Le plasma lyophilisé en transfusion préhospitalière

HCL
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Hospices Civils de Lyon
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Eric CESAREO

Absence de conflit d'intérêt

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The why and how our trauma patients die: A prospective Multicenter Western Trauma Association study

J Trauma Acute Care Surg
2019; 86: 864-70

Rachael A. Callcut,
and **Western Trauma Association Multicenter Study Group**, *San Francisco, California*

n = 1536 death
12-2015/08-2017
18 Trauma Center

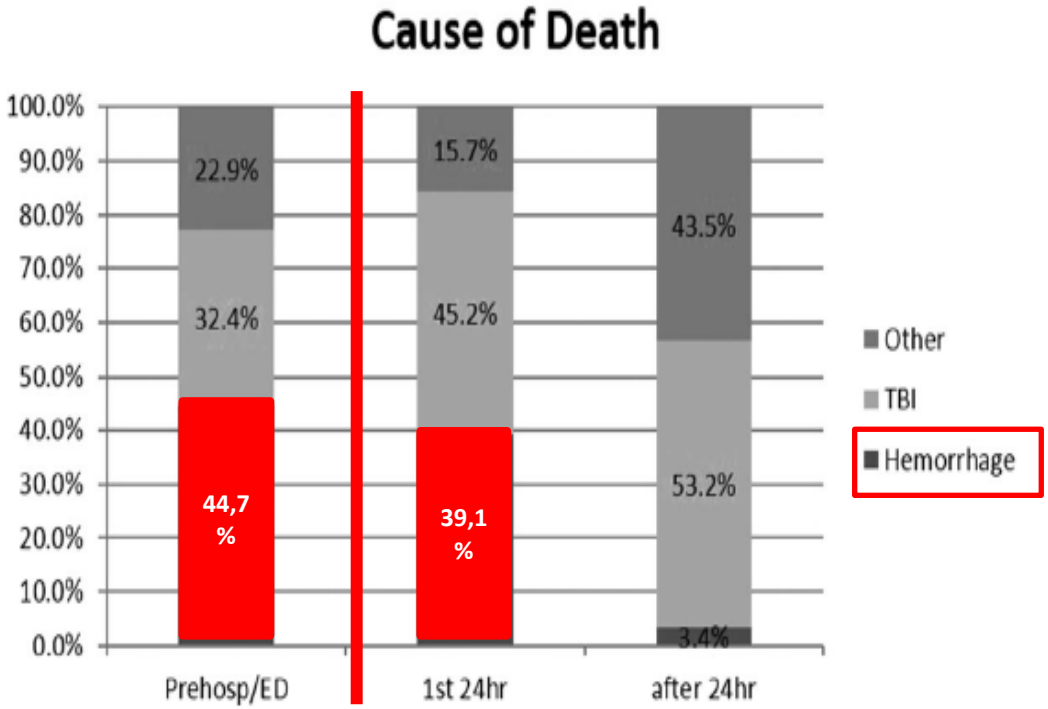
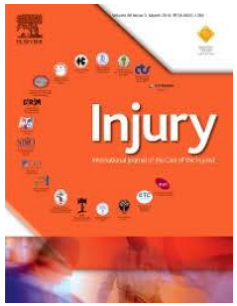


Figure 1. COD by Time. prehosp, prehospital.

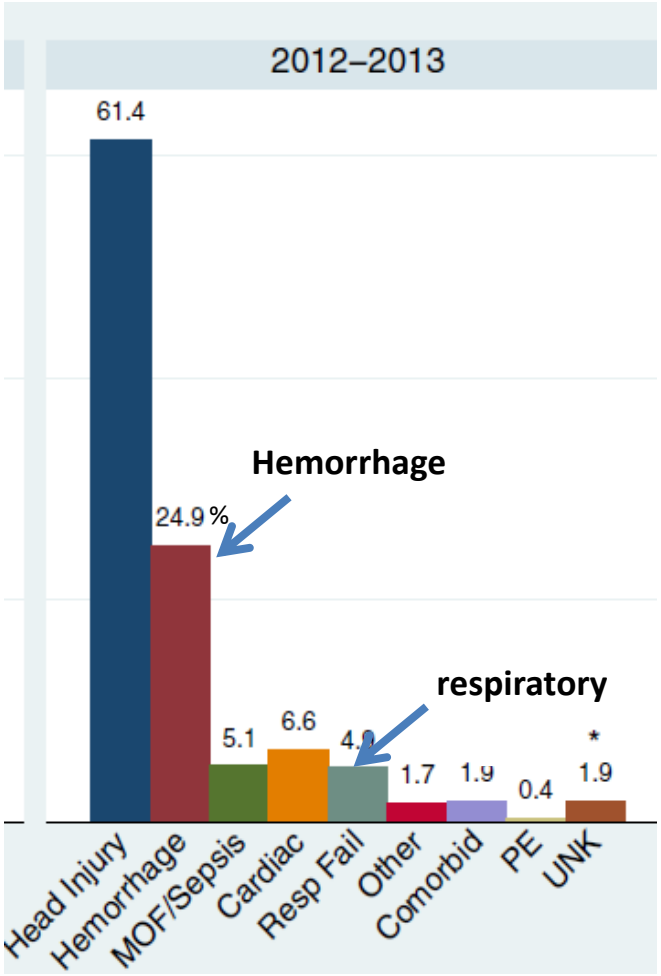
H + 1

Blunt injury (Cause of death 1029 patients)



Oyeniyi BT

Injury
2017; 48: 5-12

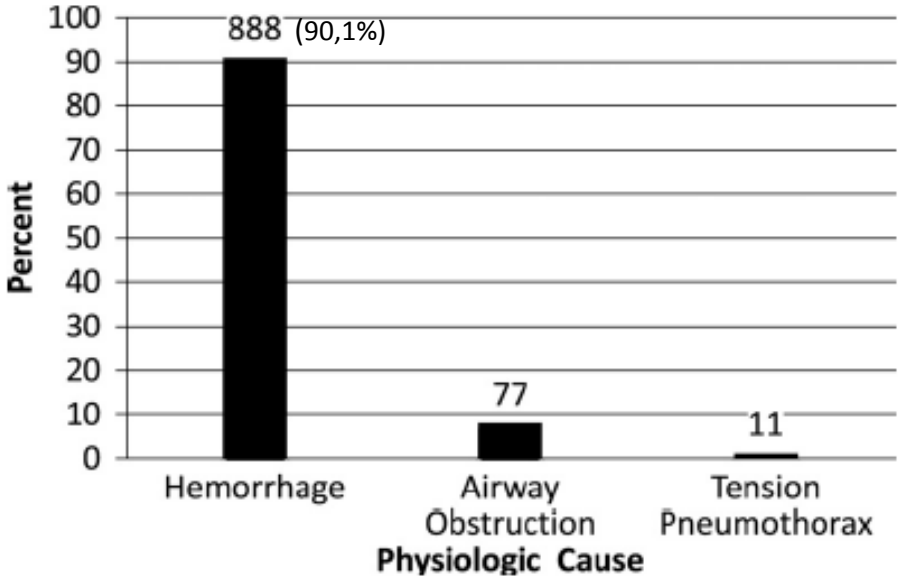


Death on the battlefield (n = 976)

2001-2011

Eastridge BJ

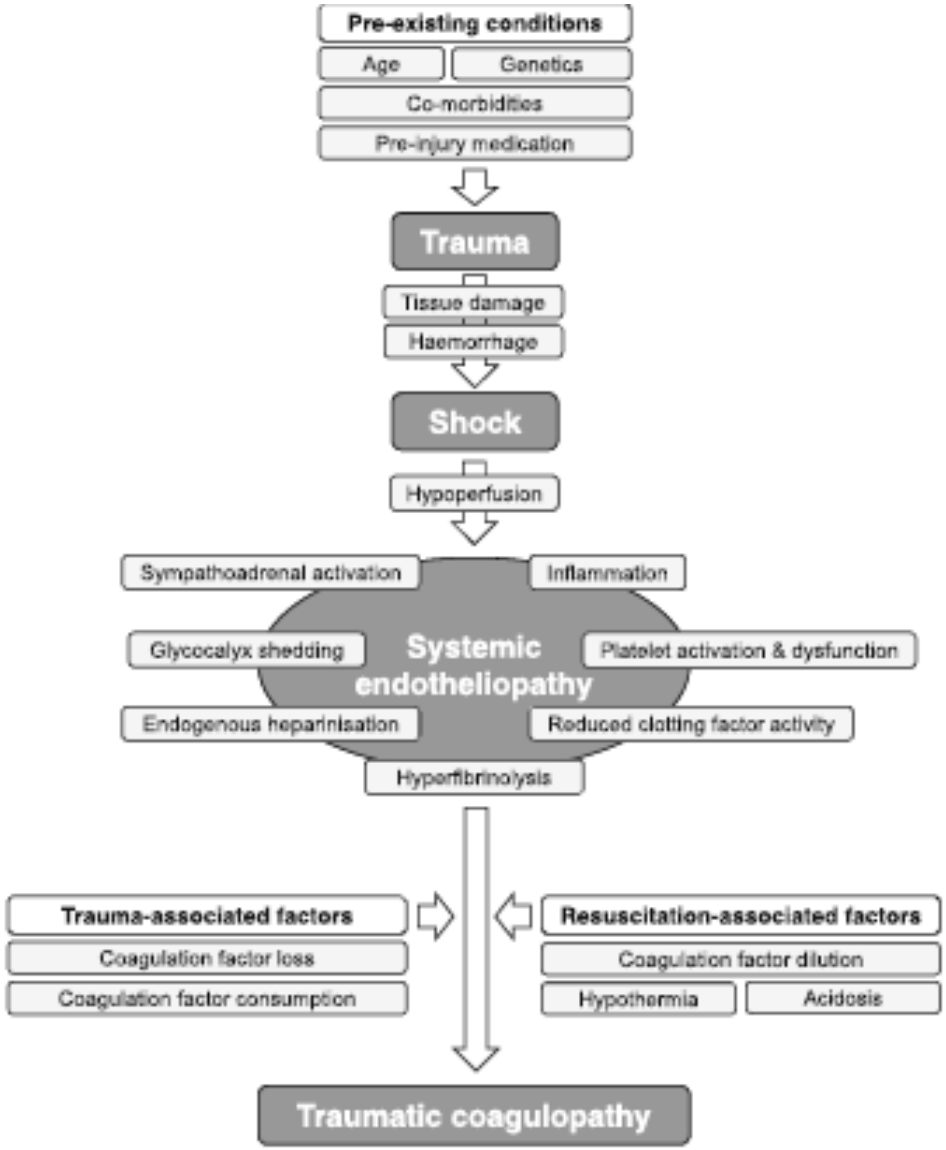
J Trauma Acute Care Surg
2012; 73:S431



The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition

Spahn et al

Crit Care. 2019



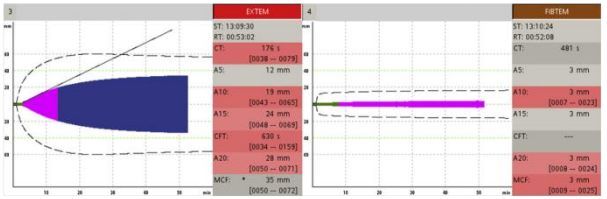


Fig. 2. Tracé obtenu à l'admission d'un patient présentant un traumatisme sévère du foie associé à un état de choc hémorragique. À l'admission, l'hémoglobine était à 52 g/dL, les plaquettes à 88 G/L, le TP à 29 % et le fibrinogène à 0,4 g/L. Le ROTEM® décrit précisément ces anomalies avec sur l'EXTEM un *clotting time* (CT) très allongé et une amplitude effondrée ; sur le FIBTEM, une amplitude à 5 minutes très diminuées. Sur ces données, le patient a reçu 4,5 g de Clottafact®, 2000 UI de Kanokad® et 4 CGR.

30% des traumatisés graves*

Triade létale

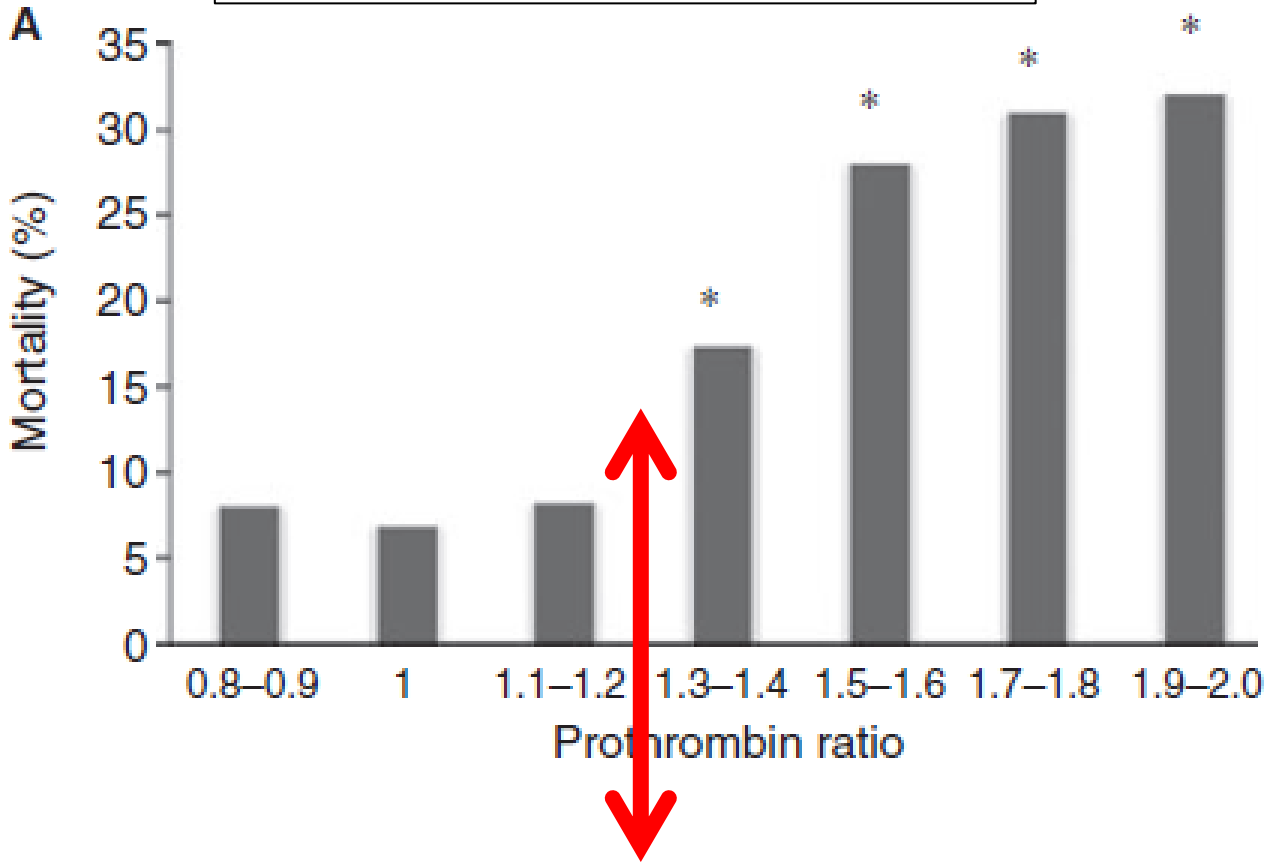
*Brohi K, Singh J, Heron M, Coast T. Acute traumatic coagulopathy. J Trauma. 2003; 54 (6): 1127-30

Definition and drivers of acute traumatic coagulopathy: clinical and experimental investigations

Frith D et al

J Thromb Haemost 2010; 8: 1919–25

Définition CAT = INR > 1,2

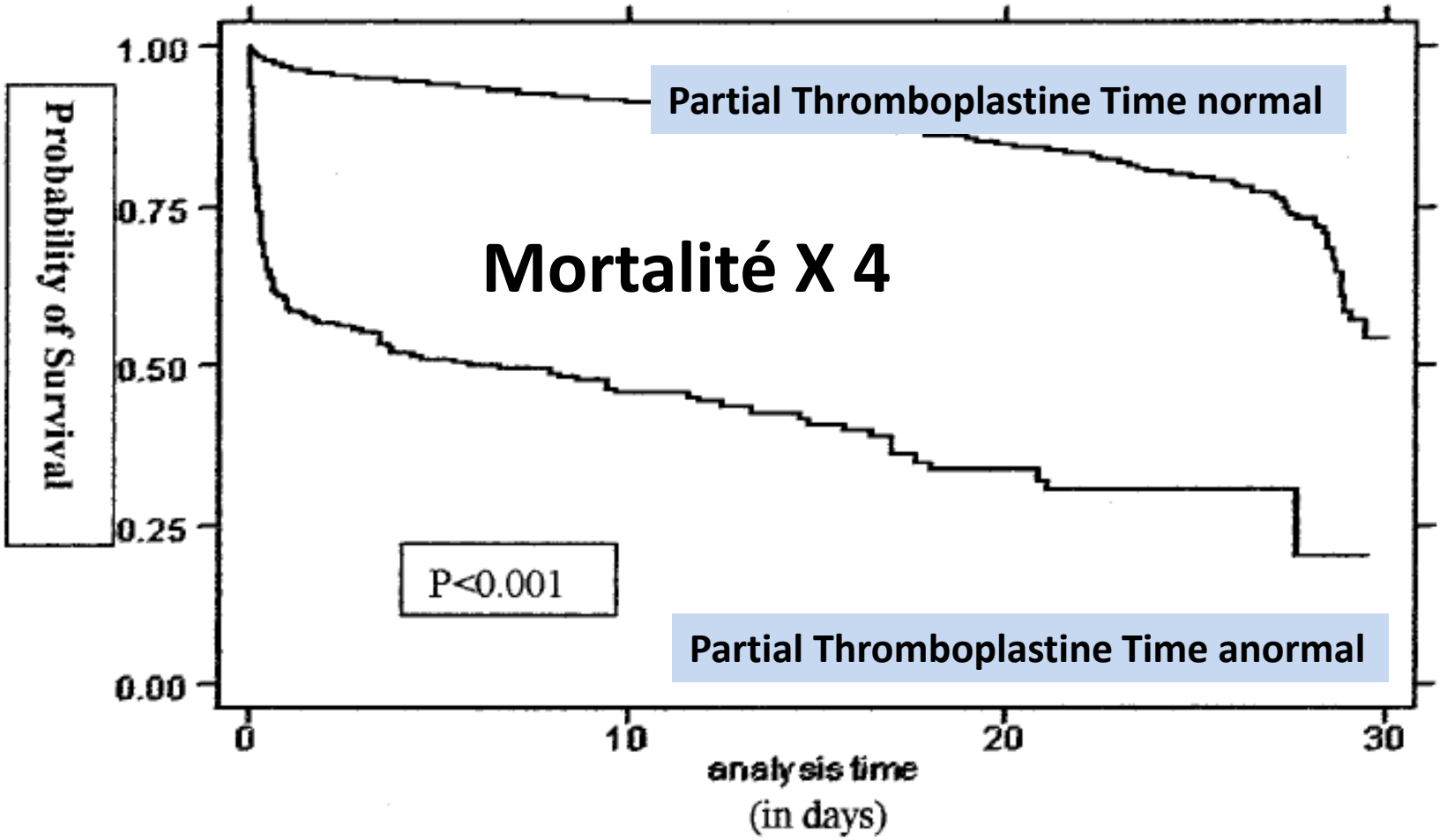


Early Coagulopathy Predicts Mortality in Trauma

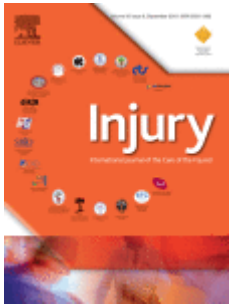
MacLeod J.B et al

J Trauma. 2003
55: 39-44

n = 7.638 traumatisés graves

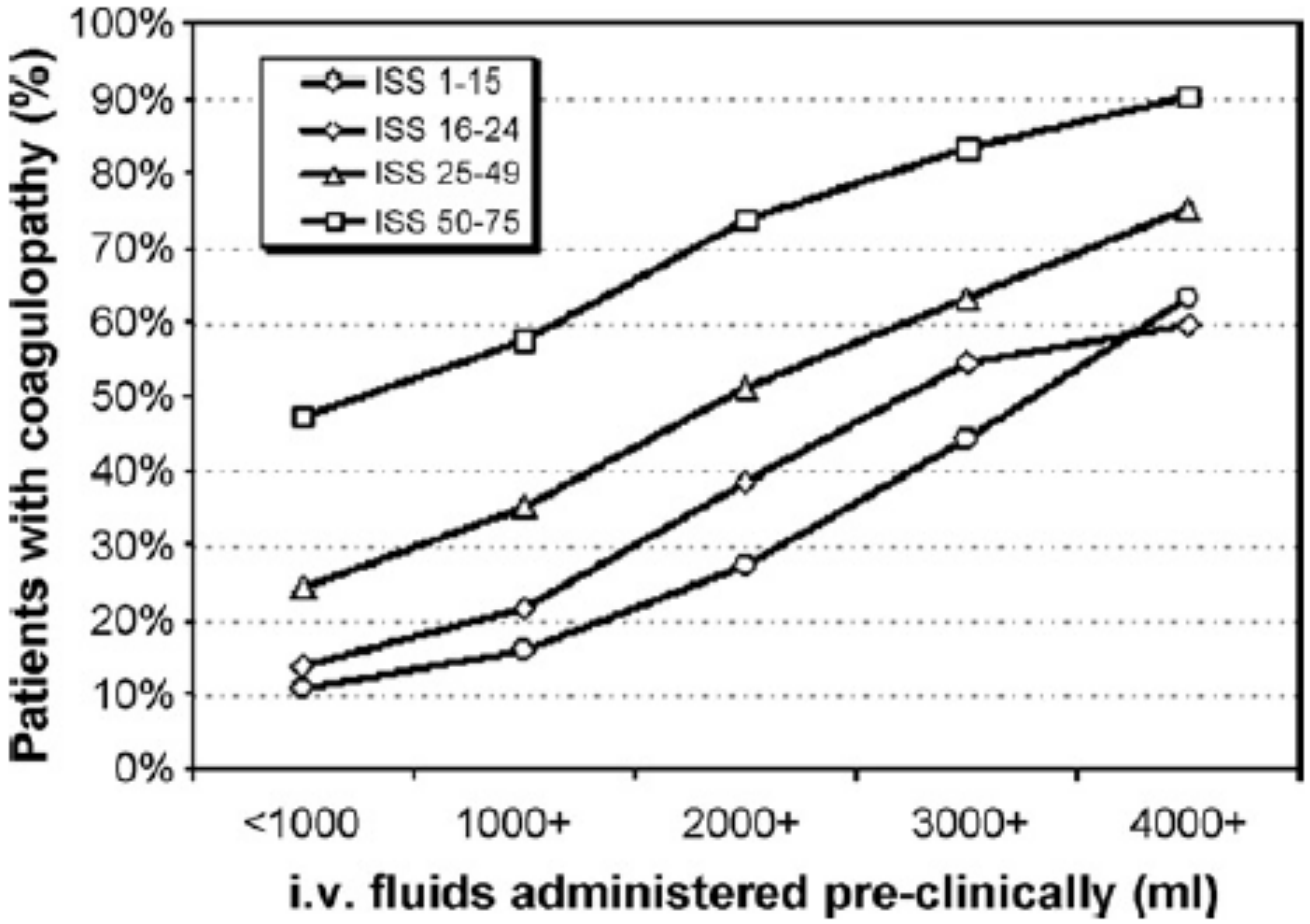


Early coagulopathy in multiple injury: An analysis from the German Trauma Registry on 8724 patients

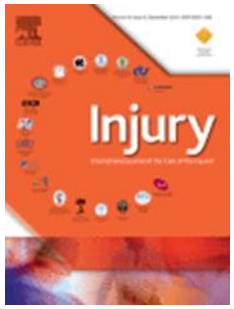


Maegele M et al

Injury 2007
38: 298-304



Early coagulopathy in multiple injury: An analysis from the German Trauma Registry on 8724 patients



Maegele M et al

Injury 2007
38: 298-304

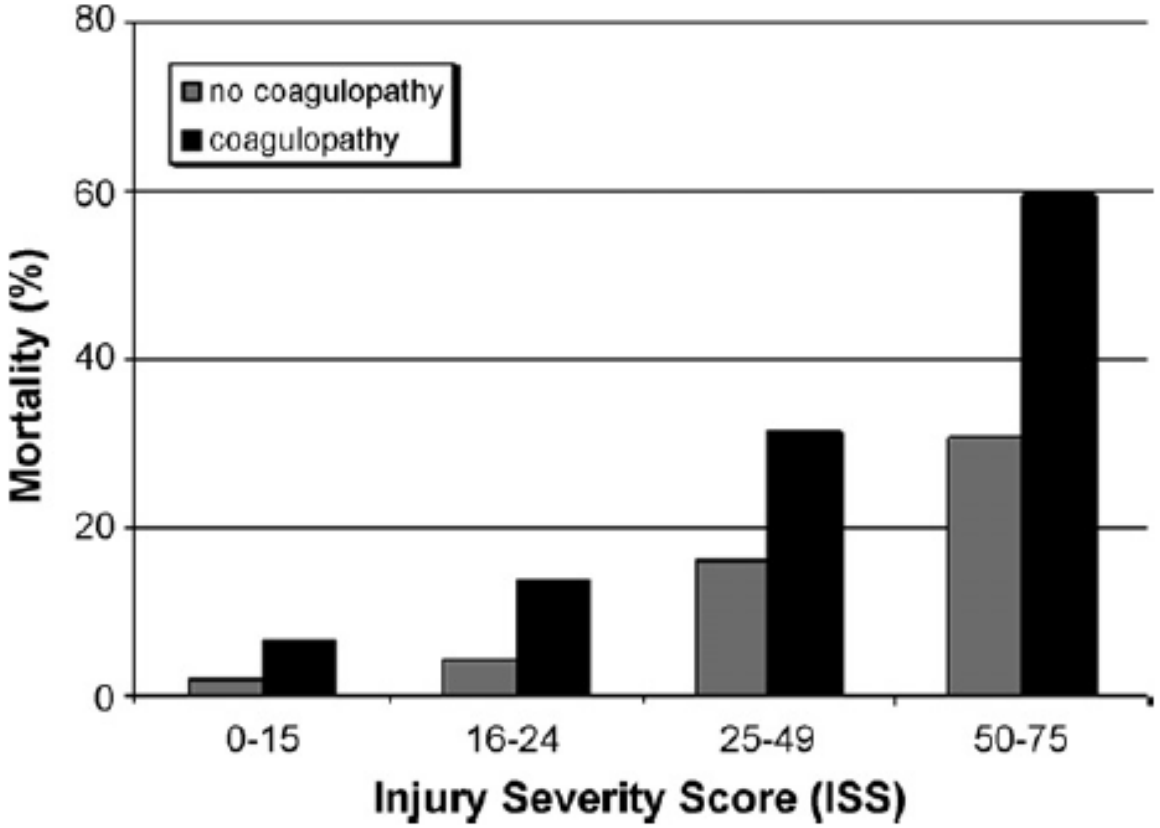
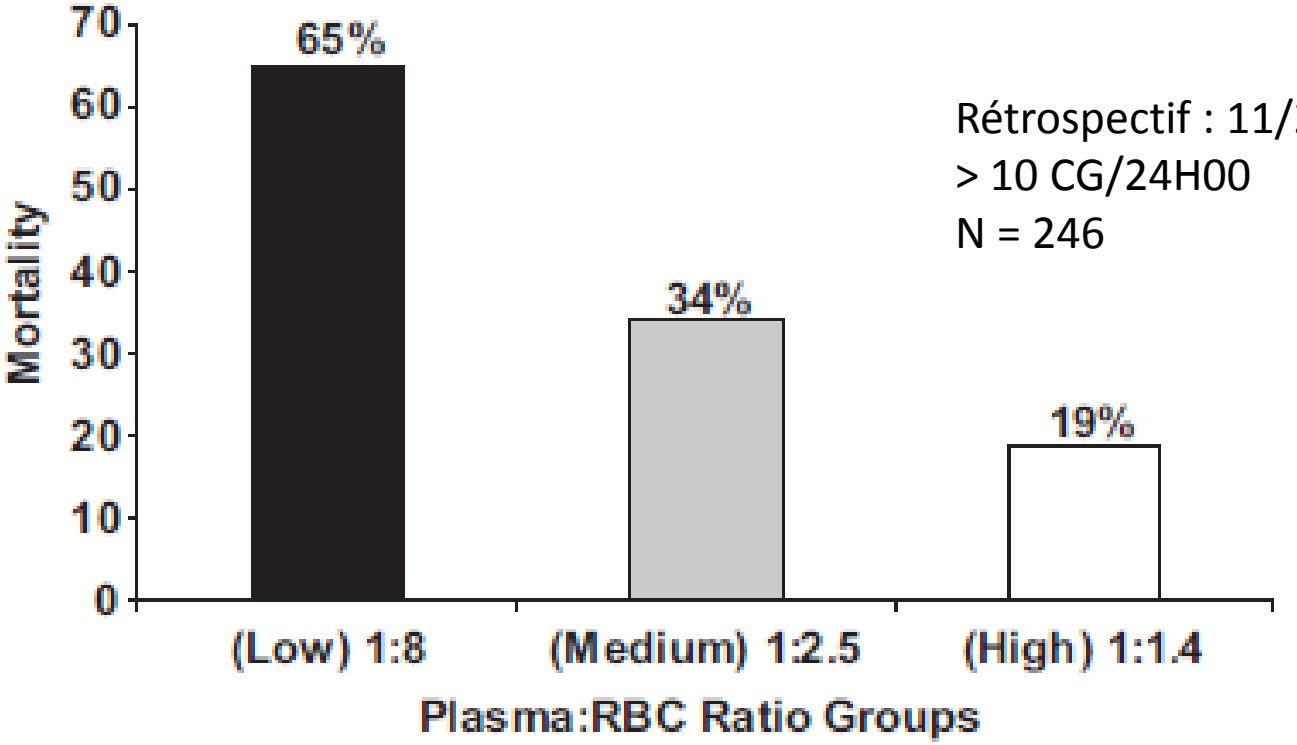


Figure 2 Mortality in patients with and without coagulopathy with respect to ISS (injury severity score).

The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital

Borgman M A et al

J Trauma. 2007
63: 805-13



Rétrospectif : 11/2003- 09/2005
> 10 CG/24H00
N = 246

Variable	Survivors	Nonsurvivors	*p* Value
Plasma:RBC ratio (n = 246)	1:1.6 (1:1.3–1:2.2)	1:2.3 (1:1.4–1:5.1)	<0.001*

Table 1 Descriptive Statistics for Each Plasma to RBC Ratio Group

Variable Median (IQR)	Low Ratio Group,* n = 31 1:8 (0:12–1:5)	Medium Ratio Group, n = 53 1:2.5 (1:3.0–1:2.3)	High Ratio Group, n = 162 1:1.4 (1:1.7–1:1.2)
ISS†	18 (16–25)	17 (13–25)	18 (16–25)
ISS >25 (%)	23	21	22
AIS score (% 4 or 5)			
Head/neck	16	6	10
Face	0	0	0.6
Thorax§	26[a]	9[ab]	7[b]
Abdomen	26	23	27
Pelvis/extremity	19	23	28
% penetrating trauma	94	92	95
% blunt trauma	6	8	5
INR, n = 212	1.78 (1.00–2.86), n = 21	1.57 (1.31–2.10), n = 42	1.54 (1.30–2.20), n = 149
Hgb,‡ n = 234	9.4 (7.1–11.1), n = 27[a]	10.8 (8.5–12.7), n = 48[ab]	10.9 (9.1–13.1), n = 159[b]

Table 2 Crystalloid and Blood Products for Each Plasma to RBC Ratio Group

Variable Median (IQR)	Low Ratio Group,* n = 31 1:8 (0:22–1:5)	Medium Ratio Group, n = 53 1:2.5 (1:3.0–1:2.3)	High Ratio Group, n = 162 1:1.4 (1:1.7–1:1.2)
Crystalloid (L)†§	7.0 (2.0–9.6)[a]	8.0 (4.4–11.5)[ab]	9.6 (6.0–12.9)[b]
Crystalloid (L/h)§	1.8 (0.36–4.2)[a]	0.6 (0.3–1.5)[ab]	0.5 (0.4–0.7)[b]
RBC	16 (12–18)	16 (12–26)	17 (12–24)
RBC/h§	4 (0.5–11.8)[a]	0.9 (0.6–4.0)[ab]	0.8 (0.6–1.3)[b]
FWB	0 (0–0) [0.1]	0 (0–2) [1.1]	0 (0–4) [3.1]
FWB/h§	0 (0–0) [0.01][a]	0 (0–0.1) [0.15][b]	0 (0–0.2) [0.23][c]
Plasma§	2 (0–3)[a]	6 (4–10)[b]	12 (9–18)[c]
Plasma/h§	0.1 (0–0.4) [0.57][a]	0.3 (0.2–1.4) [1.1][b]	0.6 (0.4–1.0) [1.1][c]
aPLT§	None received[a]	0 (0–0) [0.4][b]	0 (0–1) [0.8][c]
aPLT/h§	None received[a]	0 (0–0) [0.02][ab]	0 (0–0) [.05][b]
Cryoprecipitate§	0 (0–0) [1.6][a]	0 (0–10) [6.6][b]	9 (0–10) [9.1][b]
Cryoprecipitate/h§	0 (0–0) [0.7][a]	0 (0–1.3) [0.9][b]	0.4 (0–0.8) [0.6][b]
rFVIIa use‡	16%[a]	26%[ab]	38%[b]

Massive Transfusion Protocols: The Role of Aggressive Resuscitation Versus Product Ratio in Mortality Reduction

Riskin DJ et al

J Am Coll Surg. 209:198-205

Table 3. Mean Minutes to First Transfusion of Type-Specific Blood Products Before and after Implementation of Massive Transfusion Protocol

Product	Pre-MTP, mean (95% CI)	Post-MTP, mean (95% CI)	p Value
PRBCs	115 (85–146)	71 (49–93)	0.02*
FFP	254 (185–323)	169 (130–209)	0.04*
Platelets	418 (316–519)	241 (169–311)	0.01*

*Statistically significant; $p \leq 0.05$.

FFP, fresh frozen plasma; MTP, massive transfusion protocol; PRBCs, packed red blood cells.

urvivors
eaths

ear 4

MTP

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma: The PROPPR Randomized Clinical Trial

Holcomb JB et al

JAMA. 2015; 313: 471-82

Étude prospective multicentrique

Intervention:

comparer ratio plasma, plaquettes, PGR

338 patients (1.1.1) vs 342 patients (1.1.2)

Objectifs:

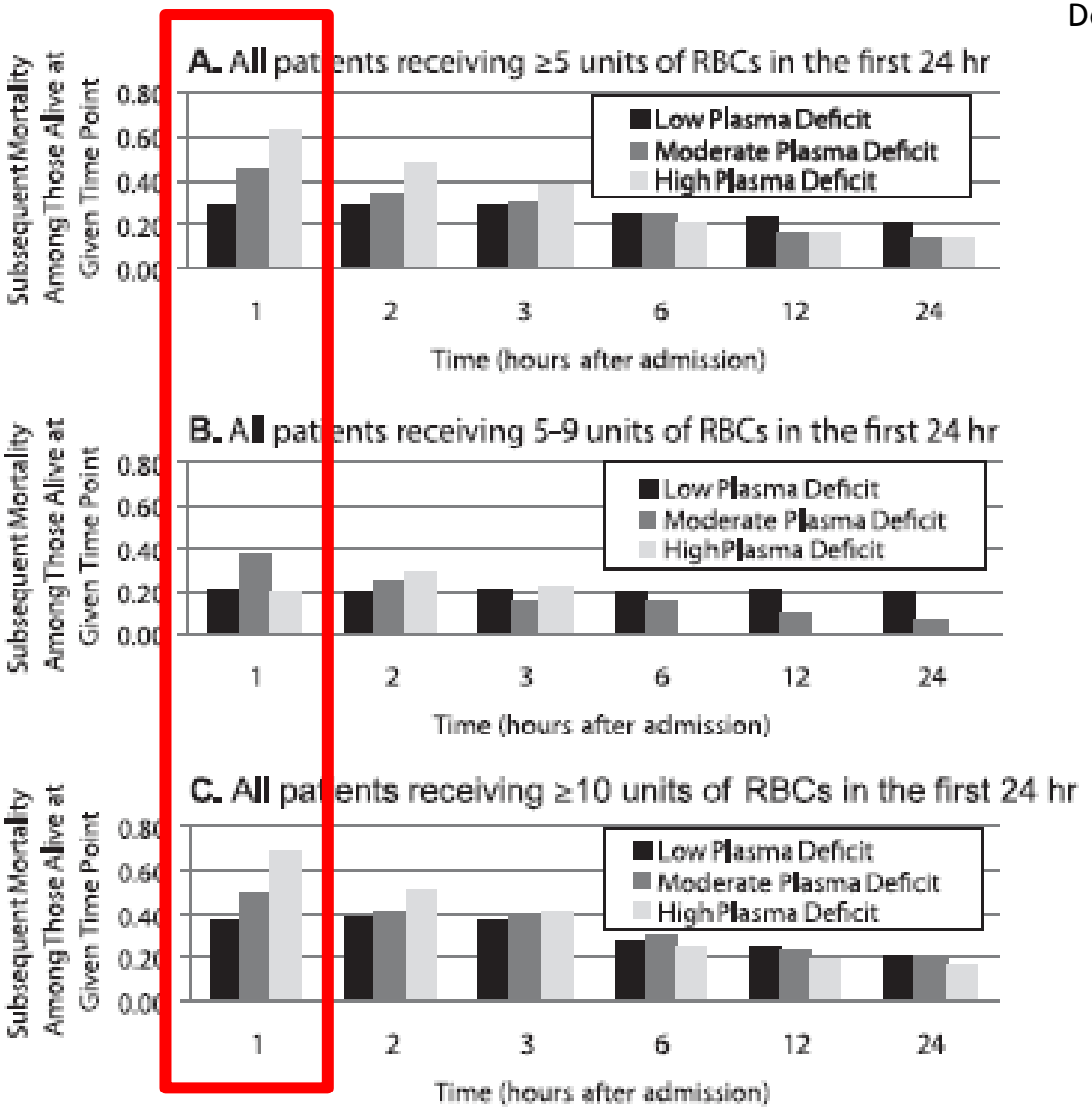
mortalité 24 H et J30

Résultats:

aucune différence significative J1 et J30

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

De Biasi AR et al



Transfusion
2011;51:1925-32

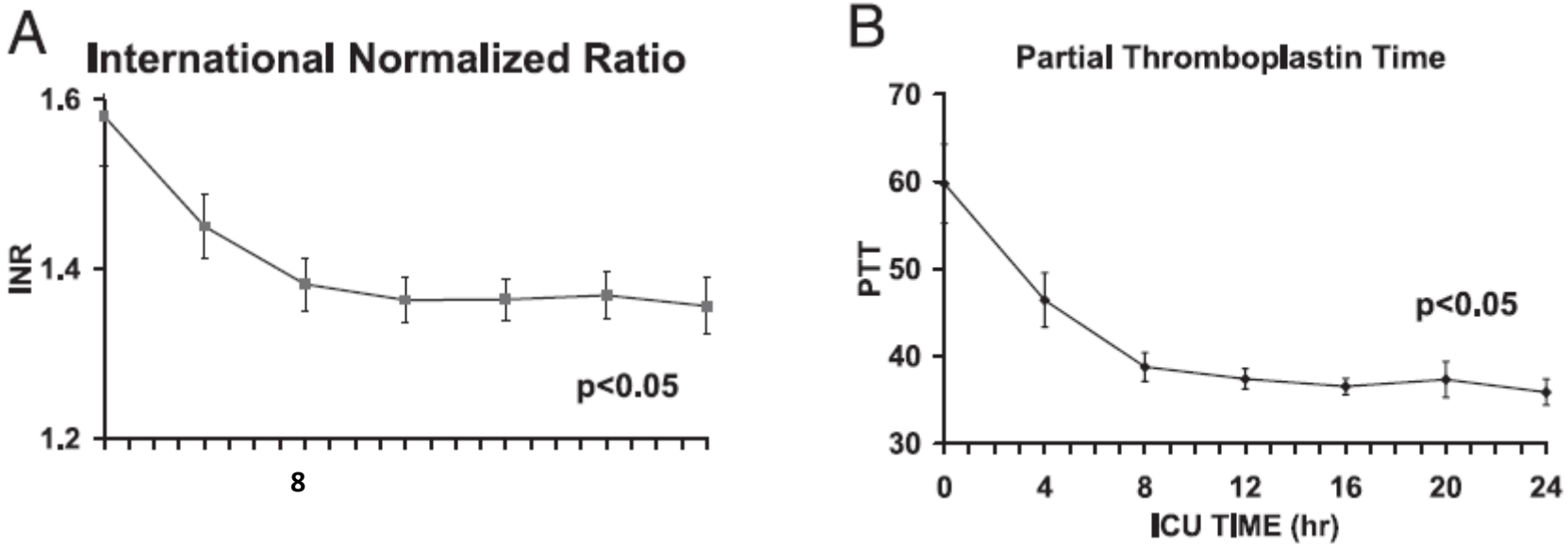
Rétrospectif
Monocentrique
N= 438

Fresh Frozen Plasma Should be Given Earlier to Patients Requiring Massive Transfusion

Gonzalez EA et al

J Trauma. 2007
62: 112-19

Rétrospectif, monocentrique (Houston)
N = 97



CONCLUSIONS

increased risk of death. For trauma patients presenting with exsanguinating hemorrhage, coagulopathy correction beginning with aggressive FFP administration pre-ICU may improve ICU resuscitation response and outcome.

Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial

Moore HB et al

Lancet. 2018; 392: 283-91

COMBAT Trial Transport en ambulance. Moyenne 19 mn

N 125 patients	Plasma group (n=65)	Control group (n=60)	Effect size (95% CI)*	p value
Clinical outcome				
Mortality at 28 days†	10 (15%)	6 (10%)	1·54 (0·60 to 3·98)	0·37
Mortality at 24 h	8 (12%)	6 (10%)	1·23 (0·45 to 3·34)	0·68
Acute lung injury within 28 days	28 (43%)	30 (50%)	0·86 (0·59 to 1·26)	0·44
Multiple organ failure within 28 days (Denver score >3)	4 (6%)	1 (2%)	3·69 (0·42 to 32·11)	0·37
Composite outcome (multiple organ failure or death) at 28 days‡	14 (21%)	7 (12%)	1·85 (0·80 to 4·26)	0·14
Coagulation (on arrival at hospital)				
INR on arrival†	1·27 (1·11 to 1·40)	1·15 (1·08 to 1·29)	0·60 (–0·01 to 0·14)	0·10
INR>1·3	28/63 (44%)	14/58 (24%)	1·84 (1·08 to 3·14)	0·02
Rapid thromboelastography				
G (dynes/cm²)‡	7·7 (6·2 to 8·9)	7·1 (5·4 to 9·7)	0·30 (–0·90 to 1·40)	0·66
Activated clotting time (s)	128 (113 to 136)	121 (113 to 136)	0 (–7·00 to 8·00)	0·76
Maximum amplitude (mm)	60·5 (55·5 to 64·0)	58·5 (52·0 to 66·0)	1·00 (–2·50 to 4·50)	0·67
Angle (°)	70·9 (66·1 to 76·1)	69·3 (63·2 to 74·4)	2·20 (–0·80 to 5·40)	0·16
LY30 (%)	1·3 (0·3 to 2·6)	1·6 (0·7 to 3·1)	–0·20 (–0·90 to 0·30)	0·32
Hyperfibrinolysis (LY30 >3·0%)	14/56 (23%)	13/51 (25%)	0·91 (0·47 to 1·78)	0·78
Physiological lysis (LY30 0·9–3·0%)	25/56 (45%)	23/51 (45%)	0·99 (0·65 to 1·51)	0·96
Lysis shutdown (LY30 <0·9%)	18/56 (32%)	15/51 (29%)	1·09 (0·62 to 1·93)	0·76
Coagulation factor on arrival at hospital (% activity)				

Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial

Moore HB et al

COMBAT Trial

Lancet. 2018; 392: 283-91

<u>Conclusions</u>:

- **Aucun bénéfice sur survie** (J.0 et J.28) si PFC < 30min

- Pas de différence sur incidence coagulopathie traumatique

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

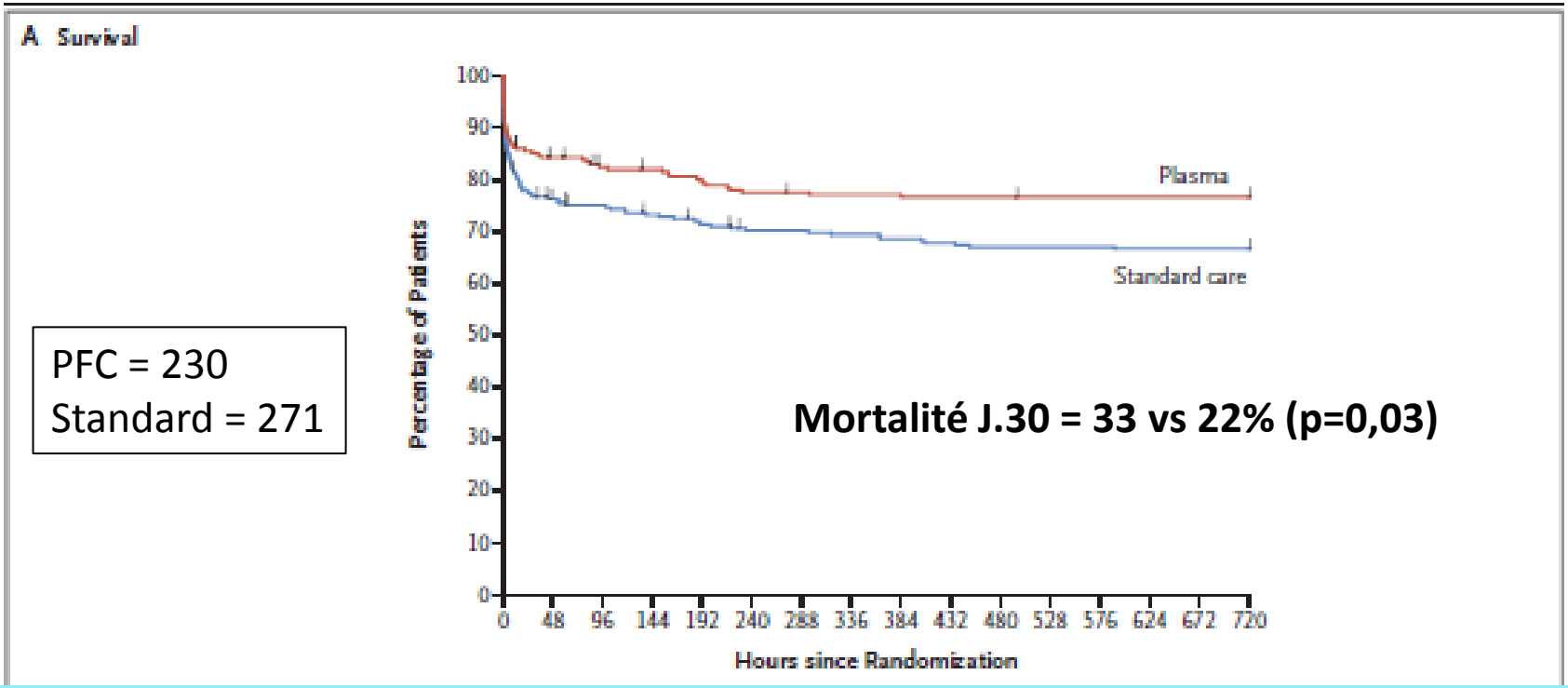
Sperry JL et al

N Engl J Med 2018
379; 4: 315-26

PAMPer Trial

N = 501 patients

Median prehospital transport time (IQR) — min	40 (33–51)	42 (34–53)



PFC = 230
Standard = 271

Mortalité J.30 = 33 vs 22% (p=0,03)

Outcome	Standard-Care Group (N=271)	Plasma Group (N=230)	Difference (95% CI)†	Observed P Value‡
24-hr mortality — no. (%)	60 (22.1)	32 (13.9)	−8.2 (−14.9 to −1.6)	0.02
In-hospital mortality — no. (%)	88 (32.5)	51 (22.2)	−10.3 (−18.0 to −2.6)	0.01

CORRESPONDENCE

Prehospital Plasma during Air Medical Transport in Trauma Patients

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Centre Hospitalier Universitaire Grenoble Alpes
Grenoble, France

N Engl J Med 2018
379;18:1783

EDITORIAL Open Access

Pre-hospital plasma transfusion: a valuable coagulation support or an expensive fluid therapy?

Christian Fenger-Eriksen[1], Dietmar Fries[2], Jean-Stephane David[3], Pierre Bouzat[4], Marcus Daniel Lance[5], Oliver Grottke[6], Donat R. Spahn[7], Herbert Schoechl[8,9] and Marc Maegele[10*]

Crit Care. 2019
23;238-42

PAMPer Trial : les critiques !

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Crit Care. 2019 23;238-42

Table 1. Patient Characteristics.* **PAMPer Trial**

Variable	Standard-Care Group (N=271)	Plasma Group (N=230)	
Median prehospital volume of crystalloid solution (IQR) — ml§	900 (0–1500)	500 (0–1250)	
Prehospital red-cell transfusion — no. (%)¶	114 (42.1)	60 (26.1)	P < 0,001
Prehospital intubation — no. (%)	141 (52.0)	115 (50.0)	
Median Injury Severity Score (IQR)††	21 (12–29)	22 (14–33)	

Table 2. Secondary Trial Outcomes.*

?

Outcome	Standard-Care Group (N=271)	Plasma Group (N=230)
24-hr mortality — no. (%)	60 (22.1)	32 (13.9)
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Crit Care. 2019 23;238-42

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Increased mortality in trauma patients who develop postintubation hypotension

Robert S. Green, MD, Michael B. Butler, MD, *and* Mete Erdogan, PhD *Nova Scotia, Canada*

J Trauma. 2017
83: 569-74

TABLE 1. Characteristics of Study Participants

Characteristics	PIH (n = 161)	Non-PIH (n = 283)	p

trial if they had at least one episode of hypotension (systolic blood pressure <90 mm Hg) and tachycardia (defined in this trial as a heart rate >108 beats per minute) or if they had any severe hypotension (systolic blood pressure <70 mm Hg), either before the arrival of air medical transport or any time before arrival at the trauma center

Rebleeding, n (%)	[illegible]	28 (17.4)	38 (13.4)	[illegible]
Volume of fluid administered, cc (±SD)	370.2 (705.6)	325.6 (856.4)	0.55

Rétrospectif
444 patients

36,6% hypo TA (PAS <90 mmHg)

Pre-hospital plasma in haemorrhagic shock management: current opinion and meta-analysis of randomized trials

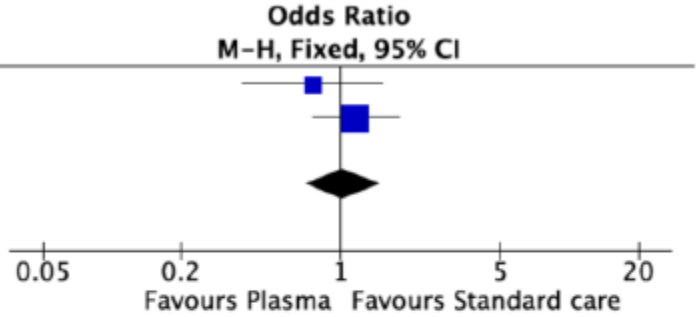
Coccolini F et al

World Journal of Emergency Surgery
2019

A

Study or Subgroup	Plasma Events	Plasma Total	Standard-care Events	Standard-care Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Moore 2018	28	65	30	60	32.8%	0.76 [0.37, 1.53]
Sperry 2018	48	230	50	271	67.2%	1.17 [0.75, 1.81]
Total (95% CI)		**295**		**331**	**100.0%**	**1.03 [0.71, 1.50]**
Total events	76		80			

Heterogeneity: $Chi^2 = 1.04$, $df = 1$ ($P = 0.31$); $I^2 = 3\%$
Test for overall effect: $Z = 0.16$ ($P = 0.87$)



B

Study or Subgroup	Plasma Events	Plasma Total	Standard-care Events	Standard-care Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Moore 2018	4	65	1	60	1.8%	3.87 [0.42, 35.63]
Sperry 2018	145	230	156	271	98.2%	1.26 [0.88, 1.80]
Total (95% CI)		**295**		**331**	**100.0%**	**1.30 [0.92, 1.86]**
Total events	149		157			

Heterogeneity: $Chi^2 = 0.96$, $df = 1$ ($P = 0.33$); $I^2 = 0\%$
Test for overall effect: $Z = 1.47$ ($P = 0.14$)

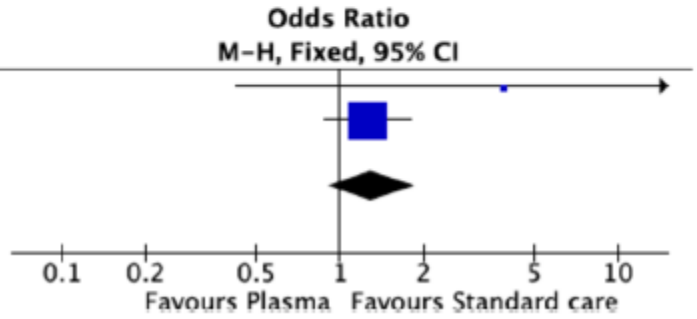


Fig. 3 Morbidity outcomes: acute lung injury (**a**), multi-organ failure (**b**)

The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition

Spahn et al

Crit Care. 2019

Fresh frozen plasma-based management

Recommendation 26 If a FFP-based coagulation resuscitation strategy is used, we recommend that further use of FFP be guided by standard laboratory coagulation screening parameters (PT and/or APTT > 1.5 times normal and/or viscoelastic evidence of a coagulation factor deficiency). (Grade 1C)

We recommend that FFP transfusion be avoided in patients without major bleeding. (Grade 1B)

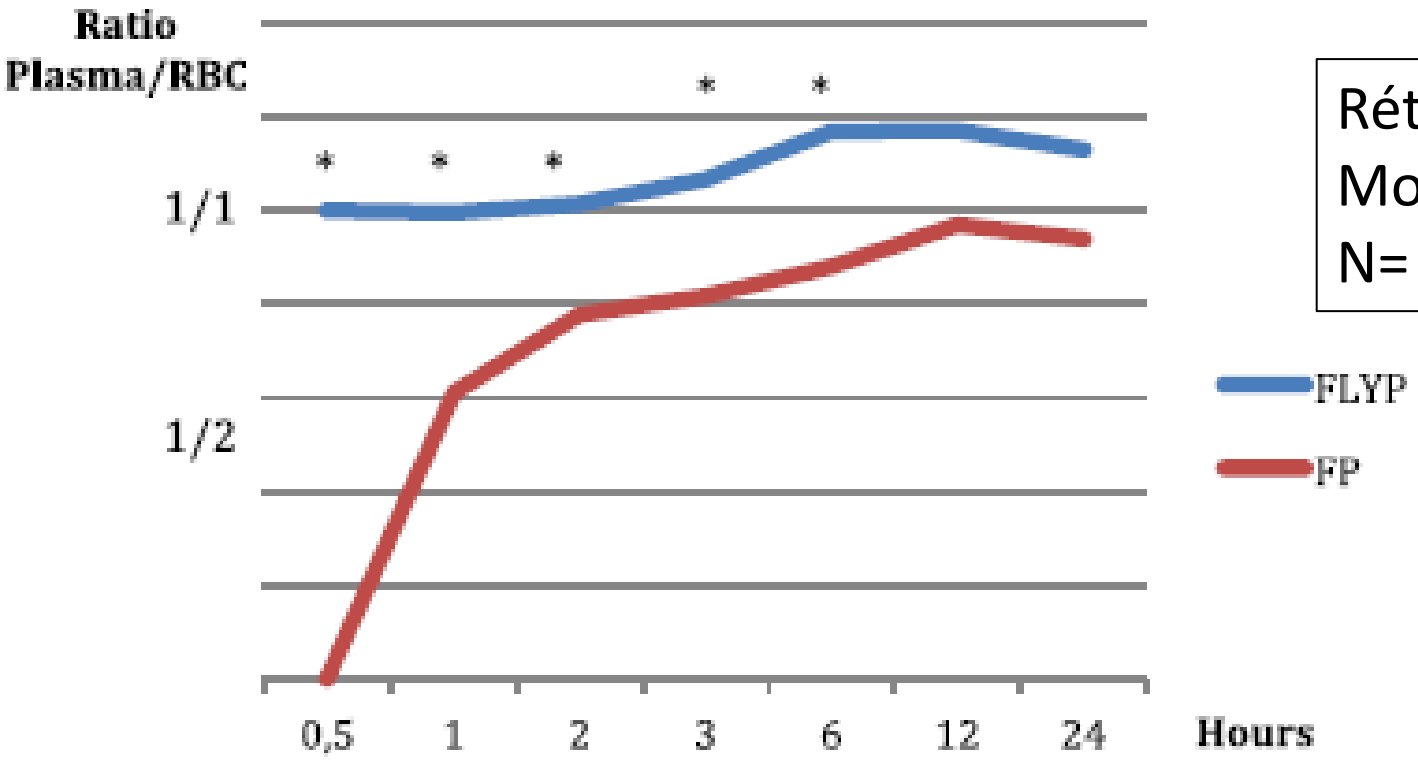
We recommend that the use of FFP be avoided for the treatment of hypofibrinogenaemia. (Grade 1C)


PLASMA CRYODESSÉCHÉ SÉCURISÉ

Use of French lyophilized plasma transfusion in severe trauma patients is associated with an early plasma transfusion and early transfusion ratio improvement

Nguyen C et al

J Trauma. 2018
84: 780-5



Rétrospectif
Monocentrique
N= 43

Figure 1. Evolution of plasma/RBC transfusion ratio over the first 24 h of trauma. FLYP, French lyophilized plasma; FP, fresh frozen plasma.

The impact of prehospital administration of freeze-dried plasma on casualty outcome

Shlaifer A and al

J Trauma. 2019
86: 108-15

Rétrospectif
Monocentrique
Population identique

n = 96 patients

TABLE 3. ED Blood Tests Results of Casualties Receiving FDP Compared With Control Group

	Controls n = 48 Median (Min-Max)	FDP n = 48 Median (Min-Max)	*p**
Hemoglobin	13.5 (7.3–18.1)	12.7 (6.2–16.7)	0.116
Platelets	274.0 (89.0–374.0)	230.0 (92.0–493.0)	0.044
INR	1.2 (1.0–1.8)	1.1 (0.9–1.7)	0.028
PT	16.7 (1.1–110.0)	16.0 (1.2–122.0)	0.910
PTT	26.1 (1.6–46.0)	26.8 (19.1–150.0)	0.977
pH	7.3 (7.0–7.5)	7.3 (6.9–7.5)	0.810
Lactate	3.1 (1.3–13.7)	3.6 (1.1–19.7)	0.535

The impact of prehospital administration of freeze-dried plasma on casualty outcome

Shlaifer A and al

J Trauma. 2019
86: 108-15

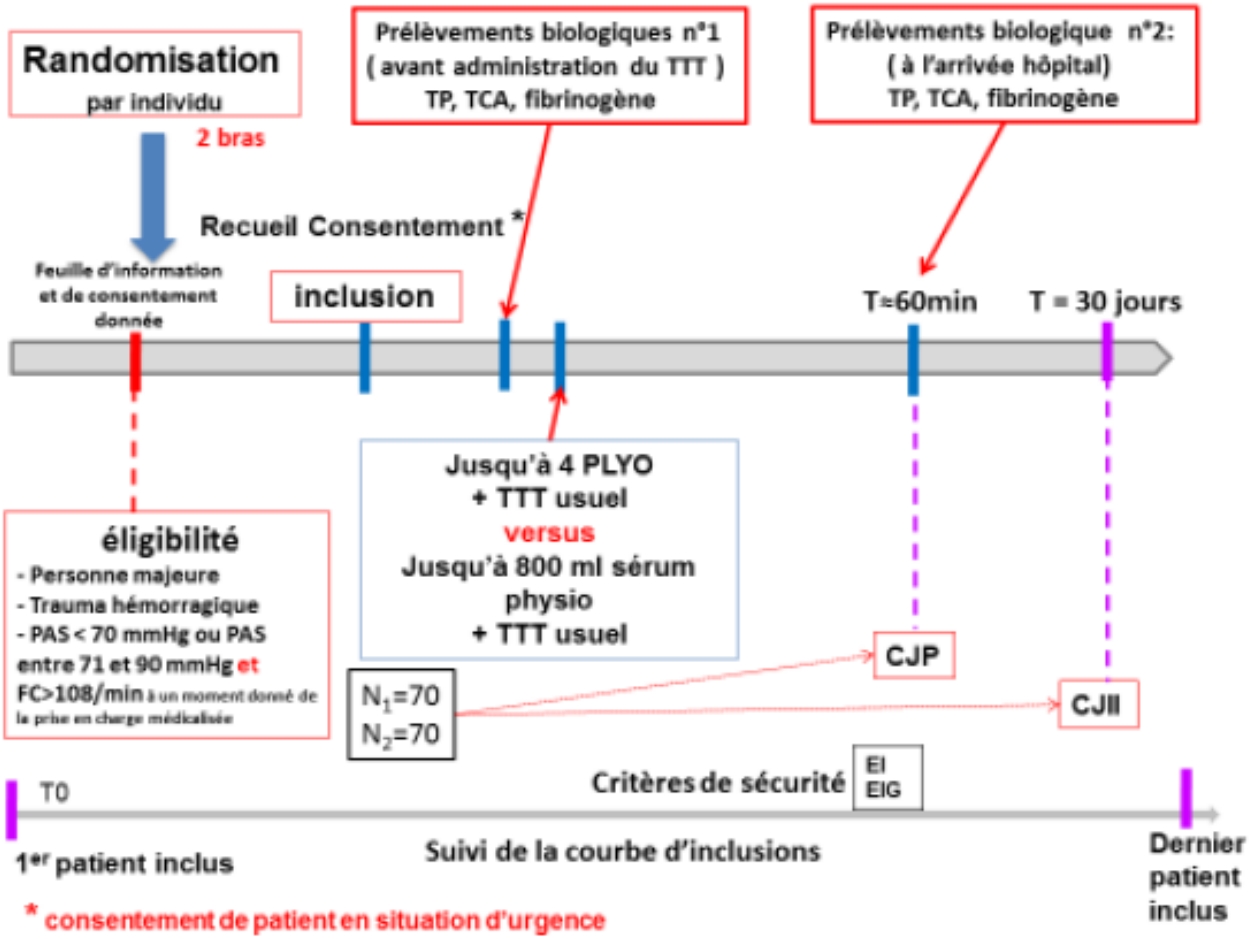
TABLE 4. Hospital Resources Utilization and Discharge Destination of Casualties Receiving FDP Compared With Control Group

	Controls		FDP		
	n = 48		n = 48		*p**
Admitted to ICU	45.8%	22	45.8%	22	1.00
Length of stay 7 + d	68.8%	33	62.5%	30	0.52
Hospital length of stay, d	19.54(±22.37); median, 9 (0–1	nedian, 8 (0–66)	0.281		
ICU length of stay, d	3.67 (±6.91); median, 0 (0–	lian, 0 (0–28)	0.631		
Discharge destination					
Death	6.2%	3	8.5%	4	0.17
Home	52.0%	25	44.7%	21	

NS

PREHO-PLYO

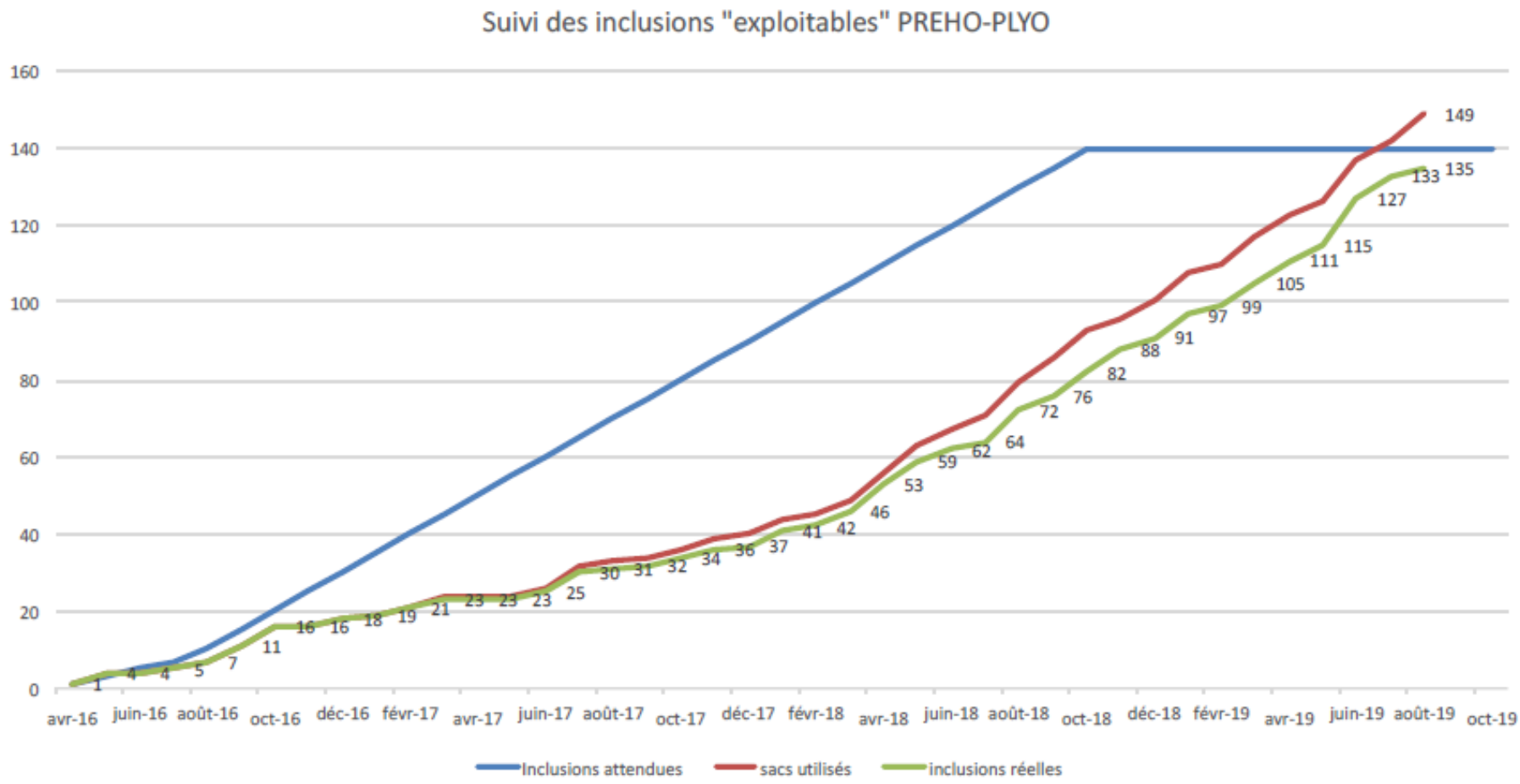
Intérêt de l'administration pré-hospitalière de plasma lyophilisé pour prévenir ou traiter la coagulopathie associée au choc hémorragique post-traumatique



Etude PREHO PLYO

Courbe d'inclusions au 28/08/2019

1er patient inclus: 14/04/2016



CONCLUSIONS

Le plasma lyophilisé en transfusion préhospitalière ?

- Niveau de preuve encore insuffisant pour PFC < 60 mn
- Préhoplyo ne pourra pas nous aider…
- Coût
- Absence de risque à évaluer
- Probablement pas dans notre pratique quotidienne
- Intérêt situation exceptionnelle (éloignement)

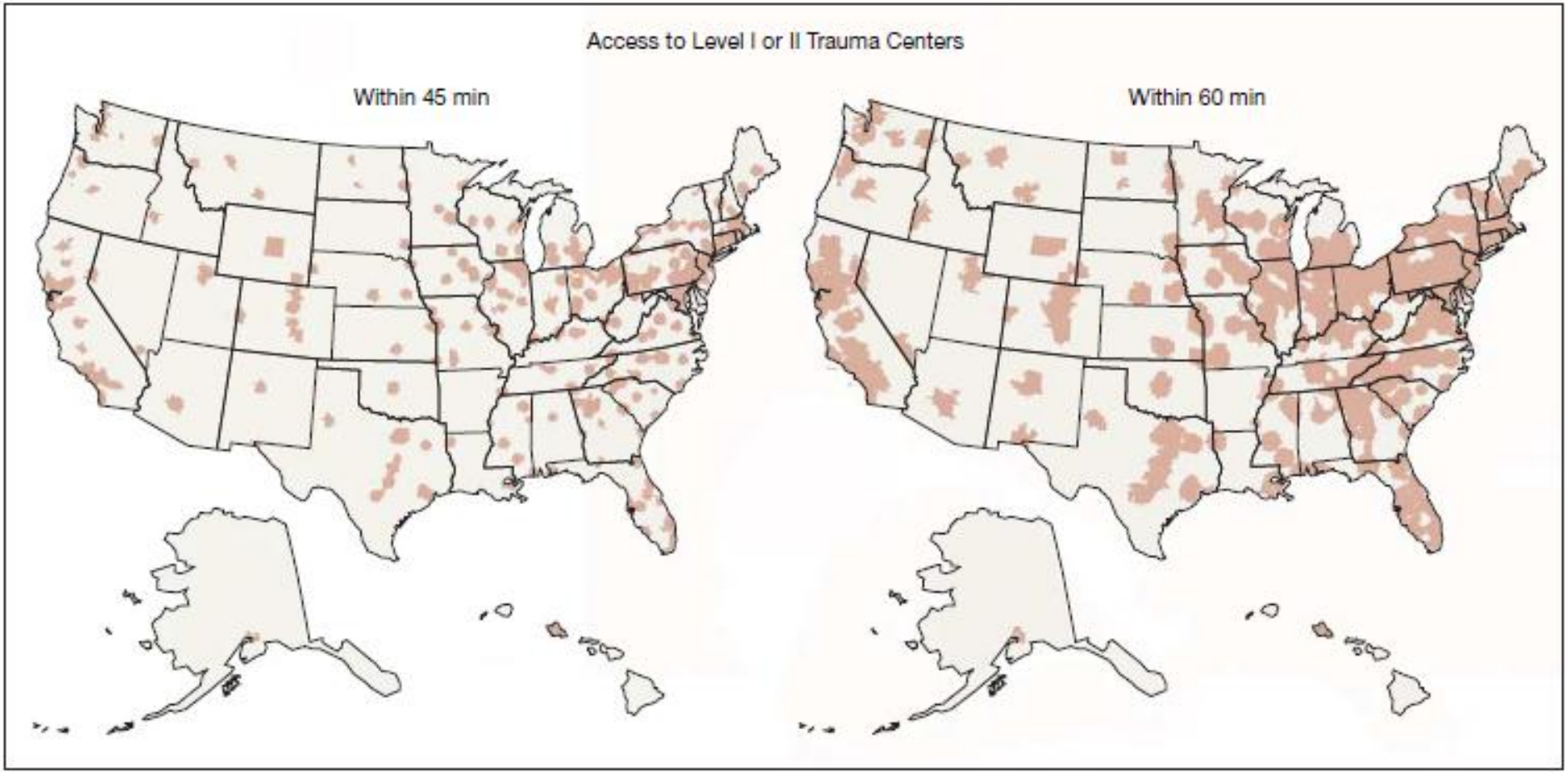
Access to Trauma Centers in the United States

JAMA®
The Journal of the American Medical Association

Branas C C and all

2005;293:2626-33

Figure 1. Areas of the United States With Access to Level I or II Trauma Centers by Ambulance or Helicopter



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Merci
pour votre attention

Questions ?

PREHO-PLYO

Intérêt de l'administration pré-hospitalière de plasma lyophilisé pour prévenir ou traiter la coagulopathie associée au choc hémorragique post-traumatique

HYPOTHESE A VERIFIER	Vérifier qu'en milieu civil extra hospitalier le PLYO administré précocement prévient ou corrige la coagulopathie post traumatique.
OBJECTIFS	***Principal*** Montrer l'efficacité du PLYO administré en pré-hospitalier au cours de prise en charge d'un choc hémorragique d'origine traumatique, sur la survenue ou le traitement d'une coagulopathie post traumatique. ***Secondaires*** - Faisabilité de l'administration de PLYO en pré-hospitalier - Montrer que le PLYO améliore le taux de fibrinogène - Montrer que l'apport de PLYO diminue les besoins transfusionnels (CGR, Plasma, facteurs de la coagulation, plaquettes) - Montrer que l'apport de PLYO diminue la durée de séjour en réanimation - Comparer la mortalité entre les 2 groupes jusqu'à J30

PREHO-PLYO

Intérêt de l'administration pré-hospitalière de plasma lyophilisé pour prévenir ou traiter la coagulopathie associée au choc hémorragique post-traumatique

CRITERES DE JUGEMENT	**Principal :** Variation du TP, entre le TP à l'admission hospitalière et le TP initialement prélevé en pré-hospitalier **Secondaires :** - Recueil des difficultés techniques et logistiques rencontrées avant, pendant et après l'administration du PLYO.
CRITERES D'INCLUSION	Personne majeure, victime de choc hémorragique d'origine traumatique avec PAS <70 ou PAS entre 71 et 90 mm Hg ET fréquence cardiaque > 108, à un moment donné de la prise en charge médicalisée. Les critères de PAS et de fréquence cardiaque n'ont pas besoin d'être simultanés.

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

De Biasi AR et al

Transfusion
2011;51:1925-32

TABLE 3. Timing of plasma transfusion, probability of survival, mortality, and time to death

Patient outcomes	Plasma repletion by third hour			Plasma repletion by sixth hour		
	>2/3 all units	<2/3 all units	p value*	>2/3 all units	<2/3 all units	p value*
All patients, n = 393 (%)	229 (58.3)	164 (41.7)		306 (77.9)	87 (22.1)	
Probability of survival (SD)	0.577 (0.359)	0.625 (0.317)	0.2	0.578 (0.343)	0.666 (0.354)	0.03
Deaths (%)	97 (42.4)	60 (36.6)	0.3	129 (42.2)	28 (32.2)	0.09
Median time to death (hr)	5.7	53.8		7.5	58.1	
5-9 units of RBCs, n = 130 (%)	81 (62.3)	49 (37.7)		105 (80.8)	25 (19.2)	
Probability of survival (SD)†	0.659 (0.338)	0.609 (0.280)	0.4	0.633 (0.333)	0.673 (0.241)	0.6
Deaths (%)	19 (23.5)	13 (26.5)	0.7	28 (26.7)	4 (16)	0.3
Median time to death (hr)	15.1	44.1		25	73	
>9 units of RBCs, n = 263 (%)	148 (56.3)	115 (43.7)		201 (76.4)	62 (23.6)	
Probability of survival (SD)	0.533 (0.364)	0.632 (0.332)	0.02	0.549 (0.365)	0.663 (0.297)	0.03
Deaths (%)	78 (52.7)	47 (40.9)	0.06	101 (50.3)	24 (38.7)	0.1
Median time to death (hr)	5.2	55.3		6.4	58.1	

* Probability of no true difference between those with minimal versus those with substantial plasma change at time interval by t test for continuous and chi square for categorical variables.

† Probability of survival: TRISS.