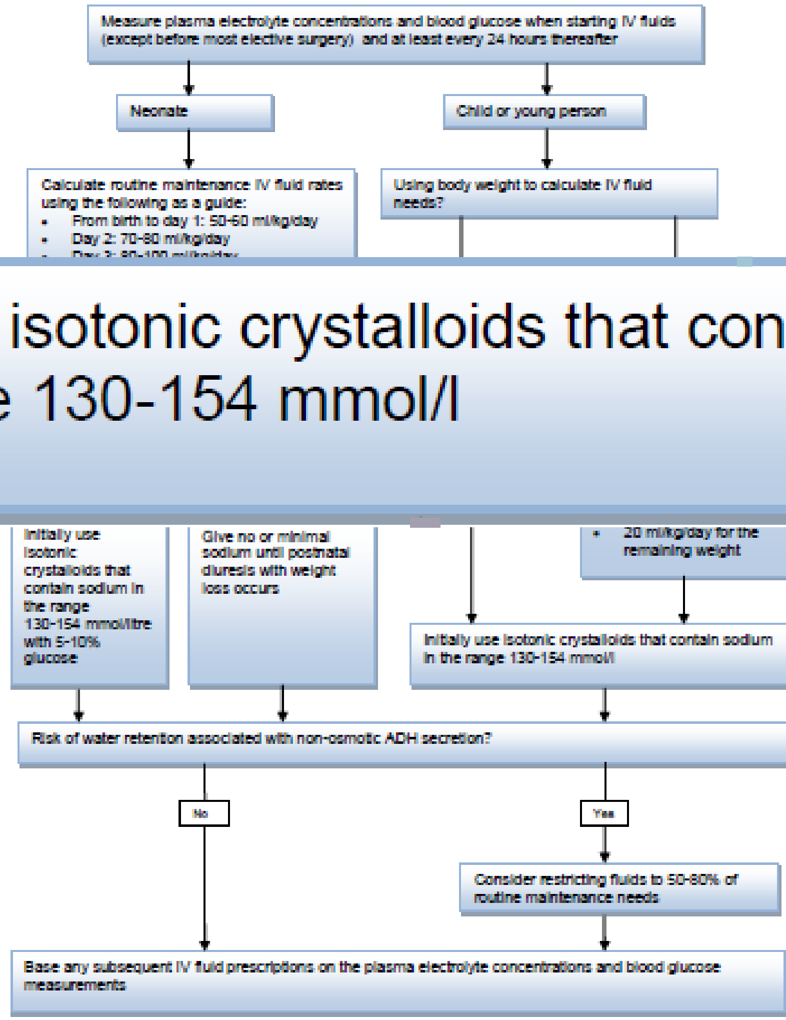
This guideline covers general principles for managing intravenous (IV) fluids for children and young people under 16 years, including assessing fluid and electrolyte status and prescribing IV fluid therapy. It applies to a range of conditions and different settings. It does not include recommendations relating to specific conditions. This guideline represents a major opportunity to improve patient safety for children and young people having IV fluid therapy in hospital.

Routine Maintenance

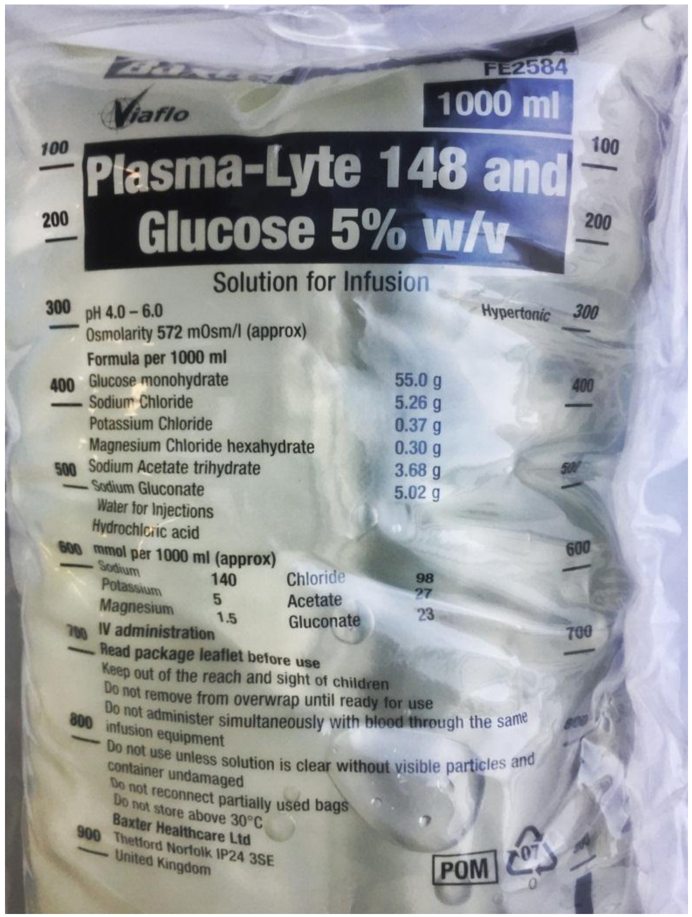


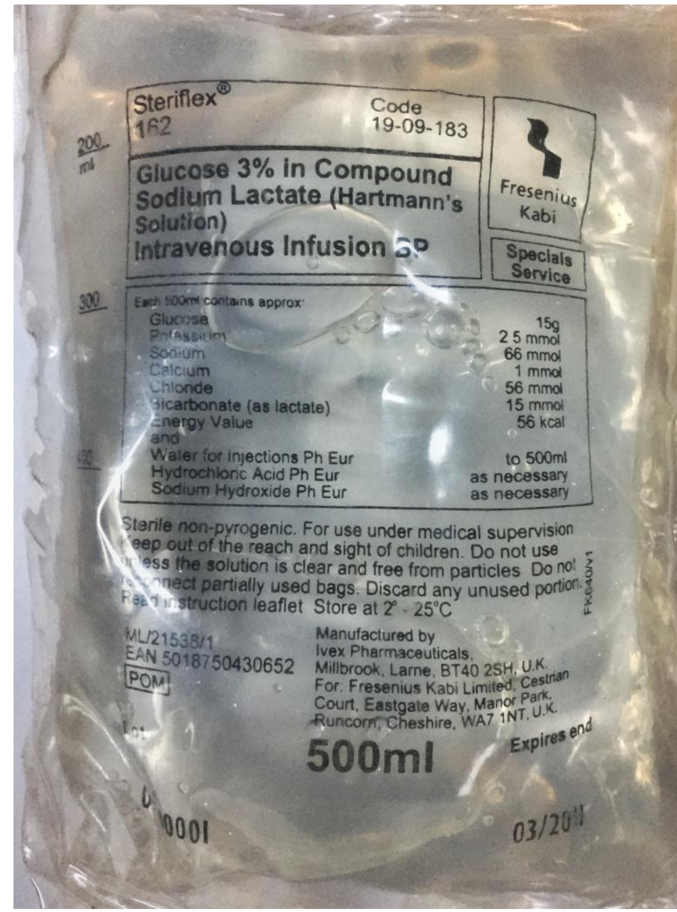
Routine Maintenance



Initially use isotonic crystalloids that contain sodium in the range 130-154 mmol/l

Isotonic fluid with dextrose…





Plasma-Lyte 148 Composition

	mmol/L								Osmolarity
	Cations				Anions				
	Na^+	K^+	Ca^{++}	Mg^{++}	Cl^-	Acetate	Lactate	Gluconate	(mosmol/L)
NaCl 0.9%[7]	154	–	–	–	154	–	–	–	309
Hartmann's[4]	131	5.0	2.0	–	111	–	29	–	278
Plasma-Lyte 148 (pH 7.4)[4]	140	5.0	0	1.5	98	27	–	23	295
Plasma[5]	136 - 145	3.5 - 5.0	2.2 - 2.6	0.8 - 1.2	98 - 106	Bicarbonate 21 - 30			290- 303[9]

Kratz A et al.[5]

No Calcium
Compatibility with blood cells

Physiological levels of sodium and chloride

Buffering capacity provided by acetate and gluconate

Physiological osmolarity

‘Normal’ saline

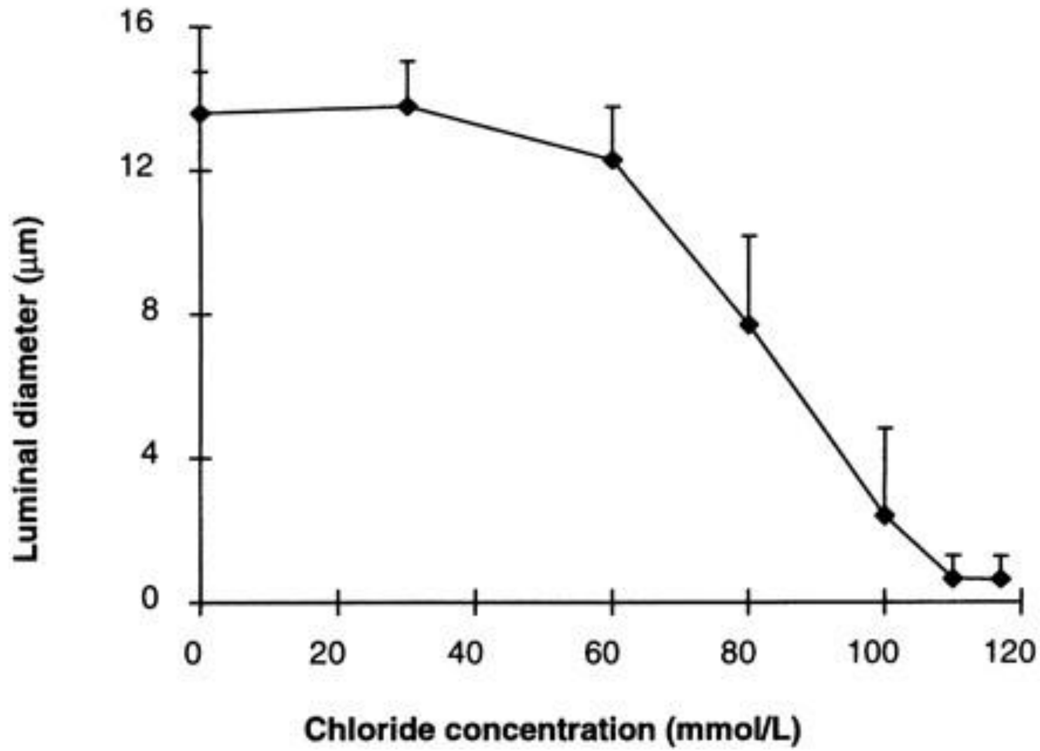
- Strongly acidic
  - pH; 4.6-5.5
  - CO_2 in the solution → 0.1% carbonic acid
  - PVC packaging
    - Diethylhexyl phthalate
  - Gamma irradiation → free radicals & HCl
  - Autoclaving → oxidation; formic and acetic acid
  - Sodium ion is an intrinsic Lewis acid

(Some) Negative effects of hyperchloraemic acidosis

- Reduced renal perfusion
- Pro-inflammatory effects
  - Increased cytokines
  - Endothelial injury
  - Acute kidney injury
- Electrolyte derangement
- Clotting derangement
- Increased blood transfusion requirement
- Death

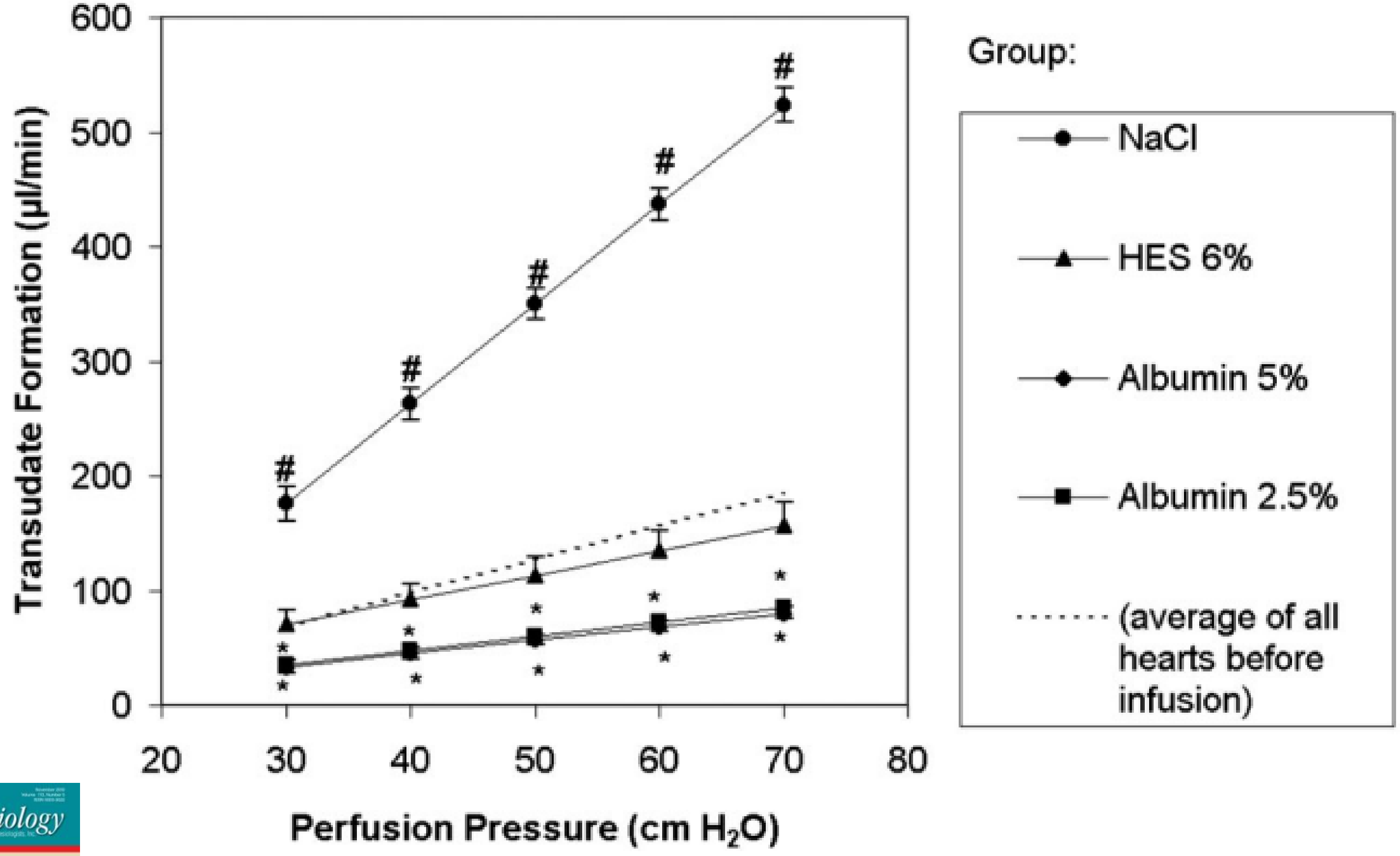
Chloride-dependent vasoconstriction

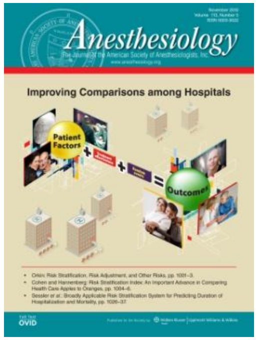
- Critical range of vasoconstriction (50-100%) lies in the physiological range of 90-110 mmol/L



Hansen PB *et al*, *Hypertension* 1998;**32**:1066-1070

Transudate formation





Anesthesiology 2006; 104:1223–31

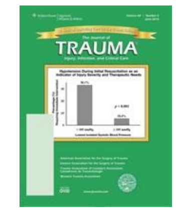
Contrasting Effects of Colloid and Crystalloid Resuscitation Fluids on Cardiac Vascular Permeability

Matthias Jacob, M.D., Dirk Bruegger, M.D.,* Markus Rehm, M.D.,† Ulrich Welsch, M.D., Ph.D.,‡ Peter Conzen, M.D.,§ Bernhard F. Becker, M.D., Ph.D.‖*

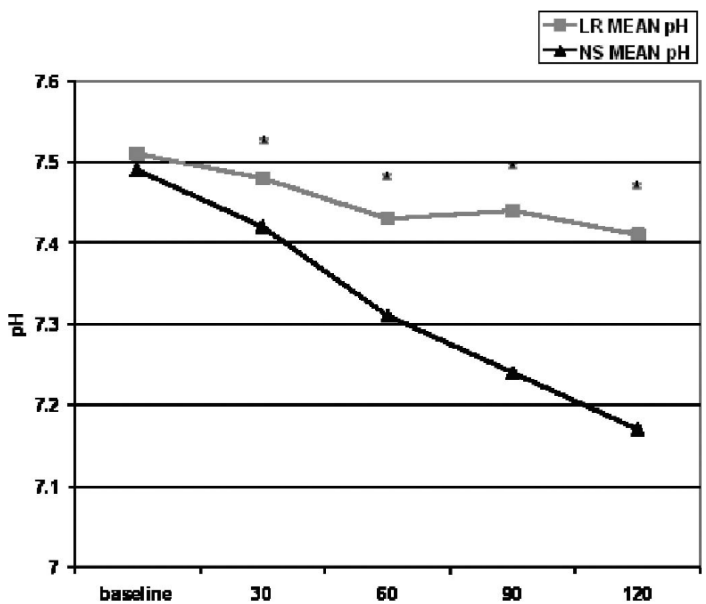
The Journal of **TRAUMA**® Injury, Infection, and Critical Care

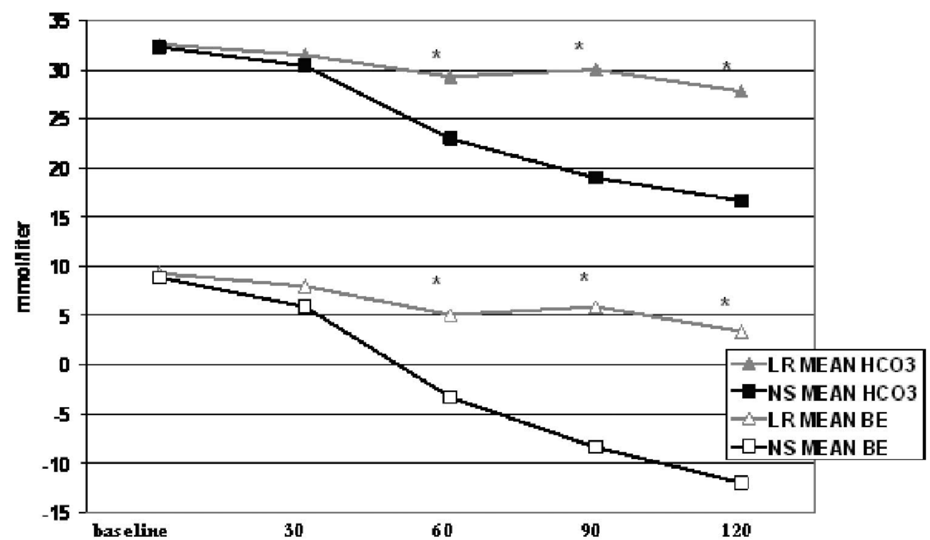
Resuscitation With Normal Saline (NS) vs. Lactated Ringers (LR) Modulates Hypercoagulability and Leads to Increased Blood Loss in an Uncontrolled Hemorrhagic Shock Swine Model

Laszlo N. Kiraly, MD, Jerome A. Differding, MS, T. Miko Enomoto, MD, Rebecca S. Sawai, MD, Patrick J. Muller, MS, Brian Diggs, PhD, Brandon H. Tieu, MD, Michael S. Englehart, MD, Samantha Underwood, MS, Tracy T. Wiesberg, MD, and Martin A. Schreiber, MD

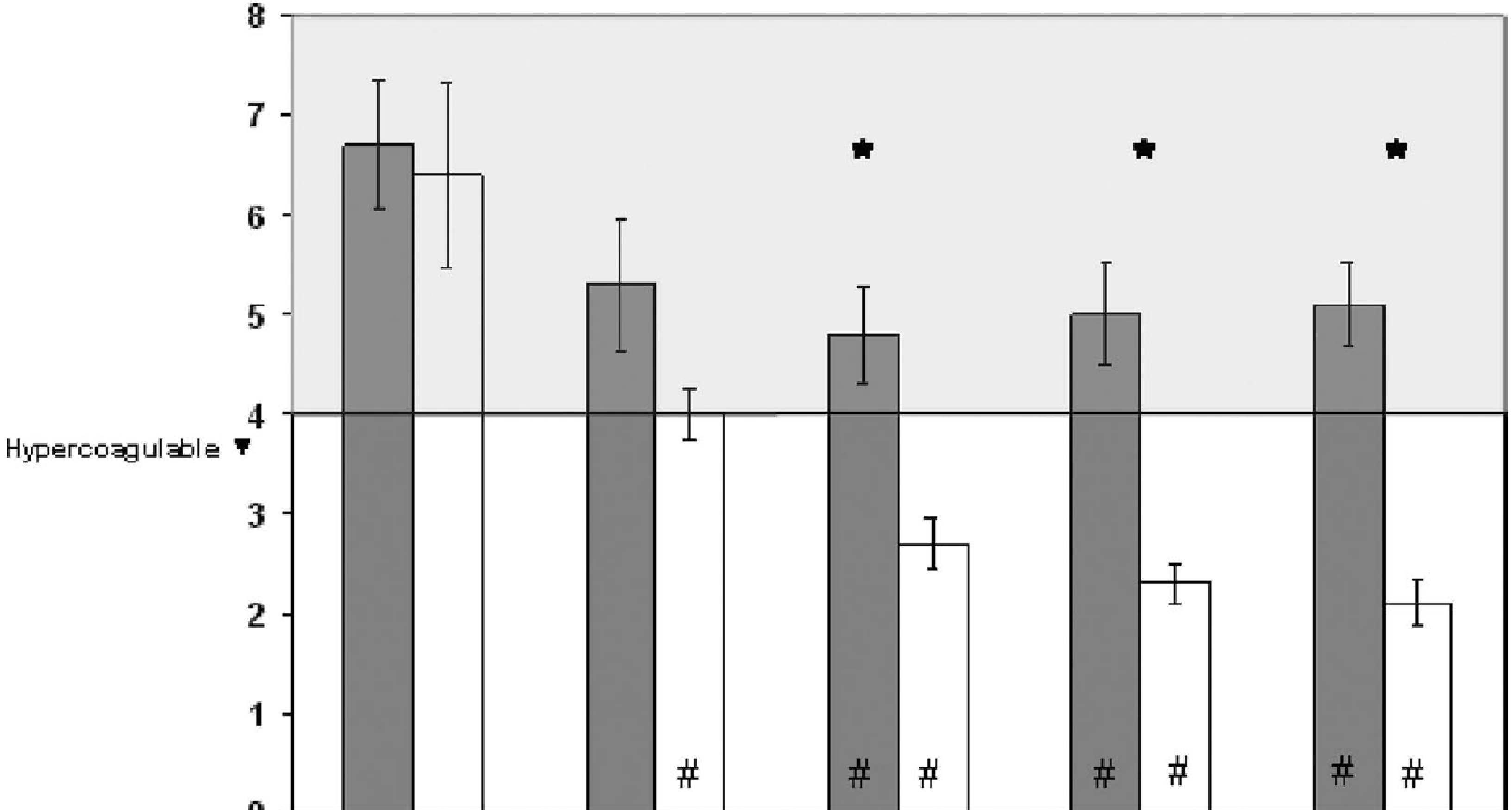


J Trauma. 2006;61:57–65.





TEG R values following injury

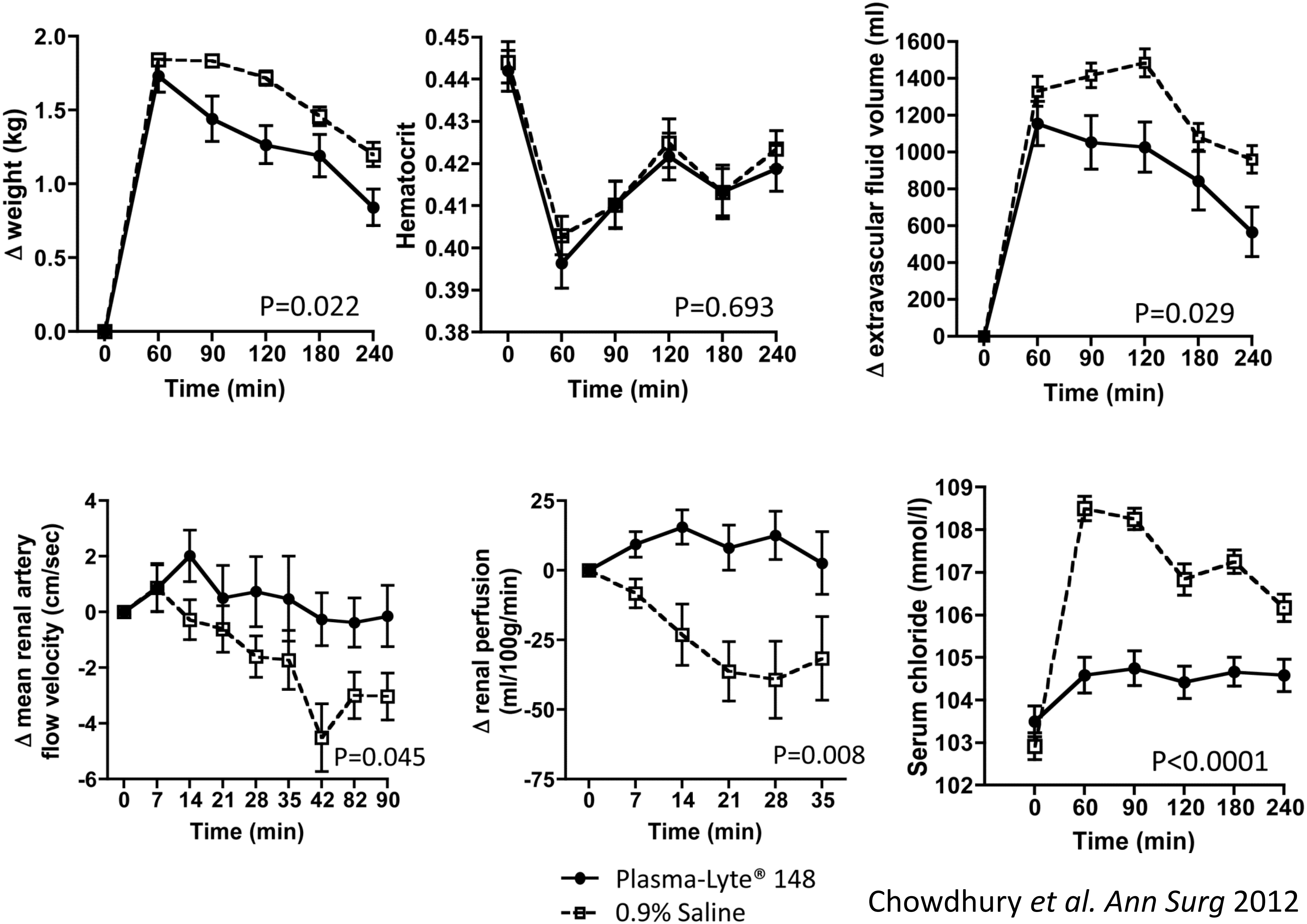


	R Baseline	R 30'	R 60'	R 90'	R 120'
MEAN NS	6.7	5.3	4.8	5	5.1
MEAN LR	6.4	4.0	2.7	2.3	2.1

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

Chowdhury AH *et al*, *Ann Surg* 2012;**256**:18-24

- Twelve healthy adult male subjects received 2-litre intravenous infusions over 1 h of 0.9% saline or Plasma-Lyte 148 in a randomised, double-blind manner
- Crossover studies were performed 7-10 days apart
  - MRI scanning to measure renal artery blood flow velocity
  - MRI scanning to measure renal cortical perfusion
  - Blood was sampled
  - Weight recorded hourly



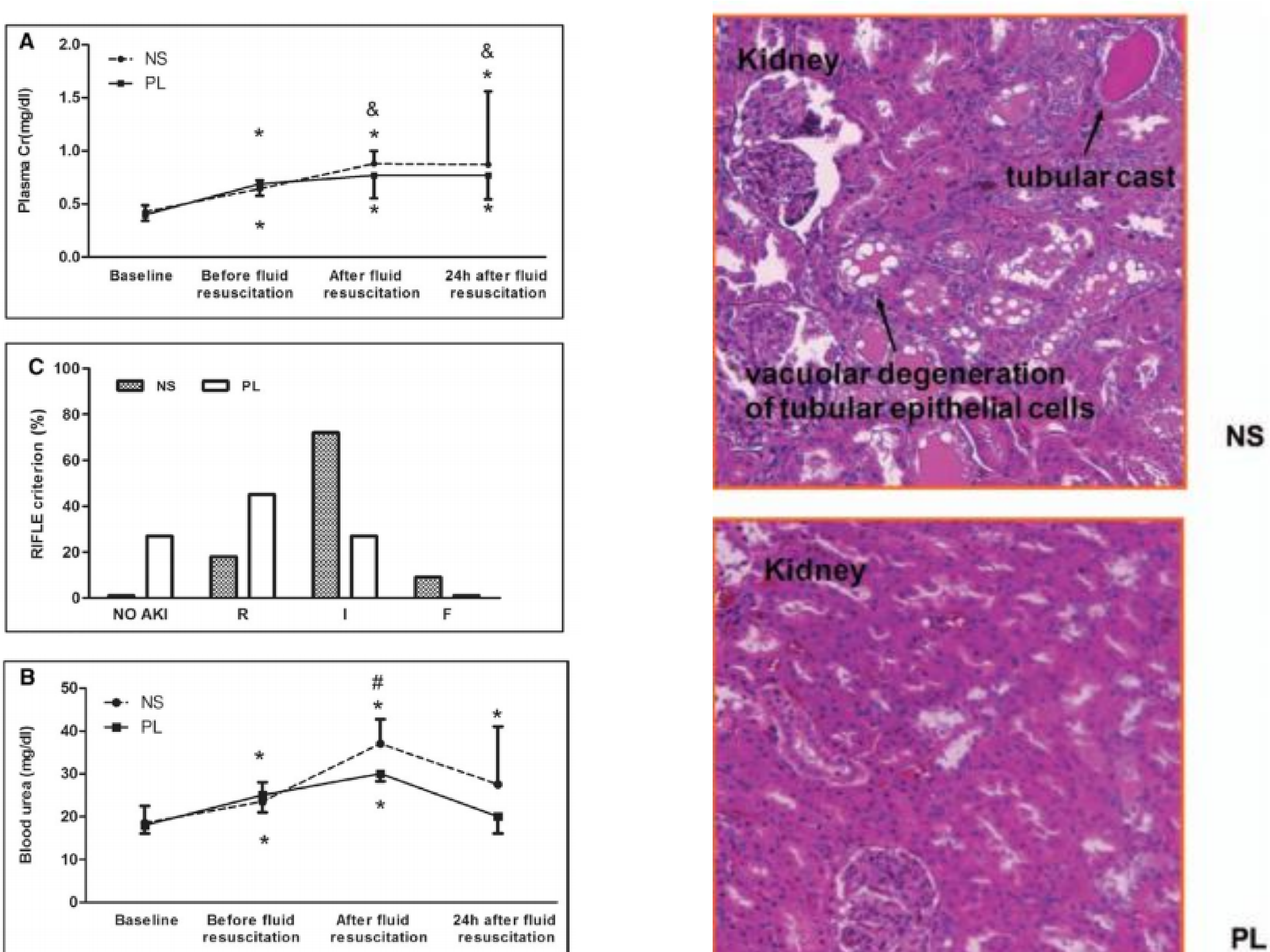
Chowdhury *et al. Ann Surg* 2012

Increase in sepsis-induced AKI

- 60 adult male, septic rats
- Saline-treated animals showed significantly higher levels of serum chloride, lactate, urea and cystatin C after fluid resuscitation ($p<0.05$)
- Saline resuscitation significantly decreased pH and base excess; and increased AKI severity (AKI-I/F, 82% Vs 27%), compared to Plasma-Lyte resuscitation ($p<0.01$)
- 24 hour survival favoured Plasma-Lyte resuscitation (76.6% Vs 53.3%; $p = 0.03$)

Effects of fluid resuscitation with 0.9% saline versus a balanced electrolyte solution on acute kidney injury in a rat model of sepsis

Zhou F, Peng Z-Y, Bishop JV, *et al. Crit Care Med* 2014;**42**:e270–e278


A
Plasma Cr(mg/dl)
2.0
1.5
1.0
0.5
0.0
NS
PL
&
*
Baseline
Before fluid resuscitation
After fluid resuscitation
24h after fluid resuscitation
C
RIFLE criterion (%)
100
80
60
40
20
0
NO AKI
R
I
F
B
Blood urea (mg/dl)
50
40
30
20
10
#
Kidney
tubular cast
vacuolar degeneration of tubular epithelial cells
NS
PL

Major Complications, Mortality, and Resource Utilization After Open Abdominal Surgery: 0.9% Saline Compared to Plasma-Lyte

Andrew Shaw *et al*, Duke University

<u>Complications</u>

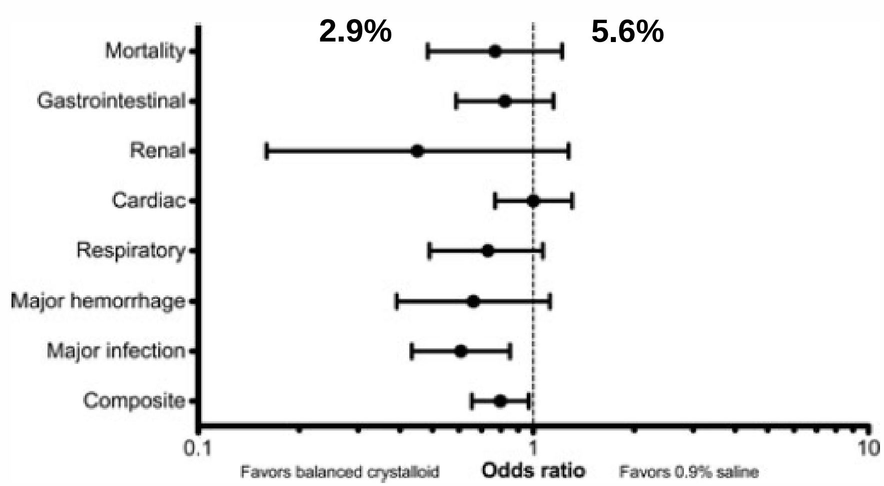


FIGURE 2. Odds ratios and 95% confidence intervals for pre-specified clinical outcomes.

<u>Interventions</u>

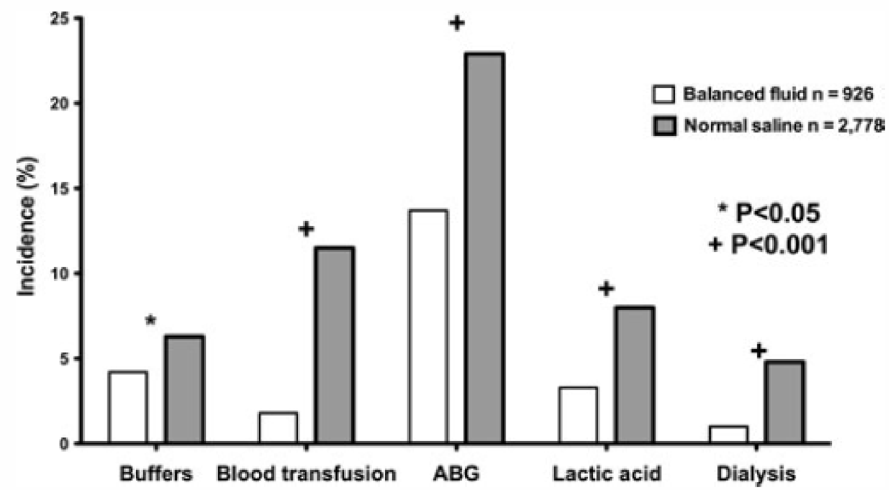


FIGURE 3. Interventions related to metaboloic acidosis diagnosis and management.

Annals of Surgery 2012:**255**;821-829

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

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

JAMA. 2012;308(15):1566-1572

Interventions During the control period, patients received standard intravenous fluids. After a 6-month phase-out period (August 18, 2008, to February 17, 2009), any use of chloride-rich intravenous fluids (0.9% saline, 4% succinylated gelatin solution, or 4% albumin solution) was restricted to attending specialist approval only during the intervention period; patients instead received a lactated solution (Hartmann solution), a balanced solution (Plasma-Lyte 148), and chloride-poor 20% albumin.

Conclusion The implementation of a chloride-restrictive strategy in a tertiary ICU was associated with a significant decrease in the incidence of AKI and use of RRT.

Table 3. Incidence of Acute Kidney Injury Stratified by Risk, Injury, Failure, Loss, and End-Stage (RIFLE) Serum Creatinine Criteria

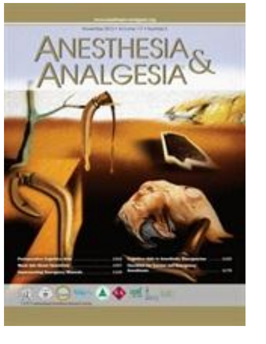
	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class			
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65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

Hyperchloremia After Noncardiac Surgery Is Independently Associated with Increased Morbidity and Mortality: A Propensity-Matched Cohort Study

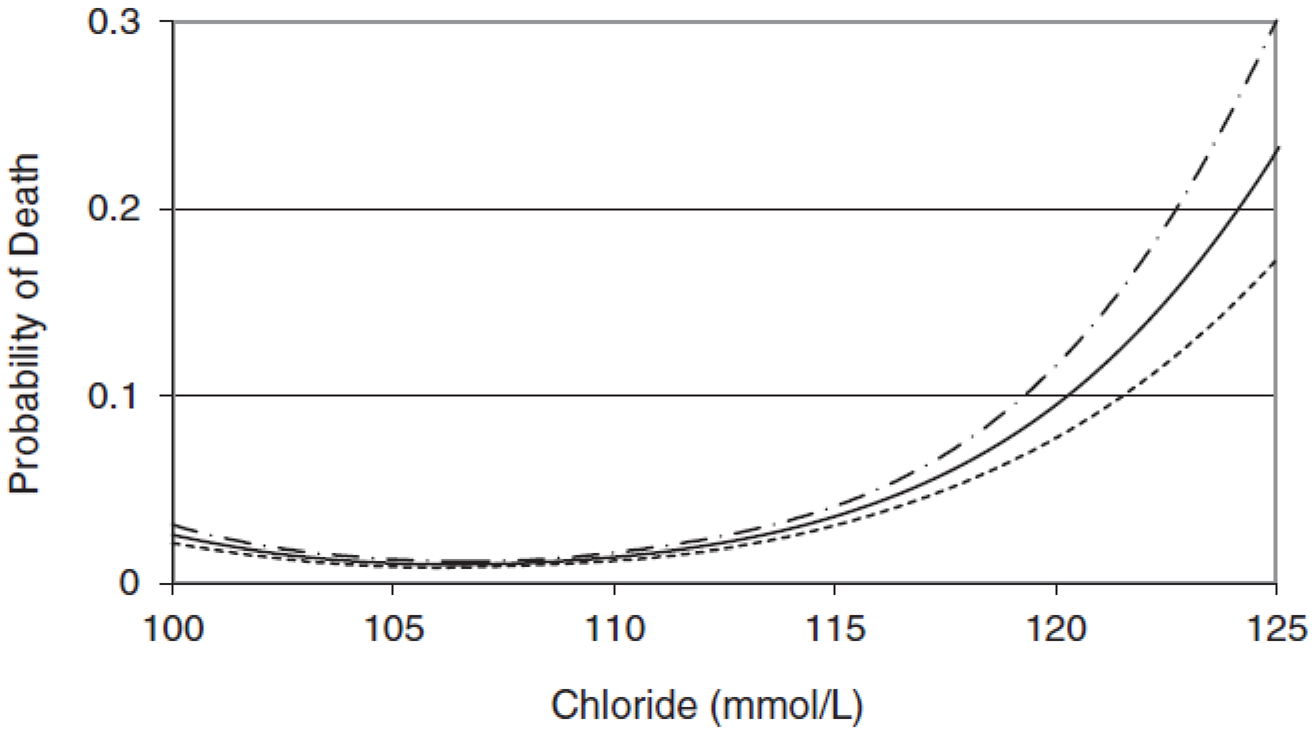
Stuart A. McCluskey, PhD, MD,* Keyvan Karkouti, MSc, MD,*† Duminda Wijeysundera, PhD, MD,* Leonid Minkovich, PhD, MD,* Gordon Tait, PhD,* and W. Scott Beattie, PhD, MD*

- Retrospective cohort trial
- 22,851 adults with normal pre-op renal function and chloride levels
- 22% incidence of post-op hyperchloraemia
- Propensity-matched with those who maintained normal chloride levels

Anesth Analg 2013;**117**:412-421



Probability of Death



Increased mortality at 30 days; 3% Vs 1.9% (Odds ratio 1.58, 95%CI: 1.25-1.98)

Systematic review

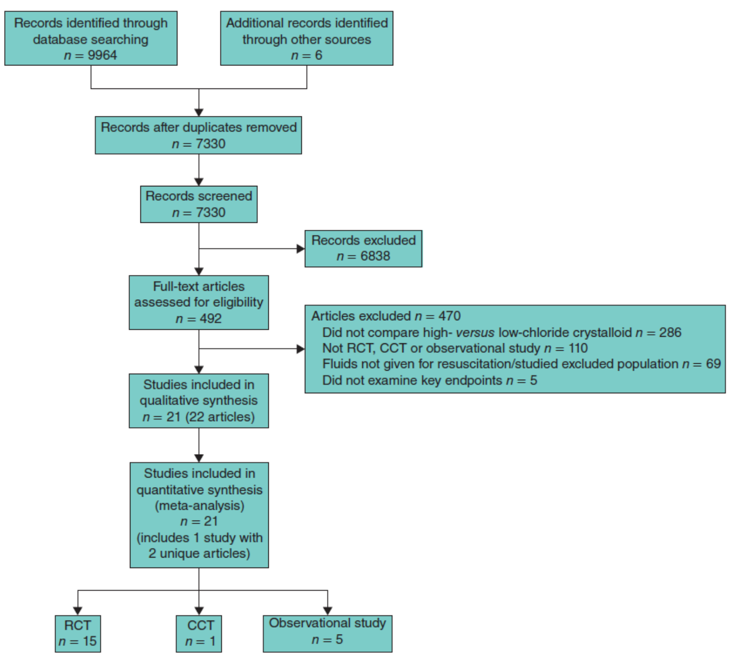
Meta-analysis of high- *versus* low-chloride content in perioperative and critical care fluid resuscitation

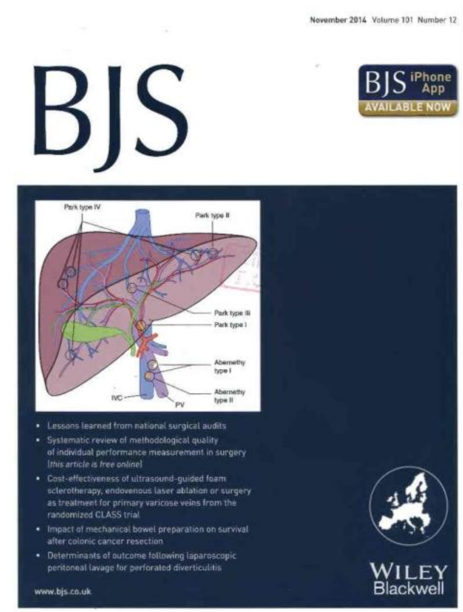
M. L. Krajewski[1], K. Raghunathan[1,2], S. M. Paluszkiewicz[3], C. R. Schermer[4] and A. D. Shaw[5]

[1]Department of Anesthesiology, Duke University Medical Center, and [2]Anesthesiology Service, Durham VA Medical Center, Durham, North Carolina, [3]Boston Strategic Partners, Boston, Massachusetts, [4]Baxter Healthcare Corporation, Deerfield, Illinois, and [5]Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Correspondence to: Professor A. D. Shaw, Division of Cardiothoracic Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee 37232–8274, USA (e-mail: andrew.shaw@vanderbilt.edu)

30 October 2014 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.9651

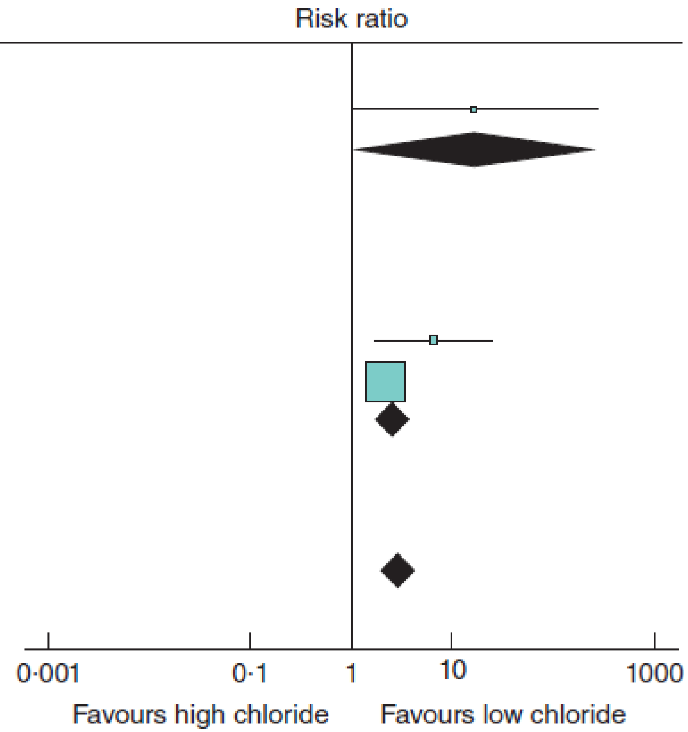




Reference	Year	Design	Country	Study population	Total study population size	Interventions compared	Key endpoints
Berger et al.[40]	2000	Retrospective	Switzerland	Adults with thermal burns	40	Bicarbonated 0·9% saline versus Ringer's lactate	Mortality, acute renal injury, ICU LOS, mechanical ventilation time, hyperchloraemia/metabolic acidosis, urine output
Cho et al.[41]	2007	RCT	Korea	Adults with rhabdomyolysis	28	0·9% saline versus Ringer's lactate	Serum chloride
Chua et al.[42]	2012	Retrospective	Australia	Adults with severe DKA	23	0·9% saline versus Plasma-Lyte® 148	ICU LOS, urine output
Cieza et al.[43]	2013	Observational	Peru	Adults with severe dehydration	40	0·9% saline versus Ringer's lactate	Serum creatinine, serum chloride
Hadimioglu et al.[12]	2008	RCT	Turkey	Adults undergoing kidney transplantation	60*	0·9% saline versus Plasma-Lyte® and Ringer's lactate	Acute renal injury, serum creatinine, serum chloride, urine output
Hasman et al.[44]	2012	RCT	Turkey	Adults with moderate or severe dehydration	60*	0·9% saline versus Plasma-Lyte® and Ringer's lactate	Serum chloride
Khajavi et al.[45]	2008	RCT	Iran	Adults undergoing kidney transplantation	52	0·9% saline versus Ringer's lactate	Serum creatinine, urine output
Kim et al.[46]	2013	RCT	Korea	Adults undergoing kidney transplantation	60	0·9% saline versus Plasma-Lyte® A	Serum creatinine, serum chloride, urine output, transfusion volume
Mahajan et al.[47]	2012	RCT	India	Children with severe dehydration	22	0·9% saline versus Ringer's lactate	Mortality, hospital LOS, serum chloride
Mahler et al.[48]	2011	RCT	USA	Adults with DKA	45	0·9% saline versus Plasma-Lyte® A	Serum chloride
Modi et al.[49]	2012	RCT	Saudi Arabia	Adults undergoing kidney transplantation	74	0·9% saline versus Ringer's lactate	Serum chloride, serum creatinine
O'Malley et al.[50]	2005	RCT	USA	Adults undergoing renal transplantation	51	0·9% saline versus Ringer's lactate	Acute renal injury, hospital LOS, hyperchloraemia/metabolic acidosis, serum creatinine, serum chloride, urine output
Scheingraber et al.[10]	1999	RCT	Germany	Adults undergoing elective abdominal gynaecological surgery	24	0·9% saline versus Ringer's lactate	Urine output
Shaw et al.[27]	2012	Retrospective	USA	Adult surgical patients	31920	0·9% saline versus Plasma-Lyte® 148 or Plasma-Lyte® A	Mortality, acute kidney injury, hospital LOS, mechanical ventilation time
Takil et al.[51]	2002	RCT	Turkey	Adult spinal surgery patients	30	0·9% saline versus Ringer's lactate	Hospital LOS, ICU LOS, serum chloride, urine output, transfusion volume
Van Zyl et al.[52]	2012	RCT	South Africa	Adults with DKA	54	0·9% saline versus Ringer's lactate	Hospital LOS, serum creatinine, serum chloride
Waters et al.[14]	2001	RCT	USA	Adult patients undergoing aortic reconstructive surgery	66	0·9% saline versus Ringer's lactate	Mortality, acute renal injury, hospital LOS, ICU LOS, mechanical ventilation time, serum creatinine, serum chloride, urine output, transfusion volume
Wu et al.[53]	2011	RCT	USA	Adults with acute pancreatitis	40	0·9% saline versus Ringer's lactate	Acute renal injury, hospital LOS
Young et al.[54]	2014	RCT	USA	Adults with traumatic injury	46	0·9% saline versus Plasma-Lyte® A	Mortality, acute renal injury, hospital LOS, ICU LOS, mechanical ventilation time, serum creatinine, serum chloride, urine output, transfusion volume
Yunos et al.[25,55]	2011, 2012	CCT	Australia	Adult ICU patients	1533	Chloride-rich fluids (0·9% saline, 4% succinylated gelatin solution, 4% albumin) versus balanced solutions (Hartmann's, Plasma-Lyte® 148, chloride-poor 20% albumin)	Mortality, acute renal injury, hospital LOS, ICU LOS, serum chloride, serum creatinine, urine output
Zunini et al.[56]	2011	Retrospective	Uruguay	Children undergoing craniofacial surgery	132	0·9% saline versus Ringer's lactate	Hyperchloraemia/metabolic acidosis

Hyperchloraemic acidosis

Reference	Hyperchloraemia/metabolic acidosis: High-chloride	Low-chloride	Weight (%)	Risk ratio
RCTs				
O'Malley *et al.*[50]	8 of 26	0 of 25	2·4	16·37 (0·99, 269·44)
Subtotal	8 of 26	0 of 25	2·4	16·37 (0·99, 269·44)
Heterogeneity: not applicable				
Test for overall effect: Z = 1·96, P = 0·05				
Observational/retrospective studies				
Berger *et al.*[41]	13 of 20	2 of 20	9·3	6·50 (1·68, 25·16)
Zunini *et al.*[56]	43 of 54	18 of 48	88·4	2·12 (1·44, 3·13)
Subtotal	56 of 74	20 of 68	97·6	2·54 (1·73, 3·72)
Heterogeneity: χ^2 = 2·66, 1 d.f., P = 0·10; I^2 = 62%				
Test for overall effect: Z = 4·78, P < 0·001				
Total	64 of 100	20 of 93	100·0	2·87 (1·95, 4·21)
Heterogeneity: χ^2 = 5·17, 2 d.f., P = 0·08; I^2 = 61%				
Test for overall effect: Z = 5·36, P < 0·001				
Test for subgroup differences: χ^2 = 1·67, 1 d.f., P = 0·20; I^2 = 40·1%				

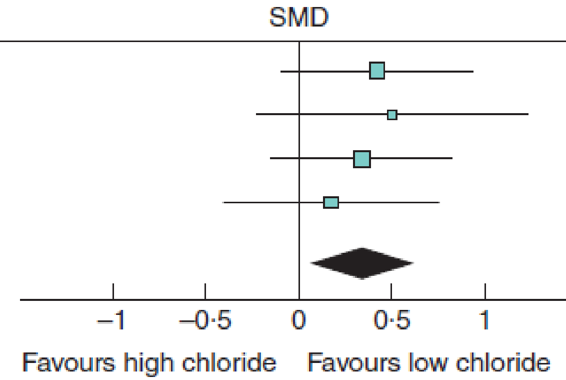


Blood transfusion requirement

Reference	Transfusion volume: High-chloride	Transfusion volume: Low-chloride	Weight (%)	SMD
Kim *et al.*[46]	459(279)	332(314)	29·6	0·42 (–0·09, 0·93)
Takil *et al.*[51]	1280(560)	960(680)	14·6	0·50 (–0·23, 1·23)
Waters *et al.*[14]	780(489)	560(776)	32·8	0·34 (–0·15, 0·82)
Young *et al.*[54]	3·2(8·3)	1·8(7·6)	23·1	0·17 (–0·41, 0·75)
Total			100·0	0·35 (0·07, 0·63)

Heterogeneity: $\chi^2 = 0{\cdot}60$, 3 d.f., $P = 0{\cdot}90$; $I^2 = 0\%$

Test for overall effect: $Z = 2{\cdot}45$, $P = 0{\cdot}01$



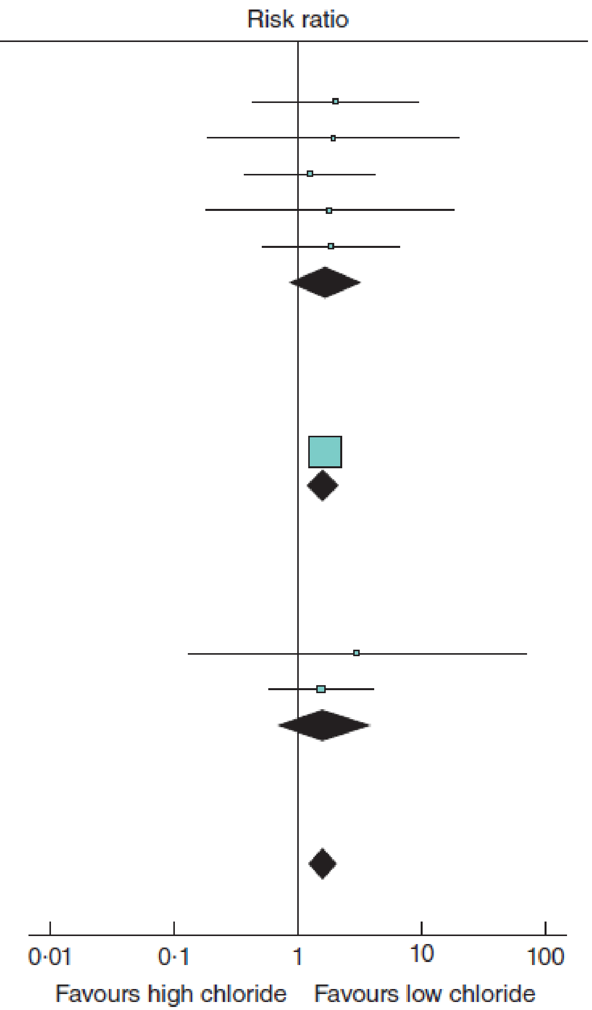
Acute Kidney Injury

Reference	AKI/renal failure: High-chloride	AKI/renal failure: Low-chloride	Weight (%)	Risk ratio
RCTs				
Hadimioglu *et al.*[12]	3 of 30	3 of 60	2·4	2·00 (0·43, 9·32)
O'Malley *et al.*[50]	2 of 26	1 of 25	1·2	1·92 (0·19, 19·90)
Waters *et al.*[14]	5 of 33	4 of 33	4·8	1·25 (0·37, 4·25)
Wu *et al.*[53]	2 of 21	1 of 19	1·3	1·81 (0·18, 18·39)
Young *et al.*[54]	6 of 24	3 of 22	3·7	1·83 (0·52, 6·46)
Subtotal	18 of 134	12 of 159	13·4	1·66 (0·83, 3·31)
Heterogeneity: $\chi^2 = 0{\cdot}31$, 4 d.f., $P = 0{\cdot}99$; $I^2 = 0\%$				
Test for overall effect: $Z = 1{\cdot}44$, $P = 0{\cdot}15$				
CCTs				
Yunos *et al.*[26,55]	105 of 760	65 of 773	77·0	1·64 (1·23, 2·20)
Subtotal	105 of 760	65 of 773	77·0	1·64 (1·23, 2·20)
Heterogeneity: not applicable				
Test for overall effect: $Z = 3{\cdot}33$, $P < 0{\cdot}001$				
Observational/retrospective studies				
Berger *et al.*[41]	1 of 20	0 of 20	0·6	3·00 (0·13, 69·52)
Shaw *et al.*[27]	23 of 2778	5 of 926	9·0	1·53 (0·58, 4·02)
Subtotal	24 of 2798	5 of 946	9·6	1·63 (0·65, 4·07)
Heterogeneity: $\chi^2 = 0{\cdot}16$, 1 d.f., $P = 0{\cdot}69$; $I^2 = 0\%$				
Test for overall effect: $Z = 1{\cdot}04$, $P = 0{\cdot}30$				
Total	147 of 3692	82 of 1878	100·0	1·64 (1·27, 2·13)

Heterogeneity: $\chi^2 = 0{\cdot}47$, 7 d.f., $P = 1{\cdot}00$; $I^2 = 0\%$

Test for overall effect: $Z = 3{\cdot}76$, $P < 0{\cdot}001$

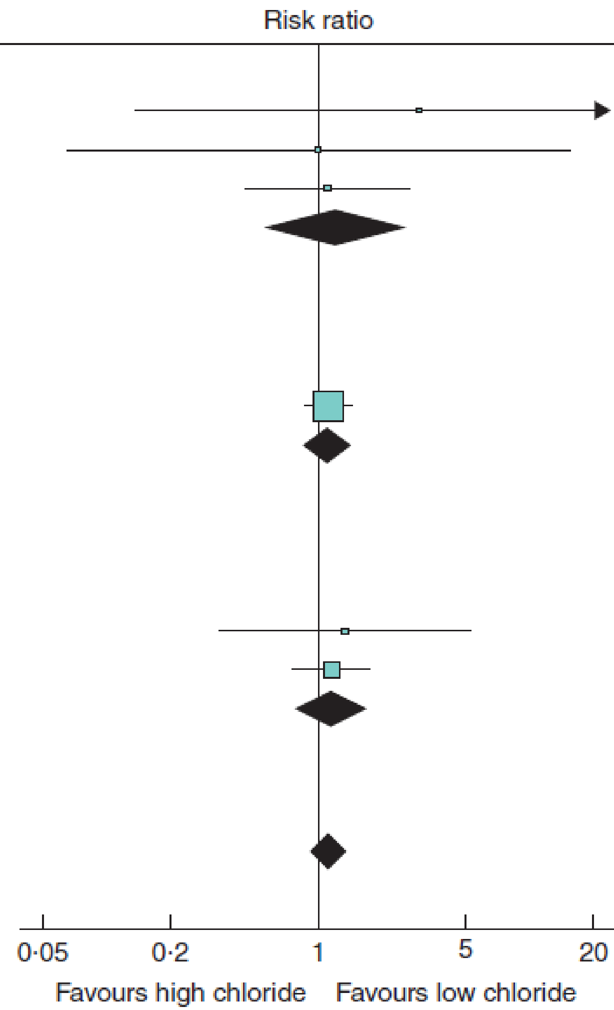
Test for subgroup differences: $\chi^2 = 0{\cdot}00$, 2 d.f., $P = 1{\cdot}00$; $I^2 = 0\%$



Mortality

Reference	Mortality: High-chloride	Mortality: Low-chloride	Weight (%)	Risk ratio
RCTs				
Mahajan *et al.*[47]	1 of 11	0 of 11	0·3	3·00 (0·14, 66·53)
Waters *et al.*[14]	1 of 33	1 of 33	0·7	1·00 (0·07, 15·33)
Young *et al.*[54]	8 of 33	7 of 32	4·6	1·11 (0·45, 2·70)
Subtotal	10 of 77	8 of 76	5·6	1·21 (0·53, 2·72)
Heterogeneity: $\chi^2 = 0{\cdot}38$, 2 d.f., $P = 0{\cdot}82$; $I^2 = 0\%$				
Test for overall effect: $Z = 0{\cdot}45$, $P = 0{\cdot}65$				
CCTs				
Yunos *et al.*[26,55]	112 of 760	102 of 773	66·0	1·12 (0·87, 1·43)
Subtotal	112 of 760	102 of 773	66·0	1·12 (0·87, 1·43)
Heterogeneity: not applicable				
Test for overall effect: $Z = 0{\cdot}87$, $P = 0{\cdot}38$				
Observational/retrospective studies				
Berger *et al.*[41]	4 of 20	3 of 20	2·0	1·33 (0·34, 5·21)
Shaw *et al.*[27]	93 of 2778	27 of 926	26·4	1·15 (0.75, 1·75)
Subtotal	97 of 2798	30 of 946	28·4	1·16 (0.78, 1·74)
Heterogeneity: $\chi^2 = 0{\cdot}04$, 1 d.f., $P = 0{\cdot}84$; $I^2 = 0\%$				
Test for overall effect: $Z = 0{\cdot}72$, $P = 0{\cdot}47$				
Total	219 of 3635	140 of 1795	100·0	1·13 (0·92, 1·39)

Heterogeneity: $\chi^2 = 0{\cdot}46$, 5 d.f., $P = 0{\cdot}99$; $I^2 = 0\%$
Test for overall effect: $Z = 1{\cdot}20$, $P = 0{\cdot}23$
Test for subgroup differences: $\chi^2 = 0{\cdot}05$, 2 d.f., $P = 0{\cdot}98$; $I^2 = 0\%$



Online First >

Original Investigation | October 07, 2015

CARING FOR THE CRITICALLY ILL PATIENT

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit

The SPLIT Randomized Clinical Trial FREE ONLINE FIRST

Paul Young, FCICM[1,2]; Michael Bailey, PhD[3]; Richard Beasley, DSc[1]; Seton Henderson, FCICM[1,4]; Diane Mackle, MN[1]; Colin McArthur, FCICM[1,3,5]; Shay McGuinness, FANZCA[1,3,6]; Jan Mehrtens, RN[4]; John Myburgh, PhD[7,8]; Alex Psirides, FCICM[2]; Sumeet Reddy, MBChB[1]; Rinaldo Bellomo, FCICM[3,9] ; for the SPLIT Investigators and the ANZICS CTG

The 0.9% Saline vs Plasma-Lyte 148 (PL-148) for ICU fluid Therapy (SPLIT) trial was a prospective, investigator-initiated, multicenter, blinded, cluster-randomized, double-crossover study conducted in 4 tertiary ICUs in New Zealand.[11] Three study ICUs were adult or mixed (adult and pediatric) general medical and surgical ICUs and 1 ICU had a predominance of cardiothoracic and vascular surgical patients (eMethods in Supplement 2).

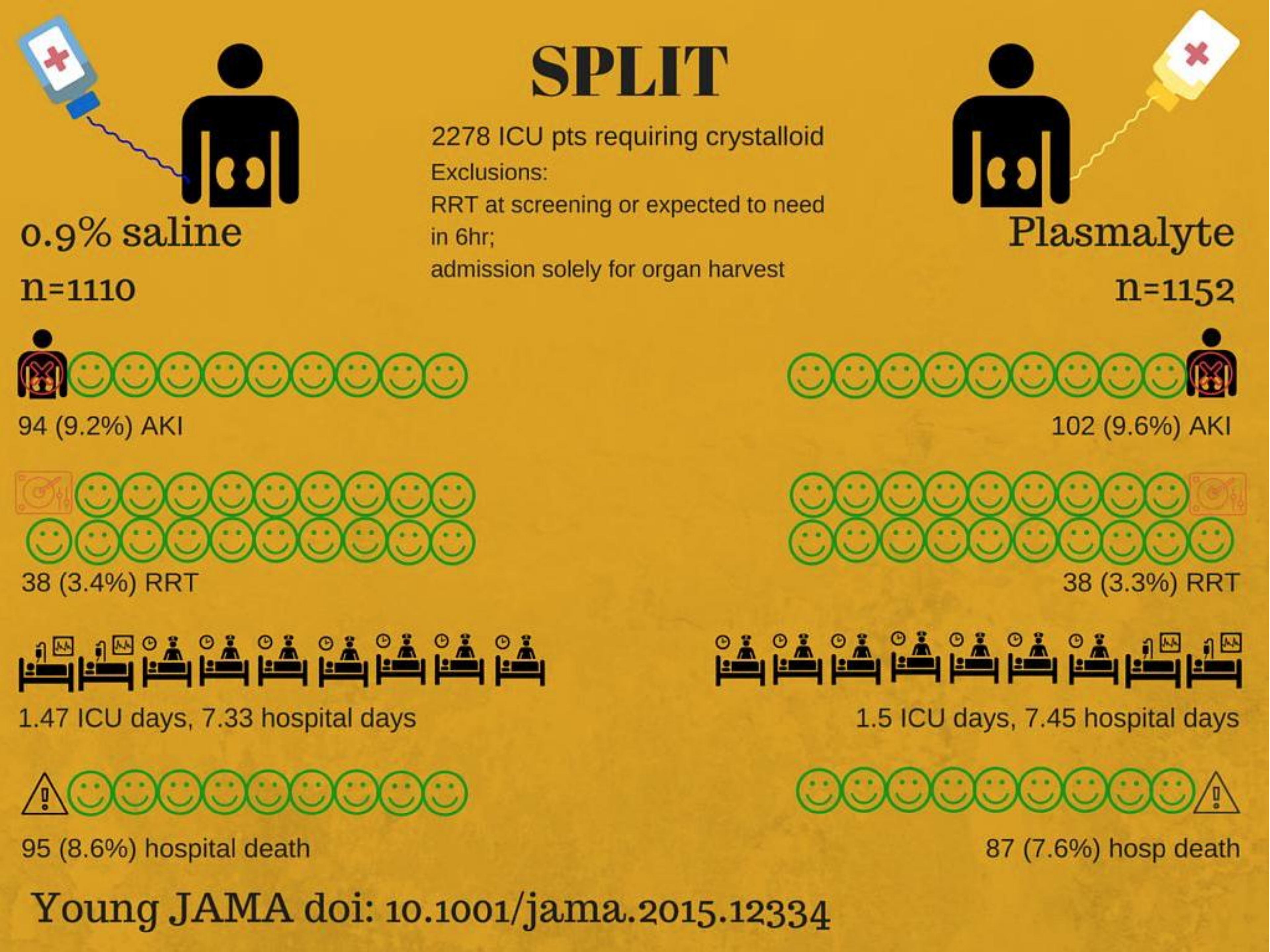

SPLIT
2278 ICU pts requiring crystalloid
Exclusions:
RRT at screening or expected to need in 6hr;
admission solely for organ harvest
0.9% saline
n=1110
Plasmalyte
n=1152
94 (9.2%) AKI
102 (9.6%) AKI
38 (3.4%) RRT
38 (3.3%) RRT
1.47 ICU days, 7.33 hospital days
1.5 ICU days, 7.45 hospital days
95 (8.6%) hospital death
87 (7.6%) hosp death
Young JAMA doi: 10.1001/jama.2015.12334

Table 2. Outcomes for Patients in the Intensive Care Unit Receiving Buffered Crystalloid vs Saline Fluid Therapy

Variable	No./Total No. (%)		Absolute Difference (95% CI)	Relative Risk (95% CI)	P Value
	Buffered Crystalloid	Saline			
Primary Outcome					
Acute kidney injury or failure[a]	102/1067 (9.6)	94/1025 (9.2)	0.4 (−2.1 to 2.9)	1.04 (0.80 to 1.36)	.77
Secondary Outcomes (Renal Outcomes)					
RIFLE[b]					
Risk	123/1067 (11.5)	107/1025 (10.4)	1.1 (−1.6 to 3.8)	1.10 (0.86 to 1.41)	.44
Injury	46/1067 (4.3)	57/1025 (5.6)	−1.2 (−3.1 to 0.6)	0.78 (0.53 to 1.13)	.19
Failure	54/1067 (5.1)	36/1025 (3.5)	1.5 (−0.2 to 3.3)	1.44 (0.95 to 2.18)	.09
Loss	2/1067 (0.2)	1/1025 (0.1)	0	1.92 (0.17 to 21.16)	>.99
End-stage renal failure	0/1067 (0)	0/1025 (0)			
KDIGO stage[c]					
1	194/1067 (18.2)	194/1025 (18.9)	−0.7 (−4.1 to 2.6)	0.96 (0.80 to 1.15)	.69
2	43/1067 (4.0)	46/1025 (4.5)	−0.5 (−2.2 to 1.3)	0.90 (0.60 to 1.4)	.67
3	62/1067 (5.8)	58/1025 (5.7)	0.2 (−1.8 to 2.1)	1.03 (0.73 to 1.45)	.93
RRT use and indications for RRT initiation					
RRT use	38/1152 (3.3)	38/1110 (3.4)	−0.1 (−1.6 to 1.4)	0.96 (0.62 to 1.50)	.91
Oliguria	10/1152 (0.9)	11/1110 (1.0)	−0.1 (−0.9 to 0.7)	0.88 (0.37 to 2.05)	.83
Hyperkalemia with serum potassium >6.5 mEq/L	4/1152 (0.3)	2/1110 (0.2)	0.2 (−0.3 to 0.6)	1.93 (0.35 to 10.50)	.69
Acidemia with pH <7.20	13/1152 (1.1)	9/1110 (0.8)	0.3 (−0.5 to 1.1)	1.39 (0.60 to 3.24)	.52
Serum urea nitrogen >70 mg/dL	5/1152 (0.4)	10/1110 (0.9)	−0.5 (−1.1 to 0.2)	0.48 (0.17 to 1.41)	.20
Serum creatinine >3.39 mg/dL	16/1152 (1.4)	13/1110 (1.2)	0.2 (−0.7 to 1.1)	1.19 (0.57 to 2.45)	.71
Organ edema	6/1152 (0.5)	11/1110 (1.0)	−0.5 (−1.2 to 0.2)	0.53 (0.20 to 1.42)	.23
Other renal failure-related indication	3/1152 (0.3)	9/1110 (0.8)	−0.6 (−1.2 to 0.1)	0.32 (0.09 to 1.18)	.09
Other non-renal failure-related indication	0/1152 (0)	2/1110 (0.2)	−0.2 (−0.4 to 0.1)		.24
Ongoing use after hospital discharge	0/1152 (0)	0/1110 (0)			
Δ Creatinine, mean (95% CI), mg/dL[d]	0.21 (0.16 to 0.25)	0.18 (0.13 to 0.23)	0.03 (−0.04 to 0.10)[e]		.42
Service utilization, geometric mean (95% CI)					
ICU, d	1.50 (1.41 to 1.60)	1.47 (1.39 to 1.57)	1.02 (0.94 to 1.11)[f]		.58
Hospital, d	7.45 (7.05 to 7.87)	7.33 (6.94 to 7.76)	1.01 (0.94 to 1.10)[f]		.72
Mechanical ventilation, h	15.32 (13.83 to 16.97)	14.24 (12.82 to 15.82)	1.05 (0.91 to 1.21)[f]		.48
Use of mechanical ventilation	790/1152 (68.6)	751/1110 (67.7)	0.9 (−2.9 to 4.8)	1.01 (0.96 to 1.07)	.65
ICU readmission required during index hospital admission	80/1152 (6.9)	57/1110 (5.1)	1.8 (−0.2 to 3.8)	1.35 (0.97 to 1.88)	.08
Mortality					
Death in ICU	76/1152 (6.6)	80/1110 (7.2)	−0.6 (−2.7 to 1.5)	0.92 (0.68 to 1.24)	.62
Death in hospital	87/1152 (7.6)	95/1110 (8.6)	−1.0 (−3.3 to 1.2)	0.88 (0.67 to 1.17)	.40

eTable 2. Intravenous fluids and blood products administered in the 24 hours prior to enrollment

	Volume of fluid administered (mL) and proportion of patients receiving fluid– mean ± SD; median [IQR]; no. (%)	
Fluid	**Buffered crystalloid group**	**Saline group**
Plasma-Lyte 148 ®	1748 ± 1964; 1200 [0-3000]; 726 (63)	1649 ± 1841;1000 [0-3000]; 675 (61)
0.9% saline	551 ± 1157; 0 [0-875]; 343 (30)	549 ± 1098; 0 [0-1000]; 351 (32)
5% dextrose	47 ± 212; 0 [0-0]; 141 (12)	42 ± 196; 0 [0-0];124 (11)
Pediatric maintenance fluids[a]	0.1 ± 4; 0 [0-0]; 1 (0)	0.3 ± 7; 0 [0-0]; 2 (0)
Other crystalloids	385 ± 1155; 0 [0-0]; 181 (16)	361 ± 1081; 0 [0-0]; 189 (18)
4% albumin	41 ± 253; 0 [0-0]; 40 (3)	34 ± 254; 0 [0-0]; 31 (3)
20% albumin	20 ± 62; 0 [0-0]; 115 (10)	20 ± 83; 0 [0-0]; 98 (9)
Gelofusine ®	13 ±137; 0 [0-0]; 17 (1)	7 ± 68; 0 [0-0]; 15 (1)
Voluven or Volulyte ®	1.7 ± 29; 0 [0-0]; 4 (0)	1.6 ± 34; 0 [0-0]; 3 (0)
Other colloids	0.3 ± 11; 0 [0-0]; 1 (0)	1.6 ± 53; 0 [0-0]; 1 (0)
Blood product		
Packed red cells	149 ± 703; 0 [0-0]; 165 (14)	122 ± 479; 0 [0-0]; 158 (14)
Fresh frozen plasma	91 ± 557; 0 [0-0]; 104 (9)	77 ± 355; 0 [0-0]; 93 (8)
Platelets	51 ± 224; 0 [0-0]; 103 (9)	43 ± 179; 0 [0-0]; 88 (8)
Cryoprecipitate	20 ± 132; 0 [0-0]; 66 (6)	17 ± 81; 0 [0-0]; 63 (6)

PLOS | ONE

RESEARCH ARTICLE

Dyschloremia Is a Risk Factor for the Development of Acute Kidney Injury in Critically Ill Patients

Min Shao[1,2,3], Guangxi Li[2,4], Kumar Sarvottam[1,2], Shengyu Wang[2,5], Charat Thongprayoon[2], Yue Dong[2], Ognjen Gajic[2,6], Kianoush Kashani[1,2,6]*

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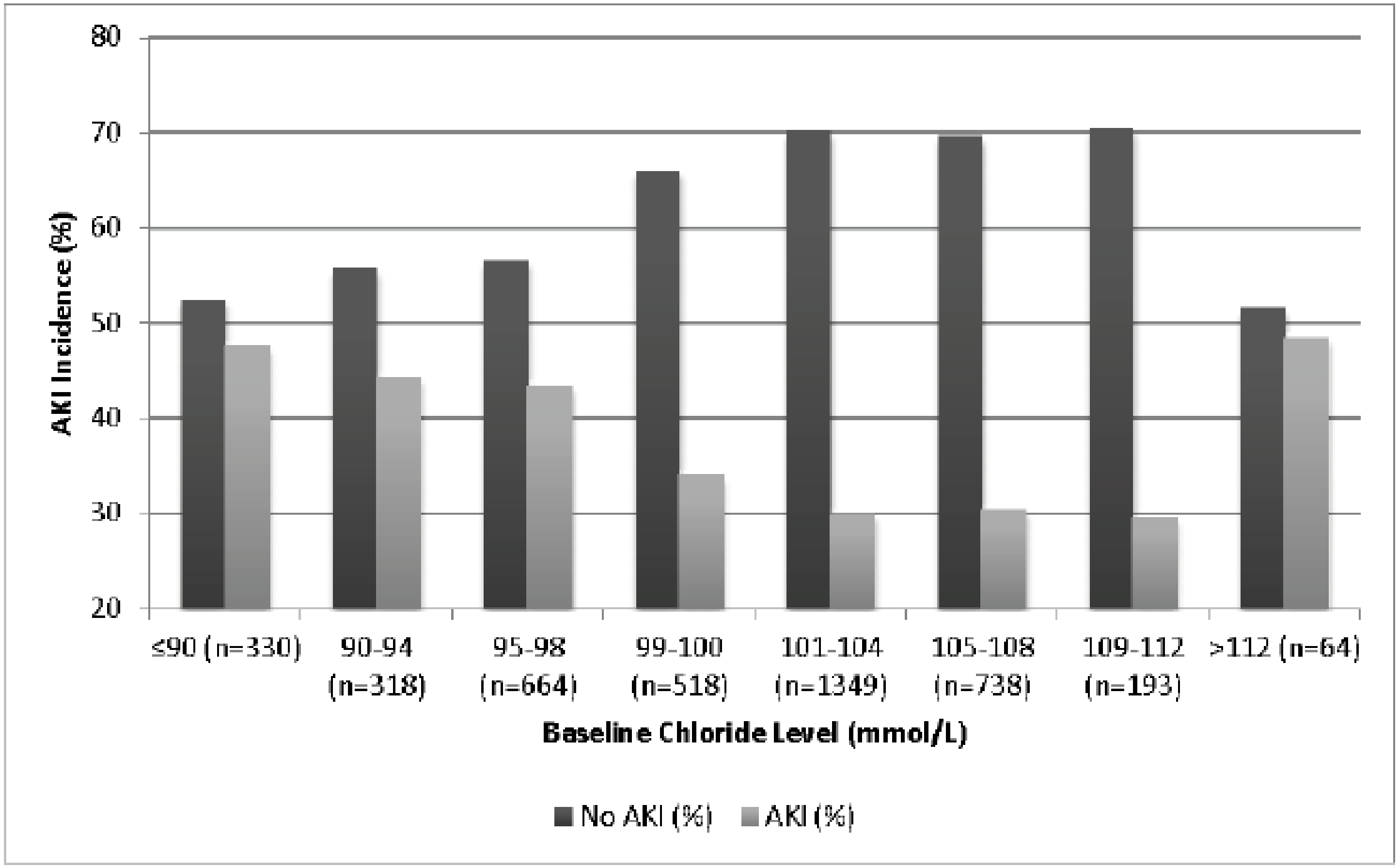
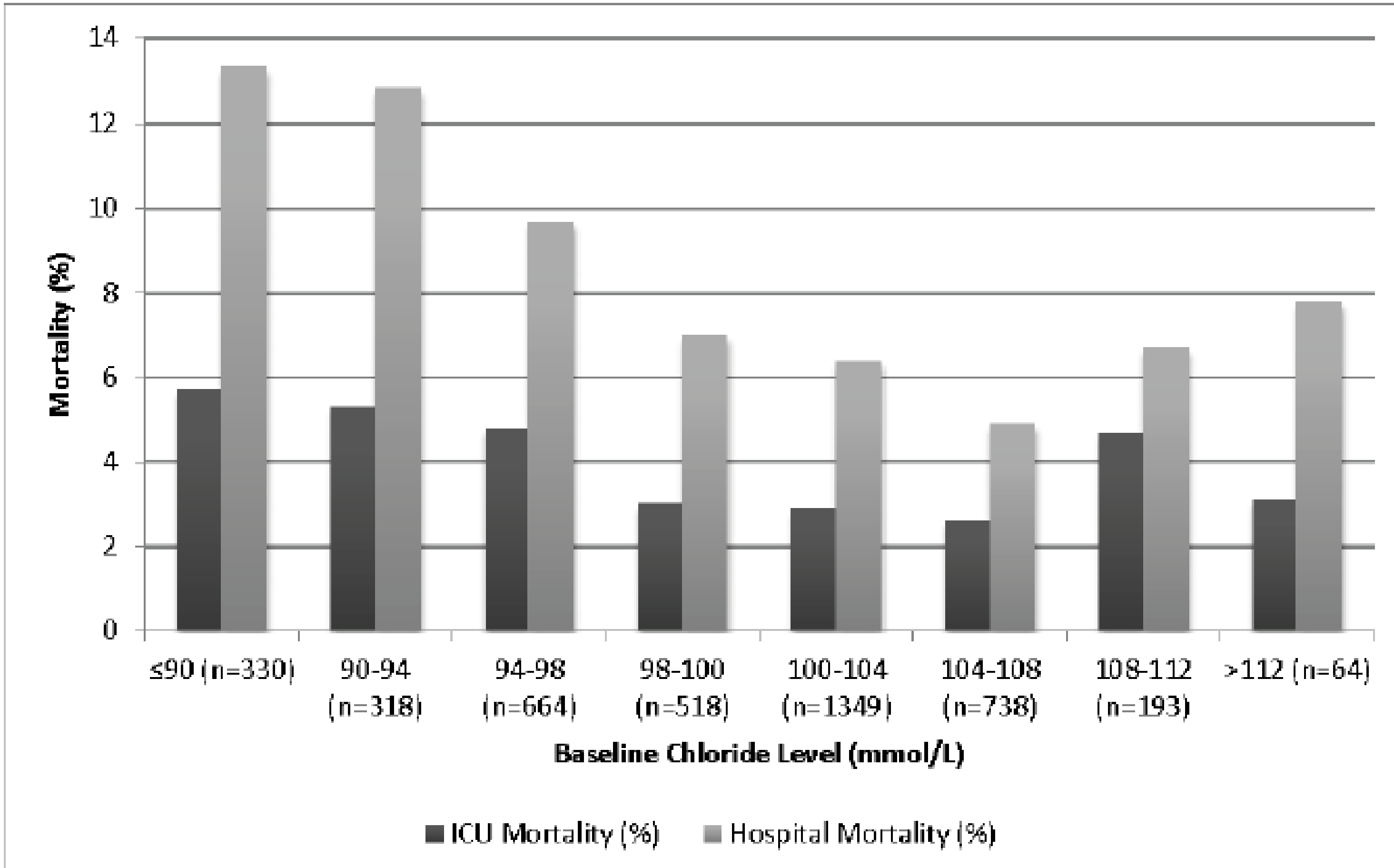
PLOS ONE | DOI:10.1371/journal.pone.0160322 August 4, 2016

Chloride and AKI incidence



Chloride and mortality



Allen *et al. BMC Pediatrics* (2016) 16:117
DOI 10.1186/s12887-016-0652-4

BMC Pediatrics

RESEARCH ARTICLE Open Access

A randomized trial of Plasma-Lyte A and 0.9 % sodium chloride in acute pediatric gastroenteritis

Coburn H. Allen[1*], Ran D. Goldman[2], Seema Bhatt[3], Harold K. Simon[4], Marc H. Gorelick[5], Philip R. Spandorfer[6], David M. Spiro[7], Sharon E. Mace[8], David W. Johnson[9], Eric A. Higginbotham[1], Hongyan Du[10], Brendan J. Smyth[11], Carol R. Schermer[10] and Stuart L. Goldstein[3]

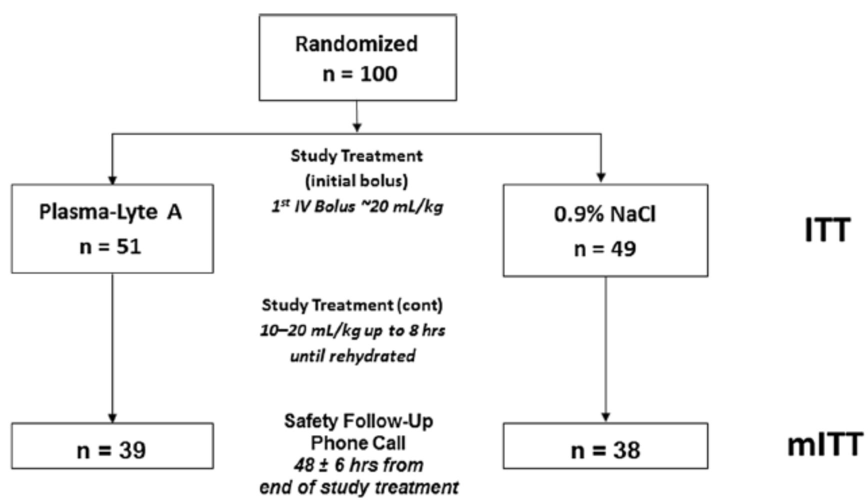


Table 2 Primary and secondary outcomes (mITT population)

	Plasma-Lyte A $n = 39$	0.9 % NaCl $n = 38$	*P* value
Bicarbonate <23 mEq/L			
Baseline (hour 0)	16.9 ± 3.51	17.8 ± 2.82	.004
Hour 4	18.5 ± 3.74	18.0 ± 3.67	
Bicarbonate <12 mEq/L			
Baseline (hour 0) (n)	9.3 ± 0.58 (3)	– (0)	NA[b]
Hour 4 (n)	14.3 ± 4.16 (3)	– (0)	
Bicarbonate ≥12–16 mEq/L			
Baseline (hour 0) (n)	14.5 ± 1.34 (13)	14.6 ± 1.29 (13)	.04
Hour 4 (n)	16.1 ± 2.28 (12)	14.7 ± 2.90 (11)	
Bicarbonate >16–22 mEq/L			
Baseline (hour 0) (n)	19.23 ± 1.86 (23)	19.51 ± 1.68 (25)	.11
Hour 4 (n)	20.35 ± 3.18 (22)	19.53 ± 2.95 (24)	
Chloride, mmol/L			
Baseline	103.03 ± 4.74	103.53 ± 4.19	<0.001
Hour 4	104.49 ± 3.18	108.51 ± 4.87	
Gorelick dehydration scale			
Baseline (hour 0)	5.2 ± 0.93	5.3 ± 1.11	.03
Hour 2	2.0 ± 1.45	2.8 ± 1.74	
Hour 4	0.81 ± 0.84	1.41 ± 1.08	.08
FLACC pain scale			
Baseline (Hour 0)	2.0 ± 1.91	1.7 ± 2.00	.03
Hour 2	0.6 ± 0.98	1.7 ± 2.59	

Shaw *et al. Critical Care* (2015) 19:334
DOI 10.1186/s13054-015-1045-z

CRITICAL CARE

RESEARCH Open Access

Impact of intravenous fluid composition on outcomes in patients with systemic inflammatory response syndrome

Andrew D. Shaw[1*], Carol R. Schermer[2], Dileep N. Lobo[3], Sibyl H. Munson[4], Victor Khangulov[4], David K Hayashida[4] and John A. Kellum[5]

Methods: This was a propensity-matched cohort study in hospitalized patients receiving at least 500 mL IV crystalloid within 48 hours of SIRS. Patient data was extracted from a large multi-hospital electronic health record database between January 1, 2009, and March 31, 2013. The primary outcome was in-hospital mortality. Secondary outcomes included length of stay, readmission, and complications measured by ICD-9 coding and clinical definitions. Outcomes were adjusted for illness severity using the Acute Physiology Score. Of the 91,069 patients meeting inclusion criteria, 89,363 (98 %) received 0.9 % saline whereas 1706 (2 %) received a calcium-free balanced solution as the primary fluid.

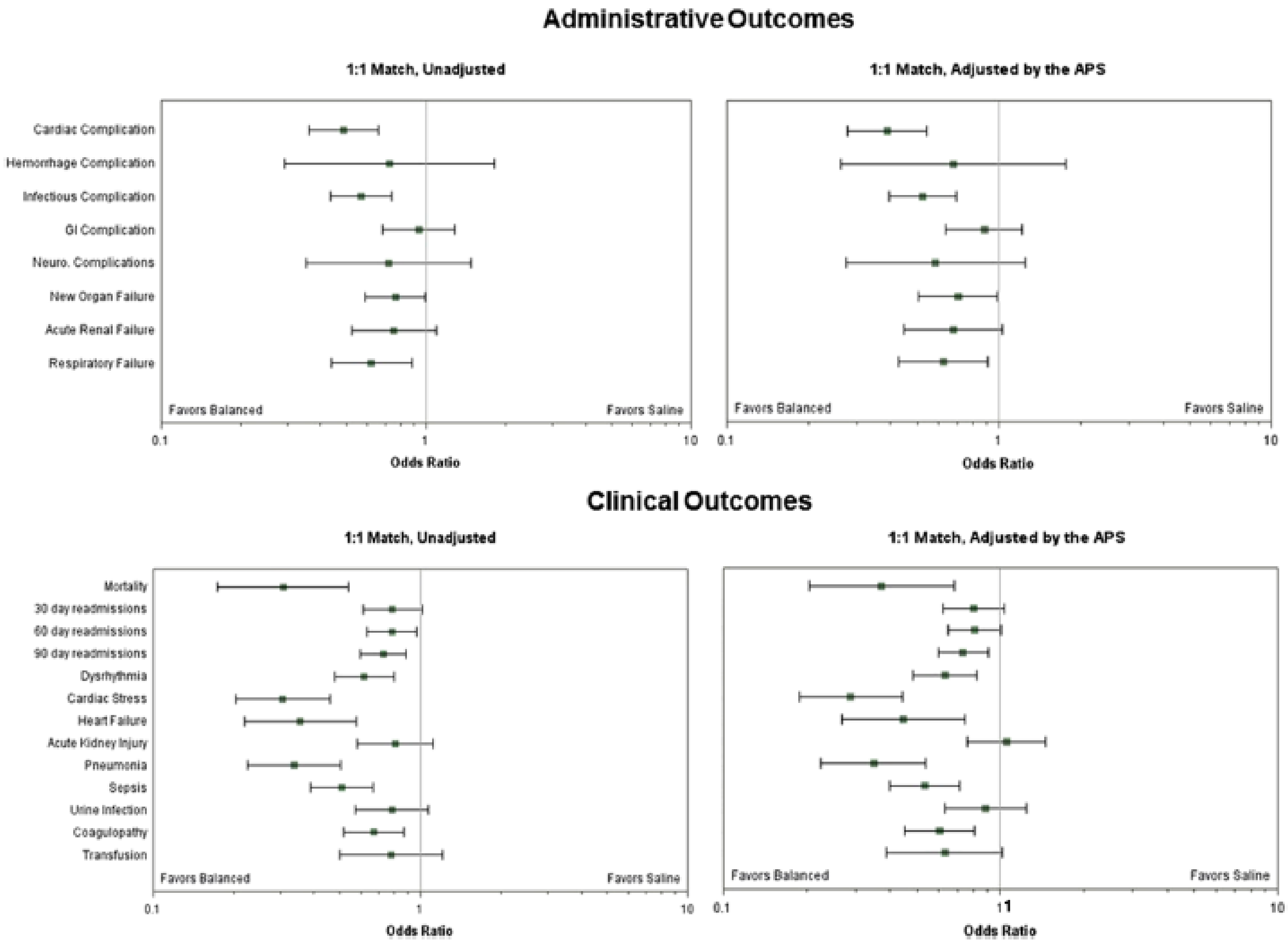


Fig. 2 Administrative and clinical outcomes unadjusted and adjusted for Acute Physiology Score

Van Regenmortel *et al. Ann. Intensive Care (2016) 6:91*
DOI 10.1186/s13613-016-0193-x

Annals of Intensive Care

RESEARCH **Open Access**

CrossMark

Impact of chloride and strong ion difference on ICU and hospital mortality in a mixed intensive care population

Niels Van Regenmortel[1,2*], Walter Verbrugghe[1], Tim Van den Wyngaert[3,4] and Philippe G. Jorens[1,4]

Methods: Retrospective cohort study in an academic tertiary intensive care unit on 8830 adult patients who stayed at least 24 h in the ICU was carried out. Patients admitted after elective cardiac surgery were treated as a separate subgroup ($n = 2350$). Analyses were performed using multivariable logistic regression. All statistical models were extensively adjusted for confounders, including comorbidity, admission diagnosis, other electrolytes and acid–base parameters.

Results: Severe hyperchloremia (>110 mmol/L), but not low (SID) was significantly associated with increased mortality in the ICU (odds ratio vs. normochloremia 1.81; 95 % CI 1.32–2.50; $p < 0.001$) and the hospital (odds ratio 1.49; 95 % CI 1.14–1.96; $p = 0.003$). Hyperchloremia and low (SID) were encountered in the majority of patients admitted after cardiac surgery (in 86.9 and 47.2 %, respectively), but were not negatively associated with mortality.

30-Day mortality

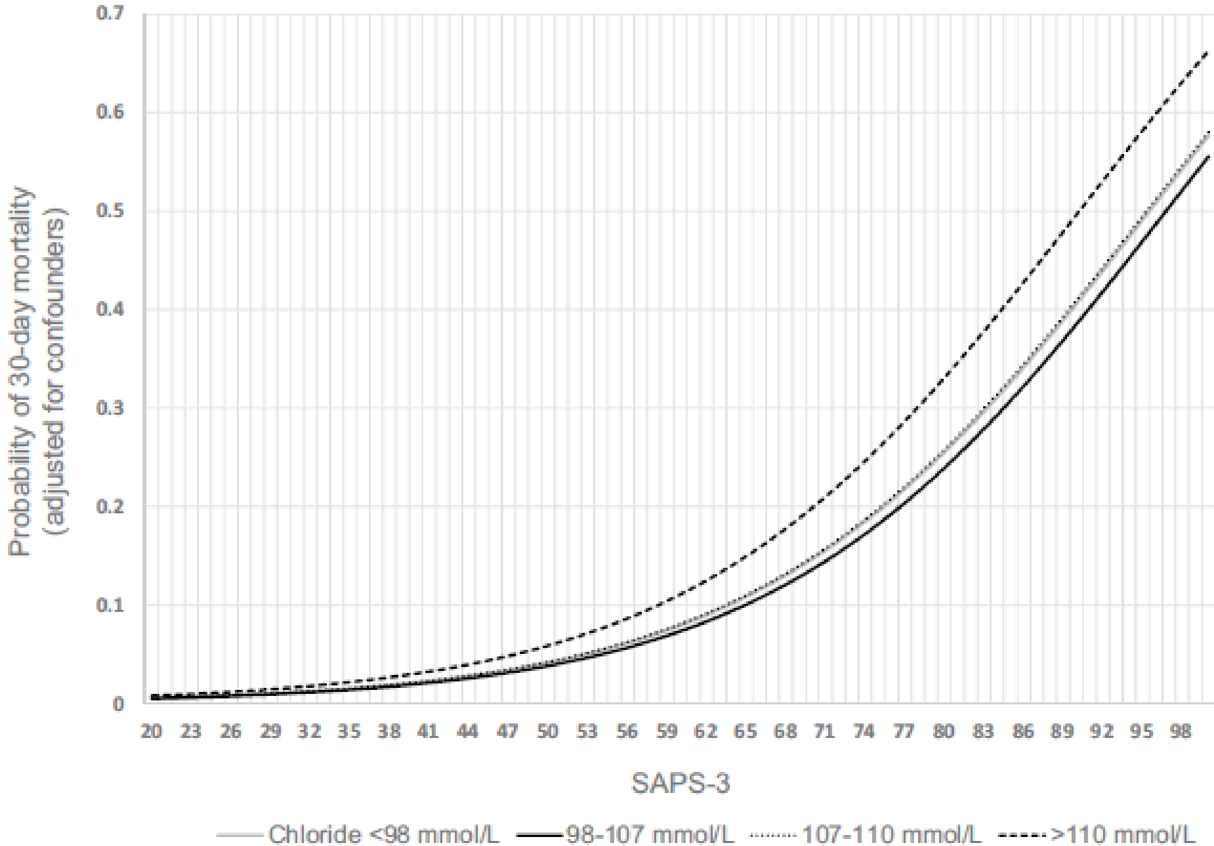


Fig. 1 Probability of 30-day mortality per chloride category based on the logistic regression model in Table 2. Simulation using a lactate level of 2 mEq/L, an admission diagnosis associated with a high risk of death (e.g., sepsis; Additional file 2: Table S2), no comorbidities and a normal sodium level

Chloride Content of Fluids Used for Large-Volume Resuscitation Is Associated With Reduced Survival

Ayan Sen, MD, MS, FCCP; Christopher M. Keener, MS; Florentina E. Sileanu, MS; Emily Foldes, MS; Gilles Clermont, MD, CM, MS; Raghavan Murugan, MD, MS, FRCP, FCCM; John A. Kellum, MD, MCCM

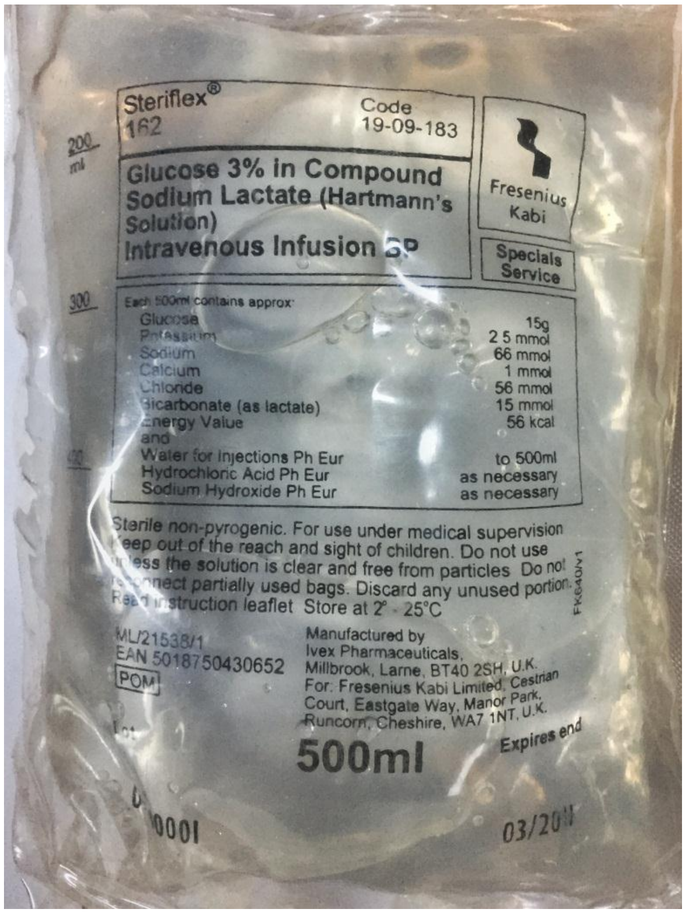
Objective: We sought to investigate if the chloride content of fluids used in resuscitation was associated with short- and long-term outcomes.
Design: We identified patients who received large-volume fluid resuscitation, defined as greater than 60mL/kg over a 24-hour period. Chloride load was determined for each patient based on the chloride ion concentration of the fluids they received during large-volume fluid resuscitation multiplied by the volume of fluids. We compared the development of hyperchloremic acidosis, acute kidney injury, and survival among those with higher and lower chloride loads.
Setting: University Medical Center.
Patients: Patients admitted to ICUs from 2000 to 2008.
Interventions: None.
Measurements and Main Results: Among 4,710 patients receiving large-volume fluid resuscitation, hyperchloremic acidosis was documented in 523 (11%). Crude rates of hyperchloremic acidosis, acute kidney injury, and hospital mortality all increased significantly as chloride load increased ($p < 0.001$). However, chloride load was no longer associated with hyperchloremic acidosis or acute kidney injury after controlling for total fluids, age, and baseline severity. Conversely, each 100 mEq increase in chloride load was associated with a 5.5% increase in the hazard of death even after controlling for total fluid volume, age, and severity ($p = 0.0015$) over 1 year.
Conclusions: Chloride load is associated with significant adverse effects on survival out to 1 year even after controlling for total fluid load, age, and baseline severity of illness. However, the relationship between chloride load and development of hyperchloremic acidosis or acute kidney injury is less clear, and further research is needed to elucidate the mechanisms underlying the adverse effects of chloride load on survival. (*Crit Care Med* 2016; XX:00–00)
Key Words: acute kidney injury; chloride; metabolic acidosis; saline; survival

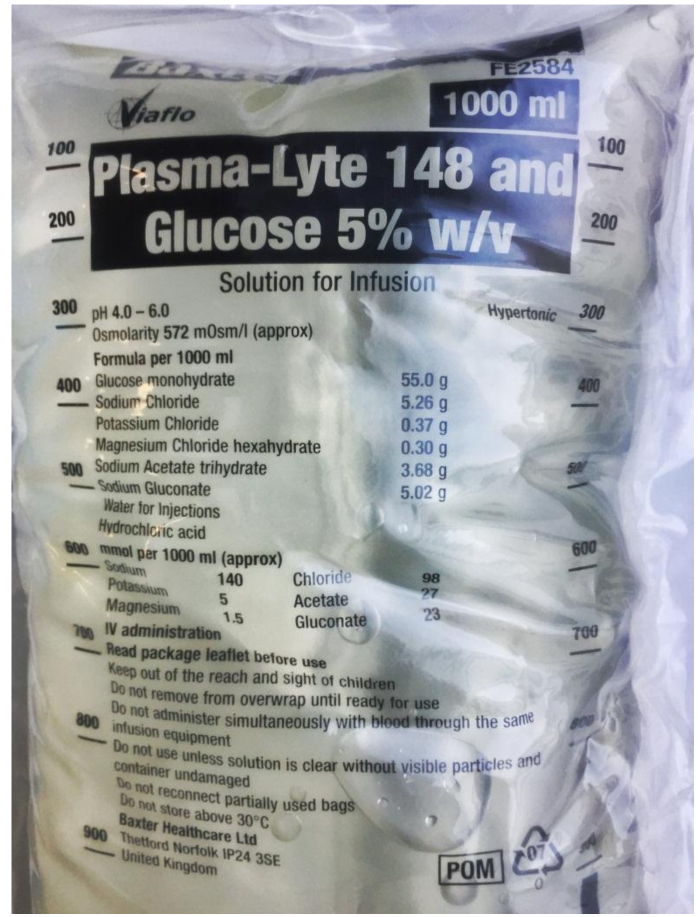
TABLE 2. Outcomes Stratified by Chloride Load

Quartile mEq	Q1 (323–491)	Q2 (492–635)	Q3 (636–848)	Q4 (849–5,432)	*p*
Hyperchloremic acidosis within 24 hr of large-volume fluid resuscitation, *n* (%)					
Missing	758 (64.4)	748 (63.5)	737 (62.6)	651 (55.3)	< 0.001
No	335 (28.5)	341 (28.9)	321 (27.2)	296 (25.1)	
Yes	84 (7.1)	89 (7.6)	120 (10.2)	230 (19.5)	
Maximum Kidney Disease: Improving Global Outcomes, *n* (%)					
No acute kidney injury	329 (27.9)	245 (20.8)	226 (19.2)	163 (13.9)	< 0.001
Stage 1	221 (18.8)	211 (17.9)	165 (14.0)	151 (12.8)	
Stage 2	371 (31.5)	421 (35.7)	433 (36.8)	362 (30.8)	
Stage 3	256 (21.7)	301 (25.5)	354 (30.1)	499 (42.5)	
Hospital mortality, *n* (%)	226 (19.2)	285 (24.2)	298 (25.3)	417 (35.4)	< 0.001
Mortality after ICU admission, days, *n* (%)					
30	207 (17.6)	266 (22.6)	289 (24.5)	387 (32.9)	< 0.001
90	294 (24.9)	343 (29.1)	374 (31.7)	480 (40.8)	< 0.001
365	407 (34.6)	432 (36.7)	481 (40.8)	553 (46.9)	< 0.001

Q1–Q4 = quartiles 1 through 4.

Lactate Vs Acetate





Lactate Vs Acetate

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BURNS

Safety of resuscitation with Ringer's acetate solution in severe burn (VolTRAB)—An observational trial

Jochen Gille[a,*], *Birgit Klezcewski*[a], *Michael Malcharek*[a], *Thomas Raff*[b], *Martin Mogk*[c], *Armin Sablotzki*[a], *Hischam Taha*[d]

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[d] *Department of Plastic & Reconstructive Surgery, Royal Devon & Exeter Hospital Foundation Trust, Exeter, Devon, UK*

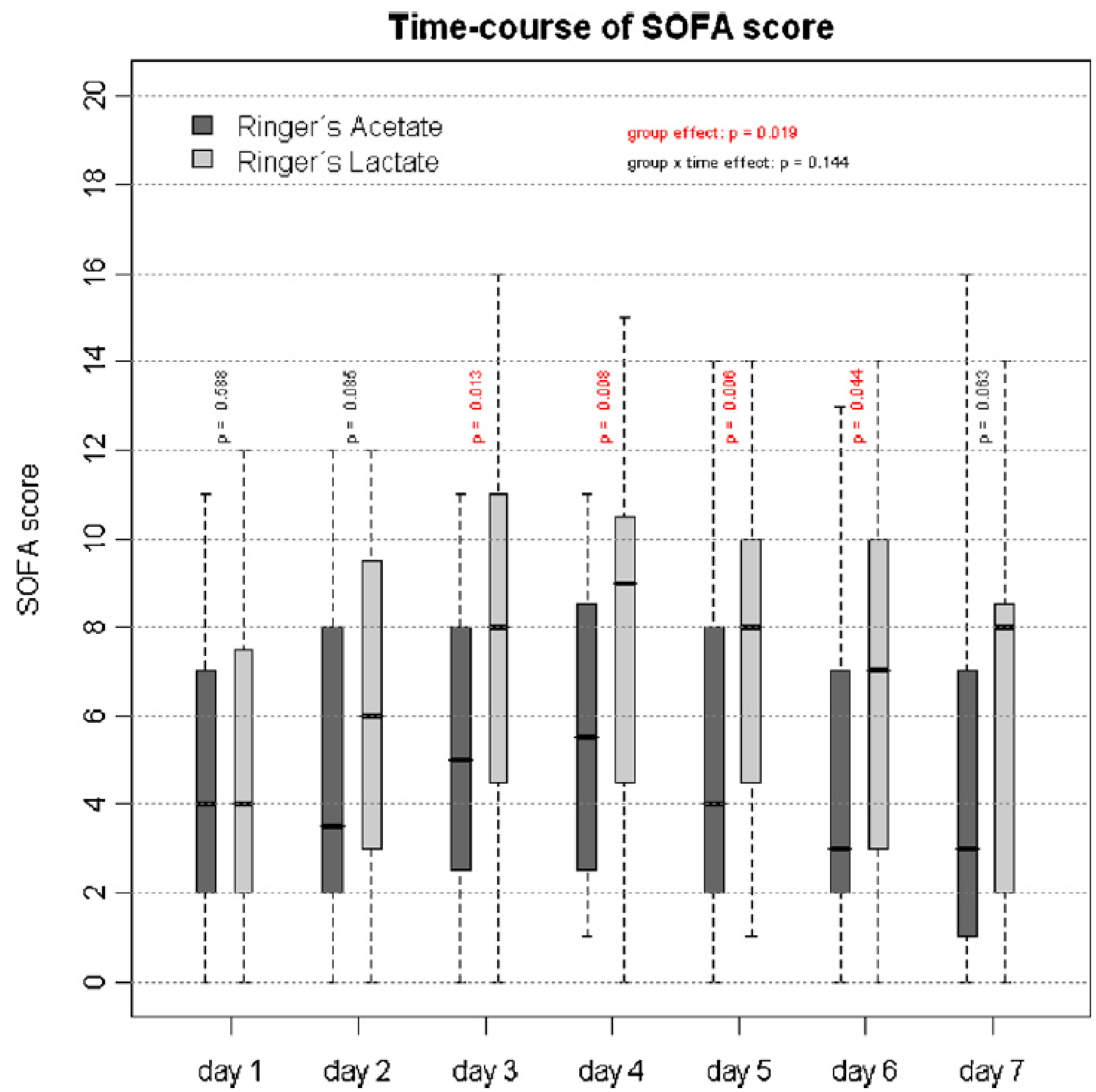


Fig. 1 – Variation of SOFA score during the first 7 days of admission.

ORIGINAL ARTICLE

The effects of plasmalyte-148 *vs.* Hartmann's solution during major liver resection: a multicentre, double-blind, randomized controlled trial

L. WEINBERG [1, 2, 3], B. PEARCE [1], R. SULLIVAN [4], L. SIU [5], N. SCURRAH [1]
C. TAN [1], M. BACKSTROM [5], M. NIKFARJAM [2], L. McNICOL [1]
D. STORY [2], C. CHRISTOPHI [2], R. BELLOMO [6]

(Minerva Anestesiol 2015;81:1288-97)

TABLE I.—*Physiochemical profiles of Plasmalyte-148 and Hartmann's solution compared to plasma. Values are an approximation, and stated exactly as printed on each litre of the solution.*

	Hartmann's	Plasmalyte	Plasma
Sodium, meq/L	129	140	140
Chloride, meq/L	109	98	104
Potassium, meq/L	5	5	4
Calcium, meq/L	2	0	2
Magnesium, meq/L	0	3	1
Acetate, meq/L	0	27	0
Gluconate meq/L	0	23	0
Lactate, meq/L	29	0	1
pH	6.5	7.4	7.4
eSID, meq/L	29	49	42
Osmolality (approximate) mOsm/L-	274	295	290-310

eSID: effective strong ion difference. Hartmann's solution and Plasmalyte manufactured by Baxter HealthCare, Toongabbie, NSW, Australia

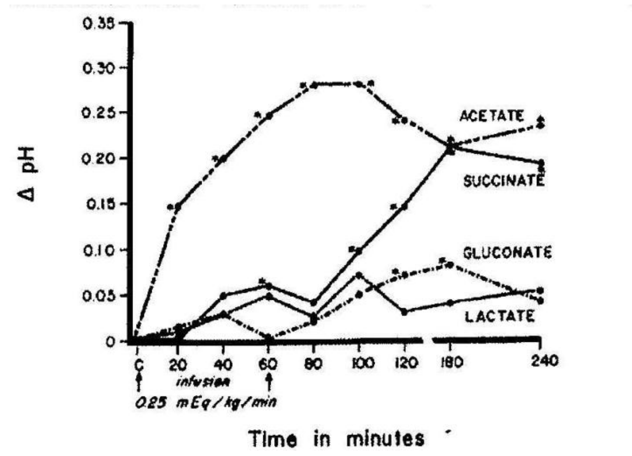
	Immediately postoperative		
	Plasmalyte N.=30	Hartmann's N.=30	p
SBE; mmol/L (N.=-2 to 2)	-0.9 (2.3)	-1.7 (2.2)	0.17
Lactate; mmol/L (N.=0.5-1.6)	1.9 (1.13)	2.9 (1.76)	**0.02**
pH (N.=7.35-7.45)	7.34 (0.05)	7.33 (0.05)	0.44
Na^+; mmol/L (N.=136-145)	139 (2.2)	138 (2.9)	0.09
Cl^-; mmol/L (N.=98-107)	106 (2.4)	108 (3.0)	**0.01**
K^+; mmol/L (N.=3.5-5.1)	4.1 (0.61)	4.4 (0.56)	0.19
Mg^{2+}; mmol/L (N.=0.66-1.07)	0.85 (0.12)	0.71 (0.11)	**<0.001**
Phosphate; mmol/L (N.=0.87-1.45)	1.2 (0.19)	1.4 (0.15)	0.32
Ca^{2+}; mmol/L (N.=2.15-2.55)	1.97 (0.37)	1.98 (0.50)	0.93
Ca^{2+} (ionized); mmol/L (N.=1.13-1.32)	1.07 (0.06)	1.14 (0.06)	**<0.001**
eSID; meq/L (N.=40-42)	37.2 (3.39)	33.5 (5.34)	**0.002**
Na^+ Cl^- difference; mmol·L^{-1} (N.=38)	32 (3.1)	29 (4.3)	**0.004**
Albumin; g/L (N.=35-52)	30 (5.5)	28 (7.2)	0.15
ALT; IU (N.<33)	251 (180.1)	347 (421.0)	0.26
Bilirubin; mmol/L (N.<18)	19.6 (10.6)	23 (12.6)	0.26
Creatinine; mmol/L (N.=44-80)	76 (23.4)	85 (18.6)	0.10
GFR; mL/min (N.=90-120)	78 (13.9)	76 (14.8)	0.75
Glucose mmol/L (N.=3.9-5.8)	8.0 (1.7)	8.3 (2.0)	0.53
Hb; g/dL (N.=115-165 for females; 130-170	119 (12.5)	102 (40.2)	0.031
Platelets; x10^9 (N.=150-400)	217 (71.4)	185 (78.3)	0.20
PT; s (N.=11-14)	12.0 (2.6)	14.4 (2.41)	**<0.001**
APTT; s (N.=22-38)	26 (2.8)	30 (7.2)	**0.007**
Fibrinogen; g/L (N.=2.0-4.0)	4.3 (5.3)	3.3 (1.2)	0.34

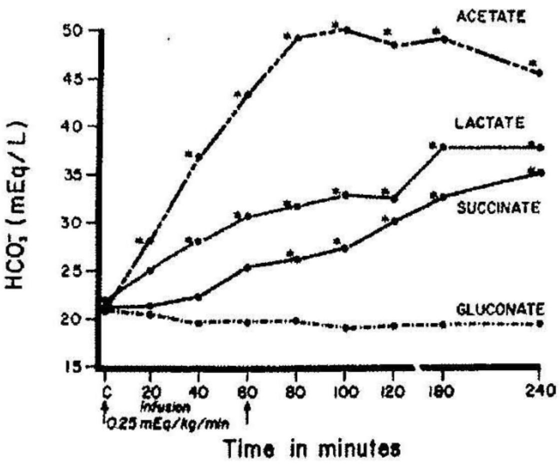
TABLE V.—*Postoperative complications and outcomes.*

	Plasmalyte N.=30	Hartmann's N.=30	P
No of patients with a complication	6 (20%)	17 (56%)	**0.007**
Total number of complications	10	30	
Clavien-Dindo Grade of highest complication			
i	0	2 (7%)	0.49
ii	2 (7%)	7 (23%)	0.14
iii	2 (7%)	2 (7%)	1.0
iv	1 (3%)	4 (13%)	0.35
v	1 (3%)	2 (7%)	1.0
Cardio-respiratory complications			
Pneumonia	0	2 (7%)	
Pulmonary congestion	1 (3%)	4 (13%)	
Pulmonary edema	1 (3%)	1 (3%)	
Pleural effusion	0	1 (3%)	
Pneumothorax	1 (3%)	0	
Myocardial infarction	0	4 (13%)	
Arrhythmias	2 (7%)	3 (10%)	
Renal complications			
Acute renal failure	0	1 (3%)	
Surgical complications			
Wound infection	1 (3%)	1 (3%)	
Postoperative ileus delaying discharge	0	3 (10%)	
Bile leak	1 (3%)	2 (7%)	
Intra-abdominal sepsis requiring re-laparotomy	1 (3%)	2 (3%)	
Liver failure with encephalopathy	1 (3%)	0	
Other			
Postoperative blood transfusion	1 (3%)	5 (17%)	
Patient Outcomes			
Length of hospital stay days (median)	5.9	7.8	**0.04**
Hospital death within 30 days of surgery	0	2 (7%)	0.49

Potential advantages of acetate

- Converted to bicarbonate in liver and extra-hepatic tissue
- More rapidly converted than lactate
- More alkalinizing ability than lactate





Kirkendol. Trans *Am Soc Artif Intern Organs* 1980;26:323-237

‘It takes 50 years to get a wrong idea out of medicine, and 100 years to get a right one into medicine’

John Hughlings Jackson

(1835-1911)

Any questions?