Effect of Restrictive Fluid Management Strategy on Outcomes in Pediatric Trauma Patients – A Multicenter Randomized Prospective Trial

Background

- Restrictive fluid administration in adult ICU and post-op patients has been associated with decreased rate of complications
- Recent studies have challenged the decades old aggressive fluid resuscitation of trauma patients, underlying the detrimental effect of positive fluid balance on cardiopulmonary function.
- Fluid overload has been associated with impaired oxygenation and morbidity in critically ill children, however data is lacking in pediatric trauma patients.
- Currently both liberal and restrictive fluid strategies are used per physician discretion

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

- NEJM 2006
- RCT (multicenter) conservative vs liberal
- 1000 adult patients with ALI
- PAC / CO driven
- Nonsignificant decreased mortality at 60 days (25.5% vs 28.4%)
- Significant improvement in OI, decrease in days on vent, decreased ICU LOS

Effects of Intravenous Fluid Restriction on Postoperative Complications: Comparison of Two Perioperative Fluid Regimens

A Randomized Assessor-Blinded Multicenter Trial

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Annals of Surgery • Volume 238, Number 5, November 2003

- Annals of Surgery 2003
- Randomized observer blinded multicenter trial
- 140 colorectal adult patients – restricted vs standard
- Fluid therapy guided by body weight changes, preloading and third space fluid loss replacement in standard; used Hetastarch boluses
- Sig decrease in overall complications, CP, tissue-healing (leak, SSI) and GI (ileus) complications

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J Trauma Acute Care Surg. 2013 May ; 74(5): 1215–1222. doi:10.1097/TA.0b013e3182826e13.

Aggressive Early Crystalloid Resuscitation adversely affects Outcomes in Adult Blunt Trauma Patients: An Analysis of the Glue Grant Database

George Kasotakis, MD, **Antonis Sideris, MD**, **Yuchiao Yang, PhD**, **Marc de Moya, MD**, **Hasan Alam, MD**, **David R King, MD**, **Ronald Tompkins, MD, ScD**, **George Velmahos, MD, MsEd, PhD**, and **The Inflammation and Host Response to Injury Investigators**

Restricted peri-operative fluid administration adjusted by serum lactate level improved outcome after major elective surgery for gastrointestinal malignancy

Yu WenKui, MD, Li Ning, MD, Gong JianFeng, MD, PhD, Li WeiQin, MD, Tang ShaoQiu, MD, Tong Zhihui, MD, Gao Tao, Zhang JuanJuan, Xi FengChan, Shi Hui, Zhu WeiMing, MD, *and* **Li Jie-Shou,**

SHOCK, Vol. 26, No. 2, pp. 115–121, 2006

Review Article

THE CELLULAR, METABOLIC, AND SYSTEMIC CONSEQUENCES OF AGGRESSIVE FLUID RESUSCITATION STRATEGIES

Bryan A. Cotton, Jeffrey S. Guy, John A. Morris Jr, and Naji N. Abumrad
Department of General Surgery, Vanderbilt University School of Medicine, Nashville, TN

Received 17 Jan 2006; first review completed 31 Jan 2006; accepted in final form 17 Feb 2006

Fluid overload before continuous hemofiltration and survival in critically ill children: A retrospective analysis*

Jason A. Foland, MD; James D. Fortenberry, MD, FAAP, FCCM; Barry L. Warshaw, MD, FAAP; Robert Pettignano, MD, FAAP, FCCM; Robert K. Merritt, MA; Micheal L. Heard, RN; Kris Rogers, RN; Chris Reid, RRT; April J. Tanner, RN; Kirk A. Easley, MS

Fluid overload is associated with impaired oxygenation and morbidity in critically ill children*

Ayse A. Arikan, MD; Michael Zappitelli, MD, MSc; Stuart L. Goldstein, MD; Amrita Naipaul, NP; Larry S. Jefferson, MD; Laura L. Loftis, MD

Pediatric Anesthesia ISSN 1155-5645

ORIGINAL ARTICLE

Effects of a restrictive fluid regimen in pediatric patients undergoing major abdominal surgery

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Study Design

- **Multicenter randomized un-blinded prospective trial** to determine difference in outcomes between critically ill pediatric trauma patients treated with LIBERAL fluid management strategy vs RESTRICTIVE fluid management strategy

- Power analysis to detect a 15% reduction in overall complication rate with 80% power, 2-sided analysis ($p = 0.05$) - requires **240 patients**

- 40% participation rate and 20% dropout rate, we anticipate that we will need 750 patients to be initially approached about the study to reach statistical significance for the primary outcome studied.

Study Timeline

- 14 pediatric trauma patients admitted to MSCHONY PICU from Oct 1 2016 to Mar 31 2017 (6 months) ~ 30 patients per year

- If 10 Level 1 pediatric trauma centers participate in the study, and admit on average 30 critically ill trauma patients to their PICU per year, we will need approximately **3 years to complete the study.**

Pilot Study

- Examine implementation of the fluid management strategies
  - Acquire estimates of treatment differences
  - Verify clarity of algorithm
  - Refine algorithm to clinical relevance
  - Assist in implementation and adherence to algorithm
- Post-op and trauma patients have similar SIRS physiology
  - Include both for pilot study – inlude ped surg, ortho, GU
- We plan to study 20-30 patients in our pilot study

Pilot Study – 5 centers

- Morgan Stanley Children’s Hospital/Columbia University Medical Center
- Cohen Children’s Medical Center
- Johns Hopkins Children’s Center
- Komansky Children’s Hospital/Weill Cornell Medical Center
- Children's Hospital at Dartmouth-Hitchcock

- Confirmed interest for RCT – TCH, UT Southwestern - Dallas

Participating centers

- Morgan Stanley Children's Hospital/Columbia University - recruiting
- Cohen Children's Medical Center - recruiting
- Johns Hopkins Children's Center – IRB in process
- Komansky Children's Hospital/Weill Cornell Medical Center – IRB in process

- Confirmed interest for RCT – TCH, UT Southwestern - Dallas

Outcomes Measured

- Major Outcomes:
  - Overall incidence of complications
    - Major: bleeding, sepsis, anastomotic leak, wound dehiscence, hardware infection, blood clot
    - Minor: SSI, ileus, pneumonia
  - Need for mechanical ventilation (number of days on vent)

- Secondary Outcomes:
  - ICU LOS
  - Hospital LOS

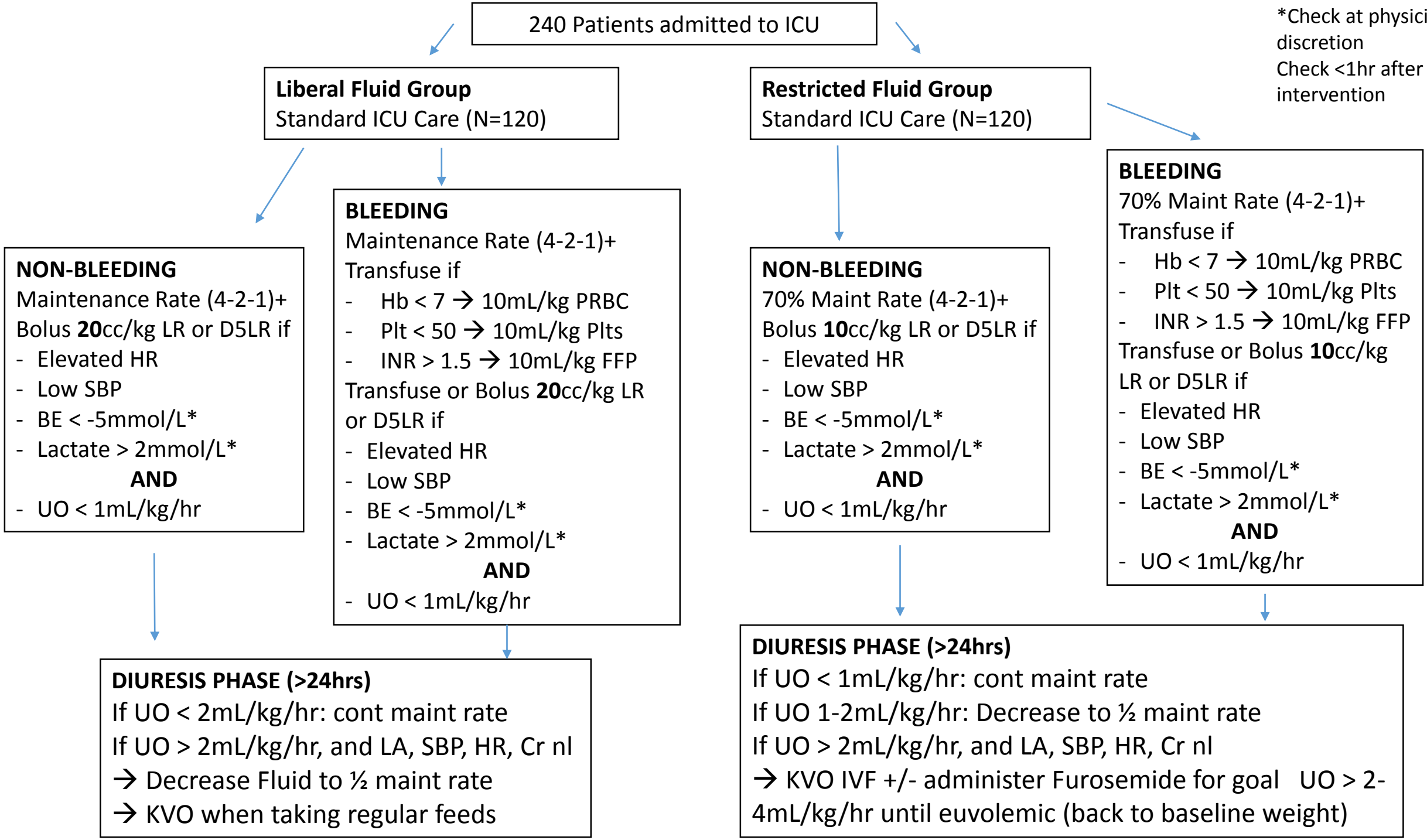
Inclusion Criteria

- Trauma Patients
  - Trauma patients 1yo to 16yo admitted to the PICU
  - Patients admitted to the PICU directly from the ED
  - Patients admitted to the PICU from the OR
  - Patients transferred to PICU from outside facility ER
    - (need to have been in ER 12hrs or less)

- For Pilot Study include:
  - Surgical Patients:
    - Patients 1yo to 18yo
    - Pediatric Surgery patients
    - Orthopedic patients
    - GU patients

Exclusion Criteria

- Patients transferred to PICU from outside PICU or inpatient floor
- Patients transferred to PICU from outside facility ER if >12hours
- Patients expected to be discharged from the PICU within 24 hours
- Patient with congenital heart disease as defined by a congenital cardiac defect requiring surgery or chronic medication
- Patient with diagnosis of chronic cardiac condition (e.g. hypertension, cardiac arrhythmia)
- Patients with chronic kidney disease as defined by an abnormality of kidney structure or function, present for more than 3 months, with implications to health
- Post-operative transplant, cardiac, and neurosurgical patients
- Patients with traumatic brain injury
- Patients with any disease that may affect baseline blood pressure and heart rate (endocrine disorders, certain genetic disorders, mitochondrial diseases)
- Hypotension requiring vasopressor therapy
- If massive transfusion protocol initiated


240 Patients admitted to ICU
*Check at physician's discretion
Check <1hr after each intervention
Liberal Fluid Group
Standard ICU Care (N=120)
Restricted Fluid Group
Standard ICU Care (N=120)
NON-BLEEDING
Maintenance Rate (4-2-1)+
Bolus 20cc/kg LR or D5LR if
- Elevated HR
- Low SBP
- BE < -5mmol/L*
- Lactate > 2mmol/L*
AND
- UO < 1mL/kg/hr
BLEEDING
Maintenance Rate (4-2-1)+
Transfuse if
- Hb < 7 → 10mL/kg PRBC
- Plt < 50 → 10mL/kg Plts
- INR > 1.5 → 10mL/kg FFP
Transfuse or Bolus 20cc/kg LR or D5LR if
- Elevated HR
- Low SBP
- BE < -5mmol/L*
- Lactate > 2mmol/L*
AND
- UO < 1mL/kg/hr
NON-BLEEDING
70% Maint Rate (4-2-1)+
Bolus 10cc/kg LR or D5LR if
- Elevated HR
- Low SBP
- BE < -5mmol/L*
- Lactate > 2mmol/L*
AND
- UO < 1mL/kg/hr
BLEEDING
70% Maint Rate (4-2-1)+
Transfuse if
- Hb < 7 → 10mL/kg PRBC
- Plt < 50 → 10mL/kg Plts
- INR > 1.5 → 10mL/kg FFP
Transfuse or Bolus 10cc/kg LR or D5LR if
- Elevated HR
- Low SBP
- BE < -5mmol/L*
- Lactate > 2mmol/L*
AND
- UO < 1mL/kg/hr
DIURESIS PHASE (>24hrs)
If UO < 2mL/kg/hr: cont maint rate
If UO > 2mL/kg/hr, and LA, SBP, HR, Cr nl
→ Decrease Fluid to ½ maint rate
→ KVO when taking regular feeds
DIURESIS PHASE (>24hrs)
If UO < 1mL/kg/hr: cont maint rate
If UO 1-2mL/kg/hr: Decrease to ½ maint rate
If UO > 2mL/kg/hr, and LA, SBP, HR, Cr nl
→ KVO IVF +/- administer Furosemide for goal UO > 2-4mL/kg/hr until euvolemic (back to baseline weight)

HR GUIDE

Age Group	50th	20% INC
12 - <18 mo	124	149
18 - <24 mo	120	144
2 - <3 y	115	138
3 - <4 y	111	133
4 - <6 y	106	127
6 - <8 y	100	120
8 - <12 y	94	115
12 - <15 y	87	104
15 - <18 y	82	98

Diuresis Phase (>24hrs)

Liberal

- If UO<2mL/kg/hr:
  - Cont maint rate
  - Bolus as per initial phase
- If UO>2mL/kg/hr, and Lactate, SBP, HR, Cr nl
  →decrease Fluid to ½ maint rate
  →KVO when taking regular feeds

Restrictive

- If UO<1mL/kg/hr
  - Cont maint rate
  - Bolus as per initial phase
- If UO 1-2mL/kg/hr
  - Decrease to 1/2 maint rate
- If UO>2mL/kg/hr, and Lactate, SBP, HR, Cr nl
  →KVO IVF +/- administer Furosemide for goal UO>2-4mL/kg/hr until euvolemic^

^Back to baseline admission weight or total even I/Os

Specifications

- Study does not take into account fluid resuscitation in OR – assumption is that the patients were given adequate fluid resuscitation

- No hypotensive patients, no patients on pressors
  - If patient requires pressor use then he/she comes off protocol
  - Aim of study is to look at normotensive pediatric trauma patients requiring fluid resuscitation

- Changes in BP and HR are compared to normal for age/weight/height vitals
  - Use isotonic fluids for first 24 hours (LR or plasmalyte) then hypotonic fluids for maintenance

- Will be Intent To Treat analysis

Interventions While on Algorithm

- If intervention is performed (crystalloid bolus or blood product administered) then parameters will be checked within 1 hr of intervention

- If patient becomes hemodynamically unstable and is not responsive to fluid/blood administration and a vasopressor needs to be started then patient comes off protocol

- Treating physician can come off protocol at any given time – reason has to be recorded

Consent

- Consent to be obtained prior to surgery if high likelihood of post-op PICU admission otherwise consent obtained upon arrival to PICU
- Obtained by either Study Site coordinator, Site PI or designated appointee (housestaff, attending, nursing)
- Study PI – Dr. Duron available **at any time** to discuss study
- English and Spanish consent ok

Pilot Study to Date

- Started recruiting patients 8/28/18
  - 24 patients recruited and consented
  - 14 pediatric trauma and surgical patients on protocol at least 24hrs
    - Trauma: 2
    - Ped Surg: 6
    - Ped GU: 2
    - Ped Ortho: 7
  - Reasons came off – d/c from PICU, started on pressors

Pilot Study to Date

- Mean Age: 9.2yo
- Mean Time on Protocol: 40hrs
- Subgroup:
  - Bleeding: 21% (n=3)
  - Non-Bleeding: 79% (n=11)

Pilot Study to Date

- The average volume of total fluid administration
  - Liberal arm: 2.74 mL/kg/hr
  - Restricted arm: 2.45 mg/kg/hr (p=0.482)

- Although not anticipating statistically significant difference between groups (as both treatment modalities meant to be within standard of care) focus group with PICU staff held and restricted maintenance rate cut to 70%

MSCHONY Staff

- PI: Vincent Duron, MD
- PICU Co-investigators:
  - N. Valerio Dorrello, MD, PhD (PICU), Steven Stylianos, MD (Ped Surg)
- Study Coordinators: Jeanne Rubsam, Jessica Price
- Study Registrar: Joseph Zwarick
- IRB Team: Amanda Alonso, Khady Ndour
- Statistics: Weijia Fan