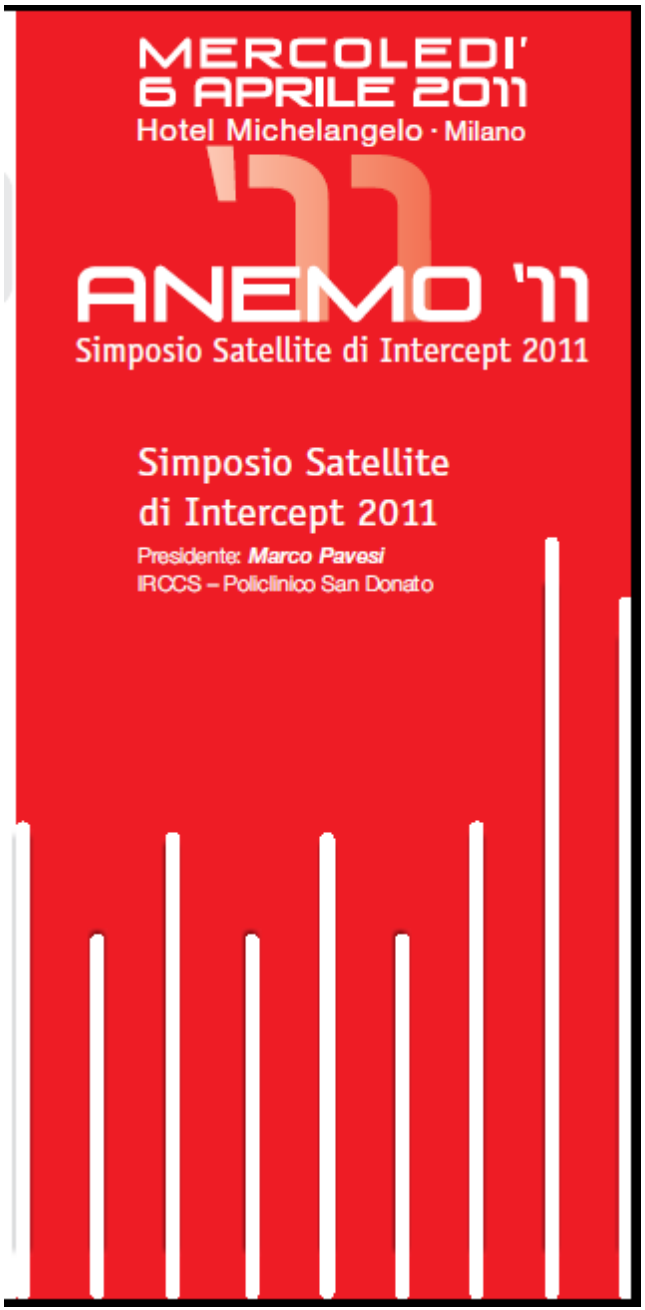


Trattamento medico delle emorragie massive

Dott. Marco Marietta

Azienda Ospedaliero-Universitaria

Modena

Due modelli epistemologici…

Modello nomotetico

Modello idiografico

Evidence-based practice guidelines for plasma transfusion

doi: 10.1111/j.1537-2995.2010.02632.x
TRANSFUSION **;**:**-**.

John D. Roback, Stephen Caldwell, Jeff Carson, Robertson Davenport, Mary Jo Drew, Anne Eder, Mark Fung, Marilyn Hamilton, John R. Hess, Naomi Luban, Jeremy G. Perkins, Bruce S. Sachais, Aryeh Shander, Toby Silverman, Ed Snyder, Christopher Tormey, John Waters, and Ben Djulbegovic

*Recommendation: We **suggest** that plasma be transfused to trauma patients requiring massive transfusion (quality of evidence = **moderate**).*

*Recommendation: We **cannot recommend** for or against transfusion of plasma at a plasma : RBC ratio of 1:3 or more in trauma patients during massive transfusion (quality of evidence = **low**).*

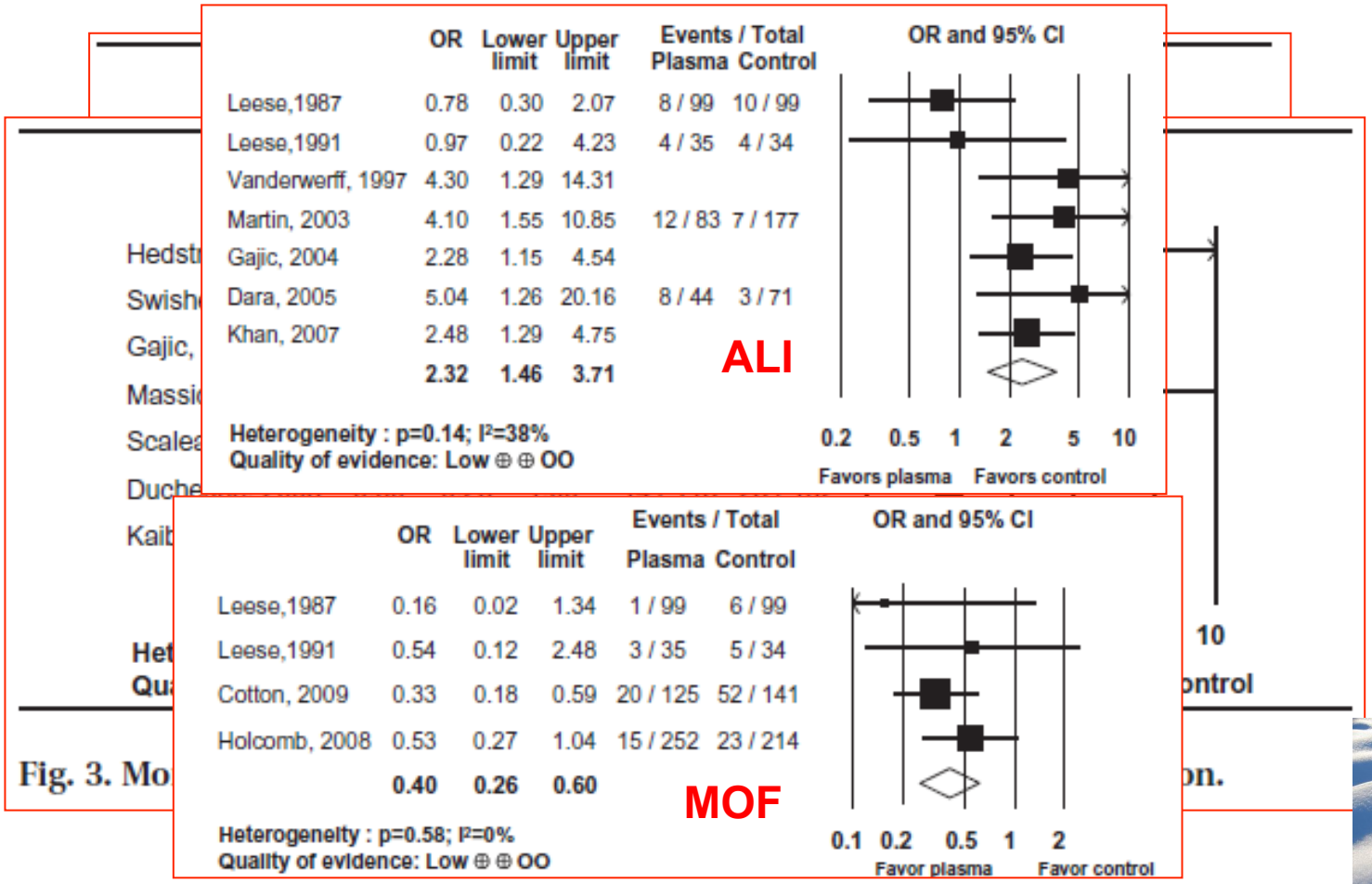
*Recommendation: We **cannot recommend** for or against transfusion of plasma for patients undergoing surgery in the absence of massive transfusion (quality of evidence = **very low**).*

*Recommendation: We **suggest against** plasma transfusion in other groups for which data were available (acute pancreatitis, organophosphate poisoning, coagulopathy*

The effect of plasma transfusion on morbidity and mortality: a systematic review and meta-analysis

doi: 10.1111/j.1537-2995.2010.02630.x
TRANSFUSION **;**:**-**.

Mohammad Hassan Murad, James R. Stubbs, Manish J. Gandhi, Amy T. Wang, Anu Paul, Patricia J. Erwin, Victor M. Montori, and John D. Roback



World J Surg
DOI 10.1007/s00268-008-9655-0

Outcome Analysis of Blood Product Transfusion in Trauma Patients: A Prospective, Risk-Adjusted Study

Grant V. Bochicchio · Lena Napolitano · Manjari Joshi · Kelly Bochicchio · Walter Meyer · Thomas M. Scalea

	PRBCs OR (CI)	FFP OR (CI)	Platelets OR (CI)
Infection	2.8 (1.96–3.94)*	1.02 (1.01–1.04)*	0.94 (0.96–1)
Hospital LOS	8.1 (6.6–9.03)*	1.3 (1.3–1.41)*	−0.15 (−0.023 to 0.07)*
ICU LOS	5.6 (4.2–7.06)*	1.25 (1.2–1.31)*	−0.08 (−0.14 to 0.01)*
Mortality	1.05 (1.03–1.07)*	1.03 (1.02–1.05)*	1.03 (1.02–1.04)

+3.5% rischio di morte per ogni unità di PFC trasfusa

Blood product use in trauma resuscitation: plasma deficit versus plasma ratio as predictors of mortality in trauma

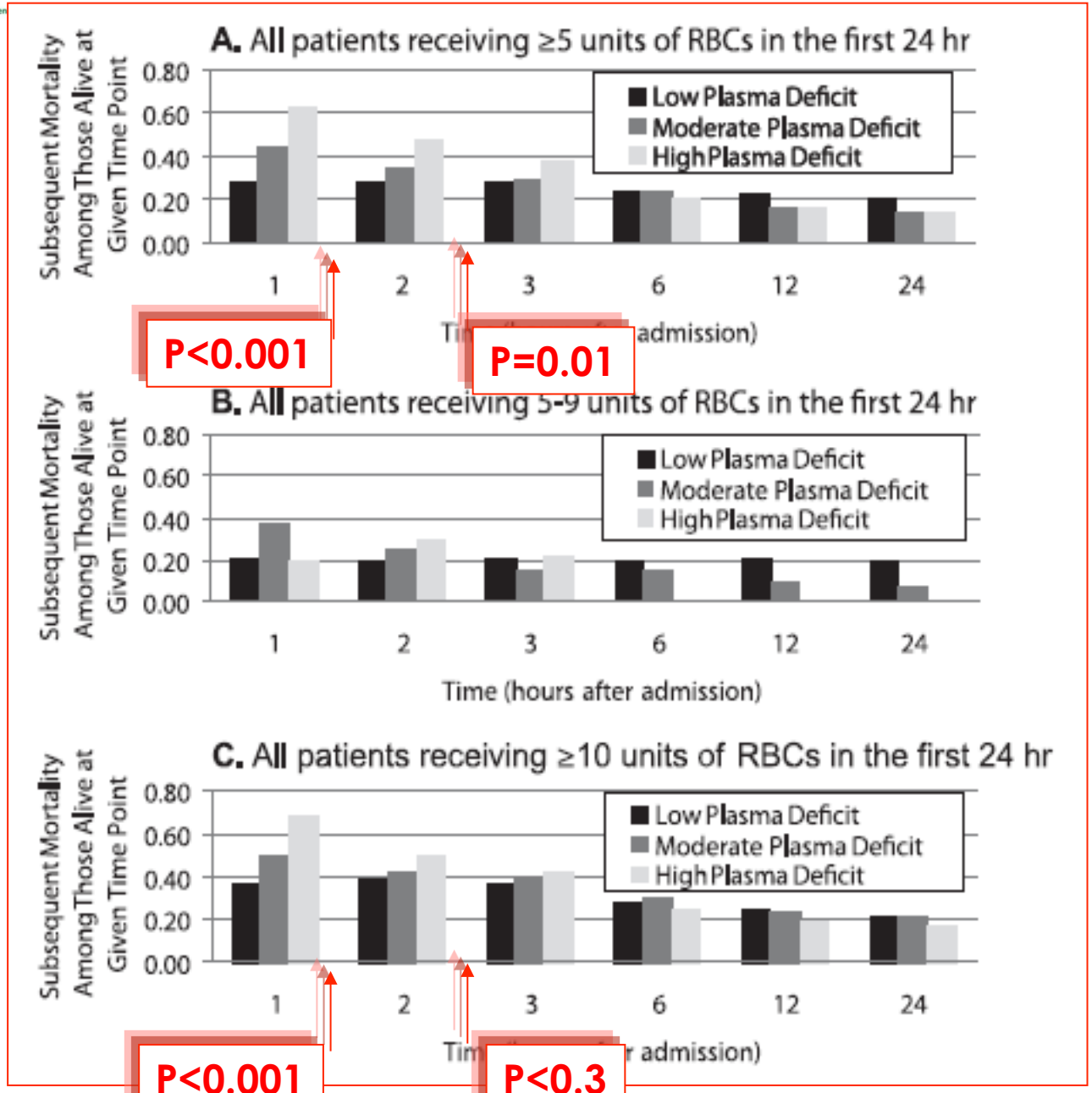
TRANSFUSION **;**:**-**.

Andreas R. de Biasi, Lynn G. Stansbury, Richard P. Dutton, Deborah M. Stein, Thomas M. Scalea,

TABLE 4. Plasma deficit (units of RBCs transfused minus units of plasma transfused) and ratio of plasma repletion (expressed as units of plasma divided by units of RBCs) as predictors of mortality in rapidly bleeding trauma patients

	Deficit status				Ratio status			
Patient characteristics	Low 0-2	3-6	High > 6	p value*	Good > 0.66	0.66-0.34	Poor < 0.34	p value
A. At 24 hr into resuscitation								
All patients (%)†	184 (40.0)	148 (33.8)	106 (24.2)		249 (56.9)	111 (25.3)	78 (17.8)	
TRISS, mean (SD)‡	0.658 (0.32)	0.571 (0.75)	0.501 (0.36)	0.001	0.625 (0.34)	0.537 (0.35)	0.559 (0.36)	0.06
Deaths, number (%)	59 (32.1)	62 (41.9)	61 (57.5)	<0.001	97 (39)	50 (45.1)	35 (44.9%)	0.5
5 to 9 units (%)	83 (49.1)	71 (42.0)	15 (8.9)		80 (43.3)	36 (21.3)	53 (31.4)	
TRISS, mean (SD)	0.659 (0.31)	0.581 (0.34)	0.586 (0.40)	0.3	0.658 (0.31)	0.580 (0.32)	0.589 (0.37)	0.1
Deaths, number (%)	21 (25.3)	25 (32.2)	6 (40.0)	0.3	21 (26.3)	9 (25)	22 (41.5)	0.1
>9 units (%)	101 (37.6)	77 (28.6)	91 (33.8)		169 (62.8)	75 (27.9)	25 (9.3)	
TRISS, mean (SD)	0.658 (0.34)	0.561 (0.36)	0.492 (0.35)	0.01	0.609 (0.35)	0.519 (0.35)	0.496 (0.34)	0.4
Deaths, number (%)	38 (37.6)	37 (48.1)	55 (60.4)	0.007	76 (45)	41 (54.7)	13 (52)	0.4
B. At 3 hr into resuscitation								
All patients (%)	176 (40.2)	170 (38.8)	92 (21)		202	117	119	
TRISS, mean (SD)‡	0.667 (0.32)	0.561 (0.35)	0.500 (0.36)	<0.001	0.622 (0.35)	0.526 (0.35)	0.602 (0.34)	0.05
Deaths, number (%)	54 (30.7)	72 (42.4)	56 (60.9)	0.001	80 (39.6)	57 (48.7)	45 (37.8)	0.2
5 to 9 units (%)	87 (51.5)	68 (40.2)	14 (8.3)		63	32	74	
TRISS, mean (SD)	0.678 (0.31)	0.562 (0.34)	0.537 (0.40)	0.06	0.674 (0.33)	0.555	0.602	0.2
Deaths, number (%)	19 (21.8)	27 (39.7)	6 (42.9)	0.03	16 (25.4)	11 (34.4)	25 (33.8)	0.5
>9 units (%)	89 (33.1)	102 (37.9)	78 (29)		139	85	45	
TRISS, mean (SD)	0.656 (0.33)	0.560 (0.35)	0.493 (0.36)	0.01	0.598 (0.35)	0.514 (0.35)	0.603 (0.34)	0.2
Deaths, number (%)	35 (39.3)	45 (44.1)	50 (64.1)	0.003	64 (46.0)	46 (54.1)	20 (44.4)	0.4

* Probability of no true difference between plasma status groups by ANOVA F statistic for continuous and chi square for categorical variables.
† All = 5 or more units of RBCs at 24 hours into resuscitation.
‡ TRISS: probability of survival.



De Biasi AR et al. Transfusion 2011

Peiniger *et al. Critical Care* 2011, **15**:R68
http://ccforum.com/content/15/1/R68

CRITICAL CARE

RESEARCH Open Access

Balanced massive transfusion ratios in multiple injury patients with traumatic brain injury

Table 3 Morbidity and mortality according to study groups[a]

	AIS score, head <3			AIS score, head ≥3		
Morbidity and mortality	**FFP:pRBC ratio ≤1:2**	**FFP:pRBC ratio >1:2**	***P* value**	**FFP:pRBC ratio ≤1:2**	**FFP:pRBC ratio >1:2**	***P* value**
Sepsis, *n* (%)	31 (21.5%)	91 (23.6%)	0.608	19 (15.7%)	98 (24.9%)	0.035
Multiorgan failure, *n* (%)	86 (58.5%)	211 (55.7%)	0.557	80 (67.2%)	276 (71.3%)	0.393
Mean ventilator-free days (±SD)	8.7 ± 11.2	12.8 ± 11.6	<0.001	4.3 ± 8.1	6.1 ± 9.0	0.006
Survivors' mean ventilation-free days (±SD)	16.9 ± 10.2	17.4 ± 10.1	0.647	11.5 ± 9.6	11.1 ± 9.7	0.825
Mean ICU LOS, days (±SD)	14.7 ± 19.4	18.5 ± 20.1	<0.001	12.5 ± 18.5	18.2 ± 21.3	<0.001
Survivors' mean ICU LOS, days (±SD)	24.7 ± 20.5	23.1 ± 20.6	0.335	29.0 ± 20.8	29.7 ± 22.3	0.703
Mean HLOS, days (±SD)	30.2 ± 40.3	43.3 ± 40.2	<0.001	20.6 ± 30.1	29.9 ± 36.4	<0.001
Survivors' mean HLOS, days (±SD)	54.3 ± 43.0	56.3 ± 38.5	0.361	49.2 ± 32.3	49.9 ± 36.8	0.934
6-hour mortality, *n* (%)	74 (34.9%)	45 (10.6%)	<0.001	55 (32.9%)	69 (15.5%)	<0.001
24-hour mortality, *n* (%)	85 (40.1%)	47 (17.4%)	<0.001	74 (44.3%)	110 (24.7%)	<0.001
30-day mortality, *n* (%)	97 (45.8%)	105 (24.6%)	<0.001	104 (62.3%)	199 (44.7%)	<0.001
In-hospital overall mortality, *n* (%)	102 (48.1%)	114 (26.8%)	<0.001	104 (62.3%)	203 (45.6%)	<0.001

[a]AIS, Abbreviated Injury Scale; FFP, fresh frozen plasma; pRBC, packed red blood cell; ICU, intensive care unit; LOS, length of stay; SD, standard deviation; HLOS, hospital length of stay.

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero-Universitaria di Modena

Policlinico

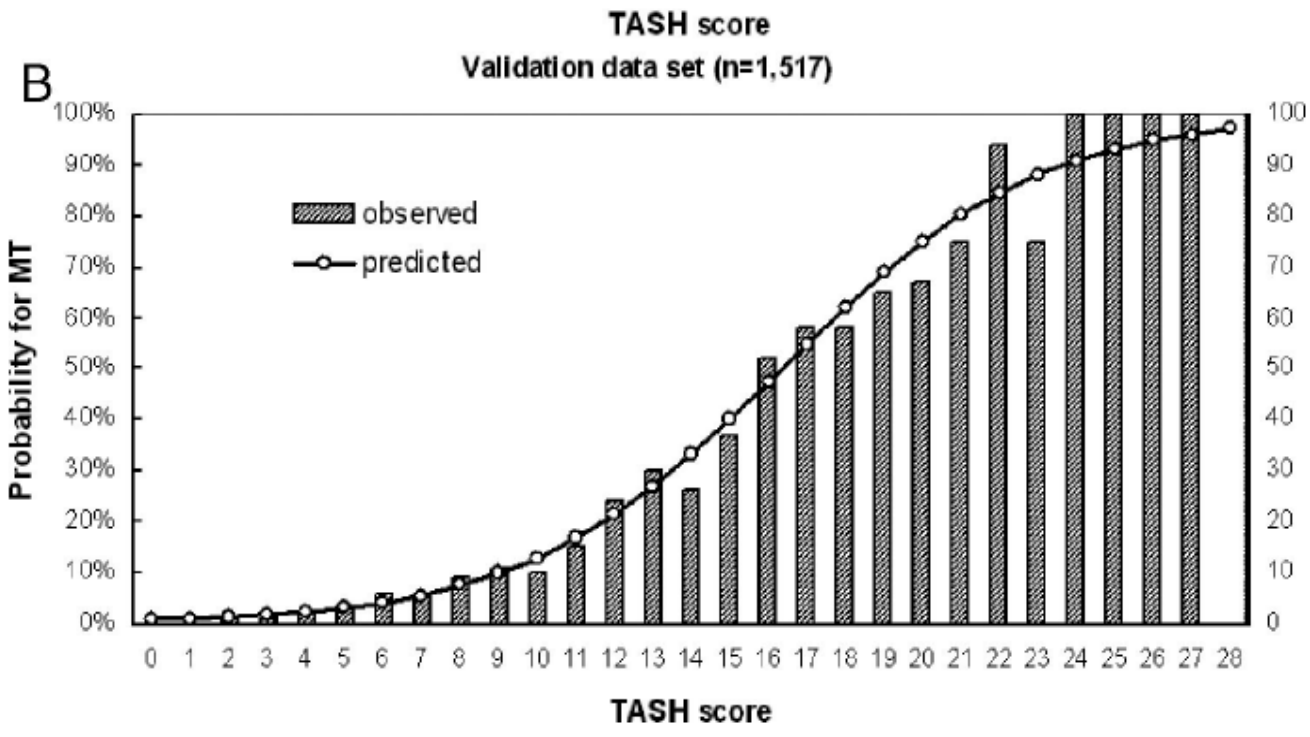
UNIVERSITÀ DEGLI STUDI
DI MODENA E REGGIO EMILIA

Trauma Associated Severe Hemorrhage (TASH)-Score: Probability of Mass Transfusion as Surrogate for Life Threatening Hemorrhage after Multiple Trauma

Nedim Yücel, MD, Rolf Lefering, PhD, Marc Maegele, MD, Matthias Vorweg, MD, Thorsten Tjardes, MD, Steffen Ruchholtz, MD, Edmund A. M. Neugebauer, PhD, Frank Wappler, MD, Bertil Bouillon, MD, Dieter Rixen, MD, and the "Polytrauma Study Group" of the German Trauma Society

J Trauma. 2006;60:1228–1237.

Table 3 Final TASH Score



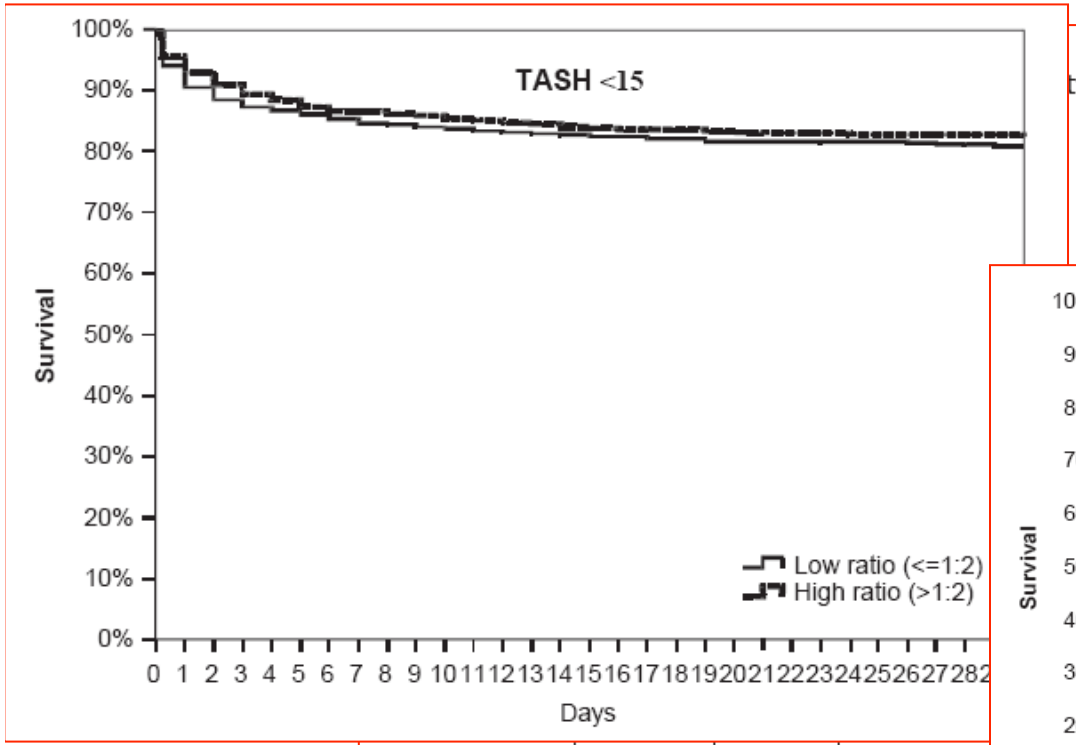
Vox Sanguinis (2011)

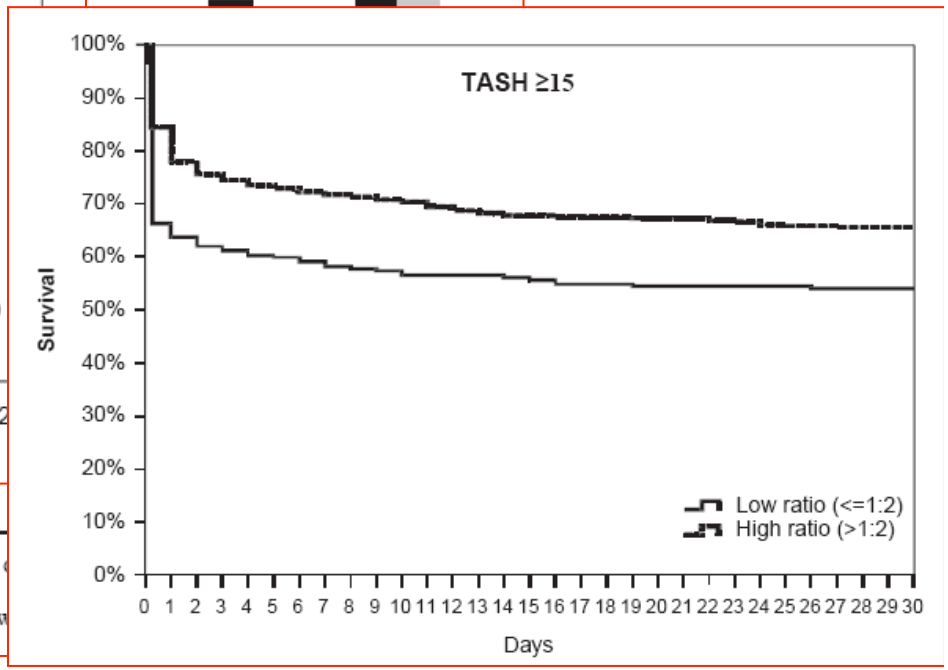
DOI: 10.1111/j.1423-0410.2011.01466.x

ORIGINAL PAPER

The effect of FFP:RBC ratio on morbidity and mortality in trauma patients based on transfusion prediction score

M. A. Borgman,[1] P. C. Spinella,[2] J. B. Holcomb,[3] L. H. Blackbourne,[4] C. E. Wade,[3] R. Lefering,[5,6,7] B. Bouillon[5,7] & M. Maegele[5,6,7]





p value *	n.s.	n.s.	n.s.

FFP:pRBC, fresh frozen plasma: packed red blood
hemorrhage; MT, massive transfusion
* Chi Square test of mortality between high and low

Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion (Review)

Cochrane Database of Systematic Reviews 2011,

Authors' conclusions

There is an absence of evidence that TEG or ROTEM improves morbidity or mortality in patients with severe bleeding. Application of a TEG or ROTEM guided transfusion strategy seems to reduce the amount of bleeding but whether this has implications for the clinical condition of patients is still uncertain. More research is needed.

Proportion of patients receiving platelets	Study population		RR 0.77 (0.47 to 1.26)	619 (6 studies)	⊕⊕⊕○ moderate[1,4]
	230 per 1000	177 per 1000 (108 to 290)			
	Medium risk population				
	171 per 1000	132 per 1000 (80 to 215)			
Combined transfusion volume (mL) of platelets		The mean Combined transfusion volume (mL) of platelets in the intervention groups was **31.95 lower** (70.43 lower to 6.52 higher)		545 (6 studies)	⊕⊕⊕○ moderate[1,4,5]
Combined transfusion volume (mL) of FFP		The mean Combined transfusion volume (mL) of FFP in the intervention groups was **96.35 lower** (277.54 lower to 84.84 higher)		545 (6 studies)	⊕⊕⊕○ moderate[1,4,6]
Rate of surgical re-intervention: TEG or ROTEM vs control	Study population		RR 0.91 (0.44 to 1.87)	708 (7 studies)	⊕⊕⊕○ moderate[1]

RESEARCH Open Access

Goal-directed coagulation management of major trauma patients using thromboelastometry (ROTEM®)-guided administration of fibrinogen concentrate and prothrombin complex concentrate

Schöchl *et al. Critical Care* 2010, **14**:R55
http://ccforum.com/content/14/2/R55

Herbert Schöchl[1,2], Ulrike Nienaber[3], Georg Hofer[1], Wolfgang Voelckel[1], Csilla Jambor[4], Gisela Scharbert[5], Sibylle Kozek-Langenecker[5] and Cristina Solomon[*6]

- ✓ 131 paz con trauma > 5 U di EC/24 ore
- ✓ Fibrinogeno in prima battuta in base a ROTEM→ se non miglioramento CP
- ✓ PCC aggiunto se TAO o ExTEM>1.5
  - 128 solo FIB, 101 anche CCP, 12 PFC, 29 plt
  - **Mortalità osservata (esclusi cranici) 14%**
  - Mortalità attesa TRISS 27.8% (p=0.0018)
  - Mortalità attesa RISC 24.3 % (p=0.014)

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero-Universitaria di Modena

Accepted for publication in the *Journal of Thrombosis and Haemostasis*
doi: 10.1111/j.1538-7836.2010.04052.x
Received 23 July 2010, accepted 31 August 2010

Treatment of massive bleeding with prothrombin complex concentrate: Argument for.

K. A. Tanaka, F. Szlam

Department of Anesthesiology, Emory University School of Medicine, Atlanta, GA

Accepted for publication in the *Journal of Thrombosis and Haemostasis*
doi: 10.1111/j.1538-7836.2010.04062.x
Received 29 July 2010, accepted 2 September 2010

Debate

Treatment of massive bleeding with prothrombin complex concentrate: Argument against

Anne Godier[1,2,3], Sophie Susen[4,5], Charles-Marc Samama[1,2,3]

EFFICACIA DEI PCC IN MODELLI ANIMALI DI EMORRAGIA MASSIVA

Autore, anno	Modello	PCC Comparatore	Efficacia In rosso i valori significativi
Dickneite, 2008	Coagulopatia diluizionale in maiali, quindi lesione ossea o splenica	35 UI/kg Salina	↓ tempo di emostasi ↓ perdite
Dickneite, 2009	Coagulopatia diluizionale in maiali, quindi lesione ossea o splenica	25 UI/kg 15 ml/kg PFC 40 ml/kg PFC	↓ tempo di emostasi ↓ perdite rispetto a entrambi
Pragst, 2009	Coagulopatia diluizionale in conigli, quindi lesione renale	25 UI/kg Salina 180 μg/kg rFVIIa	↓ tempo di emostasi ↓ perdite rispetto a entrambi
Kaspereit, 2010	Sanguinamento „a nappo“ dopo BPCP in maiali	30 UI/kg Salina	↓ perdite
Dickneite, 2010	Coagulopatia diluizionale in maiali, quindi lesione splenica	35 UI/kg Salina 180 μg/kg rFVIIa	↓ tempo di emostasi ↓ perdite

Table 3
Morbidity and mortality.

	All patients ($n=36$)	TR-DGU ($n=18$)	Innsbruck TB ($n=18$)	p-Value
Sepsis (n; %)	9 (25)	6 (33.3)	3 (16.7)	0.443
Multiple organ failure (n, %)	14 (38.9)	11 (61.1)	3 (16.7)	0.015
Ventilator days (days, range)	12 (6–20)	15 (6–22)	10 (5–20)	0.673
ICU LOS (days, range)	18 (10–29)	16 (13–25)	19 (9–33)	0.628
In-hospital LOS (days, range)	31 (19–49)	38 (21–48)	26 (19–50)	0.481
In-hospital mortality overall (n; %)	5 (13.9)	2 (11.1)	3 (16.7)	0.500

Data are presented as median (IQR_{25-75}).
ICU = intensive care unit; LOS = length of stay.

	[illegible] (n=18)	[illegible] (n=18)
PFC Unità <6 ore	0	6
PFC >24 ore	0	10
RBC Unità <6 ore	1	7.5
RBC Unità >24 ore	3	12.5
PLT (tutte >24 ore)	0	2
Fattori della coagulazione (tutti < 6 ore)	Fibrinogeno 4 gr PCC 1200 IU	0

Critical Care

CRITICAL CARE

Transfusion in trauma: thromboelastometry-guided coagulation factor concentrate-based therapy versus standard fresh frozen plasma-based therapy

Table 1. Inclusion criteria

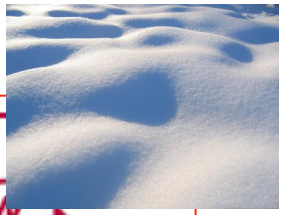
	Fibrinogen-PCC group (Salzburg Trauma Centre)	FFP group (TR-DGU)
Type of therapy	ROTEM-guided administration of coagulation factor concentrates	According to local protocols
ISS	≥ 16	
AIS thorax, abdomen, extremities	At least in one region, one injury with severity degree ≥3, $AIS_{head/neck}$ <5	
Age (years)	18–70	
Base deficit at admission	≥2 mmol/L	
FFP administered	No FFP	≥2 units FFP
Fibrinogen/PCC administered	≥1 g fibrinogen; ≥ 500 U PCC	No fibrinogen or PCC
Investigated time period	2005–2009	2005–2008
Patients included in database	353	21263
Patients fulfilling inclusion criteria	80	601

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero-Universitaria di Modena
Policlinico

Confronto fra trattamenti

GRUPPO FIBRINOGENO (n=80)	GRUPPO FFP (n=601)
6 grammi fibrinogeno 1200 UI PCC 6 UI RBC	6 UI FFP 5.5 UI RBC
No RBC 29%	No RBC 3%
No PLT 91%	No PLT 56%
Mortalità 7.5%	Mortalità 10%
LOS ICU = 14.5 gg LOS-H = 23 gg	LOS ICU = 14 gg LOS-H = 32 gg

Schoechl H et al. Critical Care 2011, 15:R83



Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

*CRASH-2 trial collaborators**

Methods This randomised controlled trial was undertaken in 274 hospitals in 40 countries. 20 211 adult trauma patients with, or at risk of, significant bleeding were randomly assigned within 8 h of injury to either tranexamic acid (loading dose 1 g over 10 min then infusion of 1 g over 8 h) or matching placebo. Randomisation was balanced by centre, with an allocation sequence based on a block size of eight, generated with a computer random number generator. Both participants and study staff (site investigators and trial coordinating centre staff) were masked to treatment allocation. The primary outcome was death in hospital within 4 weeks of injury, and was described with the following categories: bleeding, vascular occlusion (myocardial infarction, stroke and pulmonary embolism), multiorgan failure, head injury, and other. All analyses were by intention to treat. This study is registered as ISRCTN86750102, Clinicaltrials.gov NCT00375258, and South African Clinical Trial Register DOH-27-0607-1919.

	Tranexamic acid (n=10 060)	Placebo (n=10 067)	RR (95% CI)	p value (two-sided)
Any cause of death	1463 (14·5%)	1613 (16·0%)	0·91 (0·85–0·97)	0·0035
Bleeding	489 (4·9%)	574 (5·7%)	0·85 (0·76–0·96)	0·0077
Vascular occlusion*	33 (0·3%)	48 (0·5%)	0·69 (0·44–1·07)	0·096
Multiorgan failure	209 (2·1%)	233 (2·3%)	0·90 (0·75–1·08)	0·25
Head injury	603 (6·0%)	621 (6·2%)	0·97 (0·87–1·08)	0·60
Other causes	129 (1·3%)	137 (1·4%)	0·94 (0·74–1·20)	0·63

Data are number (%), unless otherwise indicated. RR=relative risk. *Includes myocardial infarction, stroke, and pulmonary embolism.

Table 2: Death by cause

The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial

Published Online
March 24, 2011

*The CRASH-2 collaborators**

	Tranexamic acid allocated	Placebo allocated	Risk ratio (95% CI)
Time to treatment (h)			
≤1	198/3747 (5·3%)	286/3704 (7·7%)	0·68 (0·57–0·82)
>1–3	147/3037 (4·8%)	184/2996 (6·1%)	0·79 (0·64–0·97)
>3	144/3272 (4·4%)	103/3362 (3·1%)	1·44 (1·12–1·84)
χ^2=23·516; p<0·0000			
Systolic blood pressure (mm Hg)			
>89	146/6878 (2·1%)	163/6761 (2·4%)	0·88 (0·71–1·10)
76–89	110/1609 (6·8%)	114/1689 (6·7%)	1·01 (0·79–1·30)
≤75	233/1562 (14·9%)	295/1599 (18·4%)	0·81 (0·69–0·95)
χ^2=2·235; p=0·33			
Glasgow coma score			
Severe (3–8)	168/1789 (9·4%)	186/1830 (10·2%)	0·92 (0·76–1·13)
Moderate (9–12)	93/1349 (6·9%)	121/1344 (9·0%)	0·77 (0·59–0·99)
Mild (13–15)	228/6915 (3·3%)	265/6877 (3·8%)	0·86 (0·72–1·02)
χ^2=1·275; p=0·53			
Type of injury			
Blunt	308/6788 (4·5%)	347/6817 (5·1%)	0·89 (0·77–1·04)
Penetrating	181/3272 (5·5%)	227/3250 (7·0%)	0·79 (0·66–0·96)
χ^2=0·923; p=0·34			
All deaths	489/10060 (4·9%)	574/10067 (5·7%)	0·85 (0·76–0·96)
Two-sided p=0·0077			

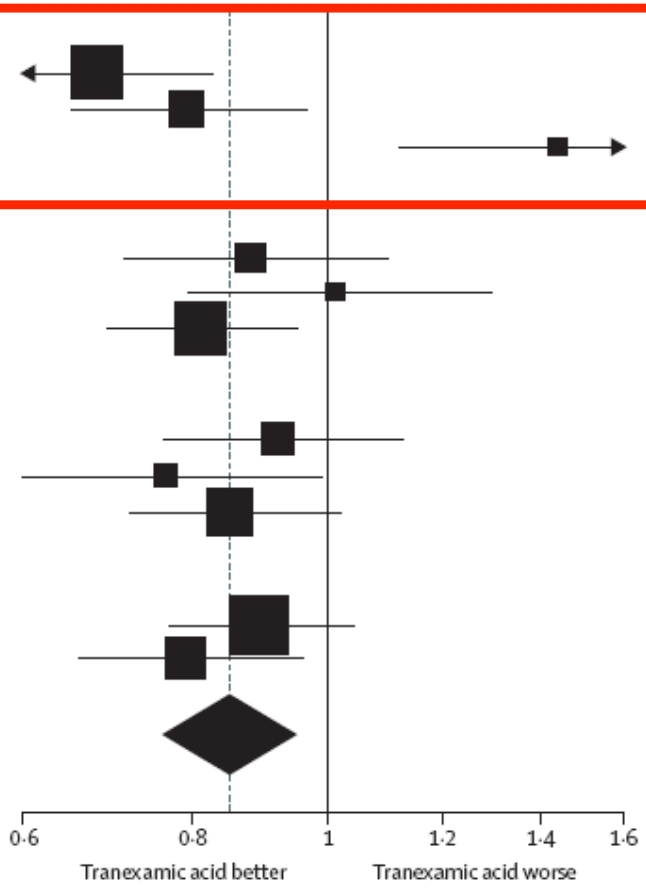


Figure 1: Mortality due to bleeding by subgroups

In sintesi…

- ✓Il rapporto PFC:EC [o meglio il deficit di PFC] è importante ma occorre distinguere meglio fra singoli pazienti
- ✓Il timing dell'intervento è fondamentale [scenari organizzativi]
- ✓Proprio per questo è molto interessante la possibilità di gestire l'emergenza emorragica con CCP/FIB/ROTEM e senza PFC
- ✓Tranexamico utile ma solo entro 3 ore


I FIOCCHI DI NEVE MI AFFASCINANO... CADONO LIEVEMENTE AL SUOLO A MILIONI...
E DICONO CHE NON CE NE SONO DUE UGUALI!
CIASCUNO COMPLETAMENTE DIVERSO DALL'ALTRO...
GLI ULTIMI TENACI INDIVIDUALISTI!
SCHULZ