What's new in trauma resuscitation

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Choice of Fluid

Can we choose fluids that improve restoration of cellular O2 delivery without massive volume?

- Hypertonic fluids
  - Mobilise interstitial to plasma volume
- Colloids
  - Increase retention in circulation
- Blood & Hb Substitutes
  - increase O2 carrying

Hypertonic saline vs Hartmanns

Cooper J, *JAMA*, 2004

- Hypotension + brain injury (n=229)
- HTS (7.5%) vs Hartmanns - 250 mls
- ISS 38, GCS 4

- Mortality equivalent: 45% (HTS) v 50%
  - No differences in secondary outcomes
- No differences in outcome at 6 mos
  - GOS, Return to work

Crystalloid vs colloid

Roberts, *Cochrane Library*, 2004

- Albumin or plasma protein fraction vs crystalloid
  - 19 trials, 7,576 patients
  - RR of death: 1.02 (0.93-1.11)
- Hydroexthyl starch (pentastarch/hetastarch)
  - 10 trials, 374 patients
  - RR of death: 1.16 (0.68-1.96)
- Dextran in hypertonic saline
  - 8 trials, 1,283 patients
  - RR of death: 0.88 (0.74-1.05)

Saline vs Albumin Fluid Evaluation study

ANZICS Clinical Trials Group

- Multicentre RCT fluid for intravascular volume in ICU
- Intervention: 4% Albumin vs NSaline during 1st 28 days
- Outcome death within 28 days, S/MOF, LOS, vent, renal.

- All pts (N Engl J Med. 2004;350(22):2247-56)
  - 6997 heterogenous ICU pts
  - RR death 0.99 (0.91-1.09), no diff other outcomes
- ➢ Albumin & NSaline equivalent

- Head Injured Pts – post hoc study (N Engl J Med. 2007;357(9):874-84.)
  - 460 pts, 69% with severe TBI
  - 24 mo. Mortality: 33% (Alb) v 20%, RR 1.63 (1.17-2.26)
- ➢ Albumin seems harmful in TBI

Comparison of Different Colloids

Bunn F, Cochrane Library, Jan 2008

- 70 trials, 4375 participants, death as outcome in 46 trials.

- Alb/PPF vs Hydroxyethyl Starch (HES): 25 trials (n=1234), RR 1.14 (0.91-1.43)
- Alb/PPF vs Gelatin: 7 trials (n=636), RR 0.97 (0.68-1.39)
- Alb/PPF vs Dextran: 4 trials (n=360), RR 3.75 (0.42-33.09)
- Gelatin vs HES: 18 trials (n=1337), RR 1.00 (0.80-1.25)
- Gelatin vs dextran and HES vs Dextran: not estimable.

- Conclusion: None safer or more effective than another.

What about Blood?

- Logical to replace what's being lost.

But:

- Red cell transfusion strongly associated with later development of MOF/infection

- Association or causation?

- Possible interventions
  - More restrictive transfusion policy
  - Manipulation of red cell preparation/storage
  - Hemoglobin substitutes

Transfusion “Trigger” in the ICU

Hebert et al, *NEJM*, 1999

- Restrictive or Liberal transfusion policy:
  - Restrictive policy: 7 to 9 g/dl (Hct 23)
  - Liberal policy: 10 to 12 g/dl (Hct 33)
- Normovolemic, non-bleeding patients

Transfusion Policy & Outcome

	Liberal	Restrictive
Mortality		
Overall	23.3%	18.7%
Age<55	13.0%	5.7%*
Apache II≤20	16.1%	8.7%*
Ventilator-free days		
Overall	16.1 d	17.5
Intubated>7 d	9.8 d	12.1*

Hebert et al, Chest, 2001

Restrictive policy: Trauma subset analysis

McIntyre, *J Trauma*, 2004

- N=203, Mean ISS ~25
- Mortality equivalent (10% vs 9%)
- MOD scores, infection rates equivalent

- Conclusion
  - Restrictive Policy is safe
  - Applicable to the resuscitated, euvolemic trauma patient
  - Cannot be extrapolated to those with active bleeding

Hemoglobin-based blood substitutes

- Human
  - Diaspirin cross-linked (DCLHb) - Hemassist™
  - Polymerized Hgb - Polyheme™
- Animal (Bovine)
  - Polymerized Hgb - Hemopure™

Trauma resuscitation

- Shock
  - Clinical syndrome arising as a result of inadequate tissue perfusion
  - Discrepancy between cellular oxygen delivery and cellular oxygen demand
- Trauma resuscitation goal:
  - Optimize oxygen consumption (delivery) at the cellular level
- Resuscitation phase typically limited to the first 24 hours after injury

Diaspirin Cross-Linked Hgb in Trauma

Sloan, *JAMA*, 1999

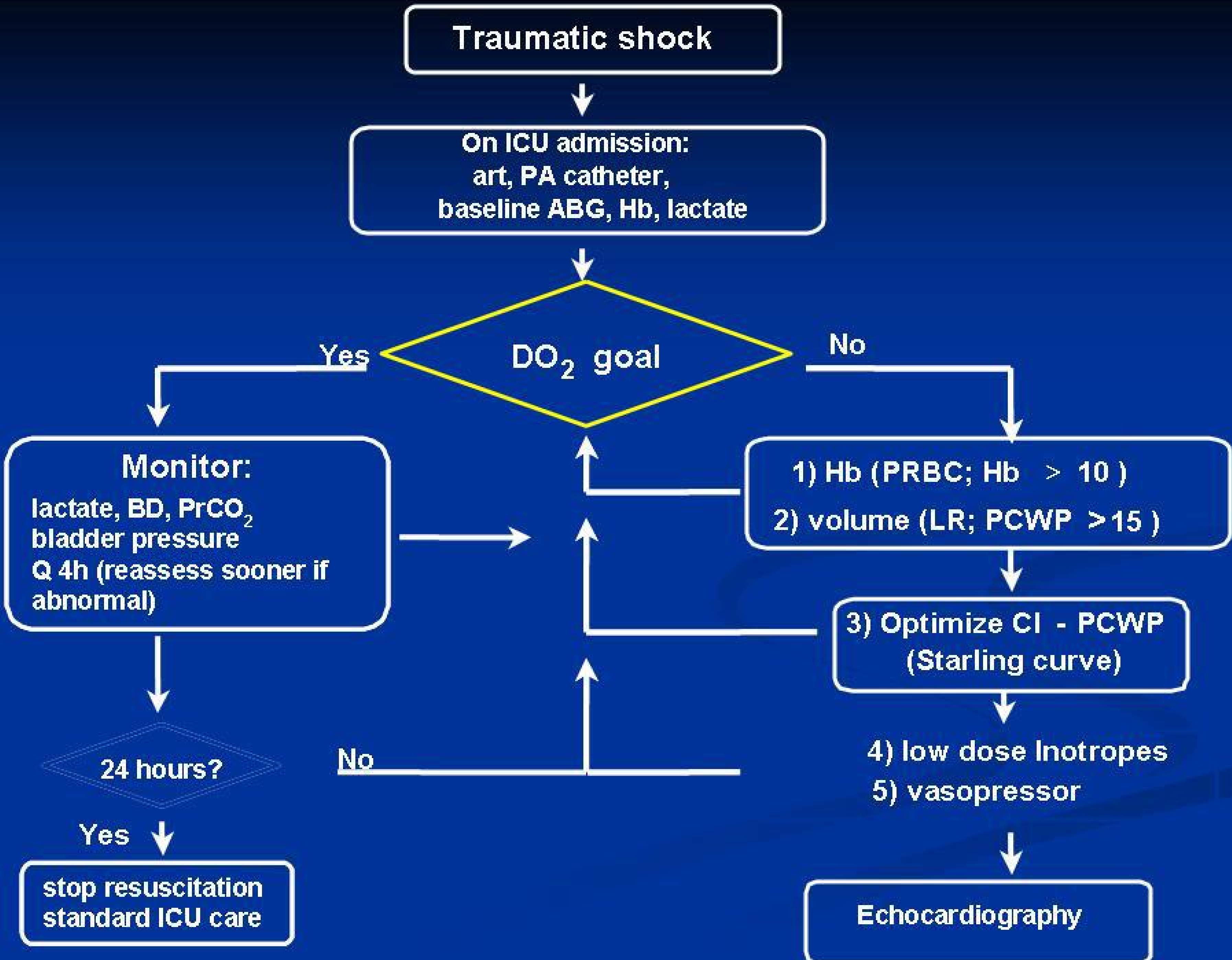
- Multicenter, RCT
- Traumatic hemorrhagic shock: SBP<90
- DCLHb versus saline: 500 or 1000 mls: 2-4 units
- Outcome: mortality

- Trial stopped at interim analysis (n=111)
  - Mortality at 48 hrs: DCLHb: 38%, Saline: 21%
  - Mortality at 28 days: DCLHb: 47%, Saline: 25%

- Unlucky randomization?
- Hb scavenging effect of NO?

How much resuscitation is enough?

- Goal Directed Therapy
  - Simple measures:
    - BP, HR, U.O.
    - CVP
    - Base Deficit, SVO2
  - Invasive measures:
    - Pulmonary Artery Catheter


Traumatic shock
On ICU admission:
art, PA catheter,
baseline ABG, Hb, lactate
DO2 goal
Yes
No
Monitor:
lactate, BD, PrCO2
bladder pressure
Q 4h (reassess sooner if abnormal)
1) Hb (PRBC; Hb > 10)
2) volume (LR; PCWP >15)
3) Optimize CI - PCWP
(Starling curve)
24 hours?
No
4) low dose Inotropes
5) vasopressor
Yes
stop resuscitation
standard ICU care
Echocardiography

Goal-directed resuscitation using a PAC in trauma

Velmahos, *Ann Surg*, 2000

- Randomized pts with hemorrhagic shock following trauma requiring operation
- Goals for control group
  - SBP>100, HCT>30, UO>1 cc/kg, BD<-3
  - IF PAC was inserted, DO2>450, VO2>130
- Goals for "optimal" group
  - CI>4.5, DO2>600, VO2>170

- Optimal endpoints
  - Reached in 70% of "optimal" group
  - Reached in 40% of control group
- Process of care
  - More inotrope use in "optimal" group & slightly more fluid given

Goal-directed resuscitation using a PAC in trauma

- Outcomes
  - Mortality 15% in optimal group, vs 11% in controls
  - ICU and hospital length of stay equivalent

- Comparison of patients who met optimal outcomes and those who didn't
    - Higher mortality
    - Longer LOS
    - More organ failure

PAPER

Supranormal Trauma Resuscitation Causes More Cases of Abdominal Compartment Syndrome

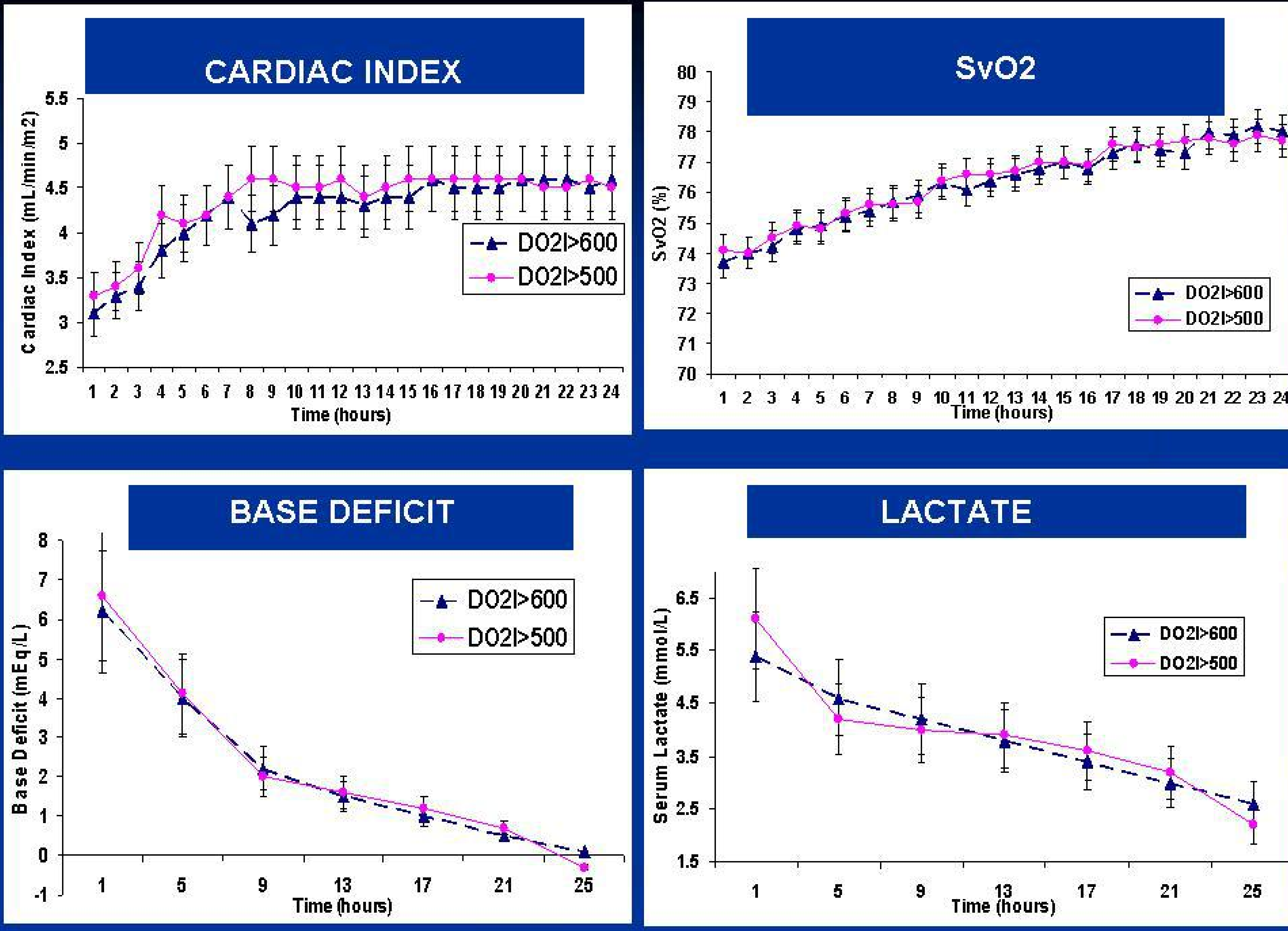
Zsolt Balogh, MD; Bruce A. McKinley, PhD; Christine S. Cocanour, MD; Rosemary A. Kozar, MD, PhD; Alicia Valdivia, RN; R. Matthew Sailors, PhD; Frederick A. Moore, MD

152 Resuscitation Protocol Patients

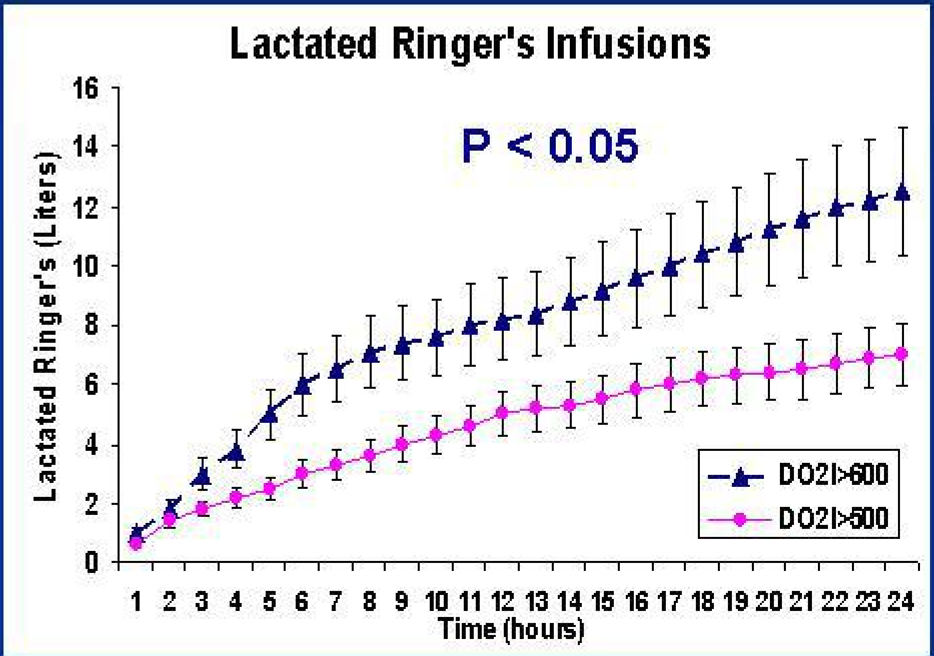
85 Patient	**71 Patients**
DO_2I Goal > 600	**DO_2I Goal > 500**

Balogh et al

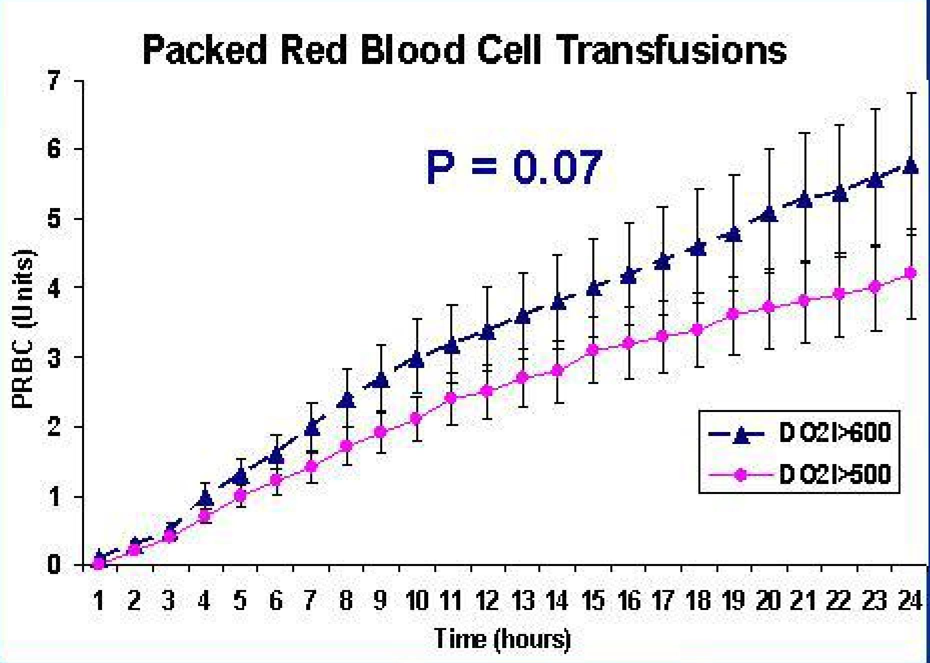
Group	Age (years)	ISS	BD (mEq/L)	Pre-ICU LR (L)	Pre-ICU PRBC (U)
DO_2I_{600}	37 ±3	28 ±3	9 ±1	6 ±1	5 ±1
DO_2I_{500}	33 ±2	27 ±2	9 ±1	5 ±1	5 ±1



CARDIAC INDEX
Cardiac Index (mL/min/m2)
5.5
5
4.5
4
3.5
3
2.5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)
DO2I>600
DO2I>500
SvO2
SvO2 (%)
80
79
78
77
76
75
74
73
72
71
70
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)
DO2I>600
DO2I>500
BASE DEFICIT
Base Deficit (mEq/L)
8
7
6
5
4
3
2
1
0
-1
1 5 9 13 17 21 25
Time (hours)
DO2I>600
DO2I>500
LACTATE
Serum Lactate (mmol/L)
6.5
5.5
4.5
3.5
2.5
1.5
1 5 9 13 17 21 25
Time (hours)
DO2I>600
DO2I>500



Lactated Ringer's Infusions
P < 0.05
Lactated Ringer's (Liters)
Time (hours)
DO2I>600
DO2I>500



Packed Red Blood Cell Transfusions
P = 0.07
PRBC (Units)
Time (hours)
DO2I>600
DO2I>500

Effect of manipulating the resuscitation goals

Group	IAH %	ACS %	MOF %	Death %
DO_2I_{600}	42 *	16 *	22 *	27 *
DO_2I_{500}	20	8	9	11

IAH = UBP > 20 mm Hg

* $p < 0.05$

Controversies

- Initial choice of resuscitation fluid
  - Massive fluid resuscitation vs controlled hypotension
  - Crystalloid vs colloid
  - Hypertonic versus isotonic
- Transfusion practices
  - Is there a role for a strict transfusion policy?
  - What is the role of blood substitutes?
- Endpoints for resuscitation

Summary so far

- Pendulum is moving away from massive volume resuss
  - No justification for routine use of colloids, hypertonic saline
- Hemorrhage control precedes significant volume resuss
- Transfusions
  - for the bleeding patient – replace what is actively being lost,
  - once bleeding stopped – restrictive policy
- PAC only for resuss failure & progressive hypoxaemia
  - Base deficit, urine output adequate in most

- Why is volume harmful?
  - Oedematous states
  - Pro-Inflammatory, gene activation?
- Are inotropes an alternative for promoting cellular 02 delivery without harm of volume?

Antioxidants in resuscitation phase: rationale

- Critically ill patients have an increase in circulating products of oxidative metabolism
  - Lipid peroxides *(Goode, 1995)*
  - Oxidation of protein thiols (*Bunnel, 1993*)
- Depletion of endogenous antioxidants
  - ↓ Total plasma antioxidant capacity
  - ↓ Plasma ascorbate (vitamin C)
  - ↓ α-tocopherol (vitamin E)
  - ↓ Reduced glutathione
- Parallels development of ARDS/MOF

Antioxidants in Reperfusion Injury

Porter, *Am Surg*, 1999

- Prospective RCT
- Penetrating trauma patients prior to complete resuscitation (n=18)
  - NAC 450 mg/kg/day
  - Vitamin C 300 mg/day
  - Vitamin E 1200 IU/day
  - Selenium 300 mg/day
- Groups well matched

	Control N=9	Antioxidant N=9
MODS	3 (33%)	0 (0)
Infections	8 (89%)	5 (56%)
ICU LOS	36 d	22 d

Antioxidants in the Resuscitation Phase

Nathens, *Ann Surg*, 2002

- Trauma/Surgical ICU, n=595
- Antioxidant arm
  - Vitamin C (ascorbic acid) 1 gm IV q8h
  - Vitamin E (*dl*-α-tocopherol acetate) 1000 IU po/NG q8h
- Control arm
  - No antioxidant supplementation, standard care

Parameter	Control	Antioxidant	Relative Risk/Decrease (95% CI)
MOF	18 (6.1%)	8 (2.7%)	0.43 (0.19-0.96)
Ventilation (d)	4.6 d	3.7 d	0.9 d (0.6-1.2)
ICU LOS	6.4 d	5.3 d	1.2 d (0.81-1.5)
28-day mortality	7 (2.4%)	4 (1.3%)	0.55 (0.2-1.9)

Surgical Glue Grant | *The Journal of TRAUMA® Injury, Infection, and Critical Care*

Inflammation and the Host Response to Injury, a Large-Scale Collaborative Project: Patient-Oriented Research Core—Standard Operating Procedures for Clinical Care

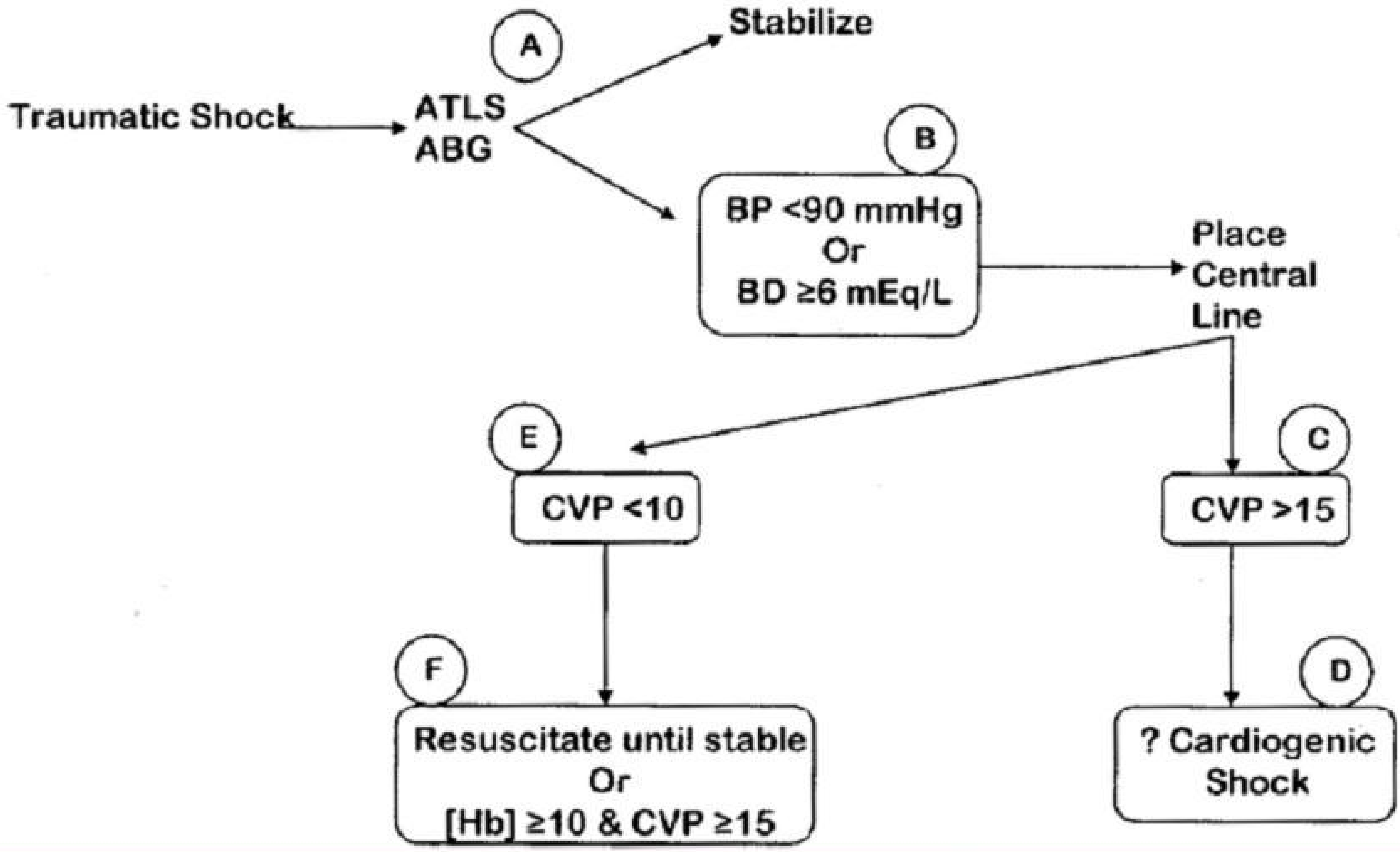
III. Guidelines for Shock Resuscitation

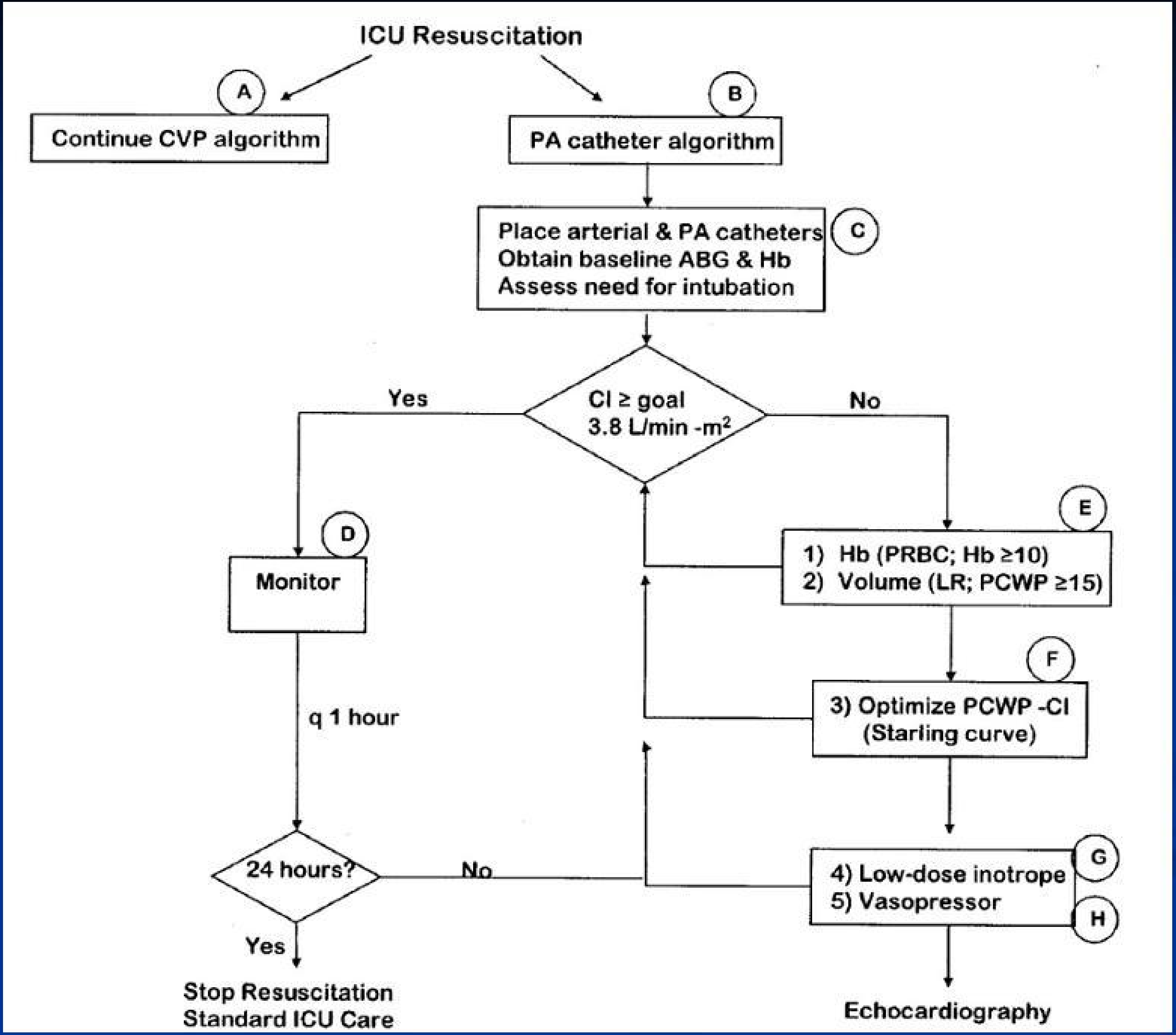
Frederick A. Moore, MD, Bruce A. McKinley, PhD, Ernest E. Moore, MD, Avery B. Nathens, MD, PhD, MPH, Michael West, MD, PhD, Michael B. Shapiro, MD, Paul Bankey, MD, PhD, Bradley Freeman, MD, Brian G. Harbrecht, MD, Jeffrey L. Johnson, MD, Joseph P. Minei, MD, and Ronald V. Maier, MD

J Trauma. 2006;61:82–89.

- Large prospective cohort study designed to characterise the genomic and proteomic response to injury
- Protocols developed to minimize variation in care across centres

INITIAL RESUSCITATION




ICU Resuscitation
A
Continue CVP algorithm
B
PA catheter algorithm
Place arterial & PA catheters
Obtain baseline ABG & Hb
Assess need for intubation
C
Yes
CI ≥ goal
3.8 L/min -m2
No
E
1) Hb (PRBC; Hb ≥10)
2) Volume (LR; PCWP ≥15)
D
Monitor
q 1 hour
F
3) Optimize PCWP -CI
(Starling curve)
24 hours?
No
G
4) Low-dose inotrope
5) Vasopressor
H
Yes
Stop Resuscitation
Standard ICU Care
Echocardiography

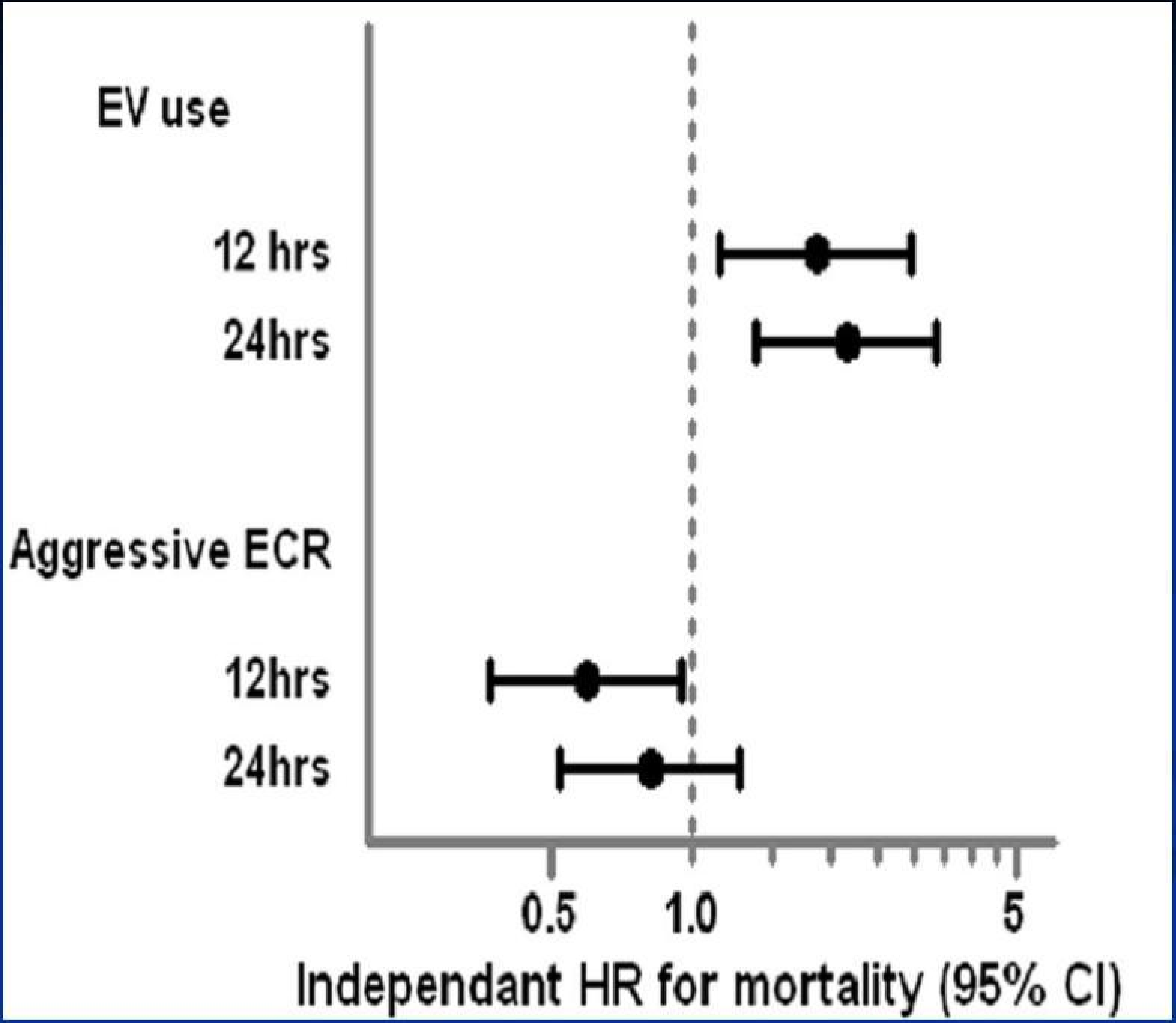
The Journal of TRAUMA® Injury, Infection, and Critical Care

Early Use of Vasopressors After Injury: Caution Before Constriction

Jason L. Sperry, MD, MPH, Joseph P. Minei, MD, Heidi L. Frankel, MD, Micheal A. West, MD, PhD, Brian G. Harbrecht, MD, Ernest E. Moore, MD, Ronald V. Maier, MD, and Ram Nirula, MD, MPH

- Observational study using Glue Grant Data
- Associations between Early Crystalloid Resuss & Mortality, and Early Peripheral-acting Vasopressor Use & Mortality
- 7 institutions 2003-2007
- 16-90 yo, Blunt trauma, Prehospital hypotension, Blood Tx in first 12/24, Not Isolated Brain/Spinal Cord Injury, not deemed "unsalvageable", survived >48/24
- Cox proportional hazards model: physiologic, injury, treatment & demographic factors

- 921 pts, 12.3% mortality
- 177 ECR>16 litres, 119 EV use
- Both ECR & EV associated with older & sicker pts who had greater physiologic disturbance & more resuscitative interventions

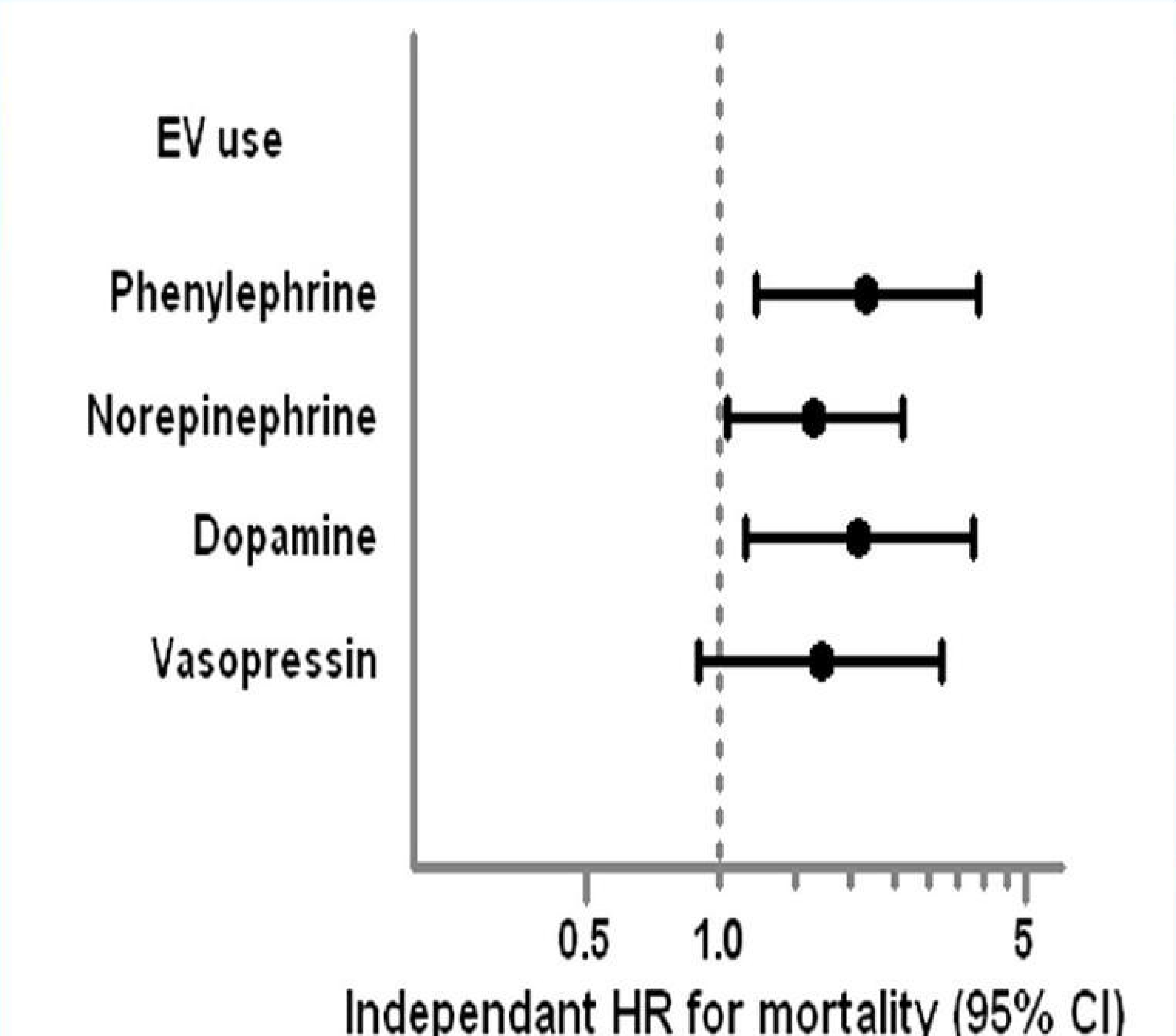

EV use
12 hrs
24hrs
Aggressive ECR
12hrs
24hrs
0.5
1.0
5
Independant HR for mortality (95% CI)

Saline/Hartmanns & Fluid Resuss

- Approach largely unchanged since 1960's
- Still using the lessons learned from Vietnam

"Fluids are good"

- Vietnam conflict
  - Aggressive use of crystalloid
  - Da Nang Lung - Shock Lung


EV use
Phenylephrine
Norepinephrine
Dopamine
Vasopressin
0.5
1.0
5
Independant HR for mortality (95% CI)

Value of this study?

- Challenges the proposition that vasopressors are an alternative to fluid resuscitation in early treatment of haemorrhagic shock

- Able to consider a wide variety of potentially confounding factors, but there may be others.

- Prospective RCT is the next step

- In the early resuscitation of most trauma patients, evidence supports giving priority to stopping bleeding, giving blood to replace what's lost, and judicious use of crystalloids.

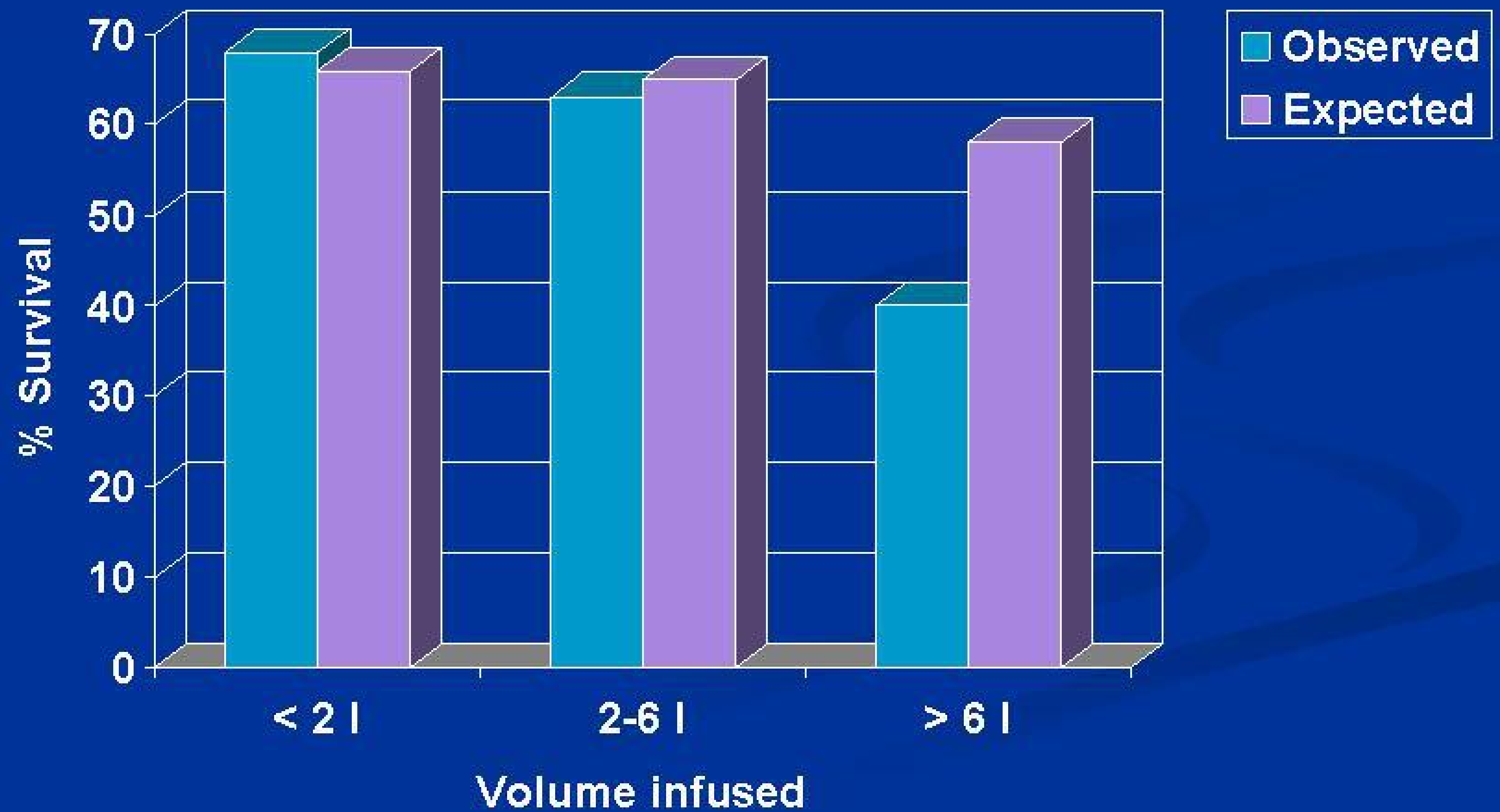
- Mean arterial pressure >70, base deficit returning to normal & production of urine are adequate monitors in most pts, with HR, CVP and SaO_2 as other important parameters to trend.

1980's more fluid = better

- Bishop, Shoemaker et al:
  - 'in critically ill patients ongoing ischemia is bad"
  - Treat "oxygen debt"
- Resuscitation *before* OR
  - Cut-downs
  - ATLS - emphasized IV access
  - Two litres then blood (became too many litres)

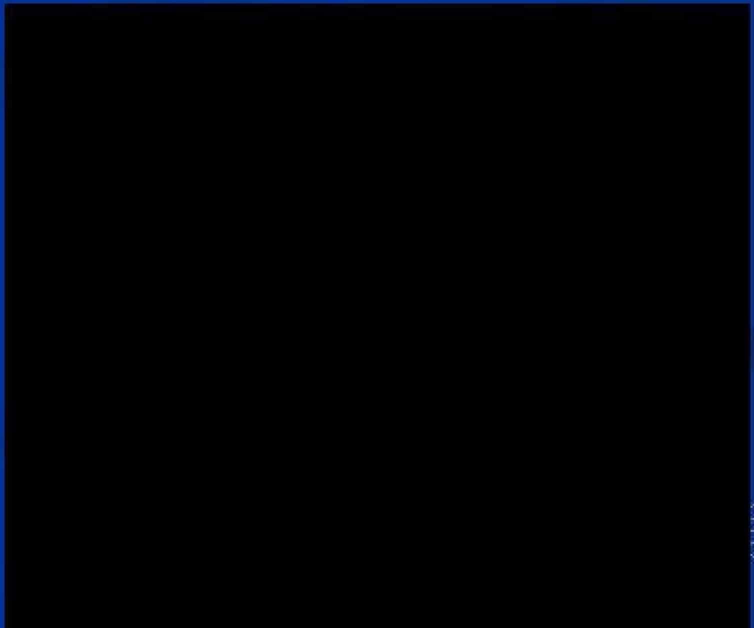
Excess mortality associated with the use of a rapid infusion system

Hambly, *Resuscitation* 1996;31:127



Secondary effects of massive crystalloid resuscitation

- ALI/ARDS
- Cerebral edema
- Ocular compartment syndrome and blindness
- Abdominal compartment syndrome (ACS)



A role for controlled hypotension?

Bickell et al, NEJM, 1994

- Randomized 598 patients with shock following penetrating truncal injury in urban Houston:
  - Immediate fluid resuscitation
  - Delayed fluid resuscitation – postponed until after OR
- Transport times <30 minutes
- Fluid administration
  - Immediate group – 2500 cc given preop (2/3 in ED)
  - Delayed group – 280 cc given preop

Results

- Delayed group
  - Slightly improved survival – 62% vs 70%
  - Shorter hospital LOS
  - Less coagulopathy
- If anything, not harmful and possibly beneficial
  - Caveats: young patients, short transport times, penetrating injury
- Main Message: Stop the Bleeding First