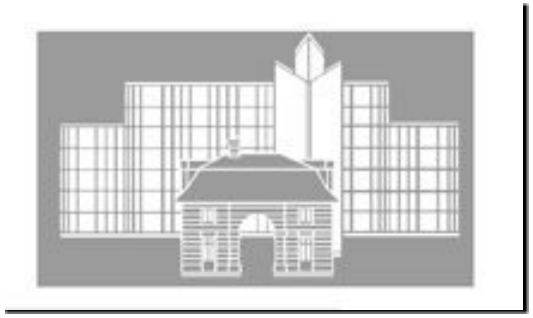
Physiopathologie et traitement du choc hémorragique



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Choc hémorragique - traumatologie

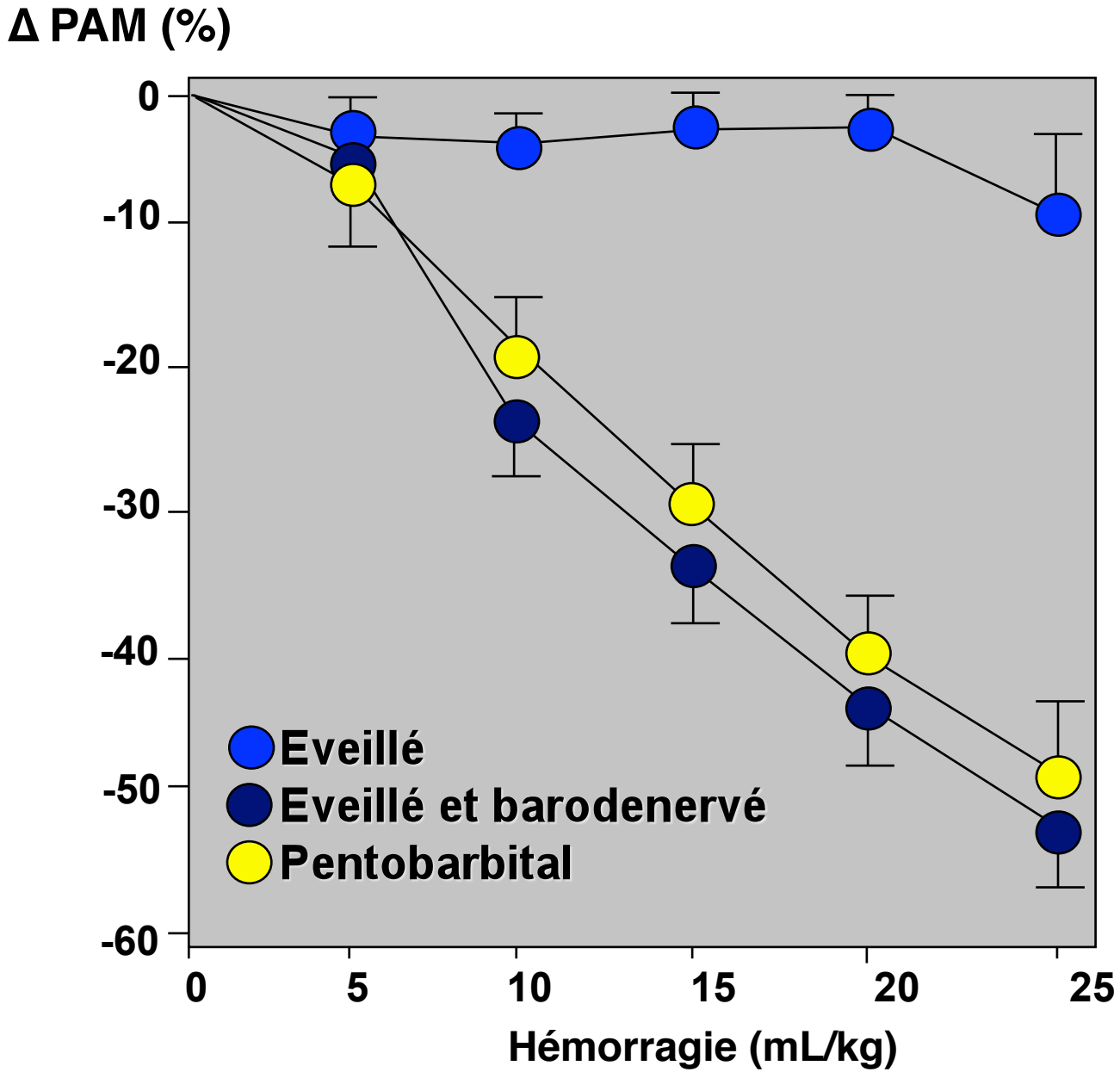
Traumatologie dans le monde

- ✓ **5 millions de mort / an**
- ✓ **>8 million en 2020**

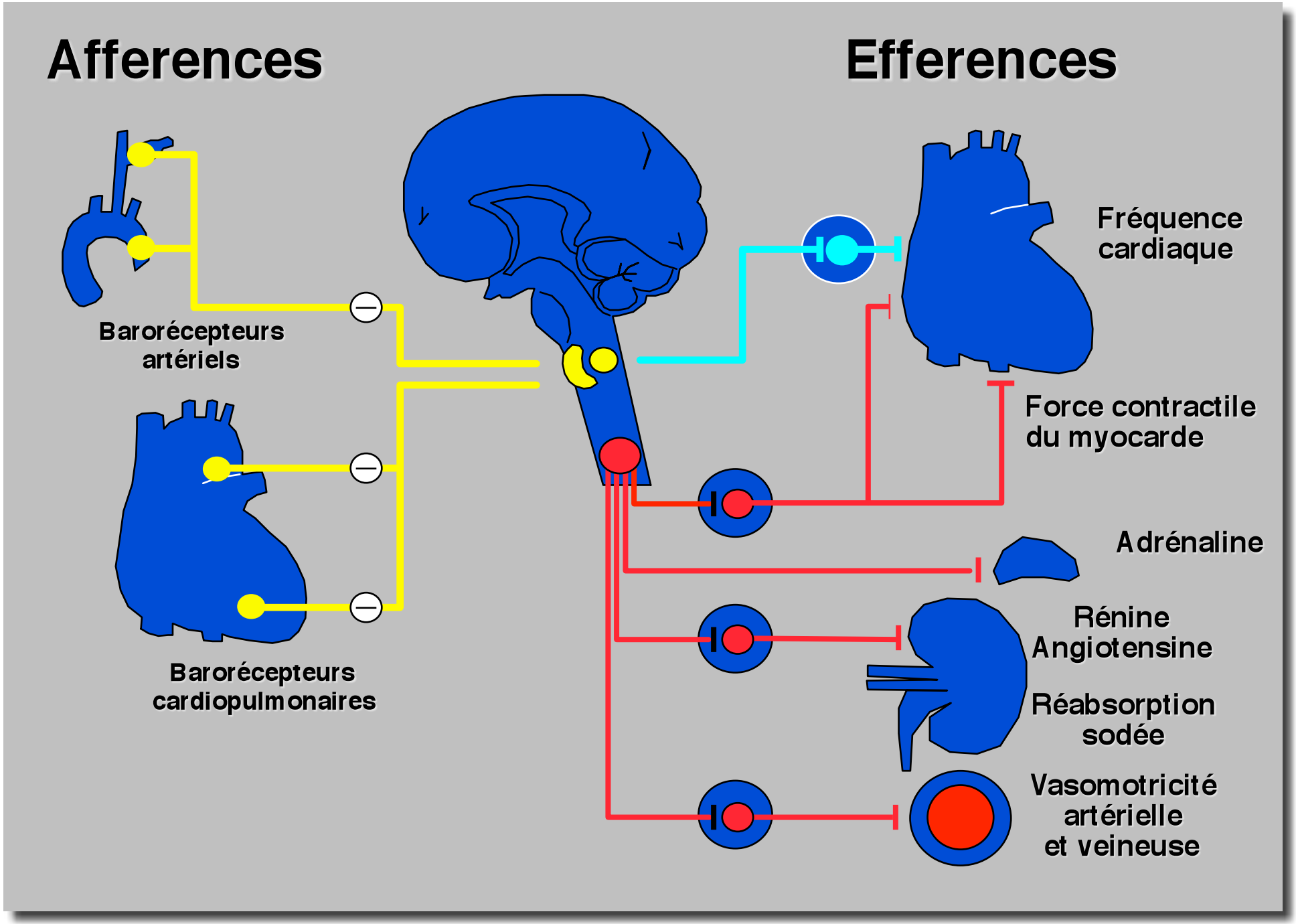
Mortalité précoce est due au choc hémorragique non controlé

Mortalité tardive est due au traumatisme cranien et aux dysfonctions d'organes

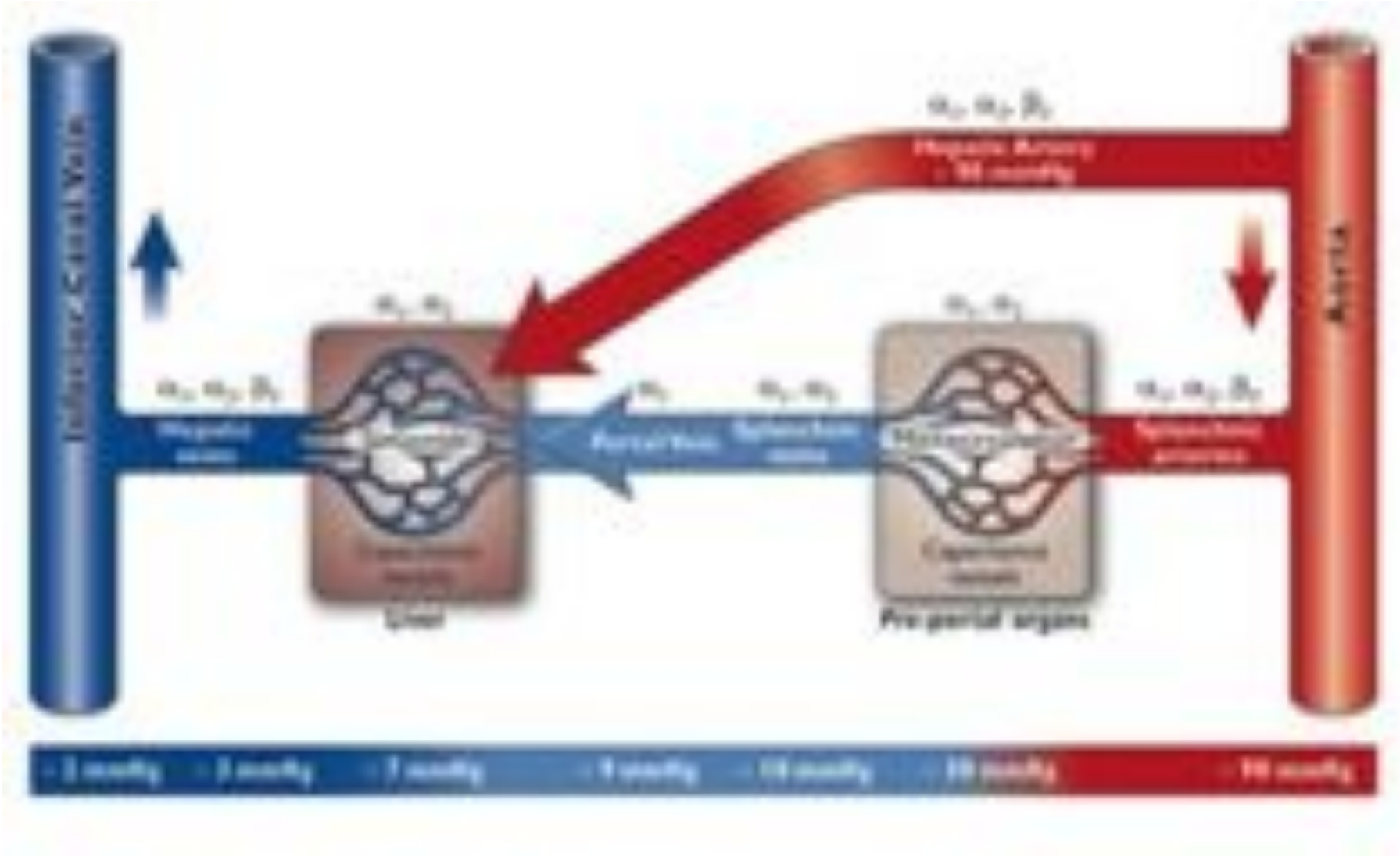
Le choc hémorragique non controlé est la cause prédominante de décès évitables chez les patients traumatisés



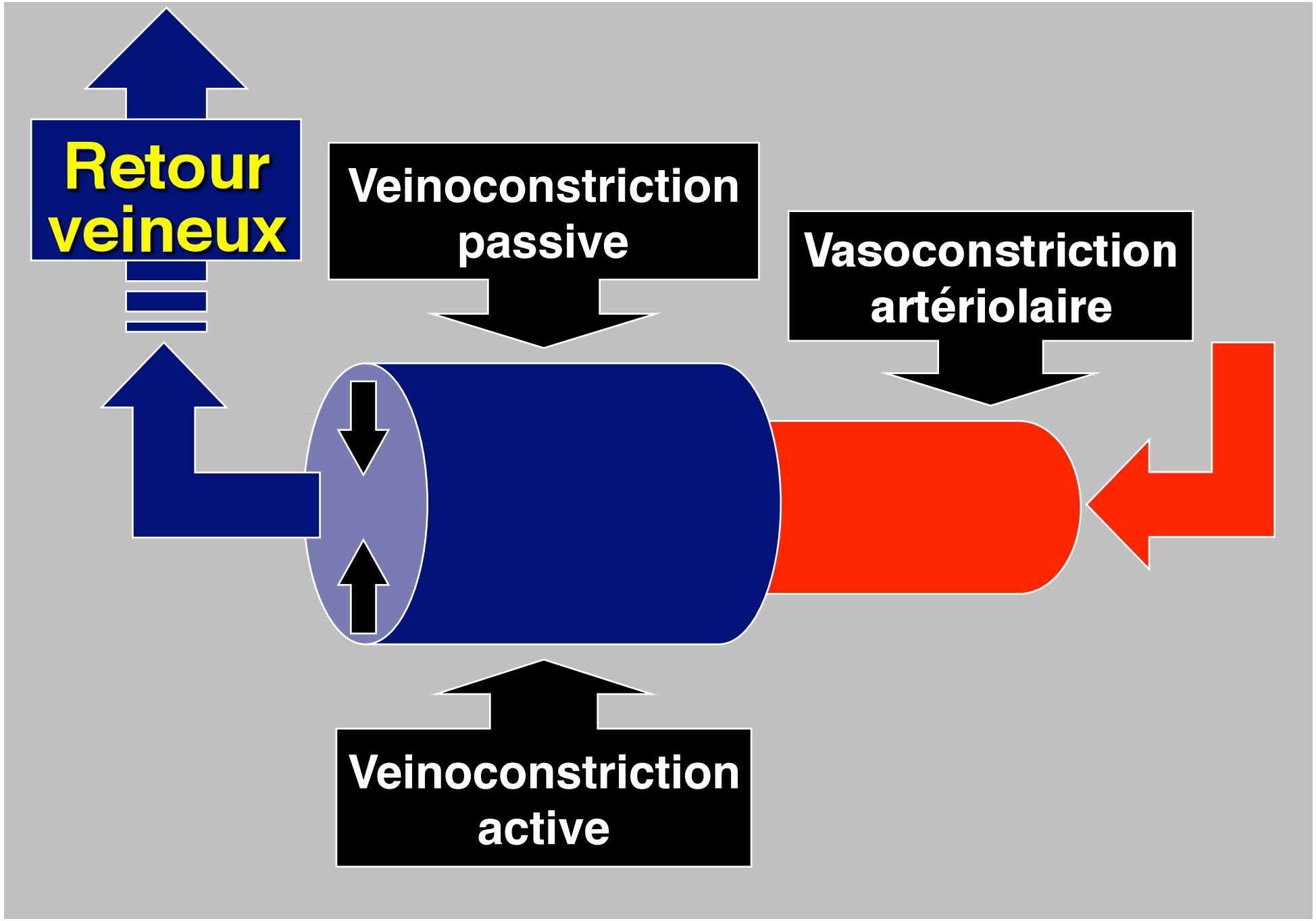
Vatner S. NEJM 1975; 293, 293:970-976.


Afferences
Efferences
Barorécepteurs artériels
Barorécepteurs cardiopulmonaires
Fréquence cardiaque
Force contractile du myocarde
Adrénaline
Rénine Angiotensine
Réabsorption sodée
Vasomotricité artérielle et veineuse

Catecholamine-induced Changes in the Splanchnic Circulation Affecting Systemic Hemodynamics



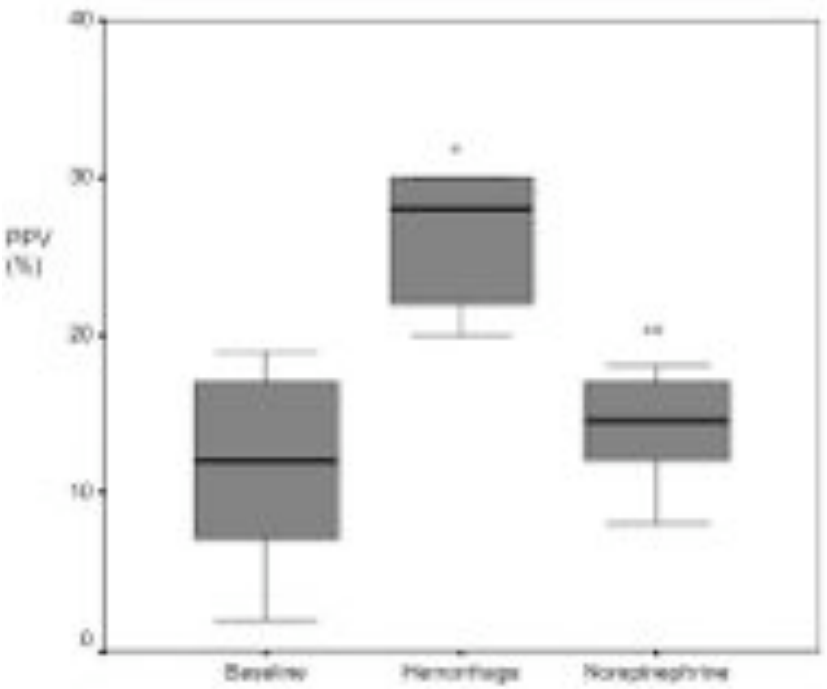
Gelman S. and Mushlin PS. Anesthesiology 2004, 100; 434.


Retour veineux
Veinoconstriction passive
Vasoconstriction artériolaire
Veinoconstriction active

Effects of norepinephrine on static and dynamic preload indicators in experimental hemorrhagic shock*

	Baseline	Hemorrhage	Norepinephrine
HR, beats · min^{-1}	167 (35)	210 (44)[a]	153 (56)[b]
MAP, mm Hg	144 (42)	85 (46)[a]	153 (36)[b]
RAP, mm Hg	5.5 (4.2)	3.0 (4.2)	2.0 (4.0)
PAP, mm Hg	18.5 (16.1)	12.0 (9.3)	18.0 (15.0)
PAOP, mm Hg	6.0 (5.1)	4.5 (4.0)	3.5 (5.1)
CO, L · min^{-1}	4.68 (3.30)	1.98 (0.86)[a]	3.08 (1.72)[b,c]

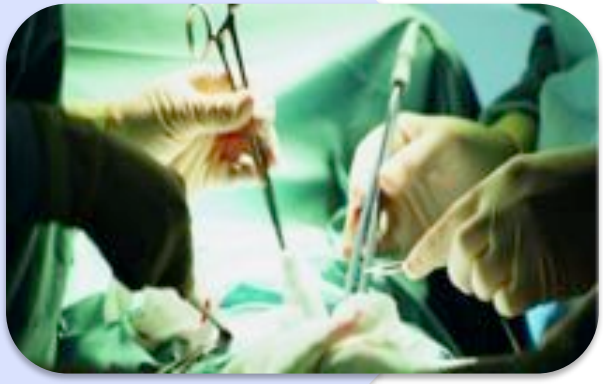
Nouira S. et al. Crit Care Med 2005:2339-2343



Choc hémorragique - traumatologie

Optimisation du temps

- ✓ **Trauma - contrôle du saignement**
- ✓ **Trauma - contrôle des lésions cérébro-spinales**



Choc hémorragique - traumatologie

Réduction du saignement et contrôle rapide de l'hémorragie

- ✓ Faible volume de remplissage vasculaire - Hypotension Permissive
- ✓ Réanimation basée sur une stratégie transfusionnelle agressive
- ✓ « Damage control surgery » - artériographie - embolisation

Identification rapide et contrôle des lésions vitales non hémorragiques

- ✓ Lésions traumatiques cérébrales – Hypertension intra-cranienne
- ✓ Lésions pulmonaires hypoxémiantes

Bleeding trauma patient

Spahn et al. Critical Care 2013, 17:R76
http://ccforum.com/content/17/2/R76

RESEARCH Open Access

Management of bleeding and coagulopathy following major trauma: an updated European guideline

Donat R Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4], Timothy J Coats[5], Jacques Duranteau[6], Enrique Fernández-Mondéjar[7], Daniela Filipescu[8], Beverley J Hunt[9], Radko Komadina[10], Giuseppe Nardi[11], Edmund Neugebauer[12], Yves Ozier[13], Louis Riddez[14], Arthur Schultz[15], Jean-Louis Vincent[16] and Rolf Rossaint[17]*

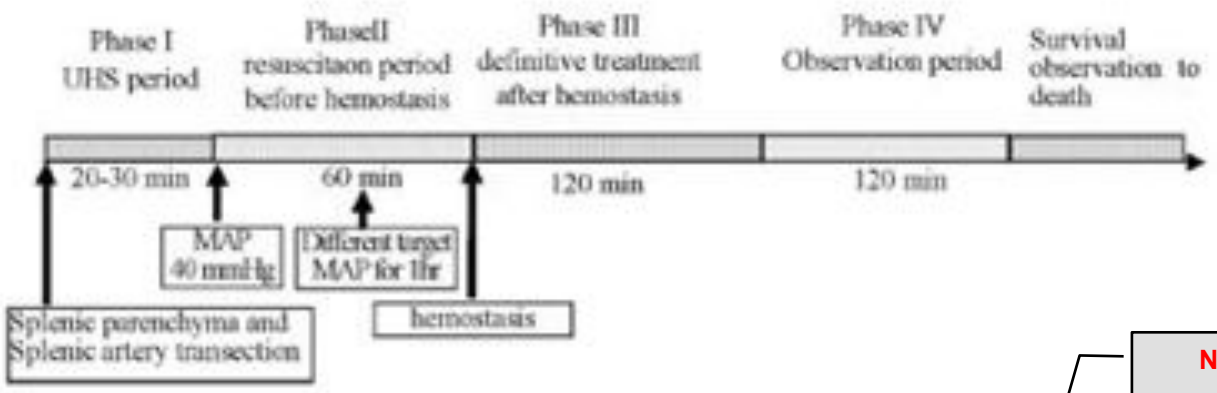
Choc hémorragique - traumatologie

Faible volume de remplissage vasculaire - Hypotension Permissive

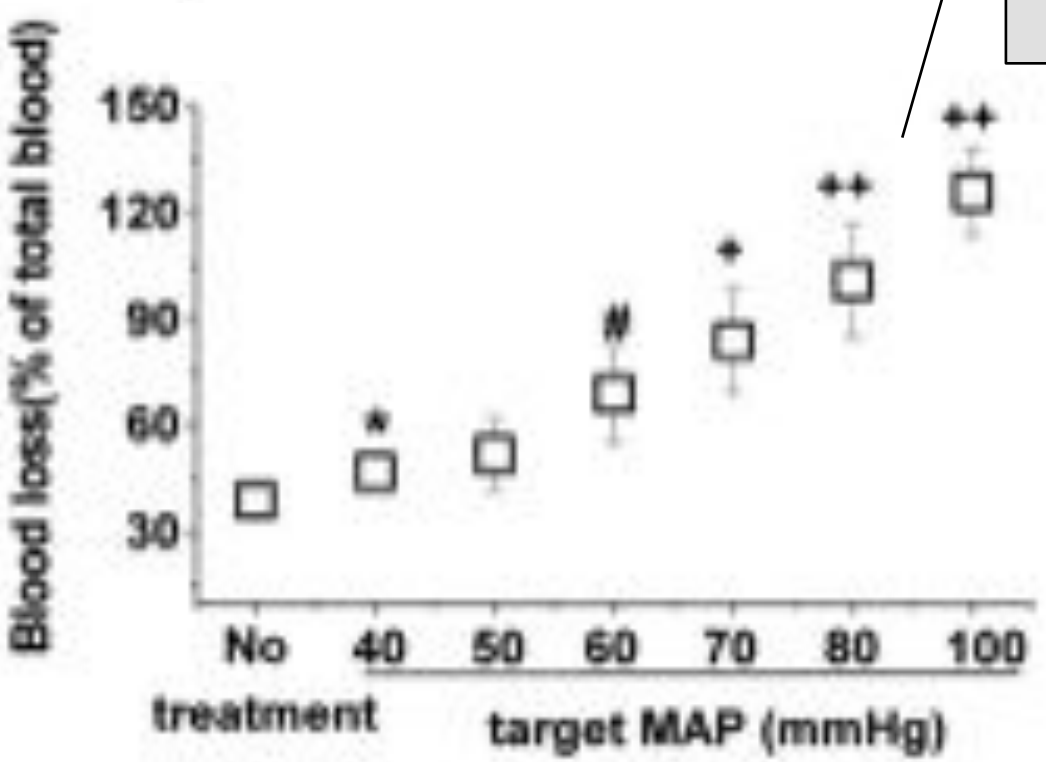
Ideal Permissive Hypotension to Resuscitate Uncontrolled Hemorrhagic Shock and the Tolerance Time in Rats

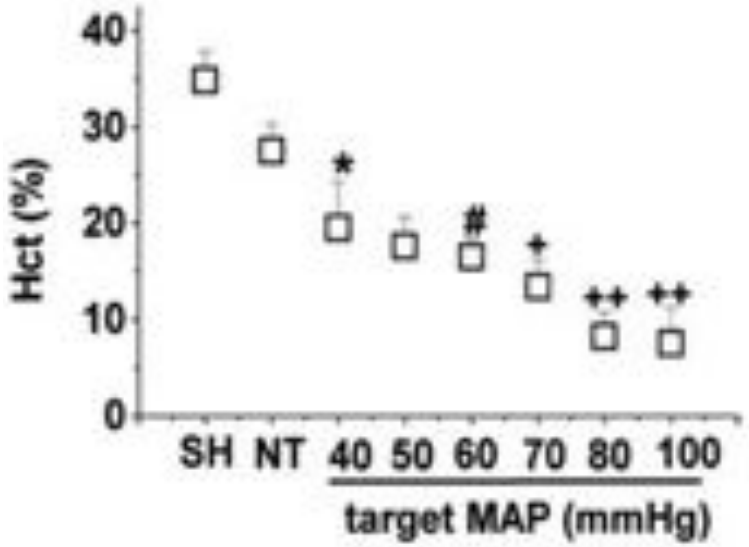
LI T et al. Anesthesiology 2011; 114:111–9

Effects of different target MAPs (40, 50, 60, 70, 80, and 100 mmHg) on uncontrolled hemorrhagic shock



Normotensive groups (80 and 100 mmHg) had increased blood loss (101%, 126% of total blood volume)





Management of bleeding following major trauma: an updated European guideline

Spahn et al. Critical Care 2013

Time elapsed between injury and operation has to be minimized

Concept of low volume fluid resuscitation
Permissive hypotension
Avoids the adverse effects of early aggressive resuscitation while maintaining a level of tissue perfusion that, although lower than normal, is adequate for short periods

Target SAP 80-90 mmHg until major bleeding has been stopped in the initial phase following trauma

MAP ≥80 mmHg in patients with combined haemorrhagic shock and severe TBI (GCS ≤8)

Immediate versus Delayed Fluid Resuscitation for Hypotensive Patients with Penetrating Torso Injuries

The NEW ENGLAND JOURNAL of MEDICINE

	Immediate resuscitation (n = 309)	Delayed resuscitation (n = 289)	P value
Before arrival at the hospital			
Ringer's lactate (ml)	870 ± 667	92 ± 309	<0.001
Trauma center			
Ringer's lactate (ml)	1608 ± 1201	283 ± 722	<0.001
Packed red cells (ml)	133 ± 393	11 ± 88	<0.001
Survival to discharge	193 (62%)	203 (70%)	0.04
Length of hospital stay	14 ± 24	11 ± 19	0.006

Bickell, WH et al. NEJM 1994

Hypotensive Resuscitation during Active Hemorrhage: Impact on In-Hospital Mortality

	SBP > 100 mm Hg	SBP = 70 mm Hg
Patients enrolled	55	55
Average SBP during bleeding (mm Hg)	114 ± 12	100 ± 17
Length of active hemorrhage (h)	2.97 ± 1.75	2.57 ± 1.46
Died	4	4
Average ISS	19.55 ± 11.6	23.91 ± 13.8
Predicted survival rate (TRISS)	94.0 ± 12%	90.2 ± 17%
Actual survival rate (%)	92.7	92.7

Titration of initial fluid therapy to a lower than normal SBP during active hemorrhage did not affect mortality

Dutton RP et al. , J. Trauma. 2002;52:1141-1146.

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Management of bleeding following major trauma: an updated European guideline

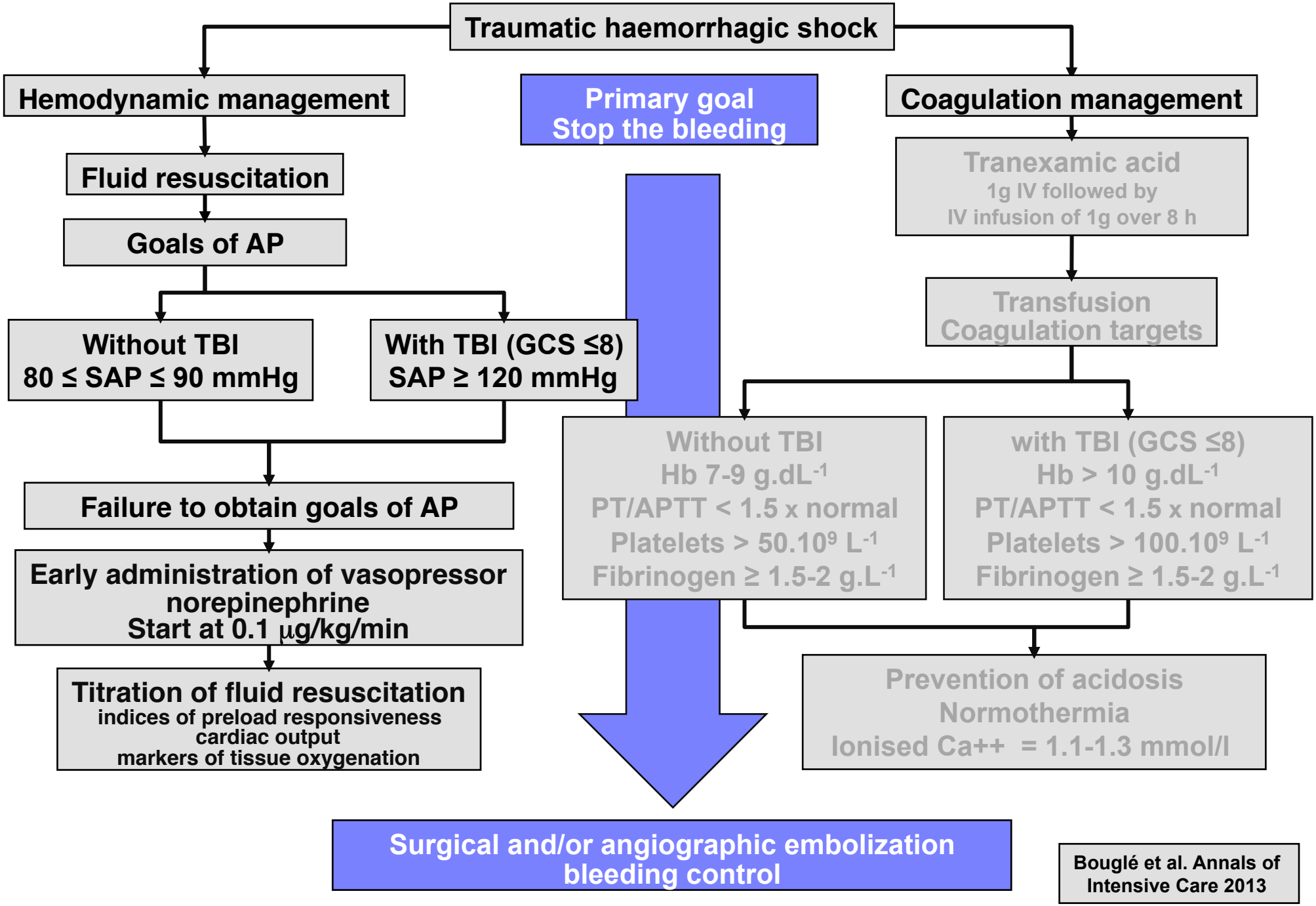
Spahn et al. Critical Care 2013

Time elapsed between injury and operation has to be minimised

The concept of low volume fluid resuscitation so-called "permissive hypotension", Avoids the adverse effects of early aggressive resuscitation while maintaining a level of tissue perfusion that, although lower than normal, is adequate for short periods

Target SAP 80-90 mmHg until major bleeding has been stopped in the initial phase following trauma

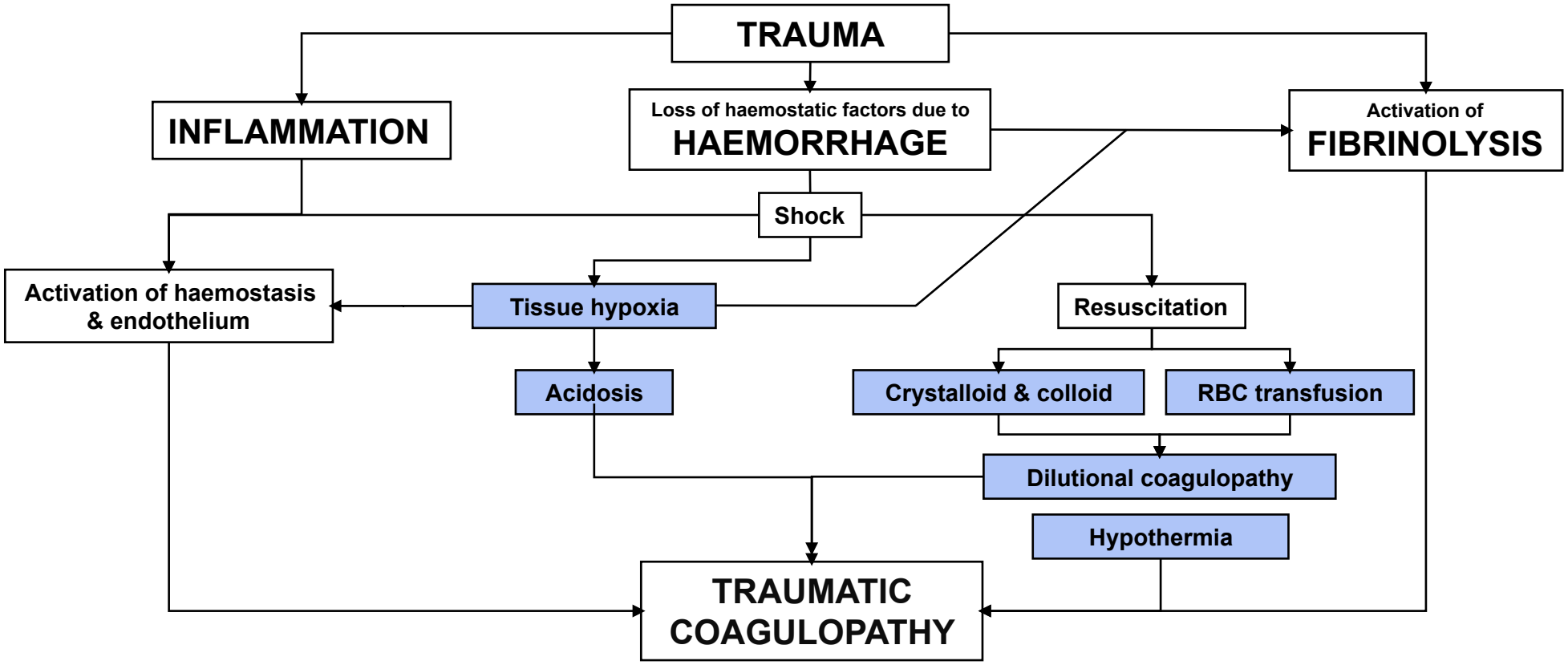
Administration of vasopressors to maintain target arterial pressure in the absence of a response to fluid therapy


Traumatic haemorrhagic shock
Hemodynamic management
Primary goal
Stop the bleeding
Coagulation management
Fluid resuscitation
Tranexamic acid
1g IV followed by
IV infusion of 1g over 8 h
Goals of AP
Transfusion
Coagulation targets
Without TBI
80 ≤ SAP ≤ 90 mmHg
With TBI (GCS ≤8)
SAP ≥ 120 mmHg
Without TBI
Hb 7-9 g.dL-1
PT/APTT < 1.5 x normal
Platelets > 50.10⁹ L-1
Fibrinogen ≥ 1.5-2 g.L-1
with TBI (GCS ≤8)
Hb > 10 g.dL-1
PT/APTT < 1.5 x normal
Platelets > 100.10⁹ L-1
Fibrinogen ≥ 1.5-2 g.L-1
Failure to obtain goals of AP
Early administration of vasopressor
norepinephrine
Start at 0.1 µg/kg/min
Titration of fluid resuscitation
indices of preload responsiveness
cardiac output
markers of tissue oxygenation
Prevention of acidosis
Normothermia
Ionised Ca++ = 1.1-1.3 mmol/l
Surgical and/or angiographic embolization
bleeding control
Bouglé et al. Annals of
Intensive Care 2013

Choc hémorragique - traumatologie

Réanimation basée sur une stratégie transfusionnelle agressive

Traumatic coagulopathy



Réanimation basée sur une stratégie Transfusionnelle agressive

- ✓ Monitorage de la coagulation
- ✓ Protocoles de transfusion massive
- ✓ Ration optimal Plasma/CG
- ✓ Fibrinogène
- ✓ Agents antifibrinolytiques
- ✓ Facteur VII recombinant

Réanimation basée sur une stratégie Transfusionnelle agressive

- ✓ **Monitorage de la coagulation**
- ✓ Protocoles de transfusion massive
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Réanimation basée sur une stratégie Transfusionnelle agressive

- ✓ **Monitorage de la coagulation**
- ✓ **Protocoles de transfusion massive**
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Damage Control Hematology: The Impact of a Trauma Exsanguination Protocol on Survival and Blood Product Utilization

Trauma exsanguination protocol (TEP): immediate and continued release of blood products from the blood bank in a predefined ratio of 10 units of PRBC to 4 units of fresh frozen plasma to 2 units of platelets.

Variable	Pre-TEP (n = 117)	TEP (n = 94)	p
30-d mortality (%)	65.8	51.1	0.030*
24-h blood product use (units)	39 ± 28	31.8 ± 19	0.017*
24-h RBC use (units)	19.8 ± 12.8	18.8 ± 11.2	0.695
24-h FFP use (units)	12.4 ± 12.5	9.9 ± 7	0.595
24-h PLT use (units)	6.8 ± 7.2	3.1 ± 3.7	<0.001*
Intraoperative RBC use (units)	11.1 ± 8.5	16 ± 11.4	0.001*
Intraoperative FFP use (units)	4.3 ± 4	8.2 ± 6.8	<0.001*
Intraoperative PLT use (units)	1.1 ± 2.6	2.2 ± 2.3	<0.001*
Intraoperative crystalloid (L)	6.7 ± 4.2	4.9 ± 3.0	0.002*
Unexpected survivors (%)	5.1	22.3	<0.001*
Unexpected deaths (%)	22.2	8.5	0.007*

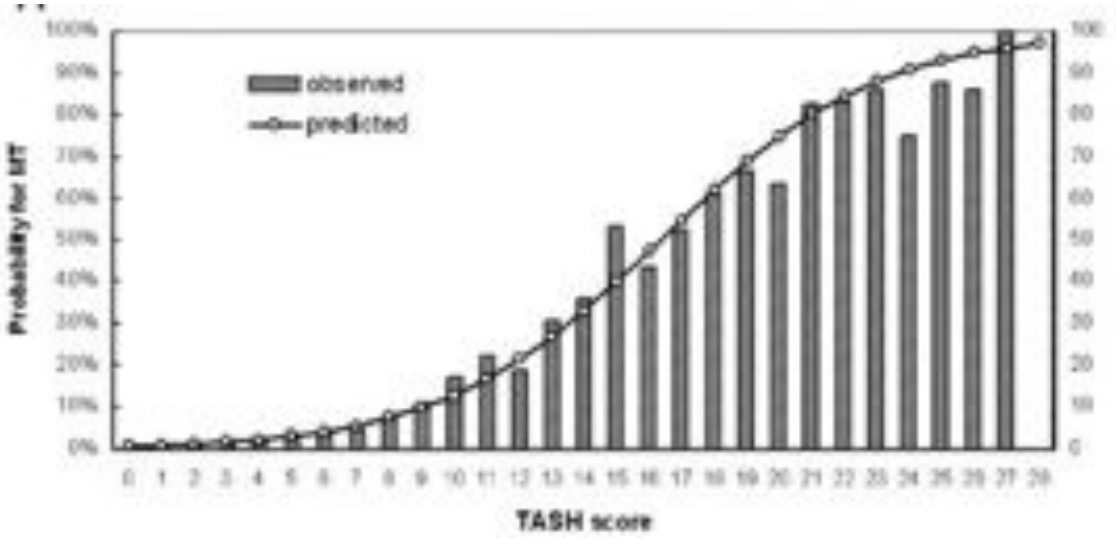
Cotton BA et al., J Trauma. 2008;64:1177–1183.

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

Variable	Value	Points
Hemoglobin (mg/dL)	<7	6
	<9	6
	<10	4
	<11	3
	<12	2
Base excess (mmol/L)	<−10	4
	<−6	3
	<−2	1
Systolic blood pressure (mm Hg)	<100	4
	<120	1
Heart rate (beats/min)	>120	2
Free intraabdominal fluid (e.g. by FAST)		3
Extremities		
Clinically instable pelvic fracture		6
Clinically femur fracture open/dislocated		3
Male patient		1

MT was defined by transfusion requirement of >10 units of packed red blood cells from emergency room (ER) to intensive care unit admission

Yücel N et al. J Trauma. 2006;60:1228–1237



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A high ratio of plasma and platelets to packed red blood cells in the first 6 hours of massive transfusion improves outcomes in a large multicenter study

- ✓ 466 massive transfusion trauma patients (≥10 U of PRBCs in 24 hours)
- ✓ 16 level 1 trauma centers were reviewed
- ✓ Transfusion ratios in the first 6 hours were correlated with outcome.
- ✓ To remove the bias of the delay in availability of plasma and platelets, all patients who died within 30 minutes of arrival to the emergency room were excluded

The American Journal of Surgery®

Product ratio	Measure	Transfusion ratio in first 6 hours <1:4	1:4-1:1	≥1:1	P
FFP:PRBC	6 hour mortality %	37.3*	15.2*	2.0*	<0.001
	In-hospital mortality %	54.9*	41.1*	25.5*	<0.04
	Ventilator free days†	9	7.9	6.3	0.35
PLT:PRBC	6 hour mortality %	22.8	19.0	3.2*	<0.002
	In-hospital mortality %	43.7	46.8	27.4*	<0.03
	Ventilator-free days†	6*	9.9**	9.1**	<0.004

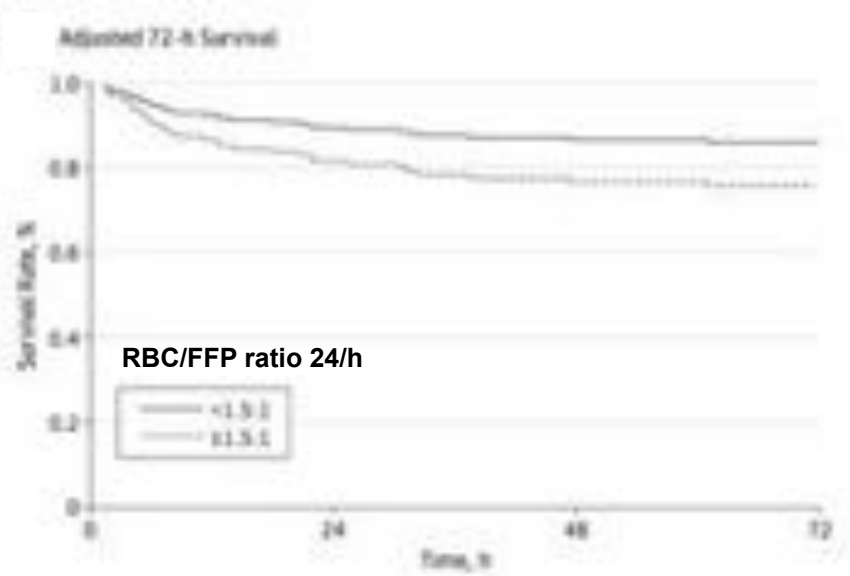
Zink KA et al., The American Journal of Surgery (2009)

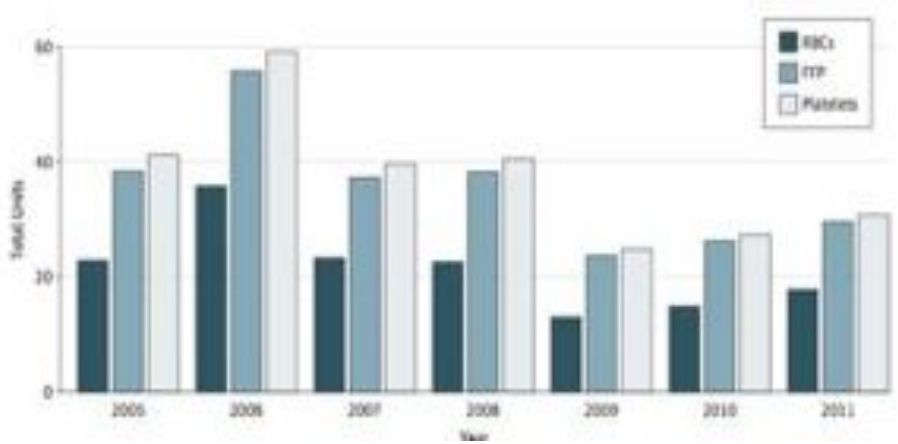
A Paradigm Shift in Trauma Resuscitation
Evaluation of Evolving Massive Transfusion Practices

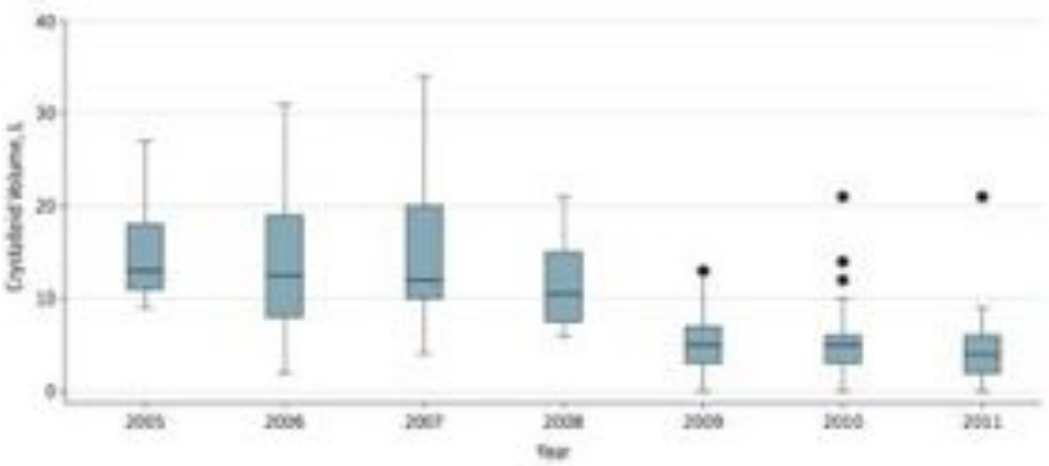
Massives transfusion practices

- ✓ 174 trauma patients receiving a **massive transfusion(>10 units RBCs in 24 hours)** or requiring the activation of massive transfusion protocol
- ✓ February 2005 to June 2011
- ✓ **% of RBCs transfused within 6 hours increased from 80.2% in 2005 to 87.6% in 2011 (*P* = .04)**
- ✓ **% of FFP transfused within 6 hours increased from 74.3% in 2005 to 87.3% in 2011 (*P* = .02)**
- ✓ Shift toward a reduced crystalloid volume and more plasma-based MT practices

ME Kutcher et al. *JAMA Surg.* 2013







Management of bleeding following major trauma: an updated European guideline

Spahn et al. Critical Care 2013

We recommend initial administration of plasma (fresh frozen plasma (FFP) or pathogen-inactivated plasma) or fibrinogen in patients with massive bleeding

we suggest an optimal plasma:red blood cell ratio of at least 1:2

We recommend that plasma transfusion be avoided in patients without substantial bleeding

Réanimation basée sur une stratégie Transfusionnelle agressive

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Management of bleeding following major trauma: an updated European guideline

Spahn et al. Critical Care 2013

We recommend treatment with fibrinogen concentrate or cryoprecipitate if significant bleeding is accompanied by thromboelastometric signs of a functional fibrinogen deficit or a plasma fibrinogen level < 1.5 to 2.0 g/l

We suggest an initial fibrinogen concentrate dose of 3 to 4 g or 50 mg/kg of cryoprecipitate

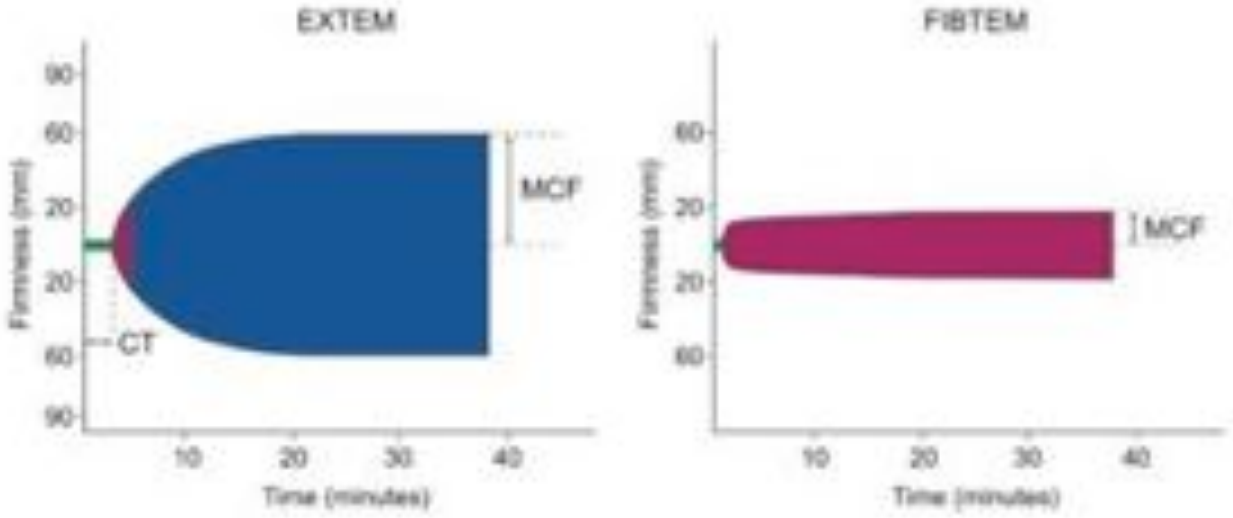
Repeat doses may be guided by viscoelastic monitoring and laboratory assessment of fibrinogen levels

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

CRITICAL CARE

131 patients / Retrospective analysis included trauma patients who received ≥ 5 units RBC within 24 hours. Coagulation management was guided by thromboelastometry

Fibrinogen concentrate was given as first-line haemostatic therapy when maximum clot firmness (MCF) measured by FibTEM (fibrin-based test) was <10 mm. Prothrombin complex concentrate (PCC) was given in case of recent coumarin intake or clotting time measured by extrinsic activation test (EXTEM) >1.5 times normal. Lack of improvement in EXTEM MCF after fibrinogen concentrate administration was an indication for platelet concentrate.



EXTEM® test (extrinsically activated test)

FibTEM® test (fibrin clot obtained by platelet inhibition with cytochalasin D)

Schöchl H et al. Crit Care. 2010;14(2):R5

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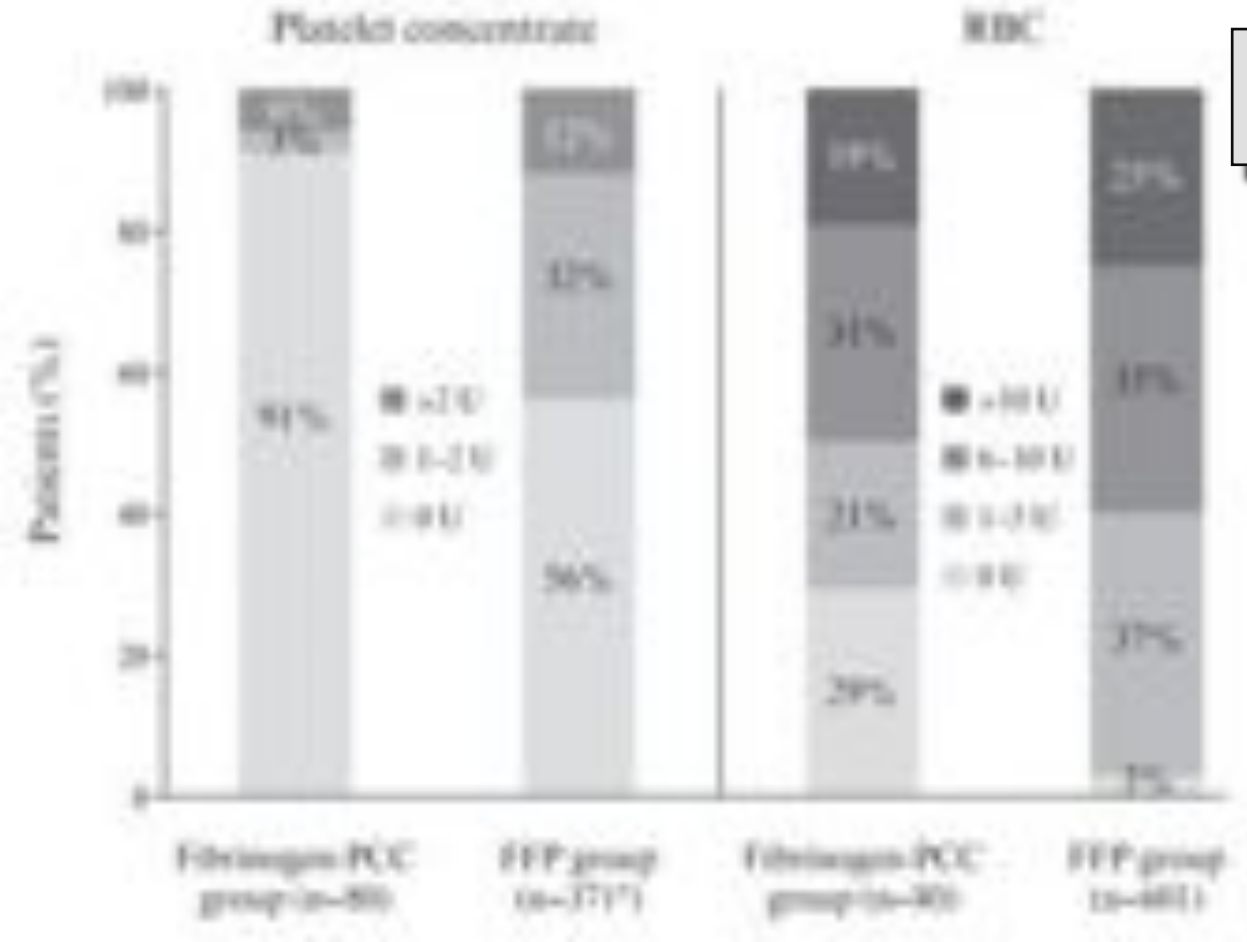
	Total administered until arrival at ICU		Total administered during 24 hours after admission to the ER	
	Number of patients treated	Dose	Number of patients treated	Dose
Fibrinogen concentrate (g)	123	6 (4, 9)	128	7 (5, 11)
PCC (U)	83	1800 (1650, 3100)	101	2400 (1800, 3600)
FFP (U)	6	10 (7, 10)	12	10 (9.75, 11.25)
PC (U)	22	2 (1, 2)	29	2 (2, 3)
RBC (U)	125	6 (4, 10)	131	10 (6, 13)

Data are presented as median (25th percentile, 75th percentile). Total number of patients = 131. ER, emergency room; FFP, fresh frozen plasma; PC, platelet concentrate; PCC, prothrombin complex concentrate; RBC, red blood cell concentrate.

Schöchl H et al. Crit Care. 2010;14(2):R5

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

Retrospective analysis compared patients from the Salzburg Trauma Centre (Salzburg, Austria) treated with fibrinogen concentrate and/or PCC, but no FFP (fibrinogen-PCC group, n = 80), and patients from the TraumaRegister DGU receiving ≥ 2 units of FFP, but no fibrinogen concentrate/PCC (FFP group, n = 601)



Mortality was comparable between groups:
7.5% in the fibrinogen-PCC group
10.0% in the FFP group

Schöchl 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

THE LANCET

Randomised controlled trial / 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.

Trauma patients with significant hemorrhage (SAP < 90 mmHg or/and HR > 100 bpm) or at risk of significant hemorrhage

	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.

Lancet. 2010 Jul 3;376(9734):23-32

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Trauma patients with significant hemorrhage (SAP < 90 mmHg or/and HR > 100 bpm) or at risk of significant hemorrhage

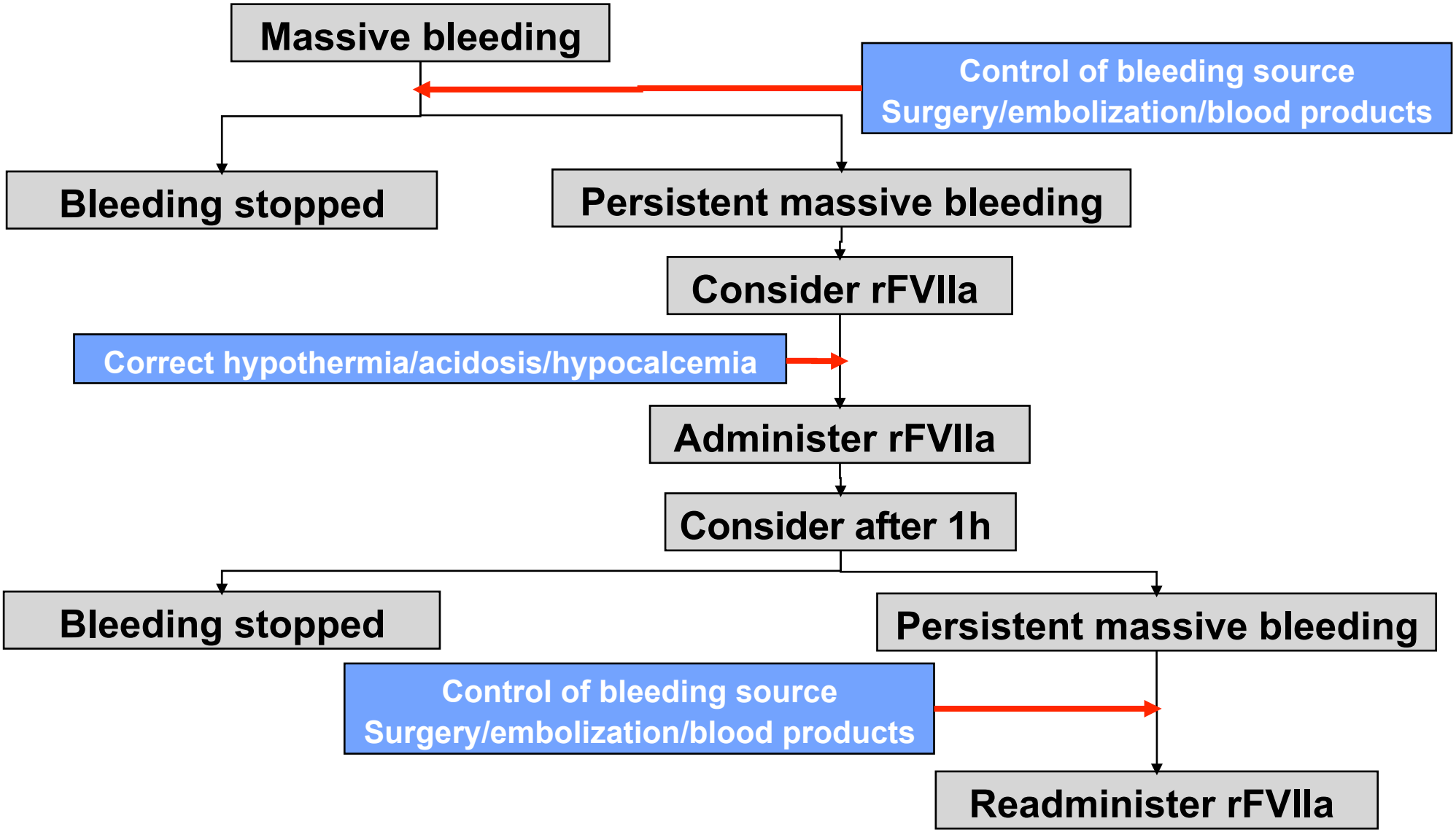
	Tranexamic acid (n=10 060)	Placebo (n=10 067)	RR (95% CI)	p value
Vascular occlusive events*				
Any vascular occlusive event	168 (1·7%)	201 (2·0%)	0·84 (0·68–1·02)	0·084
Myocardial infarction	35 (0·3%)	55 (0·5%)	0·64 (0·42–0·97)	0·035
Stroke	57 (0·6%)	66 (0·7%)	0·86 (0·61–1·23)	0·42
Pulmonary embolism	72 (0·7%)	71 (0·7%)	1·01 (0·73–1·41)	0·93
Deep vein thrombosis	40 (0·4%)	41 (0·4%)	0·98 (0·63–1·51)	0·91

Lancet. 2010 Jul 3;376(9734):23-32

Réanimation basée sur une stratégie Transfusionnelle agressive

- ✓ Monitorage de la coagulation
- ✓ Protocoles de transfusion massive
- ✓ Ration optimal Plasma/CG
- ✓ Fibrinogène
- ✓ Agents antifibrinolytiques
- ✓ Facteur VII recombinant

Recombinant factor VIIa



Management of bleeding following major trauma: an updated European guideline

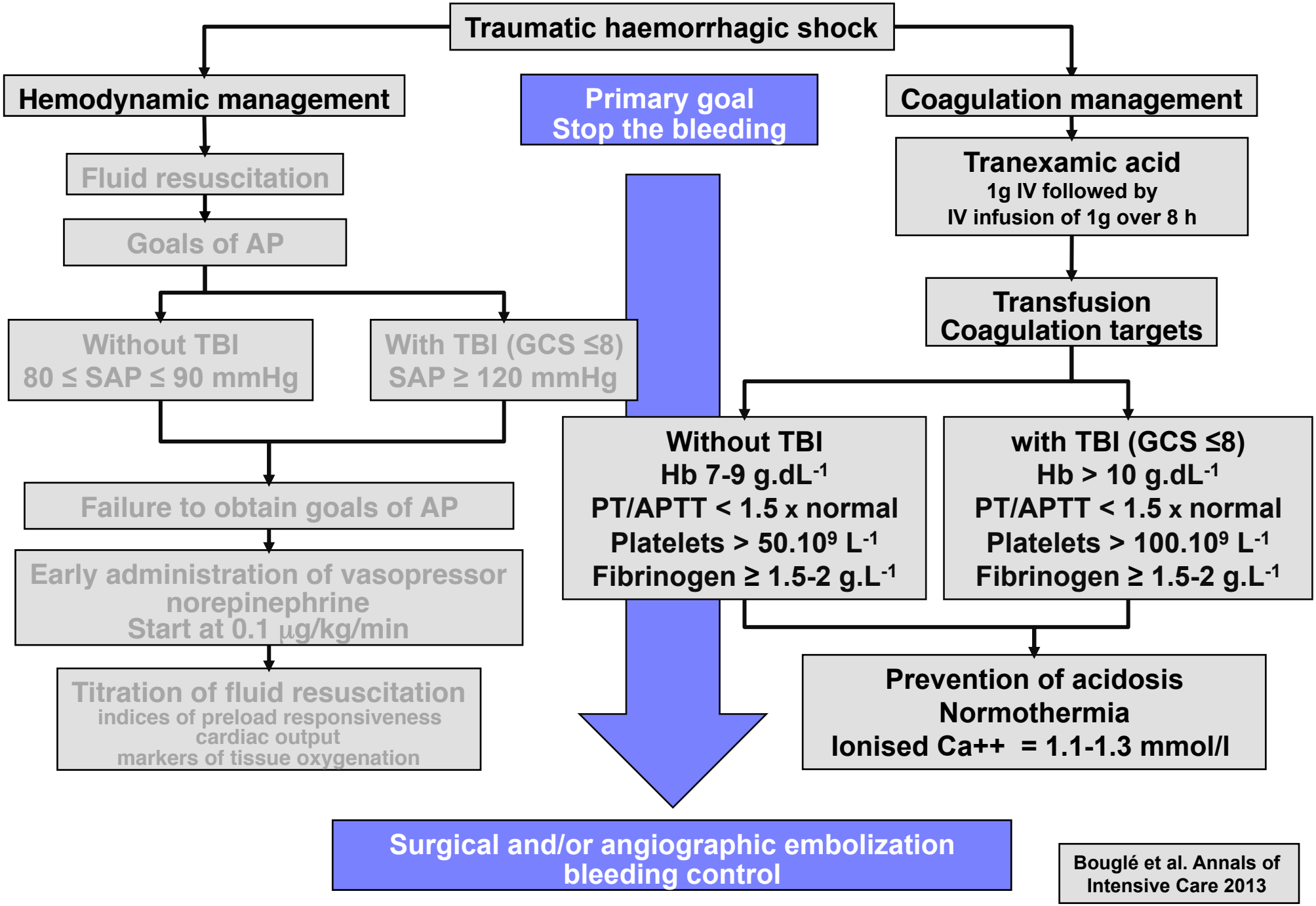
Spahn et al. Critical Care 2013

Novel anticoagulants

We suggest the measurement of substrate-specific anti-factor Xa activity in patients treated or suspected of being treated with oral anti-factor Xa agents such as rivaroxaban, apixaban or endoxaban

If bleeding is life-threatening, we suggest reversal of rivaroxaban, apixaban and endoxaban with high-dose (25 to 50 U/kg) PCC

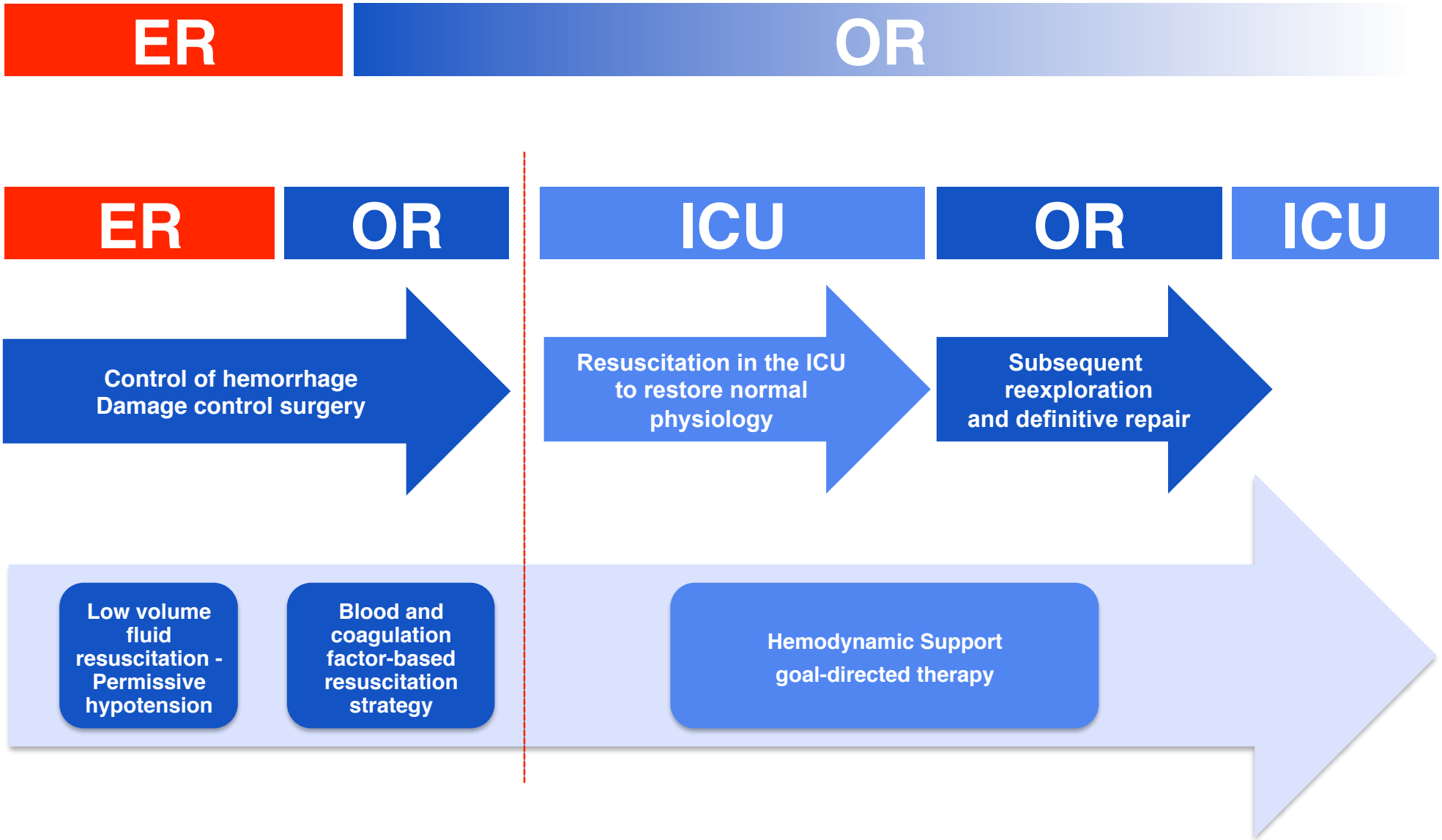
We do not suggest the administration of PCC in patients treated or suspected of being treated with oral direct thrombin inhibitors, such as dabigatran


Traumatic haemorrhagic shock
Hemodynamic management
Primary goal
Stop the bleeding
Coagulation management
Fluid resuscitation
Goals of AP
Tranexamic acid
1g IV followed by
IV infusion of 1g over 8 h
Without TBI
80 ≤ SAP ≤ 90 mmHg
With TBI (GCS ≤8)
SAP ≥ 120 mmHg
Transfusion
Coagulation targets
Failure to obtain goals of AP
Without TBI
Hb 7-9 g.dL-1
PT/APTT < 1.5 x normal
Platelets > 50.10⁹ L-1
Fibrinogen ≥ 1.5-2 g.L-1
with TBI (GCS ≤8)
Hb > 10 g.dL-1
PT/APTT < 1.5 x normal
Platelets > 100.10⁹ L-1
Fibrinogen ≥ 1.5-2 g.L-1
Early administration of vasopressor
norepinephrine
Start at 0.1 µg/kg/min
Titration of fluid resuscitation
indices of preload responsiveness
cardiac output
markers of tissue oxygenation
Prevention of acidosis
Normothermia
Ionised Ca++ = 1.1-1.3 mmol/l
Surgical and/or angiographic embolization
bleeding control
Bouglé et al. Annals of
Intensive Care 2013

Damage control resuscitation

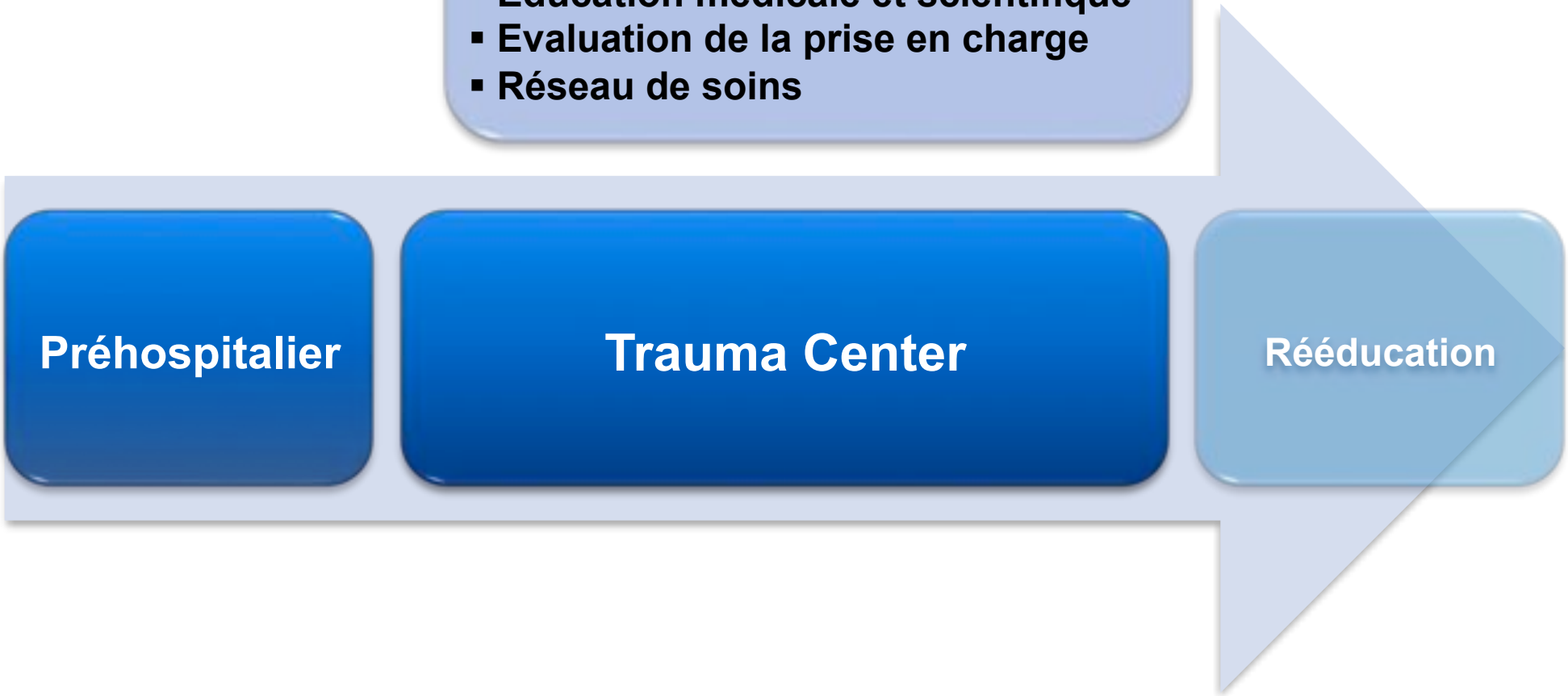
« Damage control surgery »
artériographie - embolisation

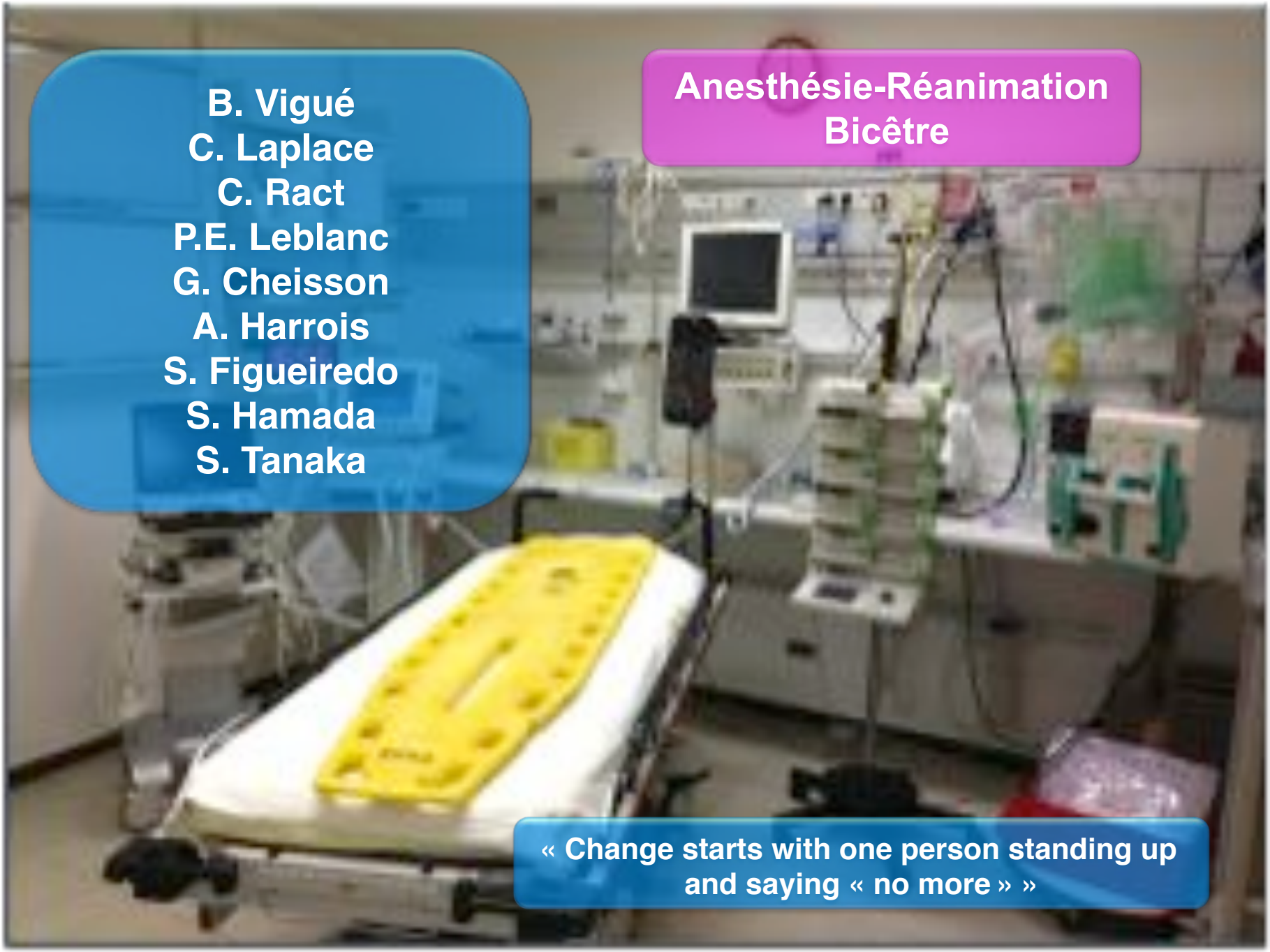
“Damage control surgery”



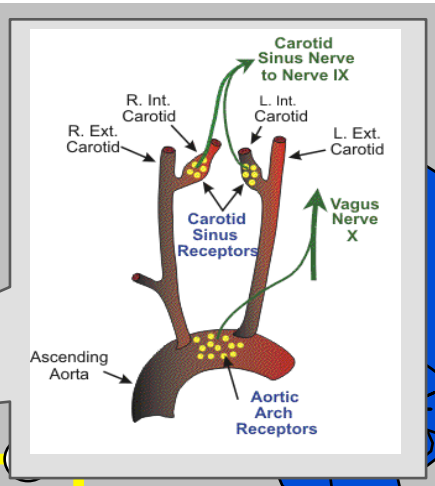
L’accueil du polytraumatisé en centre spécialisé

- Moyen humains
- Plateau technique 24h/24h
- Organisation ++
- Education médicale et scientifique
- Evaluation de la prise en charge
- Réseau de soins




B. Vigué
C. Laplace
C. Ract
P.E. Leblanc
G. Cheisson
A. Harrois
S. Figueiredo
S. Hamada
S. Tanaka
Anesthésie-Réanimation
Bicêtre
« Change starts with one person standing up and saying « no more » »

Efferences



Barorécepteurs artériels

Barorécepteurs cardiopulmonaires

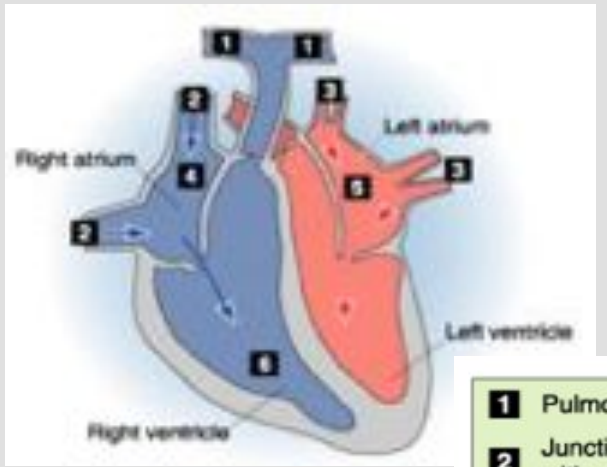
Fréquence cardiaque

Force contractile du myocarde

Adrénaline

Rénine Angiotensine

Réabsorption sodée



1 Pulmonary artery	4 Right atrium
2 Junction of right atrium with vena cava	5 Left atrium
3 Junction of left atrium and pulmonary veins	6 Ventricles