

MICROCIRCULATION ET MARQUEURS : ET CHEZ LE TRAUMATISE ?

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CHU de Nice



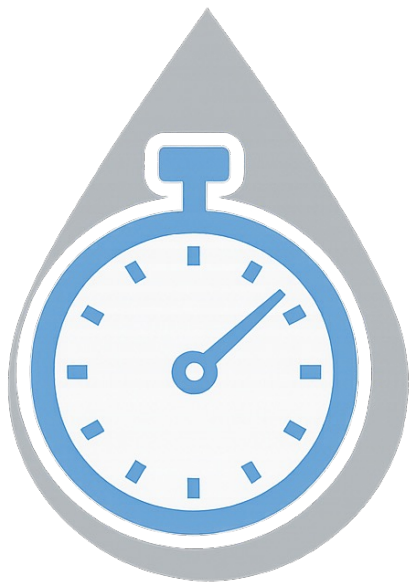
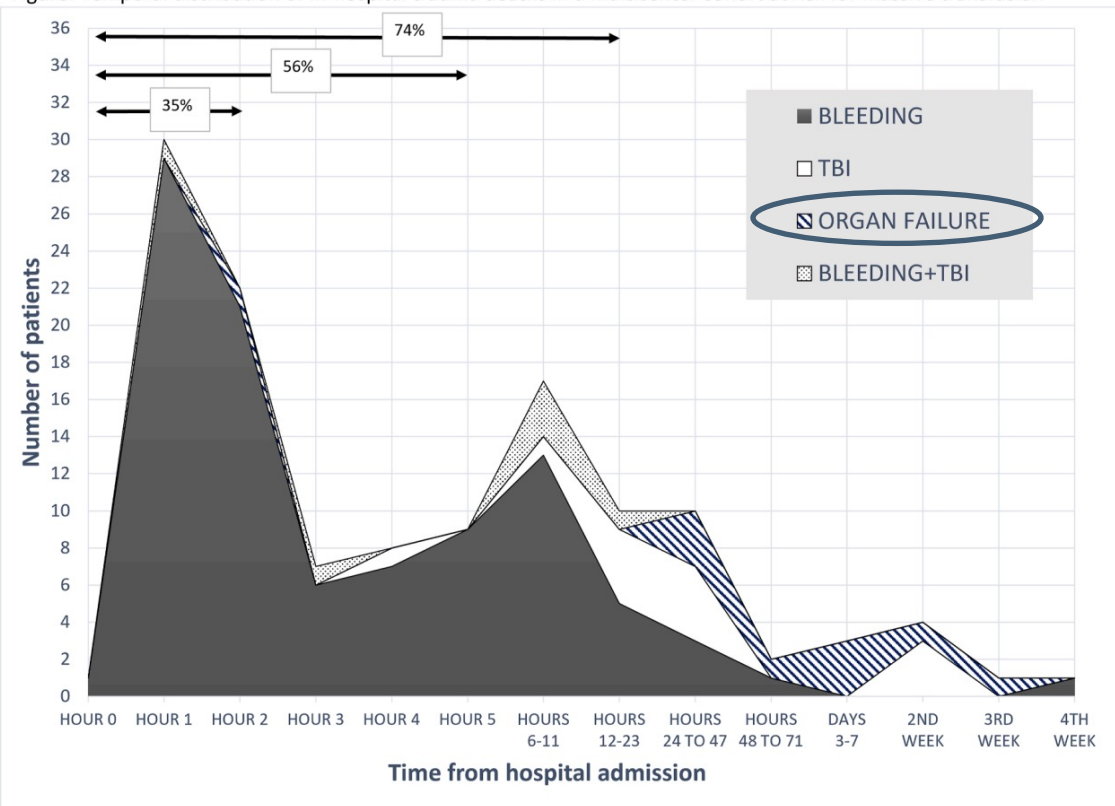


Figure: Temporal distribution of in-hospital trauma deaths in a multicenter cohort at risk for massive transfusion





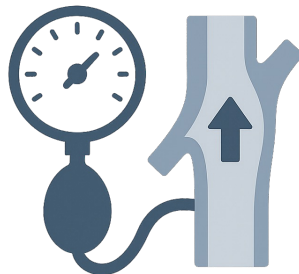
The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

II. Diagnosis and monitoring of bleeding

Initial assessment

Recommendation 5 We recommend that the physician clinically assess the extent of traumatic haemorrhage using a combination of patient physiology, anatomical injury pattern, mechanism of injury and the patient response to initial resuscitation (Grade 1C).

We recommend that the shock index (SI) and/or pulse pressure (PP) be used to assess the degree of hypovolaemic shock and transfusion requirements (Grade 1C).



III. Tissue oxygenation, volume, fluids and temperature

Volume replacement and target blood pressure

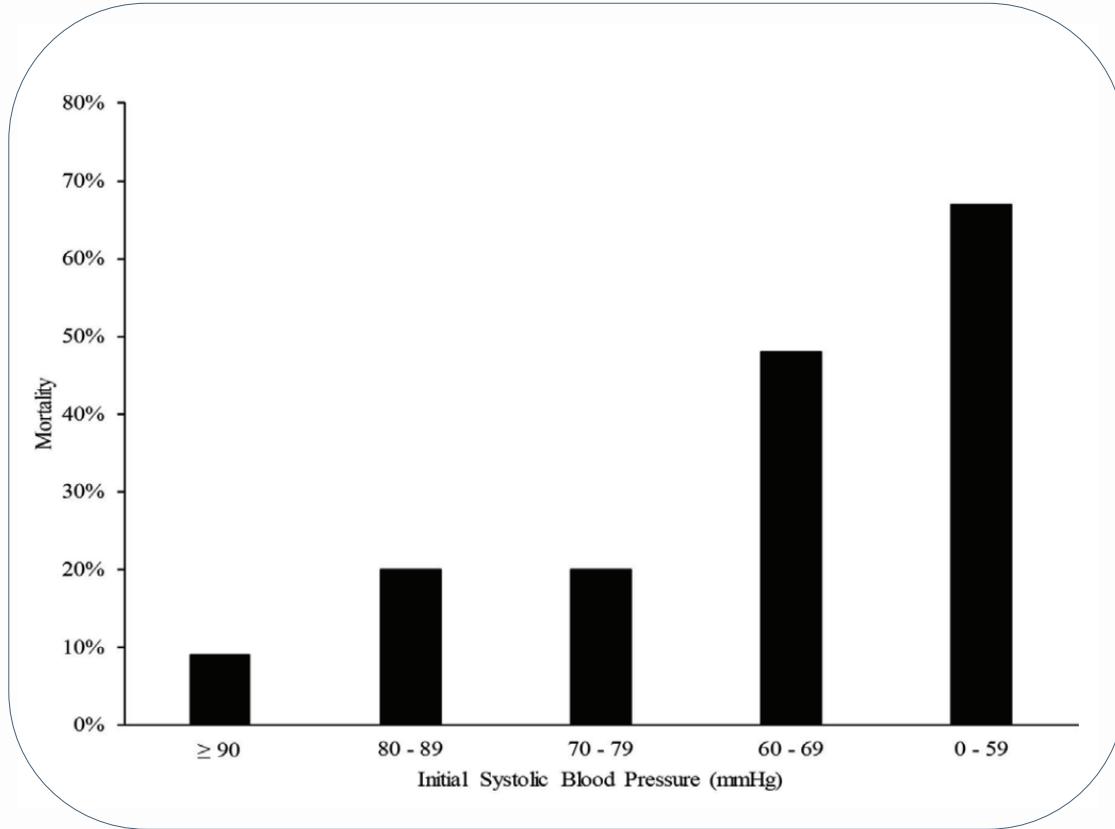
Recommendation 13 In the initial phase following trauma, we recommend the use of a restricted volume replacement strategy with a target systolic blood pressure of 80–90 mmHg (mean arterial pressure 50–60 mmHg) until major bleeding has been stopped without clinical evidence of brain injury (Grade 1B).

In patients with severe TBI ($GCS \leq 8$), we recommend that a mean arterial pressure ≥ 80 mmHg be maintained (Grade 1C).

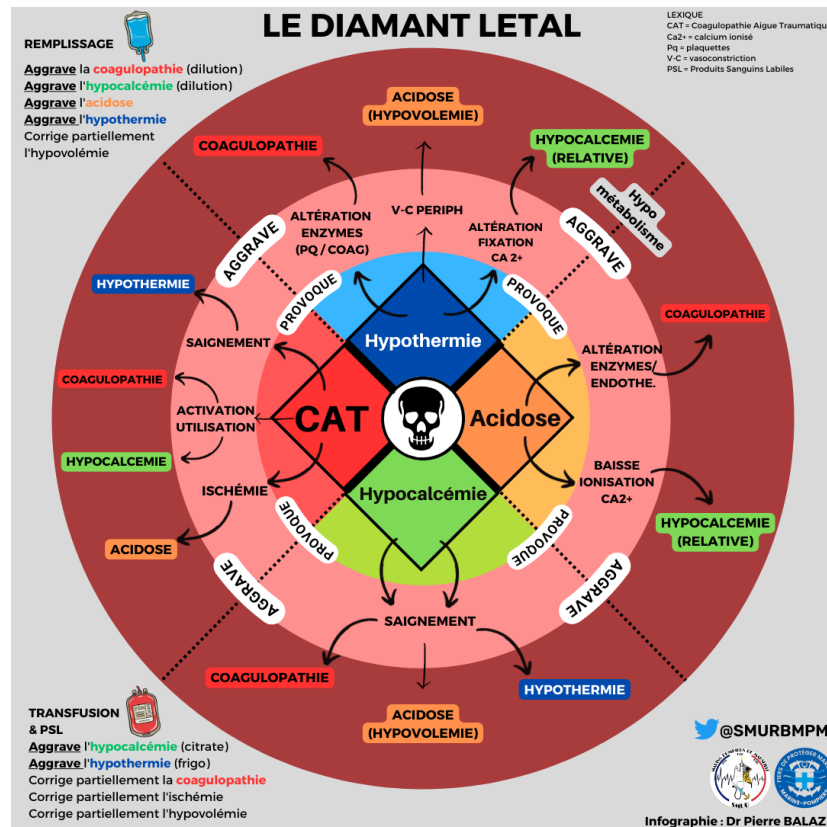
Vasopressors and inotropic agents

Recommendation 14 If a restricted volume replacement strategy does not achieve the target blood pressure, we recommend the administration of noradrenaline in addition to fluids to maintain target arterial pressure (Grade 1C).

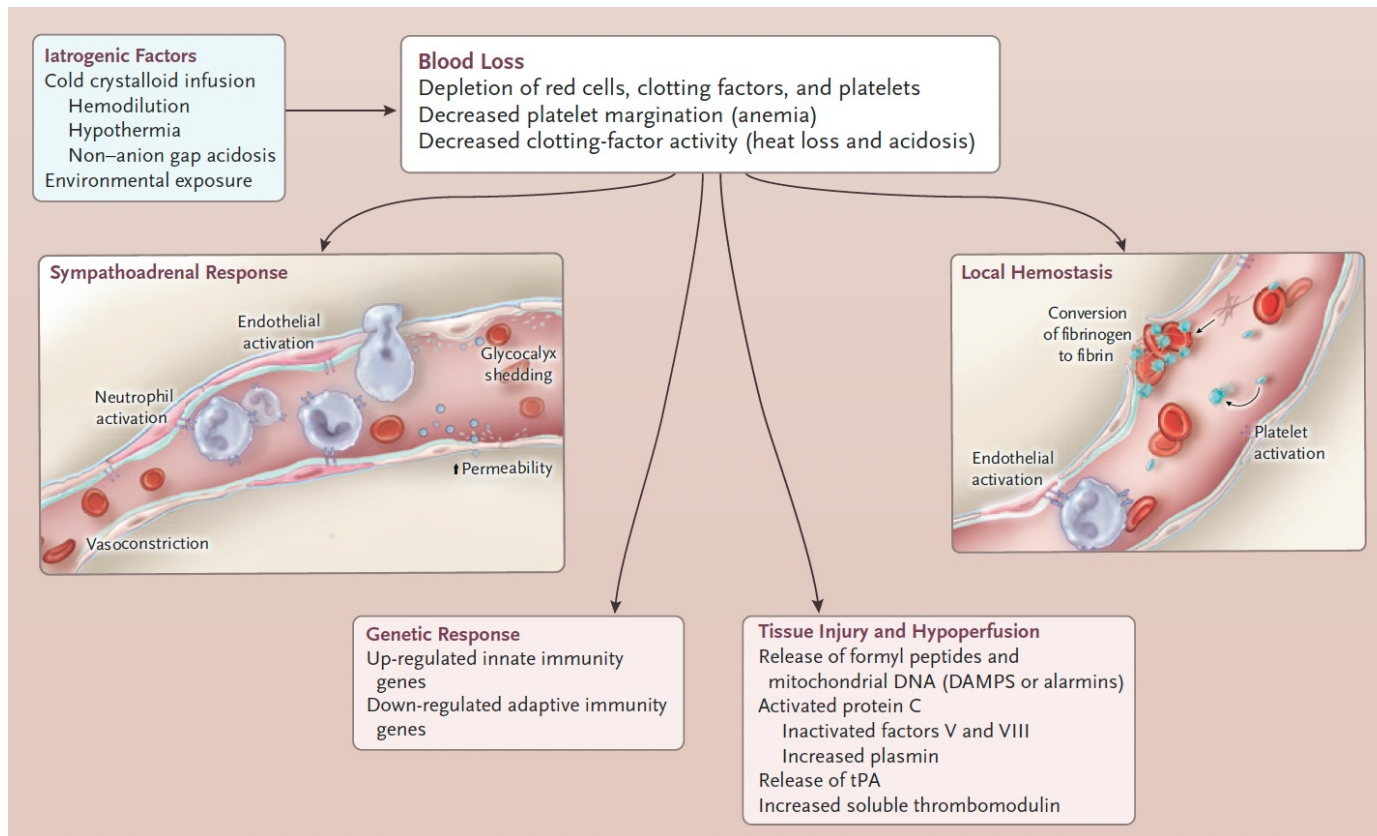
We recommend infusion of dobutamine in the presence of myocardial dysfunction (Grade 1C).



LE RÔLE CENTRAL DE LA COAGULOPATHIE



ET LE VAISSEAU ?



L'ATTEINTE MICROVASCULAIRE

Pathophysiology

TIC results from the complex interplay and balance of several mechanisms, involving both procoagulant and anticoagulant factors as well as cellular components.

Damage to the endothelium, with loss of barrier function and shedding of glycocalyx, leads to activation of inflammation and coagulation pathways; endothelial dysfunction during TIC can contribute to failures of coagulation including both hemorrhage and thrombosis.

Thrombin generation might be insufficient during early TIC, owing to dilution and consumption of procoagulant factors, but it can become excessive as TIC progresses, resulting in a prothrombotic state.

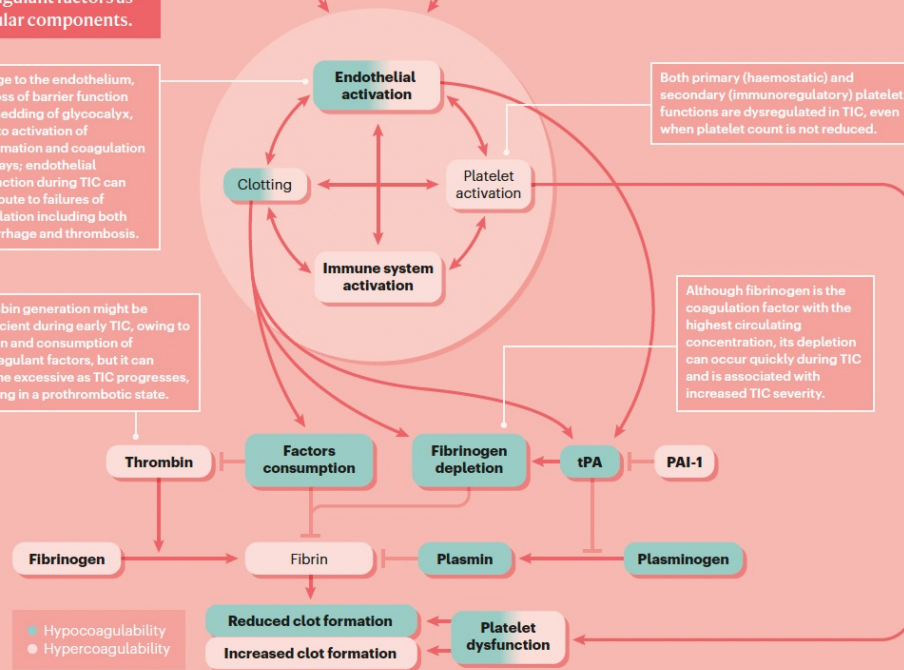
Hypoperfusion

Tissue injury

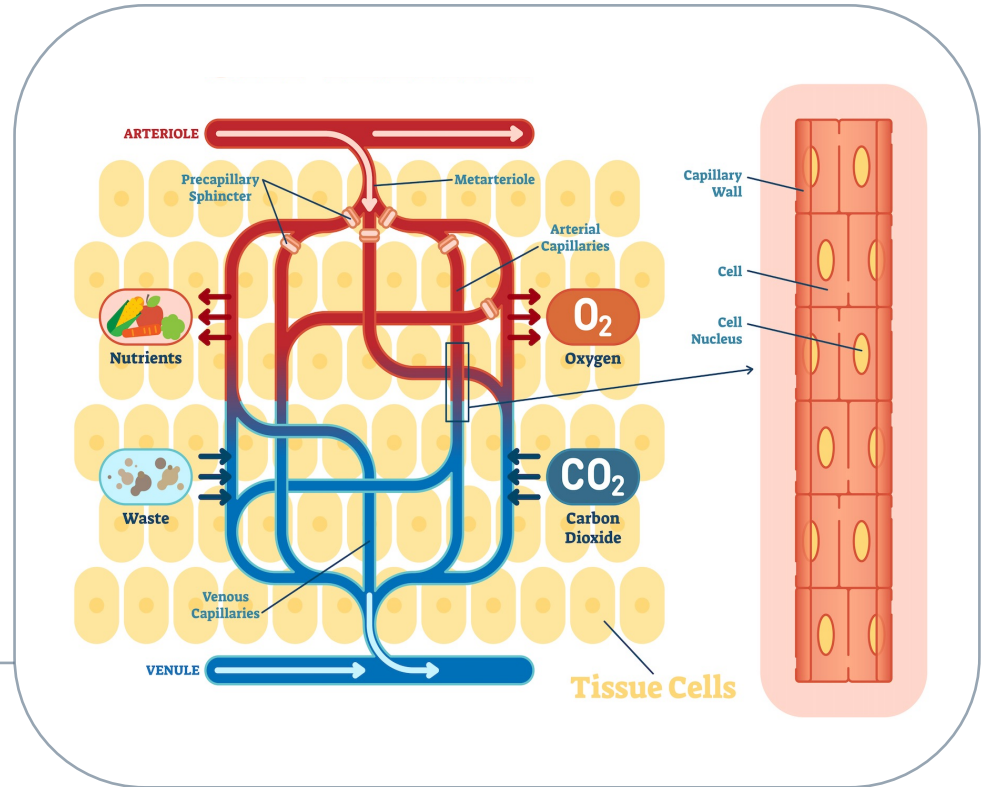
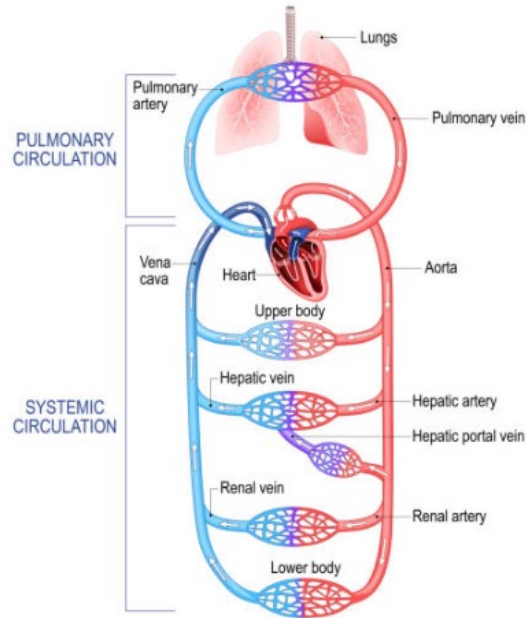
Haemorrhagic shock (leading to hypoperfusion and reduced oxygen delivery) and tissue injury (activating the coagulation cascade) synergistically trigger the development of TIC.

Both primary (haemostatic) and secondary (immunoregulatory) platelet functions are dysregulated in TIC, even when platelet count is not reduced.

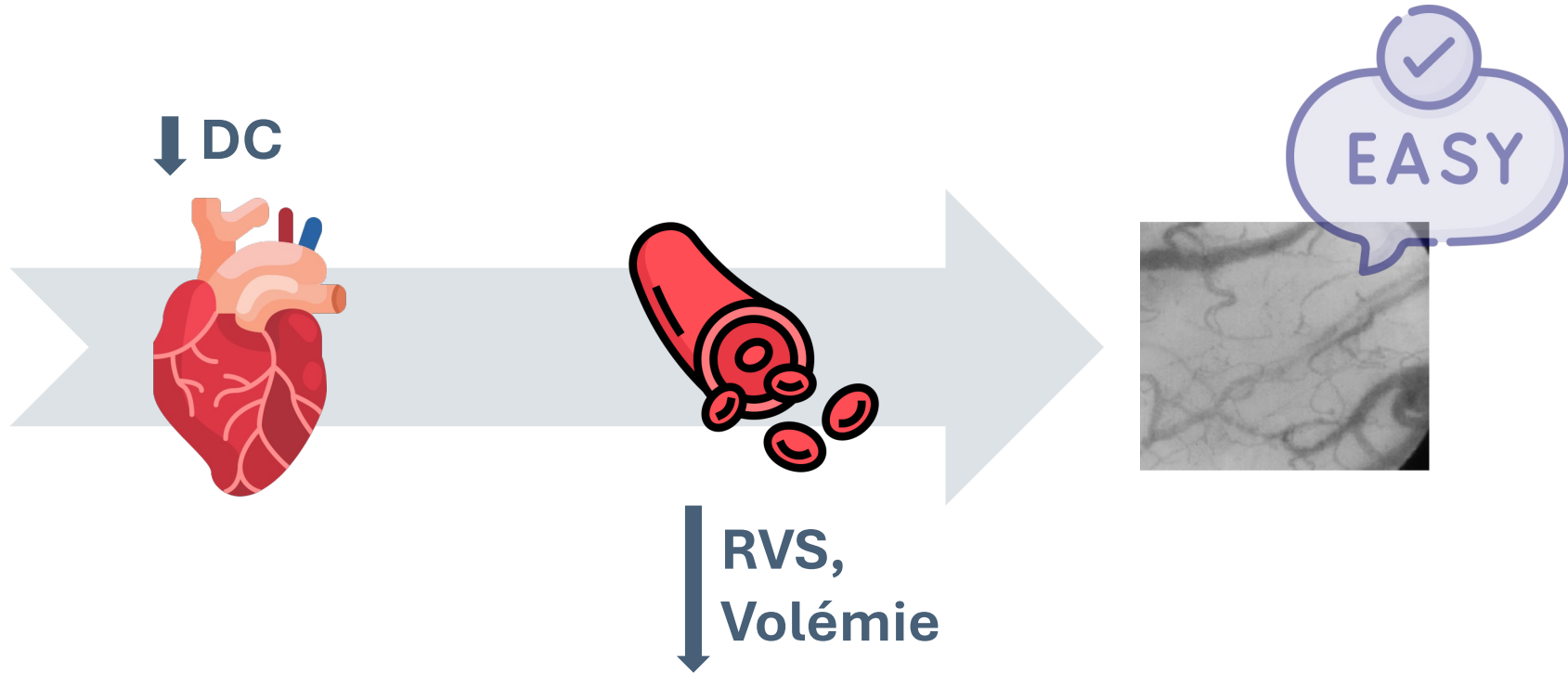
Although fibrinogen is the coagulation factor with the highest circulating concentration, its depletion can occur quickly during TIC and is associated with increased TIC severity.



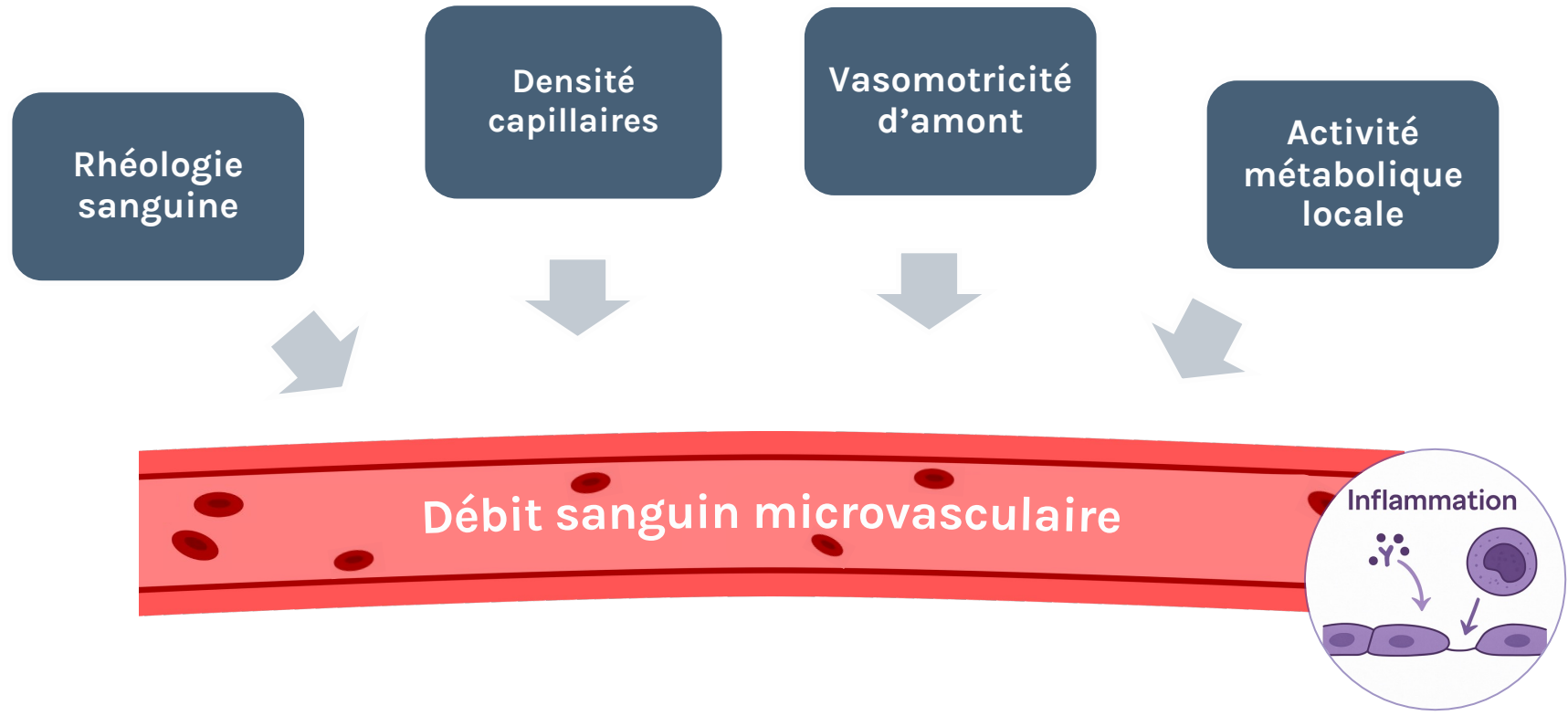
LE SYSTÈME MICROCIRCULATOIRE

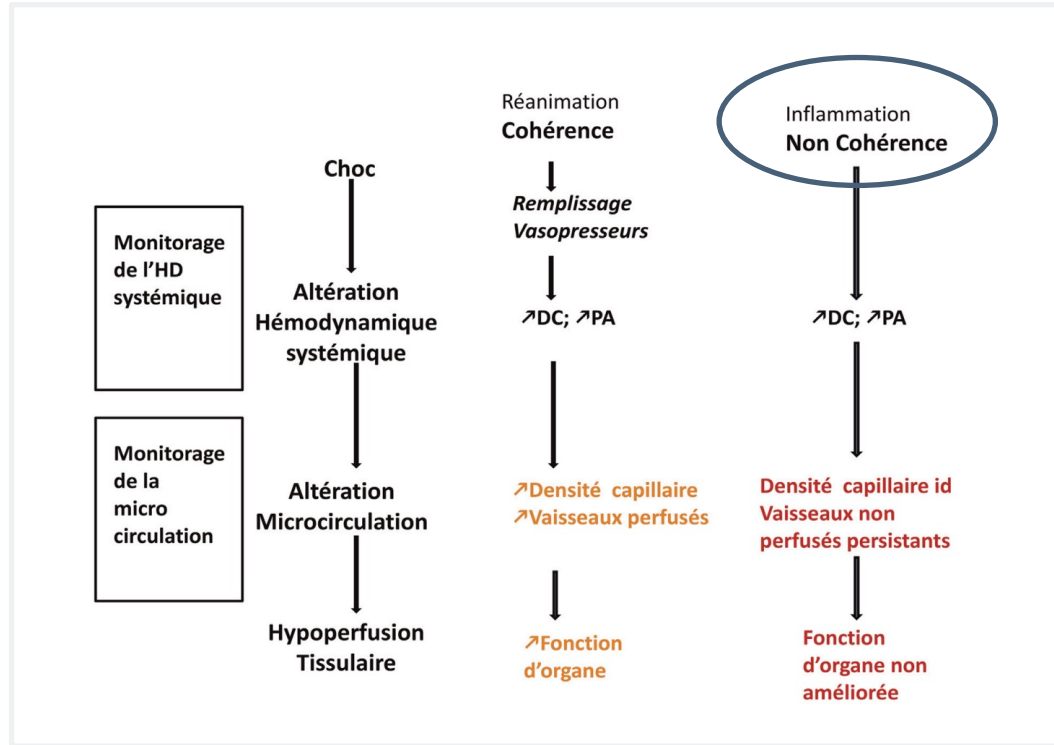


COHERENCE MACRO - MICRO



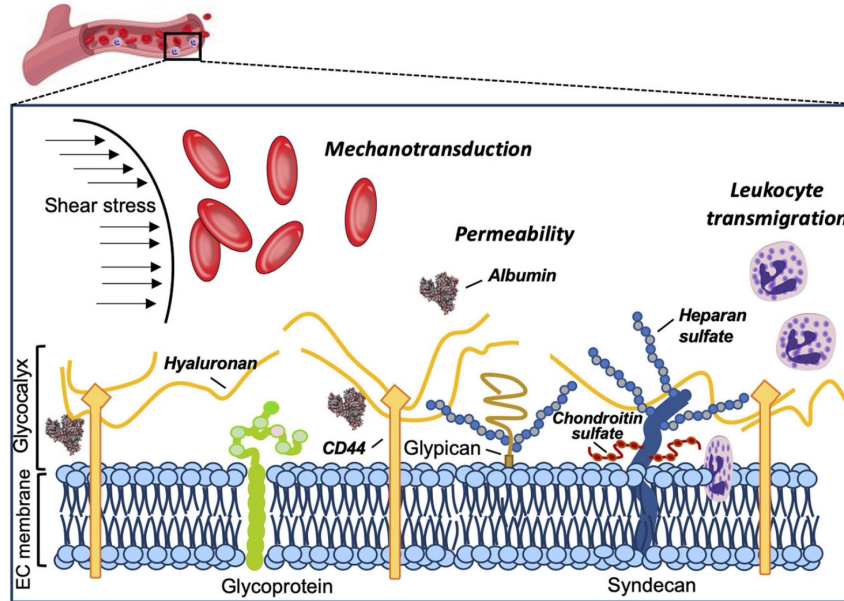
AUTO-REGULATION DU DEBIT MICROVASCULAIRE

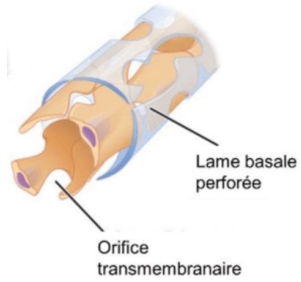




Endothelium

Glycocalyx





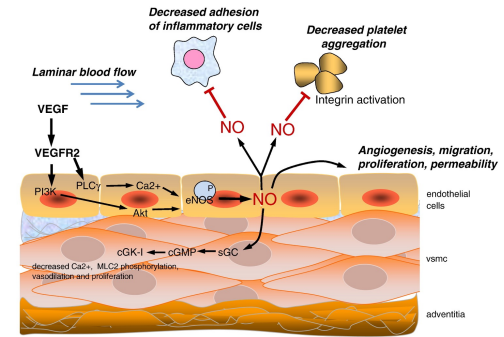
Production
substances
vasoactives

Perméabilité
vasculaire

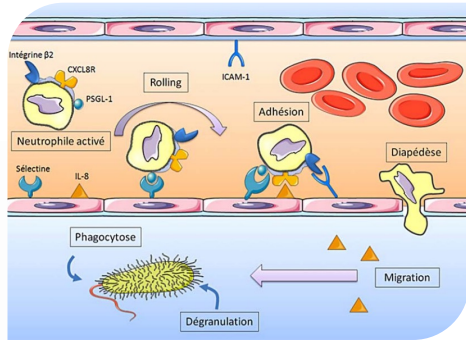
Endothelium

Glycocalyx

Propriétés
pro ou anti-
coagulantes



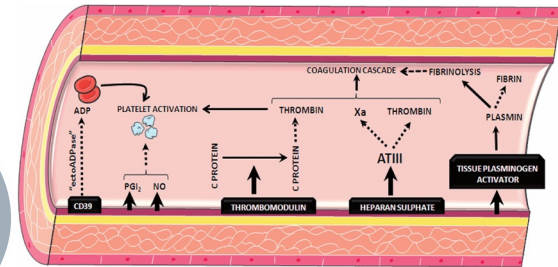
M. Rogers N et al. 2014



Libert N et al. 2010

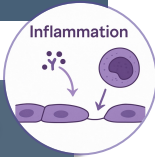
Adhésion
leucocytaire
Diapédèse

Propriétés pro
ou anti-
fibrinolytiques

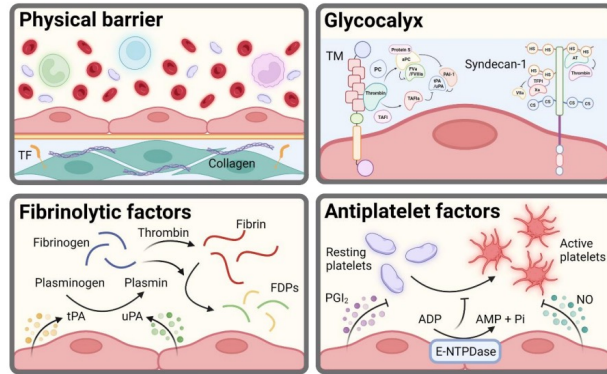


Badimon L et al. 2010

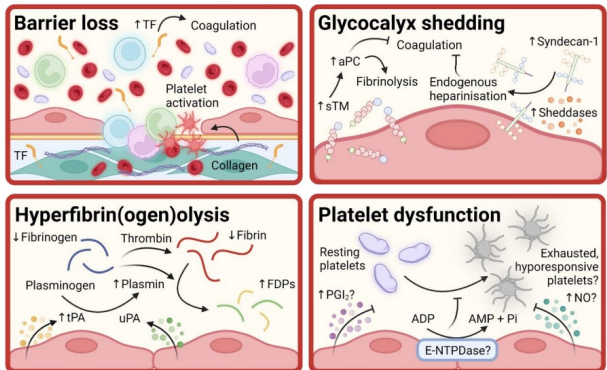
ENDOTHELIOPATHIE TRAUMATIQUE



A Health



B Traumatic injury



Perte fonction barrière = fuite capillaire

Atteinte glycocalyx

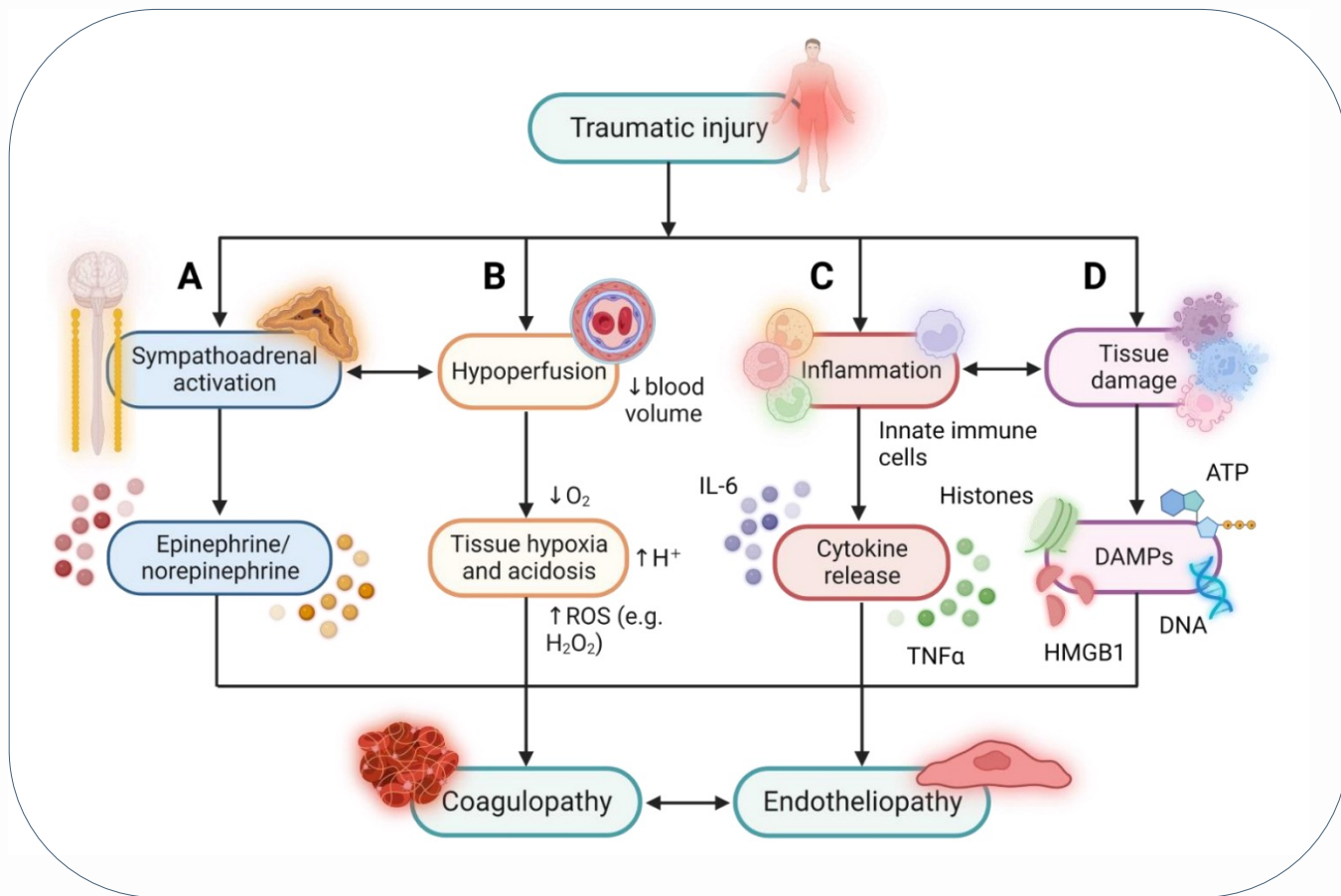
Activation plaquettaire

Etat pro coagulant, pro fibrinolytique
= microthrombi

Extravasation leucocytes = inflammation

↓ Proportion de capillaires perfusés

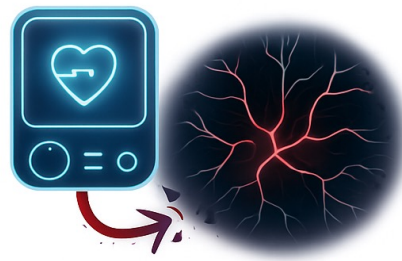
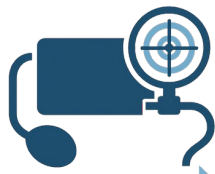
Altération oxygénation
tissulaire



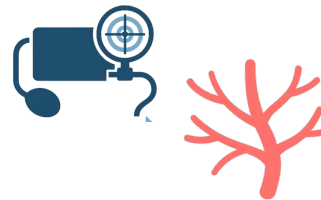
ALORS QUEL MONITORAGE ?



COHERENCE MACRO-MICRO



NON COHERENCE



MONITORER LA PAM... PAS UNE FIN EN SOI

Table 1. Hemodynamic variables in the first four days of ICU admission for the two groups of patients (SOFA* score at D4≤6.5 and SOFA score at D4>6.5).

		SOFA ≤ 6.5 at D4 15 (53.6%)	SOFA > 6.5 at D4 13 (46.4%)	p value
MAP ^a , mmHg	D1	86 [75-99]	85 [77-95]	0.964
	D2	82 [71-99]	89 [71-95]	0.648
	D3	89 [84-102]	88 [79-97]	0.413
	D4	91 [74-106]	88 [84-89]	0.932
HR ^a , bpm	D1	63 [57-83]	83 [74-102]	0.142
	D2	77 [64-100]	84 [60-101]	0.717
	D3	71 [62-88]	78 [63-92]	0.964
	D4	75 [64-87]	74 [70-85]	0.843
Norepinephrine, mcg/kg/min	D1	0.00 [0.00-0.22]	0.23 [0.026-0.48]	0.033
	D2	0.00 [0.00-0.182]	0.22 [0.02-0.28]	0.085
	D3	0.00 [0.00-0.00]	0.09 [0.04-0.33]	0.001
	D4	0.00 [0.00-0.00]	0.1 [0.04-0.17]	0.001
Arterial pH, AU	D1	7.43 [7.4-7.58]	7.45 [7.38-7.49]	0.329
	D2	7.48 [7.44-7.49]	7.45 [7.42-7.49]	0.892
	D3	7.47 [7.43-7.52]	7.48 [7.43-7.53]	0.440
	D4	7.48 [7.44-7.49]	7.47 [7.45-7.51]	0.936
BE ^a , mmol/L	D1	0.6 [-0.9-2.3]	0.6 [-12.7-3.8]	0.880
	D2	4.5 [2.2-8.5]	4.4 [1.7-6.2]	0.751
	D3	5.5 [3.7-9.4]	6.4 [2.1-7.6]	0.892
	D4	5.2 [3.7-9.7]	7.7 [4.2-11.8]	0.538
Lactate, mmol/L	D1	1.3 [0.9-2.0]	1.7 [1.1-2.2]	0.235
	D2	1.0 [0.7-2.0]	1.1 [0.7-2.0]	0.217
	D3	0.9 [0.8-1.1]	0.9 [0.7-1.2]	0.413
	D4	0.7 [0.7-1.1]	0.9 [0.6-1.4]	0.590
ScvO ₂ ^a , %	D1	79.4 [75.6-81.7]	74.3 [59.2-84.4]	0.161
	D2	74.8 [67.1-80.8]	79.3 [70.7-85.2]	0.347
	D3	75 [67.5-78.6]	72 [71.6-90.6]	0.219
	D4	72.1 [68.6-74.4]	78.6 [73.3-81.0]	0.148
Hb ^a , g/dl	D1	10.8 [9.0-12.4]	10.4 [10.2-11.2]	0.751
	D2	10.3 [9.2-11.5]	9.3 [8.4-9.9]	0.170
	D3	9.3 [8.9-11.4]	9.8 [9.5-10.9]	0.316
	D4	9.4 [8.2-11.3]	9.8 [9.3-10.8]	0.630
Hct ^a , %	D1	30.2 [27.1-3.8]	30.7 [29.2-32.]	0.856
	D2	30.9 [26.0-34.3]	27.4 [24.4-29.7]	0.170
	D3	27.7 [27.0-34.8]	29.5 [28.6-31.4]	0.440
	D4	29.0 [25.8-33.9]	29.6 [27.8-31.9]	0.79
Patients transfused, n ^a (%)				

RESEARCH ARTICLE

Association between sublingual microcirculation, tissue perfusion and organ failure in major trauma: A subgroup analysis of a prospective observational study

Roberta Domizi, Elisa Damiani, Claudia Scorcella, Andrea Carsetti, Roberta Castagnani, Sara Vannicola, Sandra Bolognini, Vincenzo Gabbanelli, Simona Pantanetti, Abele Donati*

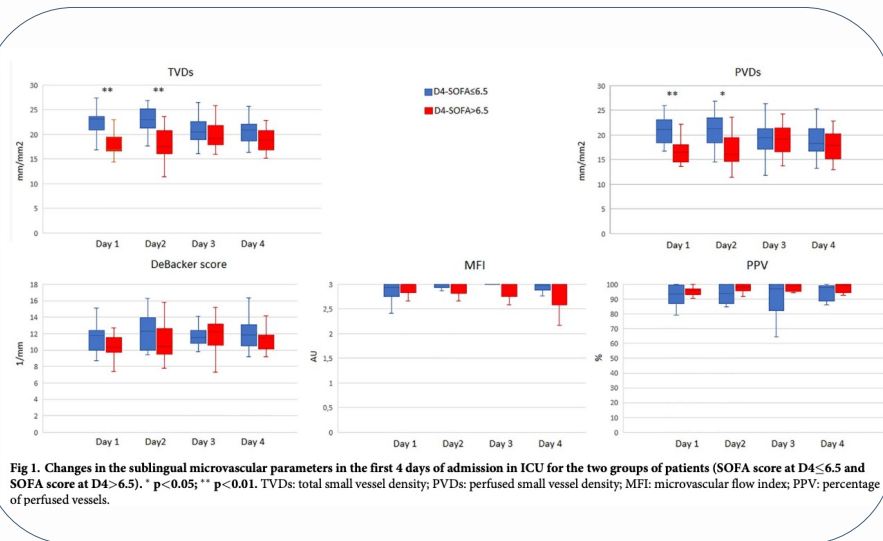


Fig 1. Changes in the sublingual microvascular parameters in the first 4 days of admission in ICU for the two groups of patients (SOFA score at D4≤6.5 and SOFA score at D4>6.5). * p<0.05; ** p<0.01. TVDs: total small vessel density; PVDs: perfused small vessel density; MFI: microvascular flow index; PPV: percentage of perfused vessels.

EVALUATION MICROCIRCULATOIRE

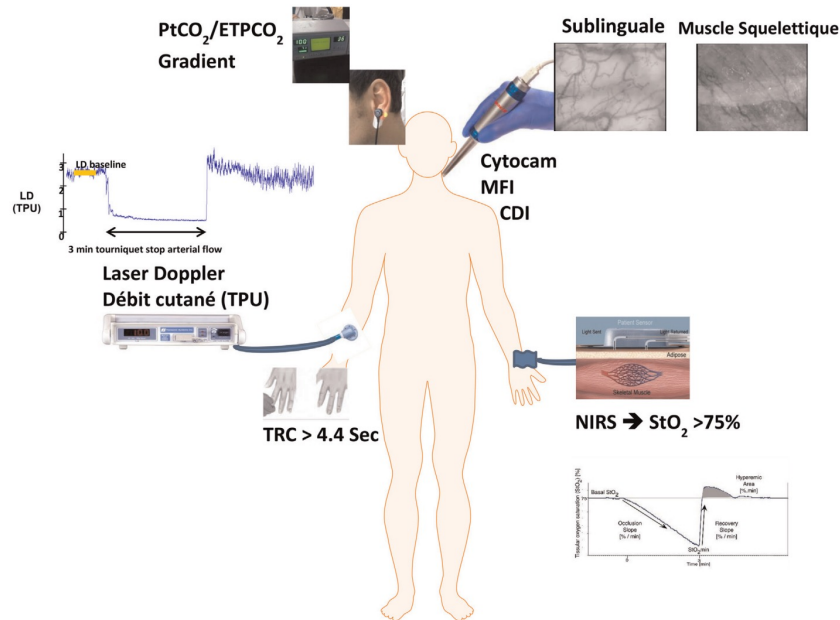


Table 1 Techniques used to evaluate the microcirculation at the bedside

	Variable measured	Main limitations
Techniques measuring microvascular perfusion		
Laser Doppler	Flow (relative), hemoglobin content/microvascular reactivity test	Global flow to relatively large sampling volume (mixture of arterioles, capillaries, and venules)
Nailfold videomicroscopy	Vascular density, heterogeneity, flow	Restricted to fingers/sensitivity to temperature and vasoconstriction
OPS and SDF	Vascular density, perfusion heterogeneity, flow	Mostly restricted to semiquantitative scoring/limited sites to investigate/movement and pressure artifacts
Techniques measuring tissue oxygenation		
SvO ₂	Adequacy of perfusion to flow	Global measurement
O ₂ electrodes	Tissue PO ₂	Global measurement in sampled volume (mixture of arterioles, capillaries, and venules)
NIRS	Tissue O ₂ saturation	Global measurement in sampled volume (mixture of arterioles, capillaries, and venules)
Reflectance spectroscopy	O ₂ saturation/microvascular reactivity test	Global measurement in sampled volume (mixture of arterioles, capillaries, and venules) unless SO ₂ histograms are provided
Gastric tonometry	Tissue CO ₂ (reflects inadequate perfusion and/or anaerobic metabolism)	Interference (feeding/reflux)/difficult discrimination between low flow and anaerobic metabolism
Sublingual capnometry	Tissue CO ₂ (reflects inadequate perfusion and/or anaerobic metabolism)	Availability limited/difficult discrimination between low flow and anaerobic metabolism
Microdialysis and equilibrium dialysis	Lactate/pyruvate	Time lag/limited sites to investigate

OPS orthogonal polarization spectral imaging technique; SDF sidestream dark field imaging technique; SvO₂ mixed-venous oxygen saturation; NIRS near-infrared spectroscopy; EMPHO Erlangen MicroPHOTometer

Marie-Reine Lossier^{1,2}, Didier Payen de la Garanderie³

Anesth Reanim. 2019; 5: 193-199

Intensive Care Med (2010) 36:1813-1825
DOI: 10.1007/s00134-010-2005-3

REVIEW

Daniel De Backer
Gustavo Ospina-Tascon
Diamantino Salgado
Raphaël Favory
Jacques Creteur
Jean-Louis Vincent

Monitoring the microcirculation in the critically ill patient: current methods and future approaches

CONFERENCE REPORTS AND EXPERT PANEL



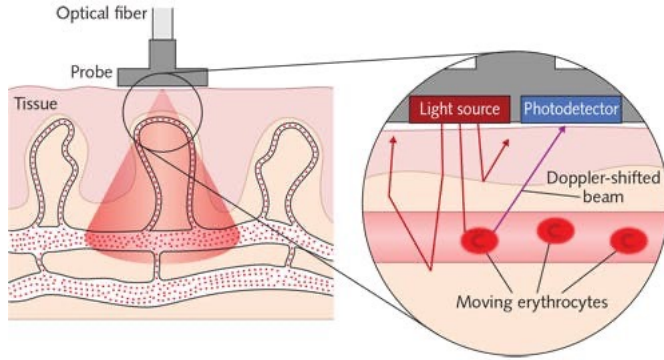
Second consensus on the assessment of sublingual microcirculation in critically ill patients: results from a task force of the European Society of Intensive Care Medicine

Table 5 Characteristics of microvascular variables

Variable	Abbreviation	Definition	Characteristics	Units	Strength/weakness
Proportion of perfused vessels	PPV	Grid-based score (3 horizontal and vertical equidistant lines). Percentage of perfused vessels per total number of vessel crossings	Binominal determinant of red blood cell velocity: flow or no-flow	%	Good reproducibility. Based upon tradition of preclinical research. Score is sensitive to isotropy (change in image size during optical magnification)
De Backer score	NA	Grid-based score (3 horizontal and vertical equidistant lines). Total number of vessel crossings per grid length	Proxy of total vessel density. Applicable to different vessel types (capillary density)	n/mm	Together with the percentage of perfused capillaries proxy of functional capillary density
Microvascular flow index	MFI	Grid-based score per quadrant. 0 = stop flow, 1 = intermittent flow, 2 = sluggish flow, 3 = normal flow	Semi-quantitative assessment of the average red blood cell velocity per quadrant	AU	Good reproducibility. Quick and possible by "eyeballing". Non-continuous separation between categories of flow. Potential loss of detail, overcome by similar score per vessel
Total vessel density	TVD	Software supported measurement of total vessel area per surface area	Determinant of capillary distance (diffusive capacity)	mm ² /mm ²	Absolute number, continuous data. Time consuming because of necessary manual correction of software-supported vessel tracing of vessels. Exact measurements of vessel diameter
Perfused vessel density	PVD	Percentage of perfused vessels × TVD	Determinant of capillary distance (diffusive capacity) and red blood cell velocity (convective capacity)	mm ² /mm ²	Equal to functional capillary density = gold standard in preclinical research. Time consuming
Space-time diagram	STD	Measurement of exact red blood cell velocity	Determinant of red blood cell velocity (convective capacity)	mm/s	Absolute number, continuous data. Time consuming, applicability limited to non-tortuous vessels of sufficient length
Heterogeneity index	HI	Coefficient of variation, expressed as (highest – lowest value)/mean	Determinant of heterogeneity of blood flow, characteristic of distributive abnormalities	AU	Provides additional information, missed by absolute numbers. Calculation may be based upon MFI or PPV

NA not applicable, AU arbitrary unit

LE LASER DOPPLER



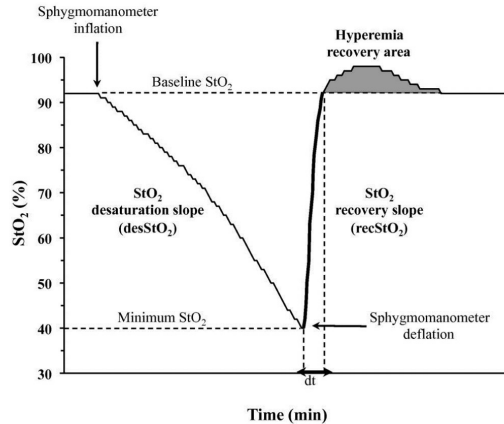
Fx laser qui rencontre les GR en mouvement
analyse changement fréquence



VELOCITE SANGUINE

*Données expé
ne cible pas les vaisseaux atteints
pas de prise compte de l'hétérogénéité*

NIRS

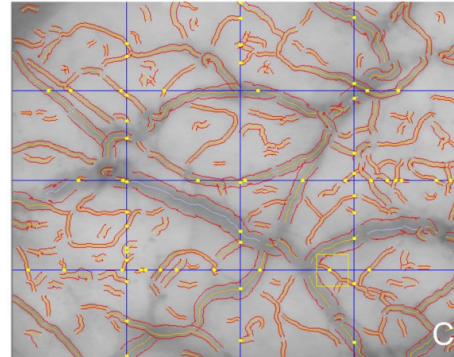
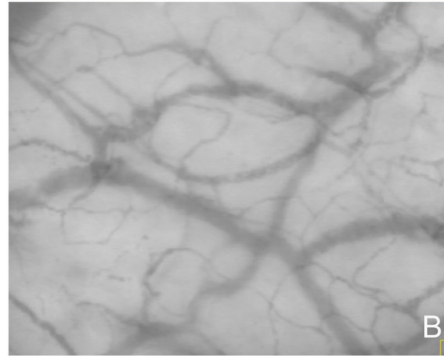
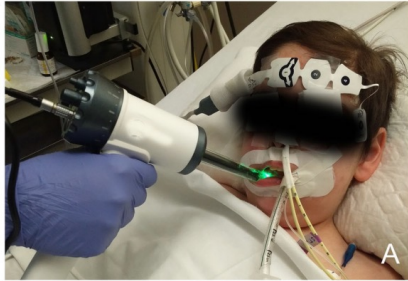


diffusion et l'absorption de lumière infra
rouge
dans les tissus

OXYGENATION TISSULAIRE
(StO2)

*Valeurs de réf variables ++
Influence épaisseur tissu cut ou gras
Mesure localisée ++
Nécessite évaluation dynamique (test occlusion)*

IMAGERIE SUBLINGUALE



González et al. *BMC Pediatrics* (2017) 17:75
DOI 10.1186/s12887-017-0837-5

BMC Pediatrics

RESEARCH ARTICLE

Open Access



Evaluation of sublingual microcirculation in a paediatric intensive care unit: prospective observational study about its feasibility and utility

Rafael González^{1,2,3}, Jorge López^{1,2,3}, Javier Urbano^{1,2,3}, María José Solana^{1,2,3}, Sarah Nicole Fernández^{1,2,3}, María José Santiago^{2,3} and Jesús López-Herce^{1,2,3,4*}



Continuous Noninvasive Tissue Oximetry in the Early Evaluation of the Combat Casualty: A Prospective Study

Alec C. Beekley, MD, Matthew J. Martin, MD, Teresa Nelson, MS, Kurt W. Grathwohl, MD, Matthew Griffith, MD, Gregory Beilman, MD, and John B. Holcomb, MD

TABLE 3. Multivariate Logistic Regression Modeling to Predict Life-Saving Intervention (LSI), Blood Transfusion, and Massive Transfusion in the Whole Group

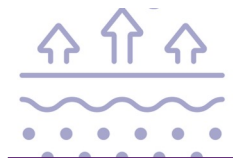
Parameters (Units)*	LSI, Odds Ratio (95% CI)†	Blood Transfusion, Odds Ratio (95% CI)†	Massive Transfusion, Odds Ratio (95% CI)†
SBP [−10 mm Hg]	Not retained	1.40 (1.1–1.8)	Not retained
DBP (5 mm Hg)	1.17 (1.0–1.4)	Not retained	Not retained
INR (0.50)	15.11 (3.7–61.3)	5.91 (1.6–21.9)	10.24 (2.5–41.9)
Hgb (−1.0 g/dL)	Not retained	Not retained	1.7 (1.1–2.6)
HCT (−5.0%)	2.39 (1.5–3.8)	3.01 (1.8–4.9)	Not retained
BD (−2 mEq/L)	1.54 (1.1–2.2)	Not retained	Not retained
THI (−1)	Not retained	1.18 (1.0–1.4)	Not retained
Logistic regression equation	$\text{Log [p/(1 - p)]} = 1.55 + 5.43 \times \text{INR} - 0.22 \times \text{BD} + 0.03 \times \text{DBP} - 0.17 \times \text{HCT}$	$\text{Log [p/(1 - p)]} = 9.88 - 0.03 \times \text{SBP} + 3.55 \times \text{INR} - 0.16 \times \text{THI} - 0.22 \times \text{HCT}$	$\text{Log [p/(1 - p)]} = 1.94 - 0.53 \times \text{Hgb} + 4.65 \times \text{INR}$
AUC (95% CI)	0.85 (0.79–0.91)	0.90 (0.84–0.96)	0.91 (0.79–1.0)

AUC, area under the receiver operating characteristic curve; SBP, systolic blood pressure; DBP, diastolic blood pressure; INR, international normalized ratio; Hgb, hemoglobin; HCT, hematocrit; BD, base deficit; THI, tissue hemoglobin index.

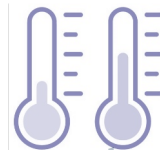
* Parameters entered into a model but not retained in any outcome equation include tissue oxygenation (StO₂), radial pulse character, heart rate, platelets, and pH.

† The odds ratio provided in the table is associated with the change in the units specified.

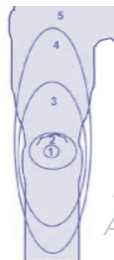
EN PRATIQUE...



T° cut



ΔT°



Marbrures

Ait-Oufella et al. Réanimation. 2012



**Perfusion
organes**



TRC

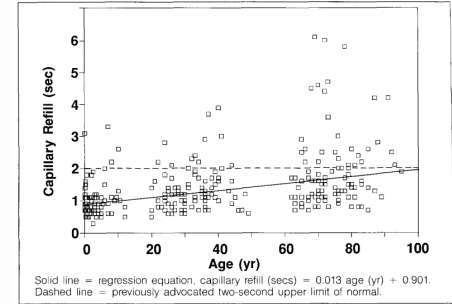


Lactate

**Defining Normal Capillary Refill:
Variation With Age, Sex, and Temperature**

David L. Schrager, MD
Larry Baraff, MD, FACEP
Los Angeles, California

Annals of Emergency Medicine
An International Journal



**Adverse Lighting Condition Effects on the
Assessment of Capillary Refill**

LAWRENCE H. BROWN, EMT-P,* N. HERAMBA PRASAD, MD,*
THEODORE W. WHITLEY, PhD†

SHORT REPORT

**Are bedside features of shock reproducible between
different observers?**

H Otieno, E Were, I Ahmed, E Charo, A Brent, K Maitland

Arch Dis Child 2004;89:977-979. doi: 10.1136/adc.2003.043901



LES BIOMARQUEURS



LE BASE EXCESS

Metabolic acidosis

Buildup of acids, i.e:

Lactic acid (trauma, hypotension), **ketoacids** (diabetes), **sulfates and phosphates** (renal failure), **hyperchloremia/dysnatremia** (excessive crystalloid resuscitation)

Metabolic alkalosis

Acids are removed, i.e:

Emesis, nasogastric tube, volume contraction from diuretics

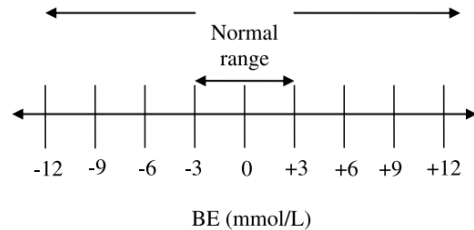


Figure 1. BE represented on a number line with common causes for metabolic acidosis and alkalosis.

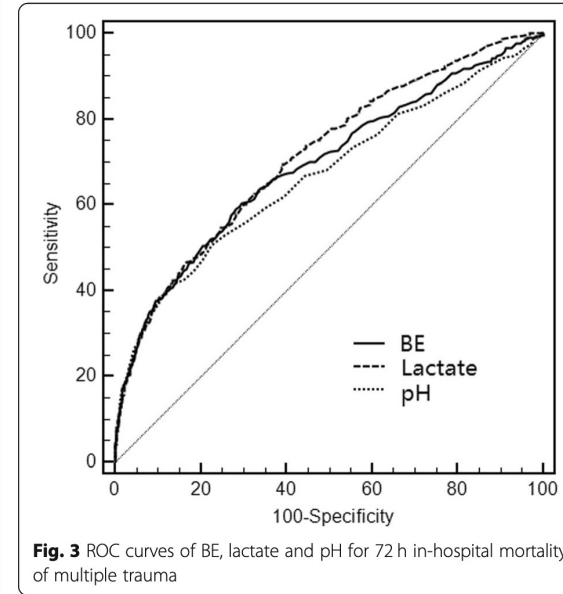


Fig. 3 ROC curves of BE, lactate and pH for 72 h in-hospital mortality of multiple trauma

Table 2 Logistic regression analyses

Variables	Univariate			Multivariate		
	OR	95%CI	P	OR	95%CI	P
BE	0.866	0.849–0.884	< 0.001	0.872	0.854–0.890	< 0.001
Lactate	1.353	1.299–1.410	< 0.001	1.353	1.296–1.413	< 0.001
pH	0.005	0.002–0.011	< 0.001	0.007	0.003–0.016	< 0.001

Variables in multivariate logistic models were adjusted for gender, age and ISS category.

LE LACTATE

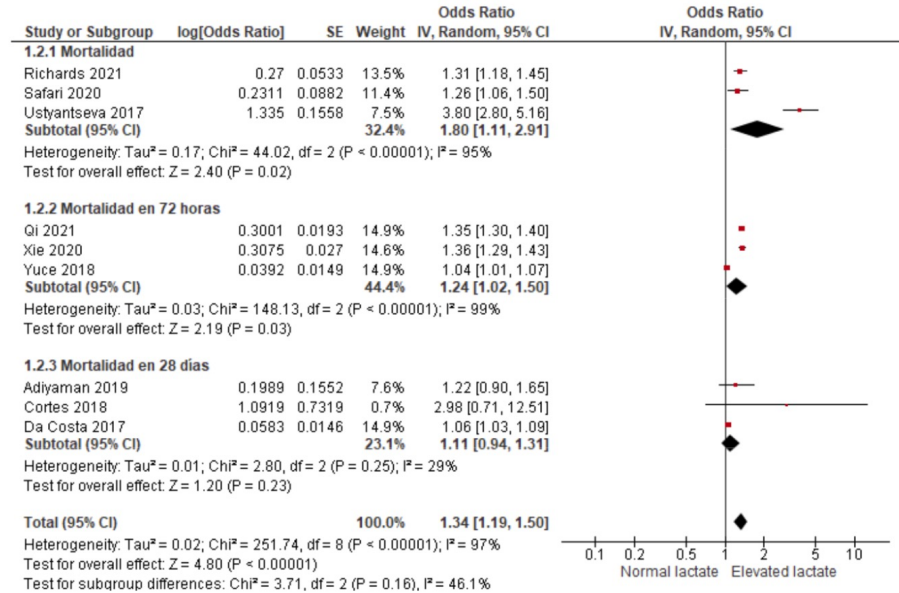
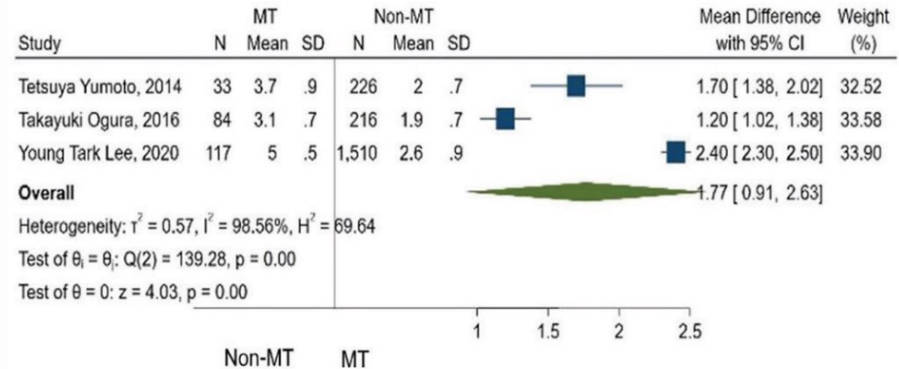


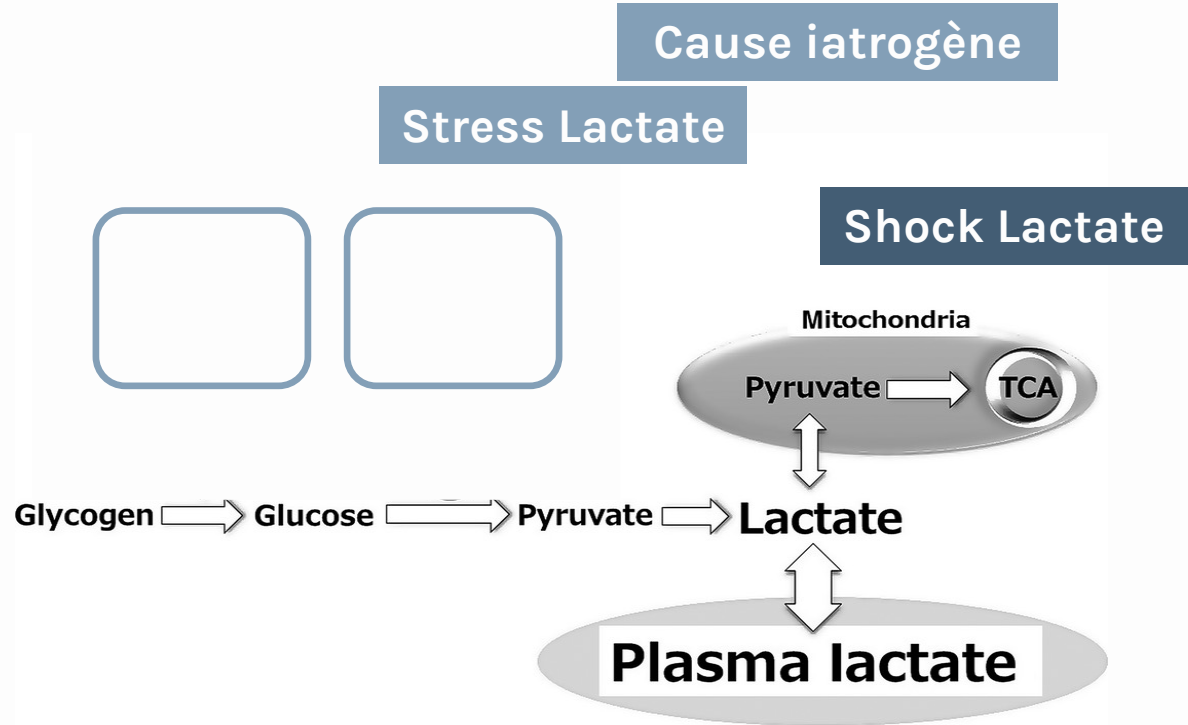
Figure 2: Forest plot of random effects of elevated lactate on mortality, 72-hour mortality, and 28-day mortality.

LE LACTATE



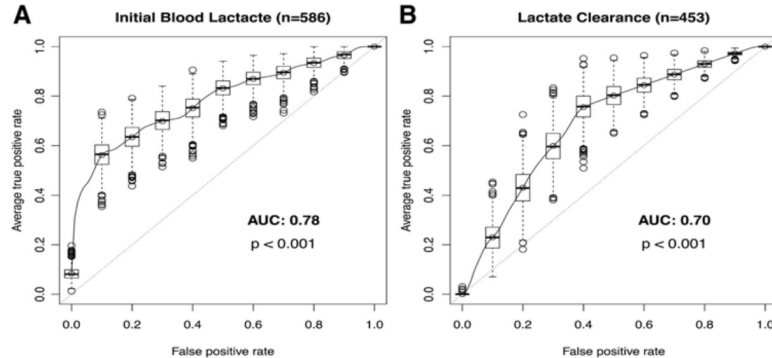
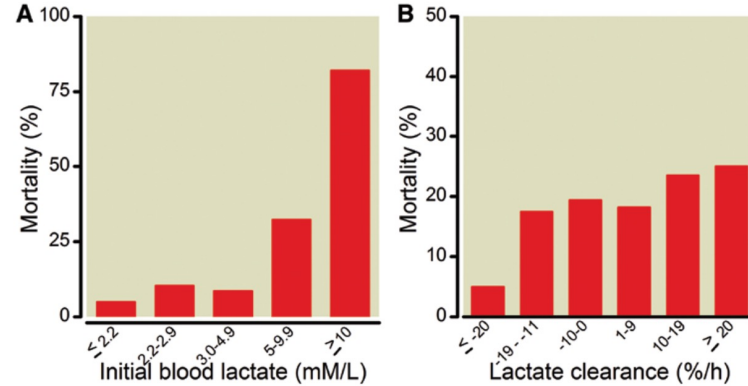
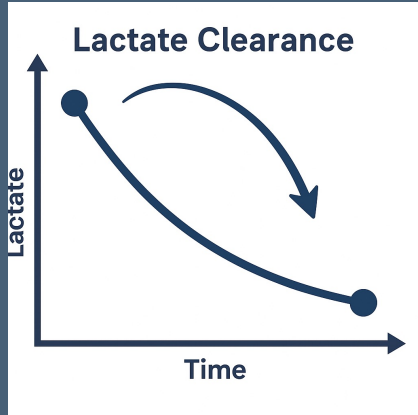
Lactate (mmol/l)

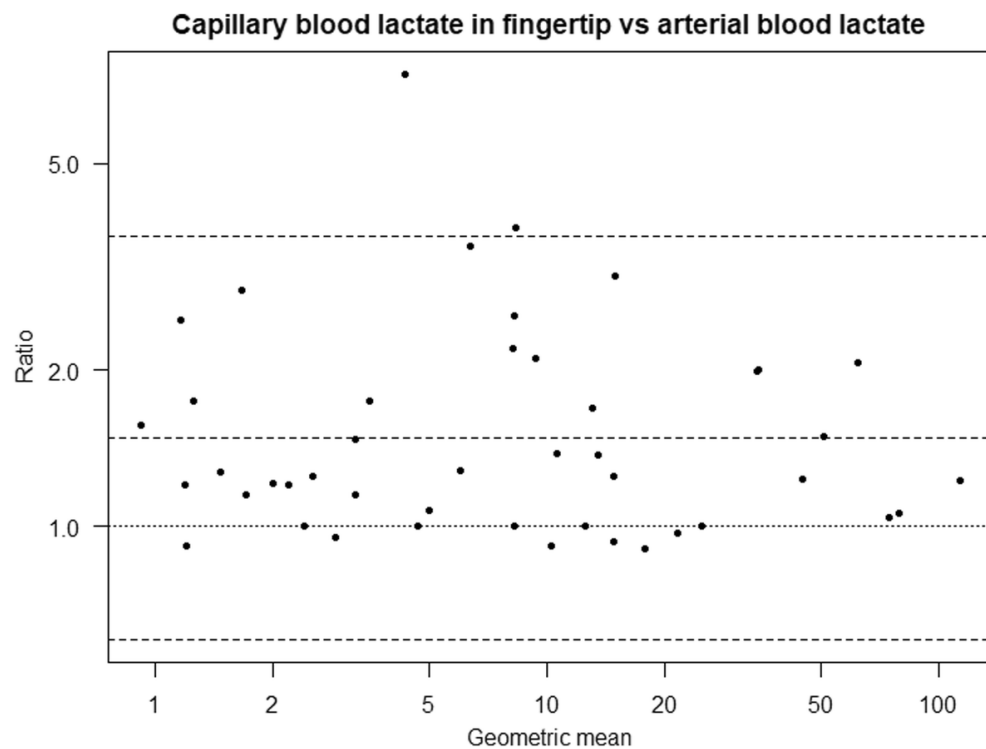




Prognostic Significance of Blood Lactate and Lactate Clearance in Trauma Patients

Marie-Alix Régnier, M.D.,* Mathieu Raux, M.D., Ph.D.,† Yannick Le Manach, M.D.,‡
Yves Asencio, M.D. M.Sc.,* Johann Gaillard, M.D.,* Catherine Devilliers, Pharm. D.,§
Olivier Langeron, M.D., Ph.D.,|| Bruno Riou, M.D., Ph.D.#





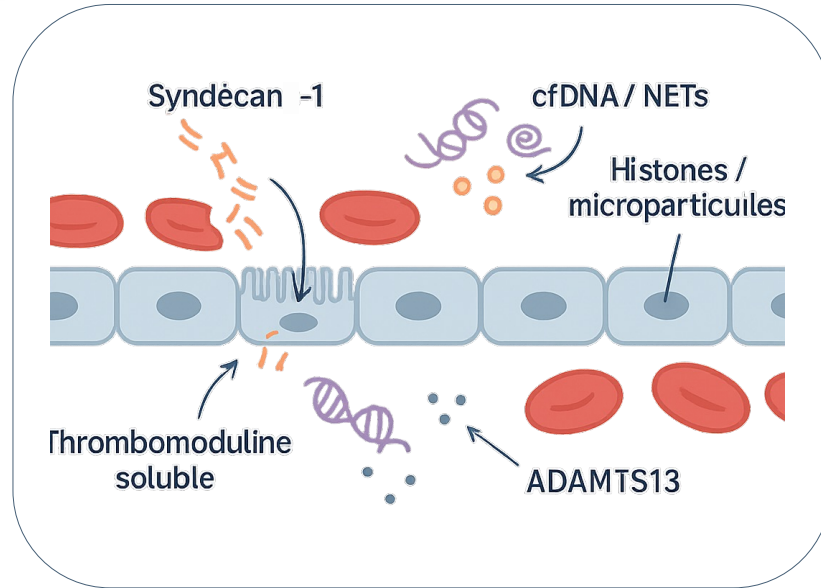
LES BIOMARQUEURS EMERGENTS

A High Admission Syndecan-1 Level, A Marker of Endothelial Glycocalyx Degradation, Is Associated With Inflammation, Protein C Depletion, Fibrinolysis, and Increased Mortality in Trauma Patients

Pär I. Johansson, MD, DMSc, MPA,* Jakob Stenballe, MD, PhD,† Lars S. Rasmussen, MD, PhD, DMSc,† and
Stavros R. Ostrowski, MD, PhD, DMSc*

Temporal phenotyping of circulating microparticles after trauma: a prospective cohort study

Matthias Freilich,^{1,2†} Nadine Schäfer,^{1†} Michael Caspers,^{1,2} Julia K. Böhm,¹ Ewa K. Stürmer,² Benil Bouillon²
and Marc Maegele²



NEUTROPHIL-DERIVED CIRCULATING FREE DNA (cfDNA/NETS): A POTENTIAL PROGNOSTIC MARKER FOR POSTTRAUMATIC DEVELOPMENT OF INFLAMMATORY SECOND HIT AND SEPSIS

Stefan Margraf,* Tim Lögters,† Jenny Reipen,† Jens Altrichter,† Martin Scholz,†
and Joachim Windolf†

Article

Shock-Driven Endotheliopathy in Trauma Patients Is Associated with Leucocyte Derived Extracellular Vesicles

Romain W. G. Dujardin,^{1,2,*†} Jeske E. C. Kisters,^{1,3,4} Mathijs R. Wirtz,¹ Najat Hajji,^{4,5} Anita M. Tuij-de Boer,¹
Jakob Stenballe,⁶ Pär I. Johansson,^{6,9} Karin Brohi,⁷ Ross A. Davenport,⁷ Christine Gaender,⁸
Simon Stanworth,^{9,10} Marc Maegele,¹¹ Rienk Nieuwland,^{4,5} Edwin van der Pol,^{4,5} and Nicole P. Juffermans,^{1,2}

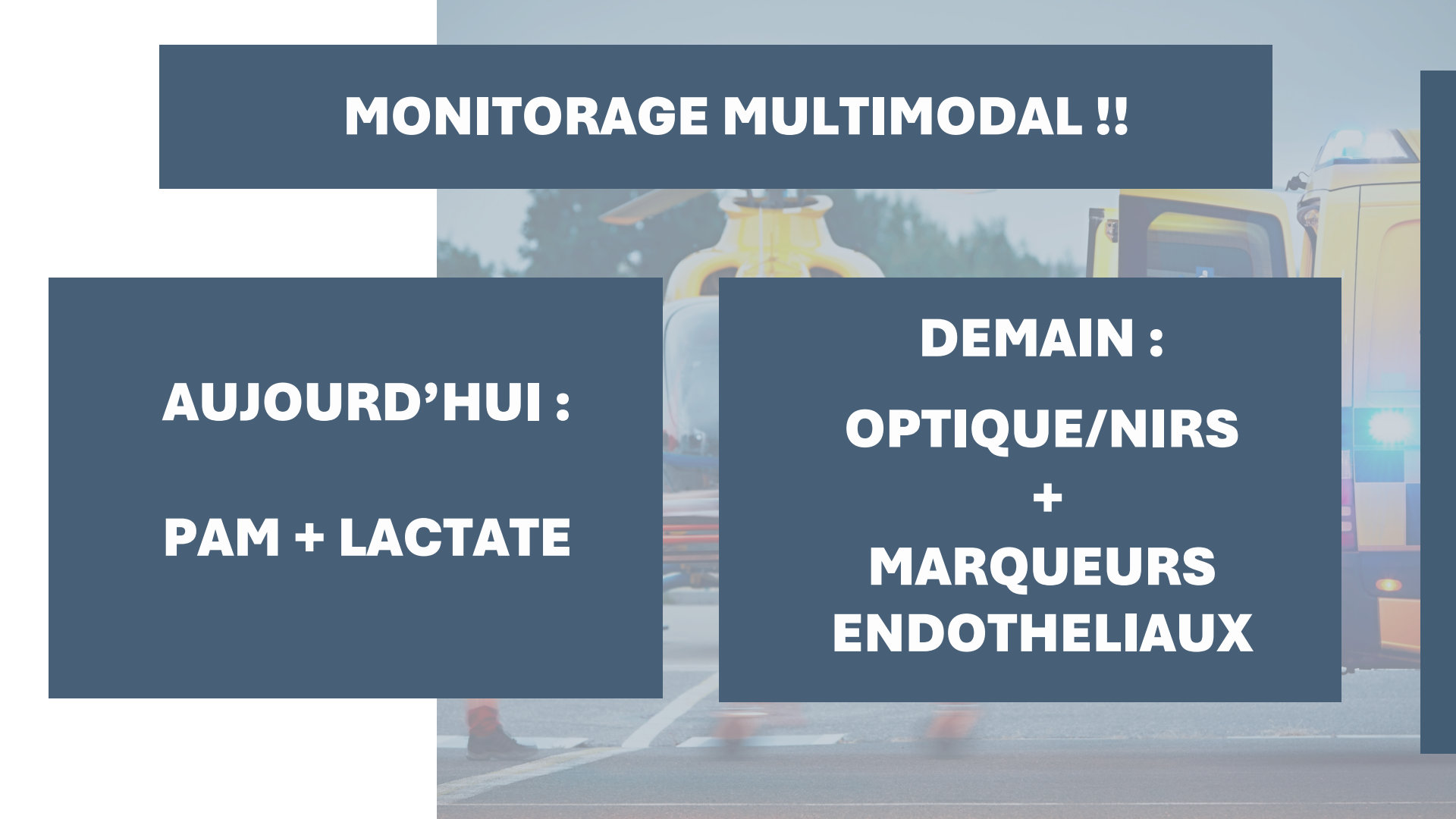
Endotheliopathy of trauma is an on-scene phenomenon, and is associated with multiple organ dysfunction syndrome

Naumann, David N; Hazeldine, Jon; Davies, David J; Bishop, Jon; Midwinter, Mark J; Belli,
Antonio; Harrison, Paul; Lord, Janet M

Angiopoietin-2, Marker and Mediator of Endothelial Activation With Prognostic Significance Early After Trauma?

Michael T. Ganter, MD,* Mitchell J. Cohen, MD,† Karim Brohi, FRCS, FRCA,†
Brian B. Chesebro, MD,* Kristian L. Staudenmayer, MD,† Pamela Rahn, BS,†
Sarah C. Christiaens, BS,* Natasha D. Bir, MD,† and Jean-François Pilleul, MD,*†

MONITORAGE MULTIMODAL !!

The background of the slide is a blurred photograph of a yellow helicopter, likely an emergency medical service (EMS) helicopter, parked on a road. The helicopter's rotors are visible, and its emergency lights are flashing. The scene is slightly out of focus, emphasizing the text overlays.

AUJOURD'HUI :

PAM + LACTATE

DEMAIN :

OPTIQUE/NIRS

+

**MARQUEURS
ENDOTHELIAUX**