Hemostatic Adjuncts: Cryoprecipitate

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In Norway, “Texas” is slang for “crazy”.


Western Trauma Association

Disclosures

- Haemonetics (TEG), Scientific Advisory Board
- Teleflex (FDP), Medical Advisory Board
- Velico (SDP), Scientific-Medical Advisory Board
- Cerus (IFC), Scientific Advisory Board

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Cryoprecipitate

- Historically, hypofibrinogenemia has been common in patients with massive blood loss (e.g.-trauma, obstetrical, or gastrointestinal bleeds).

- Although much of this may have been related to poor resuscitation (large volume crystalloid and RBCs early, with plasma late), some is due to consumption of fibrinogen in patients with severe hemorrhage.

- As with platelets, function of available fibrinogen is likely more important to hemostasis than the actual fibrinogen value.

Cryoprecipitate

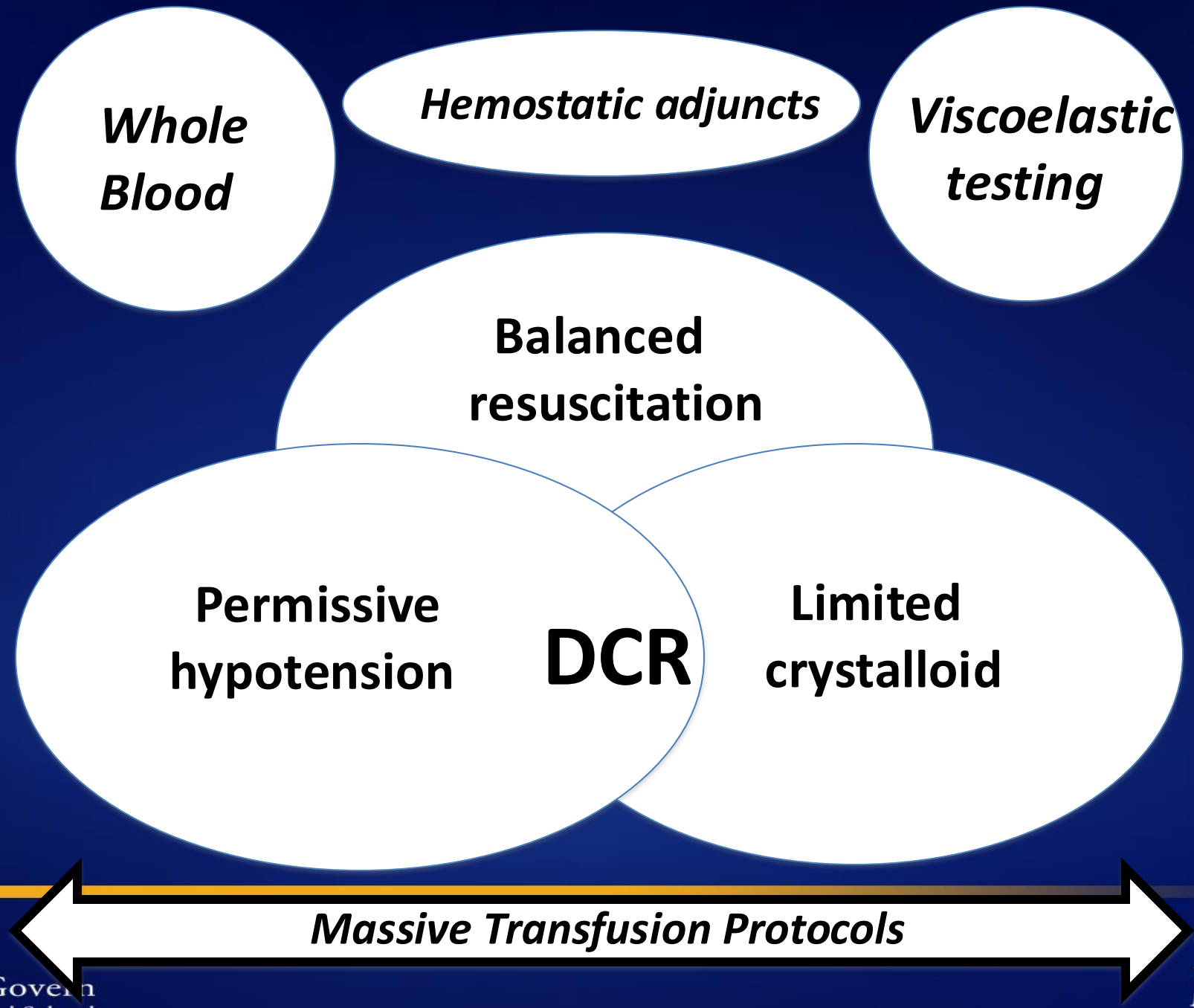
- That said, fibrinogen values less than 200 in the bleeding patient are associated with significant increases in mortality.

- The qualitative state, or fibrinogen function, can be monitored using conventional laboratory assays such as Clauss fibrinogen assay or with viscoelastic testing (TEG or ROTEM).

Cryoprecipitate

- Fibrinogen is available in plasma (approximately 400 mg per unit dose), cryoprecipitate (1500 mg or more per dose), or in concentrate.
- Cost has made cryoprecipitate product of choice in US, whereas transfusion-related complications have made fibrinogen concentrates (virally inactivated human fibrinogen) more common in Europe.
- Cryoprecipitate is usually delivered in a 10-unit dose, delivering 1500 mg per bag, where 10 to 20 units in standard-sized adults to increase the fibrinogen level by 100 to 200 mg/dL.

Cryoprecipitate?


Whole Blood
Hemostatic adjuncts
Viscoelastic testing
Balanced resuscitation
Permissive hypotension
DCR
Limited crystalloid
Massive Transfusion Protocols

Houston experience

- In 2009, cryoprecipitate was included in even numbered MTP coolers.
- After assessment of data in 2012, scheduled cryo removed and we began using as needed as directed by intra-operative TEG.
- Re-assessed in 2016 with no change in post-operative labs.
- Median ICU arrival fibrinogen: 273 to 261; median ICU arrival angle: 73 vs. 72.

Houston experience

- MT mortality rates were as high as 65% in 1997 and remained at this level through 2007, when rates began to drop <50%.
- By 2012, with EARLY (even prehospital) plasma being the centerpiece, mortality rates continued to improve dramatically and dropped to less than 30%.
- Currently 17-19% with early WB and plasma.

Increasing interest in fibrinogen

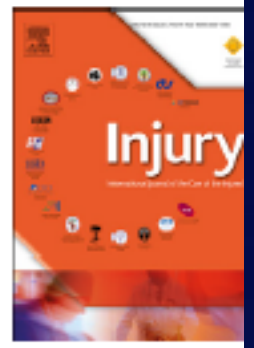
- Europe where fibrinogen concentrates are increasingly used
- UK where this has been studied and interest is growing
- Fibrinogen concentrate and IFC now available

Injury 53 (2022) 1972–1978

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury



Cryoprecipitate use during massive transfusion: A propensity score analysis

Andrew M. Fleming[a,*], Kinjal S. Shah[c], Saskya E. Byerly[b], Louis J. Magnotti[b], Peter E. Fischer[b], Catherine P. Seger[b], Andrew J. Kerwin[b], Martin A. Croce[b], Isaac W. Howley[b]

Results

- 562 patients who received at 6U or >/0-4 h.
- Cryo patients had lower RTS (6.86 vs 7.6), decreased GCS (12 vs 15), and increased lactate (7.5 vs 4.9); all $p<0.05$
- Mortality higher cryo (40 vs 24%, $p < 0.01$) on univariate analysis.
- Neither multiple logistic regression (OR 0.917; p=0.805) nor propensity score matching (average treatment effect 2.3%, p = 0.77) revealed that cryoprecipitate was associated with a difference in inpatient mortality.

Open access Original research

Trauma Surgery & Acute Care Open

Raising the bar on fibrinogen: a retrospective assessment of critical hypofibrinogenemia in severely injured trauma patients

Justin Richards [1,2] Benjamin T Fedeles,[3] Jonathan H Chow,[4] Thomas Scalea,[2,5] Rosemary Kozar [2,5]

Results

- 417 adult patients with ISS>15.
- Fibrinogen <30 min of admission:<150, 150-200, >200 mg/dL.
- Fibrinogen <150: 4.8%, 150-200: 18.2%, >200 mg/dL: 77.0%.

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Table 1 Demographic and injury characteristics by admission fibrinogen levels

	Fibrinogen <150 mg/dL (n=20)	Fibrinogen 150 mg/dL to 200 mg/dL (n=76)	Fibrinogen >200 mg/dL (n=321)	P value
Age, md (IQR)	25 (21.5–32.5)	30 (24.0–40.5)	43 (27–55)	<0.001
Blunt mechanism of injury, n (%)	5 (25)	45 (54.2)	238 (74.1)	0.03
Land transport, n (%)	8 (40)	46.0 (60.5)	189.0 (58.9)	0.23
Admission SI, mn (SD)	1.2 (1.03)	0.94 (0.46)	0.73 (0.29)	<0.001
Admission GCS, md (IQR)	3 (2-7)	14 (4–15)	14 (7–15)	<0.001
ISS, md (IQR)	34 (25–41)	27.0 (21.0–34.5)	26 (19–30)	0.001
Lactate (mmol/L), md (IQR)	6.1 (4.8–11.5)	5.2 (3.6–8.6)	3.5 (2.6–4.9)	<0.001
Platelets (×1000/µL), mn (SD)	178.6 (54.3)	223.2 (81.7)	240.4 (68.2)	0.003
INR, md (IQR)	1.8 (1.6–2.0)	1.2 (1.1–1.4)	1.1 (1.0–1.2)	0.001

Table 4 Multivariable logistic regression assessing risk of 28-day mortality

	OR	95% CI	P value
Age	1.06	1.04 to 1.08	<0.001
ISS	1.04	1.01 to 1.07	0.001
GCS	0.80	0.75 to 0.86	<0.001
Fibrinogen			
>200 mg/dL	Reference		
150 mg/dL to 200 mg/dL	1.80	0.77 to 4.24	0.32
<150 mg/dL	4.91	1.53 to 15.7	0.02

	Death due to TBI (n=48)	Non-TBI related death (n=17)	P value
Age, md (IQR)	55.5 (36.0–73.0)	35.0 (27.0–55.0)	0.09
Male, n (%)	2 (4.2)	2 (11.8)	0.27
Blunt Mechanism of Injury, n (%)	40 (83.3)	12 (70.6)	0.26
Land Transport, n (%)	22 (52.1)	7 (41.2)	0.44
Admission SI, md (IQR)	0.53 (0.4–0.95)	1.04 (0.82–1.16)	0.01
ISS, md (IQR)	29.0 (25.0–33.5)	35.0 (30.0–50.0)	0.02
Lactate (mmol/dL), md (IQR)	3.3 (2.0–5.5)	8.4 (3.1–11.8)	0.01
Platelets (×1000/μL), mn (SD)	213.3 (75.4)	194.6 (83.1)	0.4
INR, md (IQR)	1.2 (1.1–1.6)	1.2 (1.1–1.6)	0.88
Fibrinogen, n (%)			0.15
<150 mg/dL	34 (70.8)	9 (52.9)	
150–200 mg/dL	9 (18.8)	4 (23.5)	
>200 mg/dL	5 (10.4)	4 (23.5)	

Role of Fibrinogen in Trauma-Induced Coagulopathy

Jonathan P Meizoso, MD, MSPH, Ernest E Moore, MD, FACS, Fredric M Pieracci, MD, MPH, FACS, Rebecca A Saberi, MD, Arsen Ghasabyan, MPH, James Chandler, BS, Nicholas Namias, MD, MBA, FACS, Angela Sauaia, MD, PhD

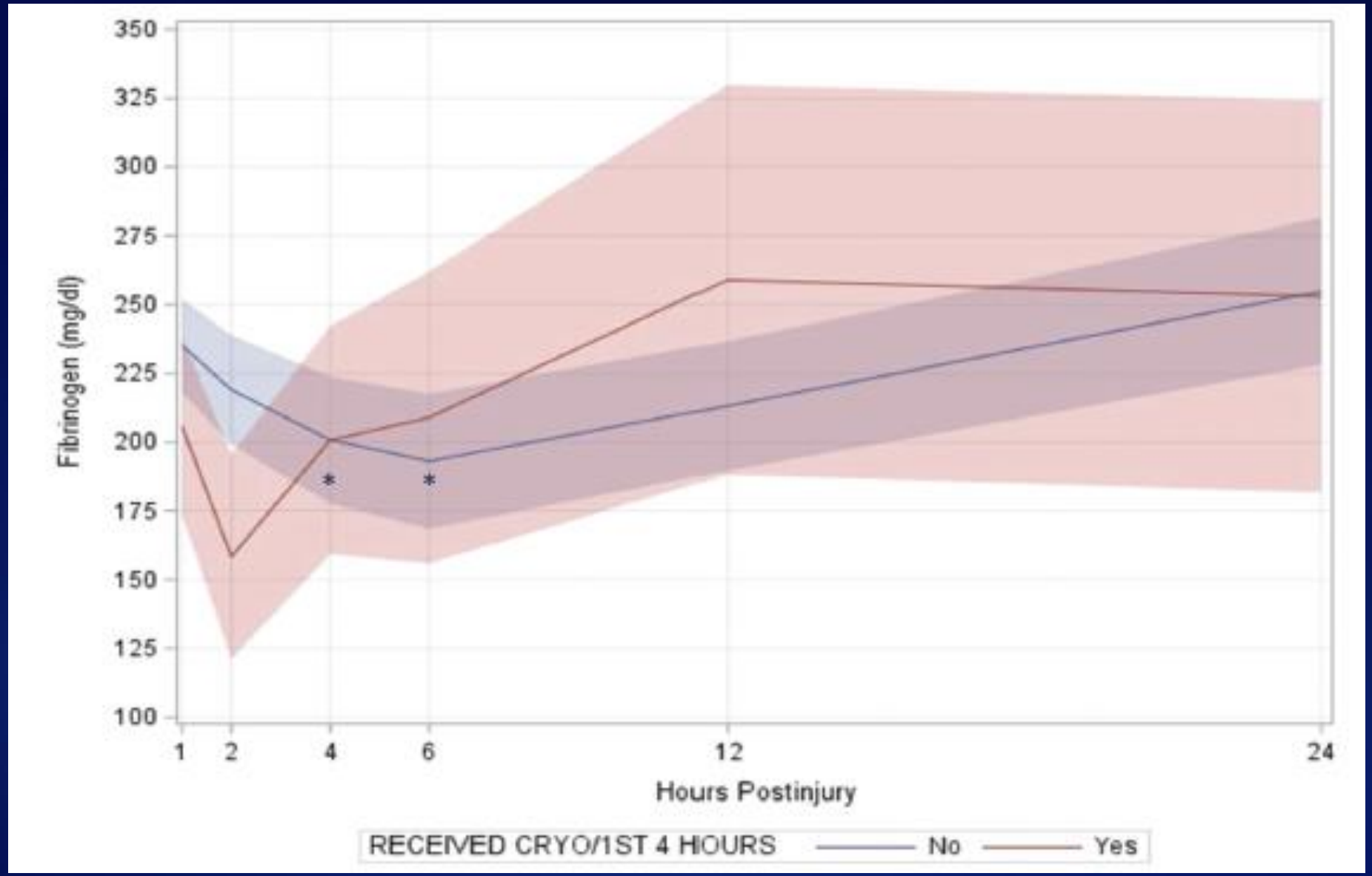
J Am Coll Surg 2022;234:465–473

Methods

- >1,000 consecutive patients, >17 yo and met the highest-level trauma activation criteria 2014-2020.
- Every patient had rTEG drawn on arrival
- For this study, patients with a fibrinogen level drawn on arrival at the attending's discretion were included.

Results

- 476 patients, 15% hypofibrinogenemic on admission
- Admission fibrinogen was an independent risk factor MT
- Early cryoprecipitate administration resulted in the fastest correction of hypofibrinogenemia.


350
325
300
275
250
225
200
175
150
125
100
Fibrinogen (mg/dl)
1
2
4
6
12
24
Hours Postinjury
RECEIVED CRYO/1ST 4 HOURS
No
Yes

Results

- 476 patients, 15% hypofibrinogenemic on admission
- Admission fibrinogen was an independent risk factor MT
- Early cryoprecipitate administration resulted in the fastest correction of hypofibrinogenemia
- In-hospital mortality 37% in hypofib patients vs 11%

Take homes

- Still confused why they used standard fibrinogen level
- Group used ratios of 4:1 (RBCs:plasma) early in study and to this date still uses 2:1 then r-TEG guided therapy
- No wonder their rates are so high!
- No difference in mortality

Open access Original research

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Does an early balanced resuscitation strategy reduce the need for cryoprecipitate in hemorrhagic shock?

David Lubkin MD; Jason Brill MD; Krislynn Mueck MD, MPH; Mariela Sandoval RN; Jessica Cardenas PhD; Bryan Cotton MD, MPH

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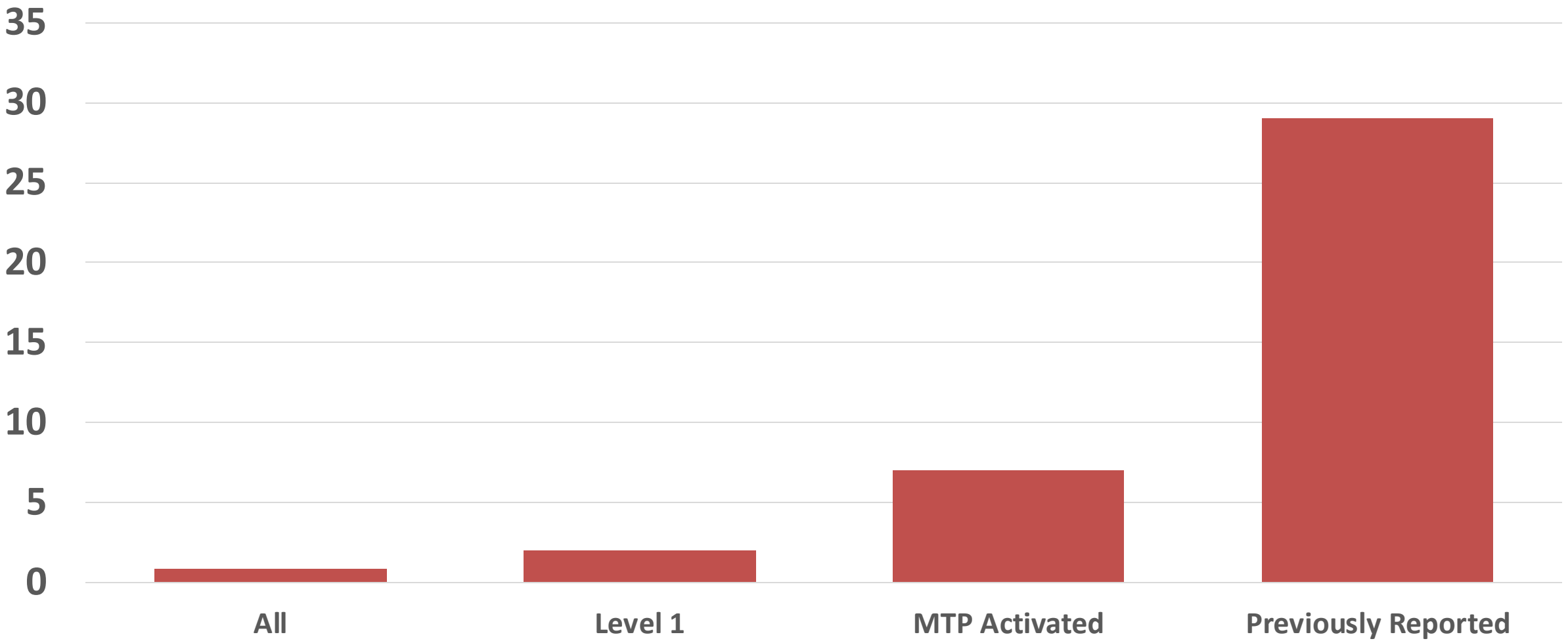
Hypothesis

- Given our institution's policy of early balanced 1:1:1 or WB resuscitation (beginning prehospital), we expected low rates of HYPOFIB on admission to our center. Lower rates would suggest empiric use of concentrated fibrinogen replacement in MTP may not be indicated

UTH experience

- Inclusion: (1) all trauma patients presenting between 11/17-4/21, (2) all level 1 patients >16 y.o., and (3) receiving pre-hospital or ED emergency-release blood products>>MTP
- HYPOFIB if admission fibrinogen <150 or r-TEG angle <60 deg
- Univariate analysis and then multivariate logistic regression were performed to determine risk factors for HYPOFIB
- Multivariate logistic regression weighted for the inverse probability of treatment was performed to assess the effect of early cryoprecipitate transfusion (0-2 hours) on survival

Percentage of HYPOFIB Patients



	HYPOFIB (n=146)	NORMAL (n=1802)	p-value
ED HR	112 (92, 133)	102 (80, 124)	<0.001
ED SBP	94 (77, 122)	100 (80, 124)	0.202
ED GCS	3 (3, 13)	9 (3, 15)	<0.001
Arrival base excess	-7 (-12, -2)	-4 (-8, -1)	<0.001
Arrival hemoglobin	12.4 (10.1, 14.0)	12.4 (10.8, 13.8)	0.928
Arrival platelet count	138 (105, 200)	218 (162, 271)	<0.001
Arrival rTEG-ACT	136 (121, 167)	113 (105, 121)	<0.001
Arrival r-TEG angle	53 (45, 57)	73 (69, 76)	<0.001
Arrival r-TEG MA	45 (38, 52)	63 (59, 68)	<0.001
Arrival r-TEG LY-30	1 (0, 2)	0 (0, 18)	0.302
ED RBC	1 (0, 4)	1 (0, 3)	0.008
ED plasma	2 (0, 5)	1 (0, 3)	<0.001
ED platelets	0 (0, 1)	0 (0, 0)	<0.001
ED WB	0 (0, 1)*	0 (0, 1)	0.013
Post-ED RBC	3 (0, 9)	1 (0, 5)	0.002
Post-ED plasma	2 (0, 6)	0 (0, 3)	<0.001
Post-ED platelets	1 (0, 2)	0 (0, 1)	<0.001

	HYPOFIB (n=146)	NORMAL (n=1802)	p-value
ICU-free days	0 (0, 23)	24 (0, 29)	<0.001
Vent-free days	28 (0, 30)	0 (0, 28)	<0.001
30-day survival	48%	82%	<0.001
Death from TBI	72%	51%	<0.001
Time to death, hrs	28 (7, 50)	36 (14, 140)	0.012

UTH experience

- Higher head AIS (5 vs 3) and ISS (38 vs 26) in HYOFIB patients who died vs those that did not
- On multivariate analysis, decreased age, increased head AIS, decreased arrival BE, and increased pre-hospital RBC:plasma were independent risk factors for HYPOFIB

UTH experience

- 10% HYPOFIB patients received early cryo (0-2 hr)
- No difference in survival in HYPOFIB patients who received early cryo vs none (40 vs 47%, p=0.63)
- On inverse probability of treatment weighted analysis, no mortality benefit for early cryoprecipitate in full cohort or in the HYPOFIB subgroup

UTH experience

- We demonstrated substantially lower rates of HYPOFIB than recent reports; due to early balanced 1:1:1 resuscitation?
- Severe TBI, shock, and unbalanced transfusion ratios were independent risk factors for hypofibrinogenemia
- Early cryo transfusion did not improve outcomes
- Routine inclusion of concentrated fibrinogen replacement in MTPs does not appear to be warranted at this time

Pediatric traumatic hemorrhagic shock consensus conference recommendations

Robert T. Russell, MD, MPH, Joseph R. Esparaz, MD, MPH, Michael A. Beckwith, MD, Peter J. Abraham, MD, Melania M. Bembea, MD, PhD, MPH, Matthew A. Borgman, MD, Randall S. Burd, MD, PhD, Barbara A. Gaines, MD, Mubeen Jafri, MD, Cassandra D. Josephson, MD, Christine Leeper, MD, Julie C. Leonard, MD, MPH, Jennifer A. Muszynski, MD, MPH, Kathleen K. Nicol, MD, Daniel K. Nishijima, MD, MAS, Paul A. Stricker, MD, Adam M. Vogel, MD, Trisha E. Wong, MD, MS, *and* **Philip C. Spinella, MD**, *Birmingham, Alabama*

3.5. In traumatically injured children with hemorrhagic shock, there is insufficient evidence for the empiric use of fibrinogen supplementation (cryoprecipitate or fibrinogen concentrates; consensus panel expertise; 87% agreement [n = 15]; median, 7; IQR, 7–8).

3.6. In traumatically injured children with hemorrhagic shock, we suggest the replacement of fibrinogen in the setting of hypofibrinogenemia (consensus panel expertise; 87% agreement [n = 16]; median, 8; IQR, 8–9).

Hypofibrinogenemia Following Injury in 186 Children and Adolescents: Identification of the Phenotype, Current Outcomes, and Potential for Intervention

Justin Gerard MD, Jan-Michael Van Gent DO, Jessica Cardenas PhD, Christian Gage MD, David Meyer MD, Charles Cox MD, Bryan Cotton MD

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Red Duke Trauma Institute at Memorial Hermann Hospital, Houston, Texas

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Background and Hypothesis

- Hypofibrinogenemia is associated with worse outcomes in trauma
- Unknown whether empiric fibrinogen administration is beneficial in the pediatric trauma population
- We set out to evaluate the prevalence of pediatric patients with hypofibrinogenemia and their outcomes, and to determine whether fibrinogen concentrated products should remain available "on demand" or be incorporated into massive transfusion protocols

Methods

- Patients <16 years old that received emergency release or MTP blood products treated at our center from 11/17-4/21

- Comparison groups:
  - Those with hypofibrinogenemia (fibrinogen < 150 or r-TEG angle < 55) versus those with normal fibrinogen or r-TEG angle values

- Outcome: Factors associated with hypofibrinogenemia, whether early fibrinogen replacement improved outcomes

Results

- 186 patients: 18 HYPOFIB vs 168 in comparison group
- HYPOFIB group younger with worse field and arrival GCS, worse arrival coagulopathy, worse head AIS, and more likely to die from head injury
- Non-HYPOFIB: more likely penetrating, +FAST, and to die of hemorrhage
- Those receiving early cryo had higher mortality on univariate but this was not sustained on multivariate analyses. There were also more likely to arrive to PICU with lower fibrinogen and r-TEG alpha angles

Discussion

- Pediatric patients with HYPOFIB are more likely to have suffered severe head injuries and to die from TBI
- Early fibrinogen replacement did not improve outcomes
- Cryoprecipitate should remain an on-demand product and not be added to massive transfusion protocols in pediatric patients

BJA

British Journal of Anaesthesia 115 (1): 76–83 (2015)

doi: 10.1093/bja/aev134
Advance Access Publication Date 19 May 2015
Clinical Practice

Early cryoprecipitate for major haemorrhage in trauma: a randomised controlled feasibility trial

N. Curry[1,*], C. Rourke[2], R. Davenport[2], S. Beer[1], L. Pankhurst[3], A. Deary[3], H. Thomas[3], C. Llewelyn[3], L. Green[4], H. Doughty[5], G. Nordmann[6,7], K. Brohi[2] and S. Stanworth[1]

[1]Department of Haematology, Oxford University Hospitals NHS Trust, John Radcliffe Hospital, Oxford, UK, [2]Centre for Trauma Sciences, Barts and the London School of Medicine & Dentistry, Queen Mary University of London, London, UK, [3]NHS Blood and Transplant Clinical Trials Unit, NHS Blood & Transplant, Cambridge and Bristol, UK, [4]Department of Haematology, Barts Health NHS Trust, London, UK, [5]NHS Blood and Transplant, Birmingham, UK, [6]Plymouth Hospitals NHS Trust, Plymouth, UK, and [7]The Academic Department of Military Anaesthesia and Critical Care, Royal Centre for Defence Medicine, Birmingham, UK

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	CRYO	STANDARD
SUBJECTS		
N	20	21
Age	31 (16–83)	50 (16–85)
Male	17 (85)	15 (71.4)
TIMELINES		
Injury to Hospital (min)	95 (76–119)	96 (75–106)
INJURIES & PHYSIOLOGY		
Blunt	18 (90)	15 (71)
ISS	28 (22–42)	41 (29–45)
Systolic arterial pressure (mm Hg)	84 (56–104)	79 (65–90)
HR (per min)	124 (91–160)	113 (102–130)
GCS	13 (5–15)	8 (3–15)
Lactate (mEq litre^{-1})	5.0 (3.9–6.0)	6.9 (3.6–12.3)
Base Excess (mEq litre^{-1})	−9.0 (−12.7–6.9)	−14.5 (−20.0–7.1)
Fibrinogen (g litre^{-1})	1.6 (1.43–2.14)	1.55 (1.43–2.24)
PT (sec)	12.6 (11.1–13.4)	13.2 (11.8–15.8)

	INTENTION TO TREAT		
	CRYO	STANDARD	P value
SUBJECTS			
N	20	21	
28 day mortality	2 (10.0)	6 (28.6)	0.14
ICU Days	11 (5–17)	18 (16–20)	0.56
In patient Days	31 (29–33)	30 (22–38)	0.66

	CRYO (*n*=20)	STANDARD (*n*=21)	P value
TIME FROM ADMISSION TO FIRST TRANSFUSION			
RBC (min)	6 (4–15)	11 (6–17)	0.14
FFP (min)	22 (11–42)	32 (15–53)	0.33
Platelets (min)	83 (64–150)	111 (67–160)	0.41
Cryoprecipitate (min)	60 (57–76)	108 (67–147)	0.002
UNITS AT 6 h			
RBC	7 (4–10)	7 (4–8)	0.49
FFP	7 (4–8)	5 (3–8)	0.31
Platelets	1 (0–1)	1 (0–1)	0.89
Cryoprecipitate	2 (2–4)	2 (0–2)	0.03
UNITS AT 24 h			
RBC	8 (5–11)	7 (6–9)	0.83
FFP	7 (4–8)	6 (3–8)	0.36
Platelets	1 (0–2)	1 (1–2)	0.56
Cryoprecipitate	2 (2–4)	2 (0–2)	0.23

BJA

British Journal of Anaesthesia, 117 (6): 775–82 (2016)

doi: 10.1093/bja/aew343

Critical Care

Randomized patients predicted to be at risk for hemorrhage (SBP<100 mHg) and received any emergency-release blood product to 6g of FC/placebo

CRITICAL CARE

Fibrinogen in the initial resuscitation of severe trauma (FiiRST): a randomized feasibility trial

B. Nascimento[1,*], J. Callum[1], H. Tien[1], H. Peng[2], S. Rizoli[3], P. Karanicolas[1], A. Alam[1], W. Xiong[1], R. Selby[1], A-M. Garzon[1], C. Colavecchia[1], R. Howald[1], A. Nathens[1], and A. Beckett[4]

[1]Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Defence Research and Development Canada, Toronto, ON, Canada, [3]Saint Michael's Hospital, Toronto, ON, Canada and [4]Montreal General Hospital, Montreal, Quebec, Canada

BJA

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doi: 10.1093/bja/aew343

Critical Care

Excluded if they had: received any blood products before admission; presented more than 6h after injury; estimated body weight<50 kg; had known or suspected pregnancy; catastrophic brain injury

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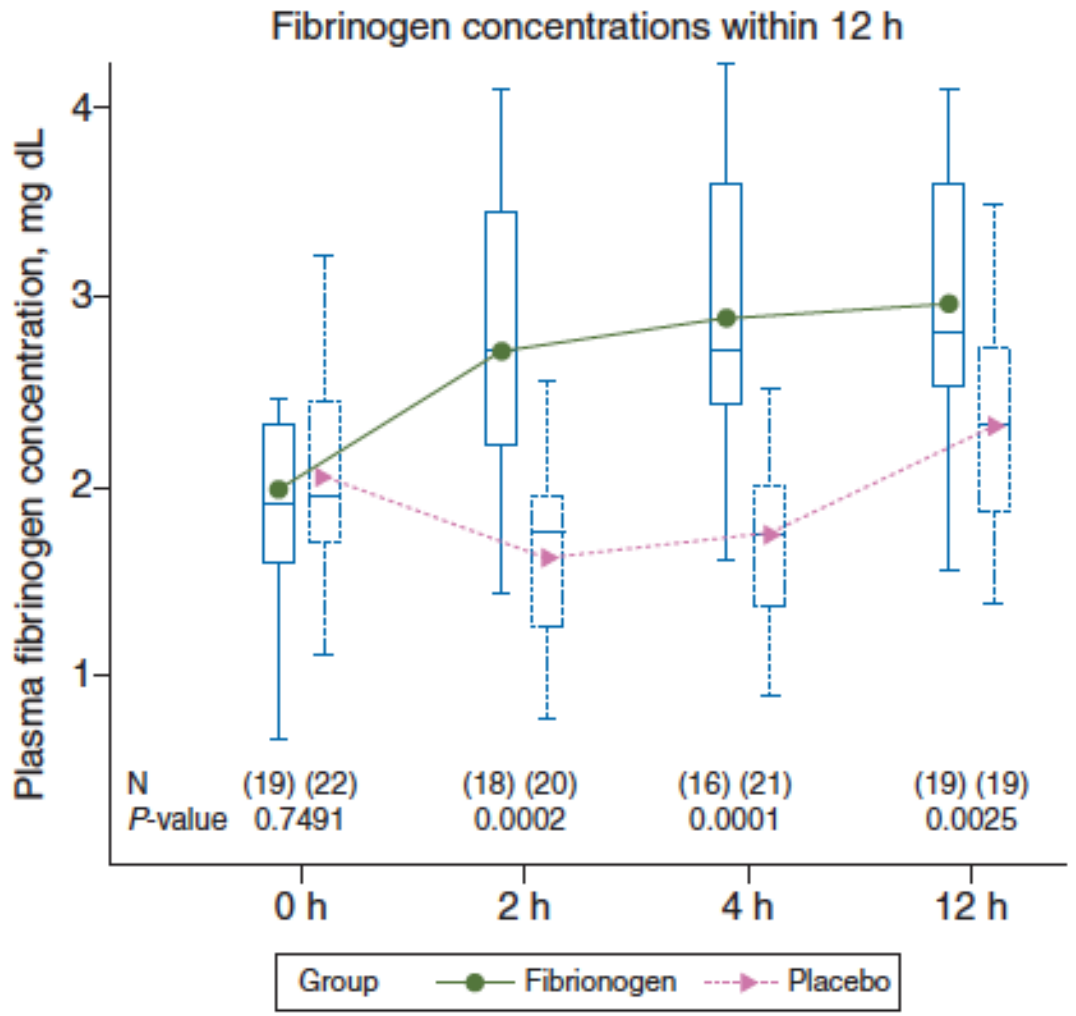
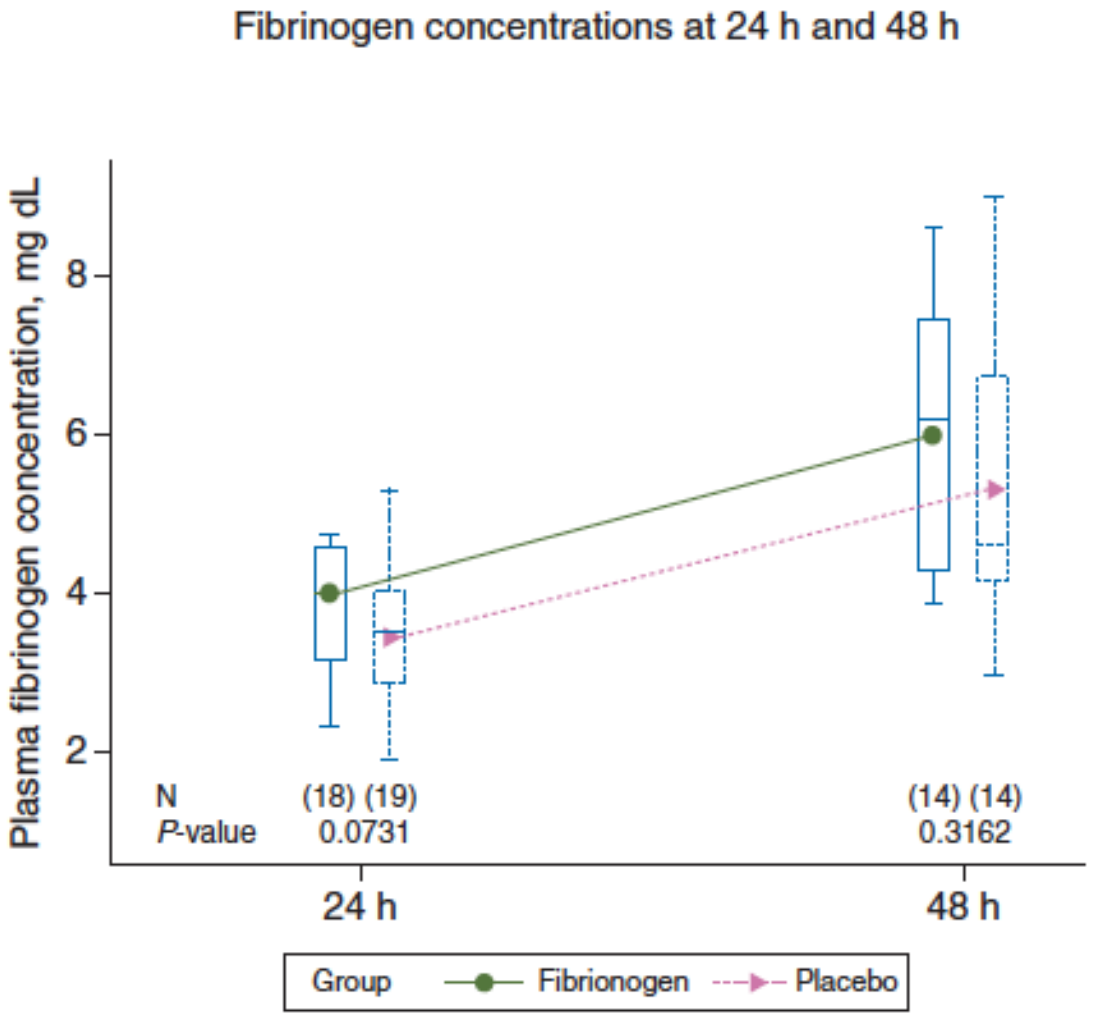

Fibrinogen concentrations within 12 h
Plasma fibrinogen concentration, mg dL
1
2
3
4
N (19) (22) (18) (20) (16) (21) (19) (19)
P-value 0.7491 0.0002 0.0001 0.0025
0 h
2 h
4 h
12 h
Group Fibrionogen Placebo


Fibrinogen concentrations at 24 h and 48 h
Plasma fibrinogen concentration, mg dL
2
4
6
8
N (18) (19) (14) (14)
P-value 0.0731 0.3162
24 h
48 h
Group Fibrionogen Placebo

	Placebo n=24	FC n=21	Relative Risk	95% CI
All-cause 28-day mortality[1]	1/24 (4.2)	2/20[2] (10)	2.4	−0.2 to 23
Death by exsanguination[3]	0	1/21 (4.8)	NA	NA
Symptomatic Deep Venous Thrombosis	0	0	NA	NA
Deep Venous Thrombosis on Leg Doppler	3/14 (21.4)	2/15 (13.3)	0.62	−0.1 to 3.2
Pulmonary Embolism	1/24 (4.2)	2/21 (9.5)	2.3	−0.2 to 23.4
Myocardial Infarction	0	0	NA	NA
Stroke	0	0	NA	NA
Acute Lung Injury	2/24 (8.3)	0	NA	NA
Acute Respiratory Distress Syndrome	2/24 (8.3)	0	NA	NA
Acute Kidney Injury	2/24 (8.3)	3/21 (14.3)	1.7	−0.3 to 9.3
Multiple Organ Failure	2/24 (8.3)	2/21 (9.5)	1.1	−0.2 to 7.4
Infection	8/24 (33.3)	5/21 (23.8)	0.7	−0.3 to 1.8

CRYOSTAT - 2 trial?

- International multi-center trial including trauma centers in England and the United States. Four US Level 1 trauma center sites planned to participate (UCSF, Shock Trauma, USC, UTH).

- Purpose: Determine the effect of cryoprecipitate given in addition to standard blood products to provide the best outcomes for the patients.

- Plan: Enroll approximately 1500 patients (400 in the US) who are severely bleeding due to trauma and predicted to receive significant amounts of blood products into a protocol using cryoprecipitate (fibrinogen) with the standard massive transfusion (MT) blood products compared to a control group receiving the standard MT products.

Patient Selection

Inclusion

- Severely injured
- 16 years or older or greater than/equal to 50 kg if unknown
- Directly from scene
- Received at least 1U unit blood in the first two hours of injury
- MTP started by attending surgeon

Exclusion

- Transfer
- > 3 hours from time of injury
- Non-survivable injuries
- Prisoners directly from jail
- 15 years or less, <50 kg
- Obvious pregnancy
- Severely burned
- Known “DNR” status
- Enrolled in concurrent interventional, RCT
- “opt-out” bracelet

CRYOSTAT-2 results

- US sites were asked to join after the fact
- Then there's the FDA/IND…
- And…we had COVID

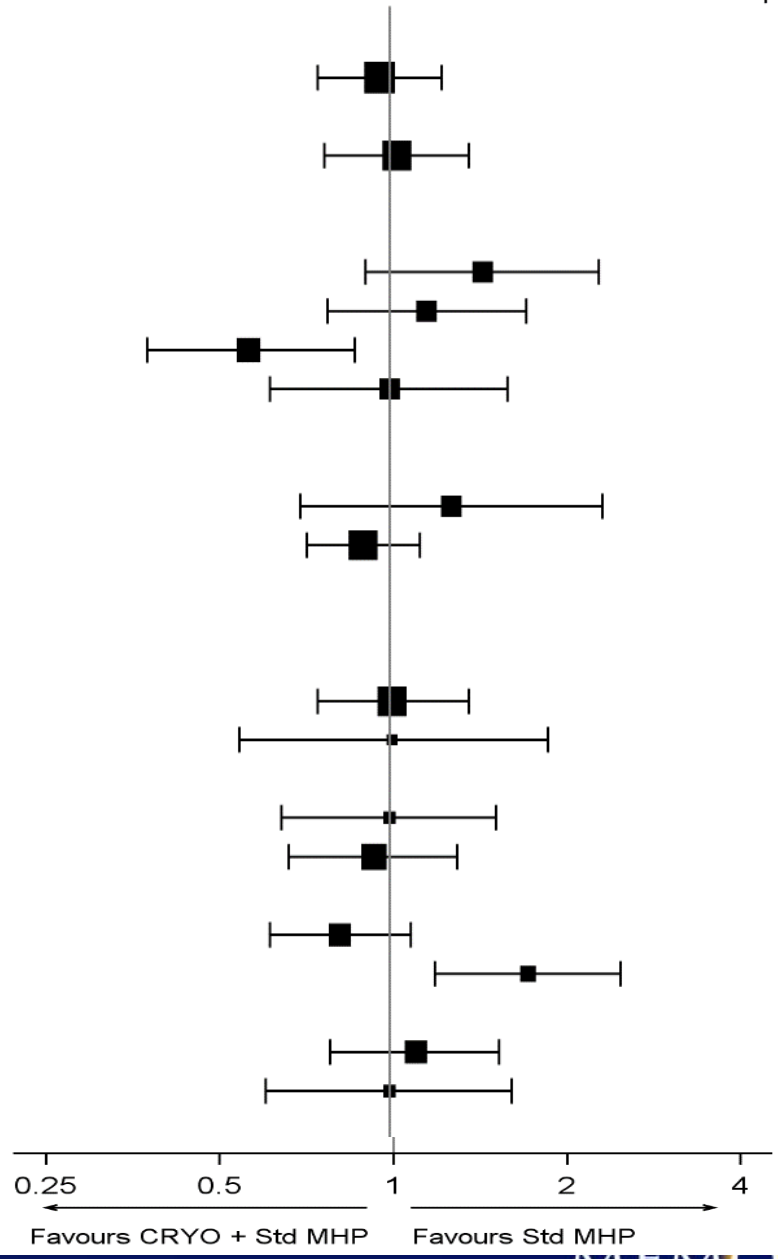
CRYO-STAT-2

- CRYOSTAT-2 enrolled 1604 patients; 805 (STD) vs 799 (CRYO).
- Primary outcome data was unavailable in 73 participants leaving 1531 patients available for analysis.
- Median ISS 29 (IQR 18-43), 36% penetrating injury, 33% SBP<90 mmHg prehospital, 79% received TXA and 43% received blood prehospital.
- Median time from admission to first cryo was 68 minutes in the CRYO arm vs 120 minutes in the STD arm; 68% of cryo patients receiving their first dose within the study goal of 90 minutes after admission

CRYO-STAT-2

- All-cause 28-day mortality in the ITT analysis was 26.1% (STD) vs 25.3% (CRYO) (OR 0.96, p=0.74).
- Mortality was similar at 6 hours (CRYO vs STD: 7.1% vs 8.6%, OR 0.82, p=0.26) and 24 hours (CRYO vs STD: 11.2% vs 12.2%, OR 0.91, p=0.61).
- Deaths from bleeding at 6h, 24h and 28-days was not different.
- Median time to death from hemorrhage was 191 minutes in the CRYO arm vs 86 minutes in the STD arm

	Std MHP n/N (%)		CRYO + Std MHP n/N (%)		Odds Ratio (95% CI)	p-value
Main ITT	201/771	(26.1%)	192/760	(25.3%)	0.96 (0.75, 1.23)	0.74
Per-Protocol	154/683	(22.5%)	163/706	(23.1%)	1.03 (0.77, 1.37)	0.83
Cryoprecipitate timing	201/771	(26.1%)				
CRYO <= 45m from adm			33/96	(34.4%)	1.45 (0.91, 2.31)	0.12
CRYO 46-60m from adm			42/144	(29.2%)	1.16 (0.78, 1.73)	0.46
CRYO 61-90m from adm			44/267	(16.5%)	0.57 (0.38, 0.87)	0.01
CRYO > 90m from adm			31/123	(25.2%)	1.00 (0.62, 1.60)	0.99
Cryoprecipitate administered	201/771	(26.1%)				
CRYO - no cryoprecipitate			39/123	(31.7%)	1.28 (0.70, 2.34)	0.41
CRYO - some cryoprecipitate			153/637	(24.0%)	0.90 (0.72, 1.13)	0.36
Subgroup Analyses						
Participant Age						
<70 years	146/681	(21.4%)	149/687	(21.7%)	1.01 (0.75, 1.37)	0.93
≥70 years	49/84	(58.3%)	40/69	(58.0%)	1.01 (0.55, 1.88)	0.97
Participant Sex						
Female	53/155	(34.2%)	56/164	(34.1%)	1.00 (0.65, 1.53)	1.00
Male	148/616	(24.0%)	136/596	(22.8%)	0.94 (0.67, 1.31)	0.69
Injury Type						
Blunt	174/500	(34.8%)	147/483	(30.4%)	0.82 (0.62, 1.09)	0.16
Penetrating	27/271	(10.0%)	45/277	(16.2%)	1.74 (1.20, 2.51)	0.01
Head AIS Score						
<4	79/472	(16.7%)	92/506	(18.2%)	1.11 (0.79, 1.55)	0.55
≥4	94/191	(49.2%)	77/157	(49.0%)	1.00 (0.61, 1.63)	0.99



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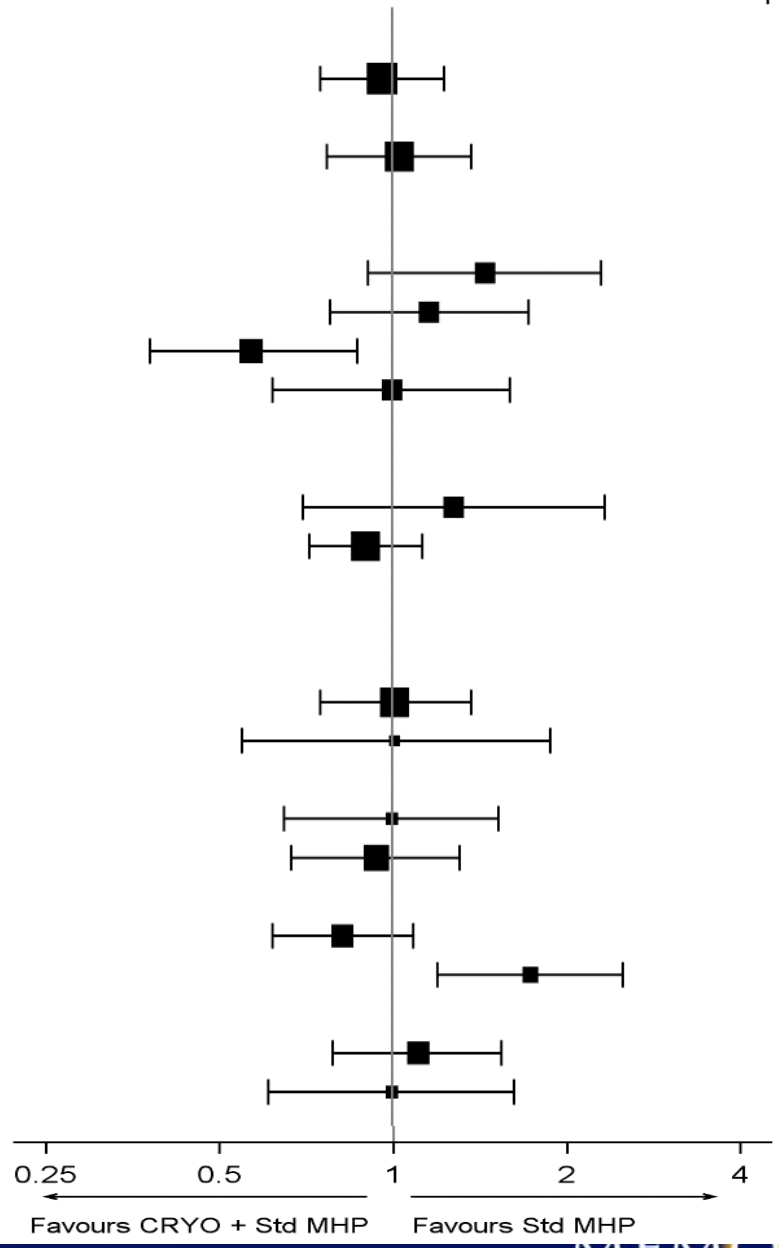


UTH Only


41
OR3 41
OR 41
CAUTION:
Radiation
Area

	CRYO (n=23)	STANDARD (n=26)	p-value
Field SBP, mmHg	86 (67, 107)	92 (82, 124)	0.484
Field HR, bpm	126 (106, 133)	122 (110, 134)	0.989
Field GCS	13 (13, 15)	6 (3, 15)	0.086
Field fluids, L	0 (0, 0)	0 (0, 0)	0.602
Field RBC, U	0 (0, 1)	0 (0, 0)	0.967
Field plasma, U	0 (0, 0)	0 (0, 0)	0.326
Field whole blood, U	0 (0, 1)	0 (0, 0)	0.293

	CRYO (n=23)	STANDARD (n=26)	p-value
Median age, years	44 (49, 26)	34 (27, 40)	0.065
Male sex	74%	76%	0.867
Race			
White	47%	30%	0.221
Black	29%	35%	
Hispanic	24%	18%	
Other	0%	17%	
Blunt mechanism	52%	46%	0.663
Head AIS	4 (3, 5)	4 (3, 5)	0.518
Chest AIS	3 (3, 4)	3 (3, 4)	0.613
Abdominal AIS	4 (3, 4)	4 (3, 4)	0.467
Extremity AIS	3 (3, 4)	3 (2, 3)	0.335
ISS	33 (24, 42)	27 (22, 41)	0.487

	CRYO (n=23)	STANDARD (n=26)	p-value
Arrival SBP, mmHg	80 (70, 100)	86 (78, 118)	0.197
Arrival HR, bpm	125 (101, 136)	128 (99, 136)	0.866
Arrival GCS	15 (13, 15)	13 (3, 15)	0.128
ED RBC, U	1 (0, 1)	0 (0, 1)	0.331
ED plasma, U	0 (0, 1)	0 (0, 1)	0.547
ED platelets, U	0 (0, 0)	0 (0, 0)	0.973
ED whole blood, U	0 (0, 1)	0 (0, 1)	0.989
Post-ED RBC, U	15 (9, 24)	12 (6, 17)	0.495
Post-ED plasma, U	15 (6, 23)	9 (5, 17)	0.383
Post-ED platelets, U	2 (1, 3)	1 (0, 2)	0.135
Post-ED cryo, U	3 (3, 3)	0 (0, 0)	<0.001

	CRYO (n=23)	STANDARD (n=26)	p-value
ED creatinine	1.4 (1.2, 1.8)	1.2 (1.1, 1.5)	0.204
ED potassium	3.8 (3.3, 4.5)	3.7 (3.3, 4.0)	0.775
ED hemoglobin	12.2 (11.6, 13.8)	12.1 (11.7, 13.3)	0.418
ED platelets	202 (150, 214)	227 (163, 270)	0.159
ED pH	7.16 (7.03, 7.28)	7.25 (7.19, 7.31)	0.130
ED base deficit	-10 (-14, -6)	-8 (-10, -5)	0.108
ED lactate	7.1 (4.8, 9.6)	4.6 (3.6, 6.8)	0.093
ED r-TEG ACT	113 (105, 113)	113 (105, 113)	0.467
ED r-TEG k-time	2.0 (1.5, 2.7)	1.8 (1.2, 2.1)	0.261
ED r-TEG alpha angle	70 (65, 72)	72 (66, 76)	0.337
ED r-TEG MA	59 (54, 64)	60 (56, 64)	0.624
ED r-TEG LY-30	0.9 (0.0, 5.8)	0.2 (0.0, 0.9)	0.125

	CRYO (n=23)	STANDARD (n=26)	p-value
OR arrival R-time, min	5.2 (4.2, 7.2)	5.9 (5.0, 10.3)	0.080
OR arrival K-time, min	1.6 (1.3, 3.0)	1.5 (1.3, 2.8)	0.586
OR arrival alpha-angle, deg	71 (62, 73)	71 (58, 73)	0.752
OR arrival MA, mm	56 (43, 61)	57 (51, 59)	0.952
OR arrival heparinase R, min	5.1 (4.0, 6.2)	6.0 (4.9, 10.8)	0.073
OR arrival FF-MA, mm	16.5 (12.3, 20.6)	16.9 (16.1, 18.6)	0.456
OR arrival FF-fibrinogen, mg/dL	300 (257, 374)	306 (293, 327)	0.606
OR repeat R-time, min	8.9 (7.4, 10.6)	8.3 (6.2, 13.0)	0.971
OR repeat K-time, min	2.1 (1.4, 4.2)	2.2 (2.1, 2.3)	0.933
OR repeat alpha-angle, deg	66 (52, 73)	68 (66, 69)	0.800
OR repeat MA, mm	57 (54, 64)	52 (51, 53)	0.266
OR repeat heparinase R, min	7.7 (6.7, 9.6)	7.5 (5.7, 11.1)	0.743
OR repeat FF-MA, mm	19.0 (17.1, 28.0)	16.4 (10.4, 17.7)	0.210
OR repeat FF-fibrinogen, mg/dL	345 (311, 510)	299 (189, 323)	0.228

	CRYO (n=23)	STANDARD (n=26)	p-value
Delta R-time, min	2.3 (-4.3, 4.6)	-1.6 (-3, 14.5)	1.000
Delta K-time, min	-0.3 (-3.7, 2.5)	-1.1 (-1.7, -0.5)	0.800
Delta alpha-angle, deg	-3.1 (-20.2, 3.4)	11.8 (7.3, 16.2)	0.200
Delta MA, mm	10.8 (4.5, 16.9)	-0.5 (-3.4, 2.4)	0.200
Delta Heparinase R-time, min	0.2 (-3.4, 2.3)	-0.7 (-5.2, 6.7)	1.000
Delta MA-FF, mm	7.4 (-0.6, 15.1)	-0.1 (-4.6, 0.3)	0.400
Delta FF-fibrinogen, mg/dL	135 (-11, 276)	-1.8 (-84, 5.5)	0.400

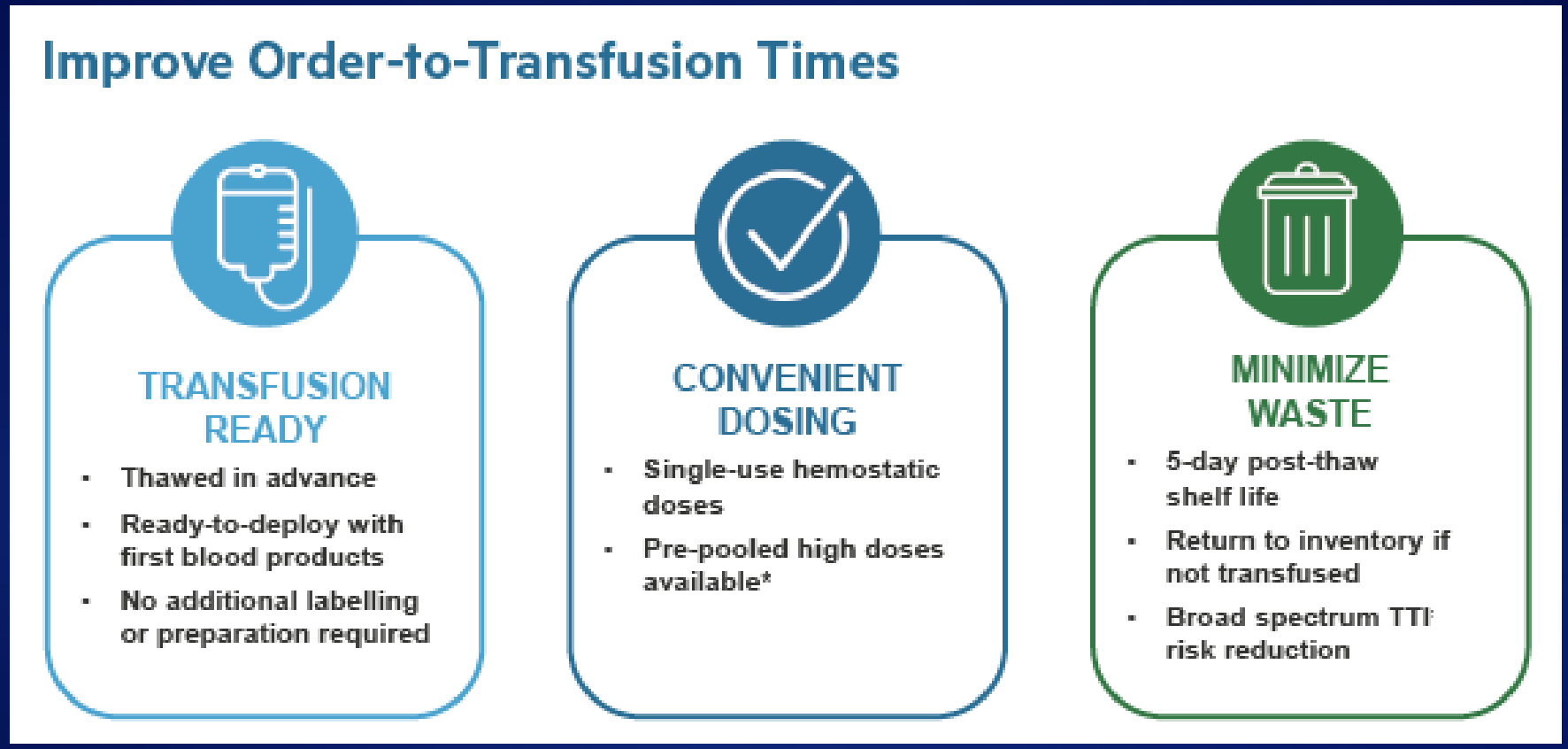
	CRYO (n=23)	STANDARD (n=26)	p-value
Acute renal failure	39%	28%	0.479
Venous thromboembolism	17%	12%	0.559
Sepsis	33%	44%	0.494
Pneumonia	33%	39%	0.728
UTI	0%	6%	0.310
24-hour P/F	310 (175, 381)	280 (180, 474)	0.838
48-hour P/F	284 (131, 324)	338 (200, 498)	0.363
72-hour P/F	235 (102, 280)	188 (147, 328)	0.905
Discharge GOSE	3 (1, 5)	4 (3, 5)	0.218
In-hospital mortality	22%	12%	0.405
Hemorrhage	40%	0%	
TBI	40%	67%	
MOF	20%	33%	

	CRYO (n=23)	STANDARD (n=26)	p-value
Time to randomization, min	28 (11, 43)	20 (13, 39)	0.676
Time to cryoprecipitate, min	41 (37, 48)	N/A	N/A

Take home?

- Is cryo necessary on an empric basis?
- Not when it takes 40 minutes after ordering
- Do any of the studies mean anything if you can't get the product in quick enough?

Intercept (IFC): Pathogen-reduced Cryoprecipitate



Efficacy of a new pathogen-reduced cryoprecipitate stored 5 days after thawing to correct dilutional coagulopathy in vitro

Melissa M. Cushing[1,2] *Lars M. Asmis,*[3] *Rebecca M. Harris,*[1] *Robert A. DeSimone*[1] *Shanna Hill,*[2] *Natalia Ivascu,*[2] *and Thorsten Haas*[4]

Pathogen reduced cryo

- Specimens from 10 healthy volunteers, diluted 1:1 with crystalloid and supplemented with PR Cryo and Cryo (at a dose replicating transfusion of two pooled doses [10 units]) and FC at a dose replicating 50 mg/kg.

- Changes in clot firmness (thromboelastometry) and in coagulation factor activity were assessed at baseline, after dilution, and after supplementation.

Pathogen reduced cryo

- FC contained 24/36% more fibrinogen vs PR Cryo/Cryo, resp.
- Baseline FIBTEM-MCF 13.5 mm, 6.5 mm > 50% dilution $p<0.05$
- After PR Cryo, median MCF 13 vs 9.0 mm for Cryo ($p<0.05$) and 16.5 mm for FC ($p<0.05$)
- Factor XIII after PR Cryo (65%) vs Cryo (48%); $p<0.05$, fibrinogen after FC (269) vs PR Cryo (187) or Cryo (193); $p<0.05$

Conclusions

- Is empiric cryo replacement necessary when your resuscitation doesn't suck? Balanced/WB, true DCR starting in the field
- Based on international, RCT, empiric cryoprecipitate transfusion does not appear to be indicated, based on labs?
- However, these recommendations are based on delays inherent in the ordering/thawing/transport process
- Can an immediately available product (IFC, FC) demonstrate clinical benefit of empiric fibrinogen replacement therapy?
- Is there a phenotype that truly benefit? TBI?

Hemostatic Adjuncts: Cryoprecipitate

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