Syndrome inflammatoire en chirurgie cardiaque

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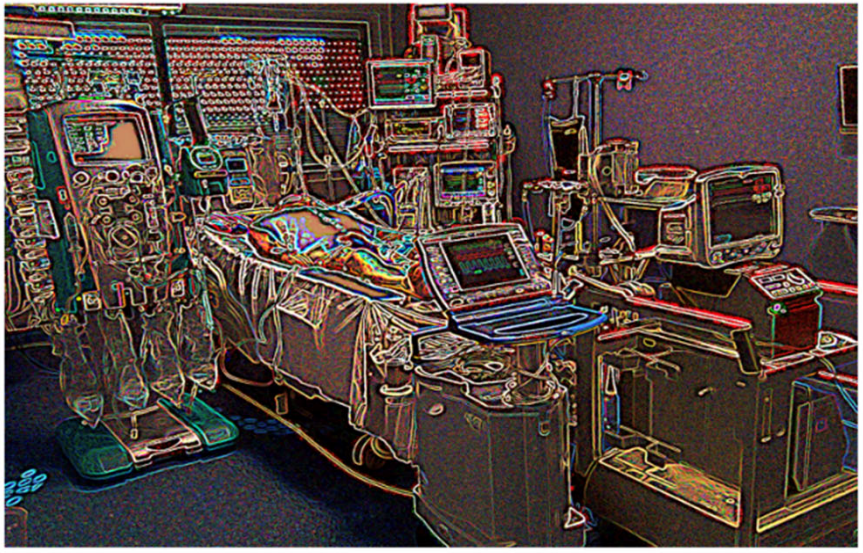

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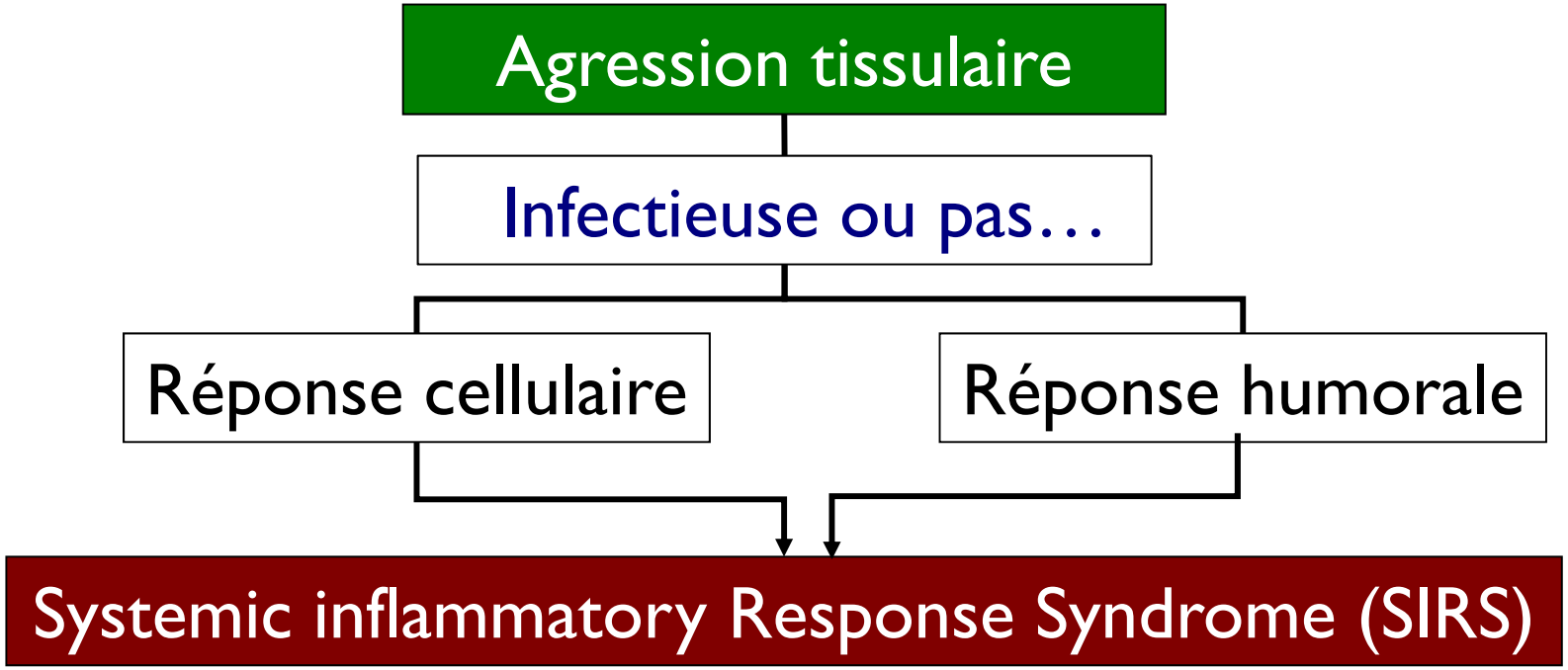
Inserm
La science pour la santé
From science to health

CHU BDX ANESTHÉSIE-RÉANIMATION CARDIOVASCULAIRE

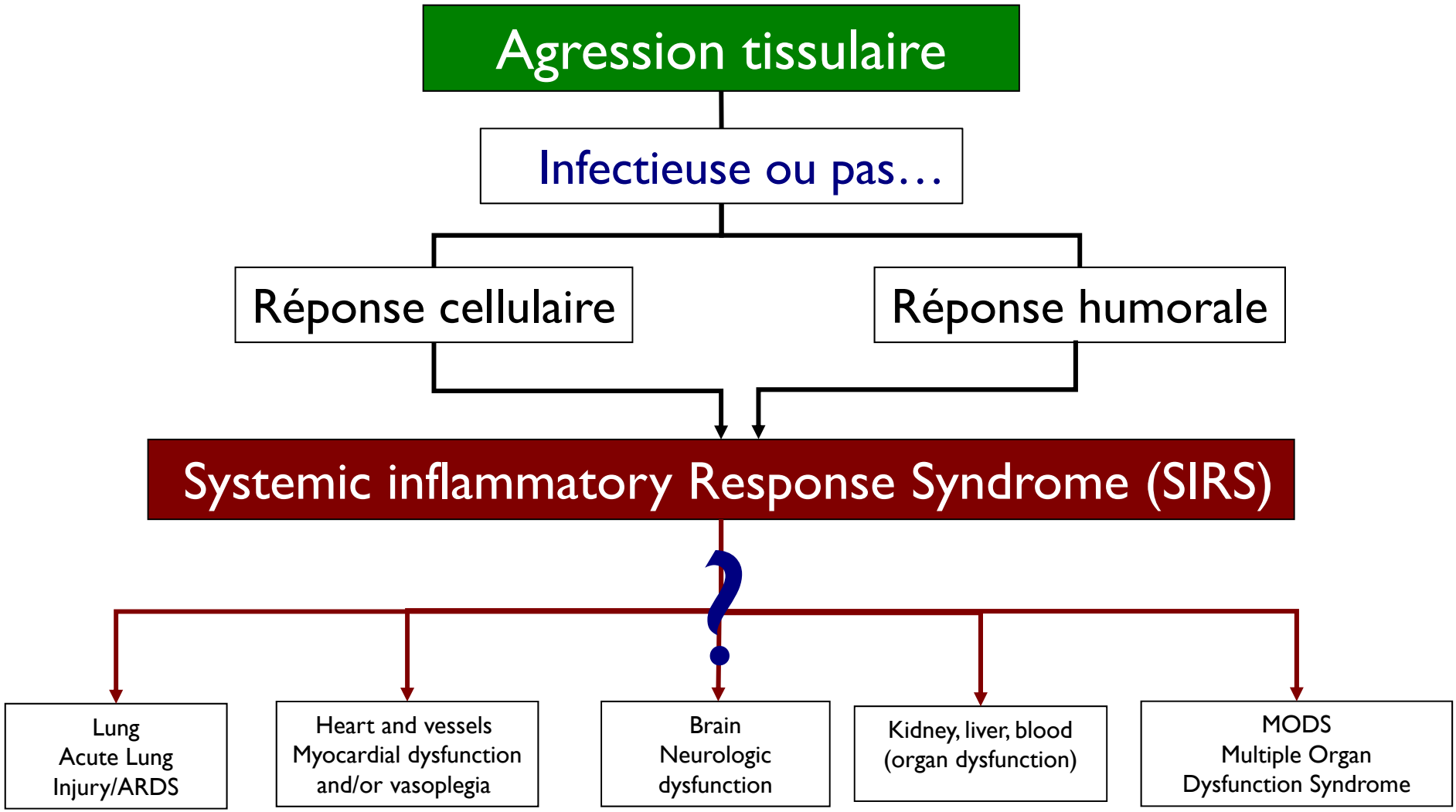

Agression tissulaire
Infectieuse ou pas…
Réponse cellulaire
Réponse humorale
Systemic inflammatory Response Syndrome (SIRS)

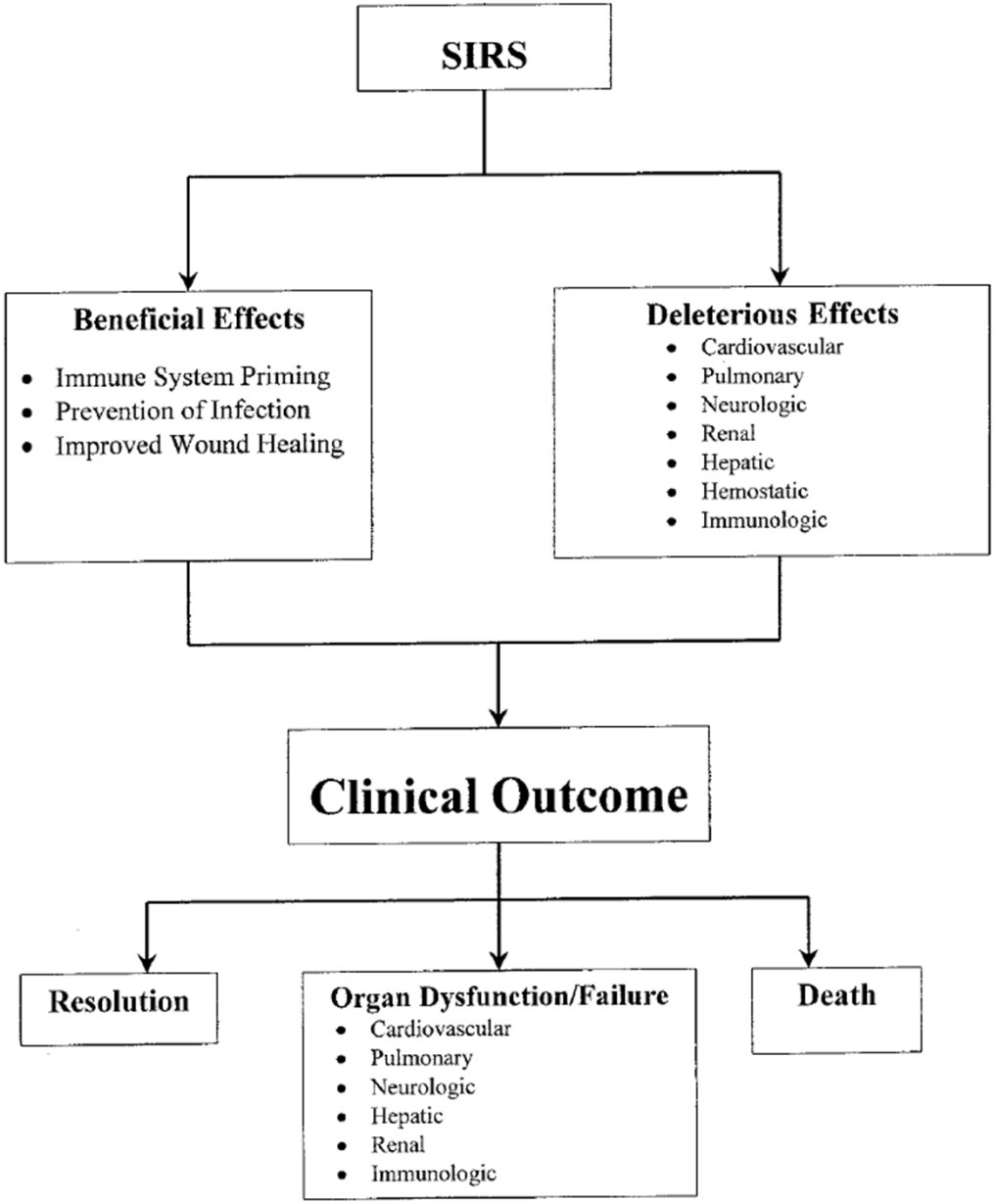
SIRS (Systemic Inflammatory Response Syndrome)

Two or more of:

- Temperature >38°C or <36°C
- Heart rate >90/min
- Respiratory rate >20/min or $Paco_2$ <32 mm Hg (4.3 kPa)
- White blood cell count >12 000/mm^3 or <4000/mm^3 or >10% immature bands

Bone RC et al. JAMA 1992; 268:3452-5


Agression tissulaire
Infectieuse ou pas…
Réponse cellulaire
Réponse humorale
Systemic inflammatory Response Syndrome (SIRS)
?
Lung
Acute Lung
Injury/ARDS
Heart and vessels
Myocardial dysfunction
and/or vasoplegia
Brain
Neurologic
dysfunction
Kidney, liver, blood
(organ dysfunction)
MODS
Multiple Organ
Dysfunction Syndrome



Laffey JG et al. Anesthesiology 2002;97:215-52

Réaction inflammatoire systémique et chirurgie cardiaque

Constante!

Expression biologique et clinique variables…

(CRP, hyperleucocytose, hyperfibrinogénémie, vasoplégie, SDMV…)

(Incidence 5-60% selon la définition retenue)

Réponses individuelles variables

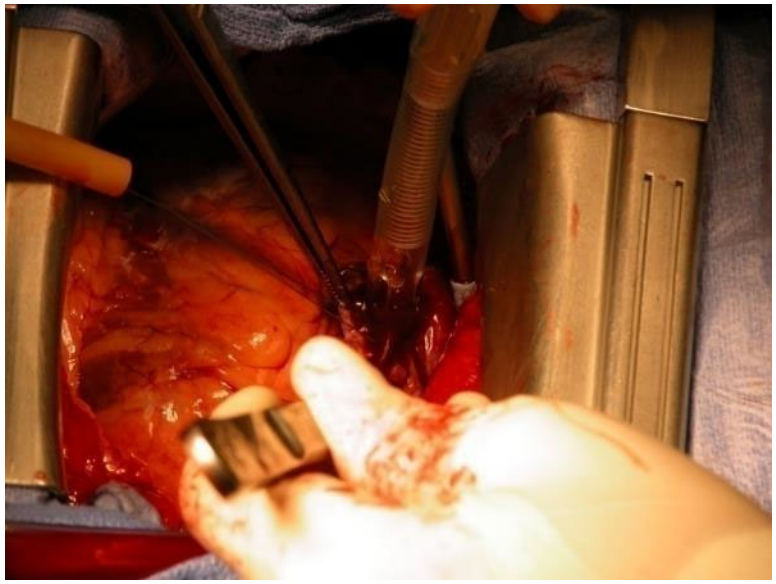
- Contexte chirurgical (urgence, hémorragique, CEC longue…)
- Phénomènes hypoperfusion d'organes (conduite optimale+++)
- Prédisposition génétique (???)

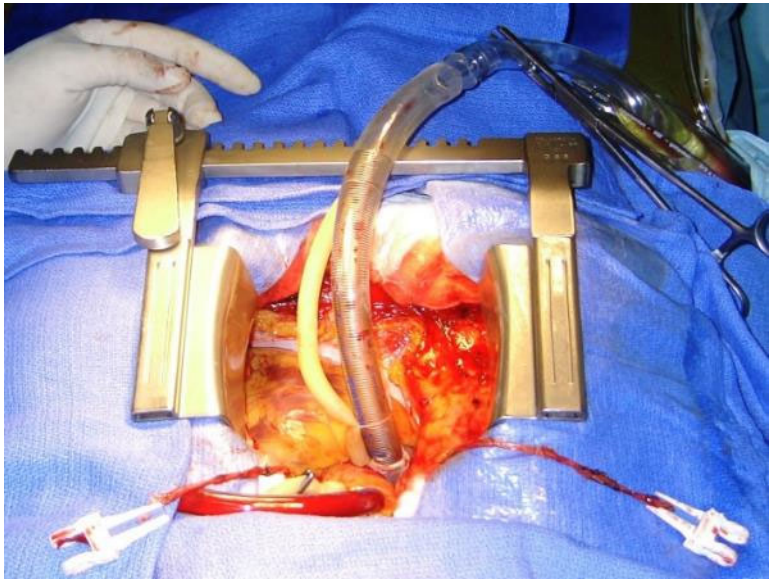
Facteurs initiateurs de la réponse inflammatoire

- Agression tissulaire (chirurgicale mais pas uniquement…)
- Exposition du sang à surface non-épithéliale (activation phase contact)
- Interface air/sang (réservoir de cardiotomie, médiastin, cavité pleurale…)
- Hypoperfusion organes (poumon, tube digestif,…+++)
  - Translocation bactérienne
  - Libération endotoxines (lipopolysaccharides bactériens…)
- Phénomènes d'ischémie-reperfusion d'organes (cardiaque, cérébrale, rénale, pulmonaire, digestive, hépatique…)
- Héparinisation (complexe héparine/protamine)

Davies SW et al. J Thorac Cardiovasc Surg 1993; 105:979-87

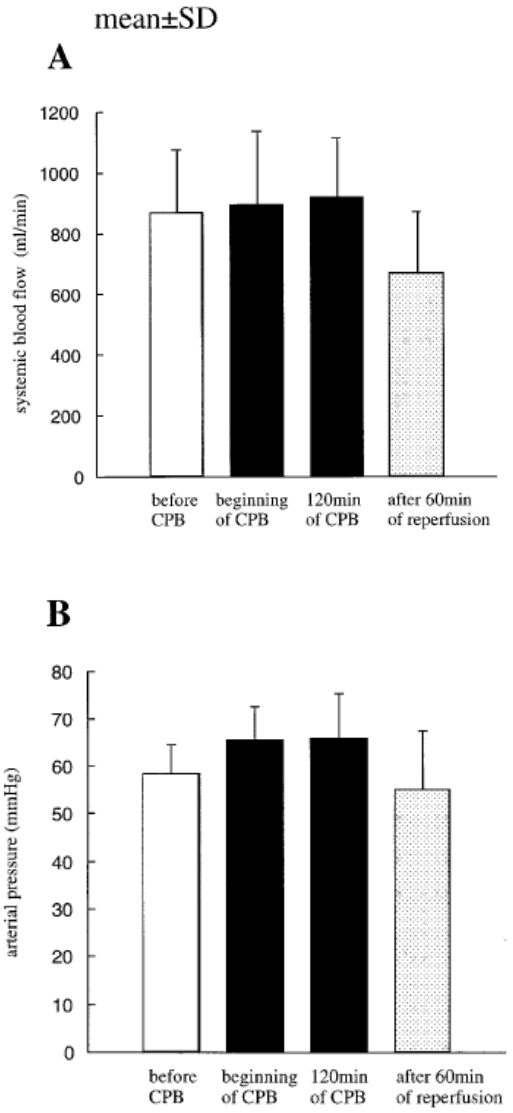
Sawa Y et al. J Thorac Cardiovasc Surg 1996;111:29-35

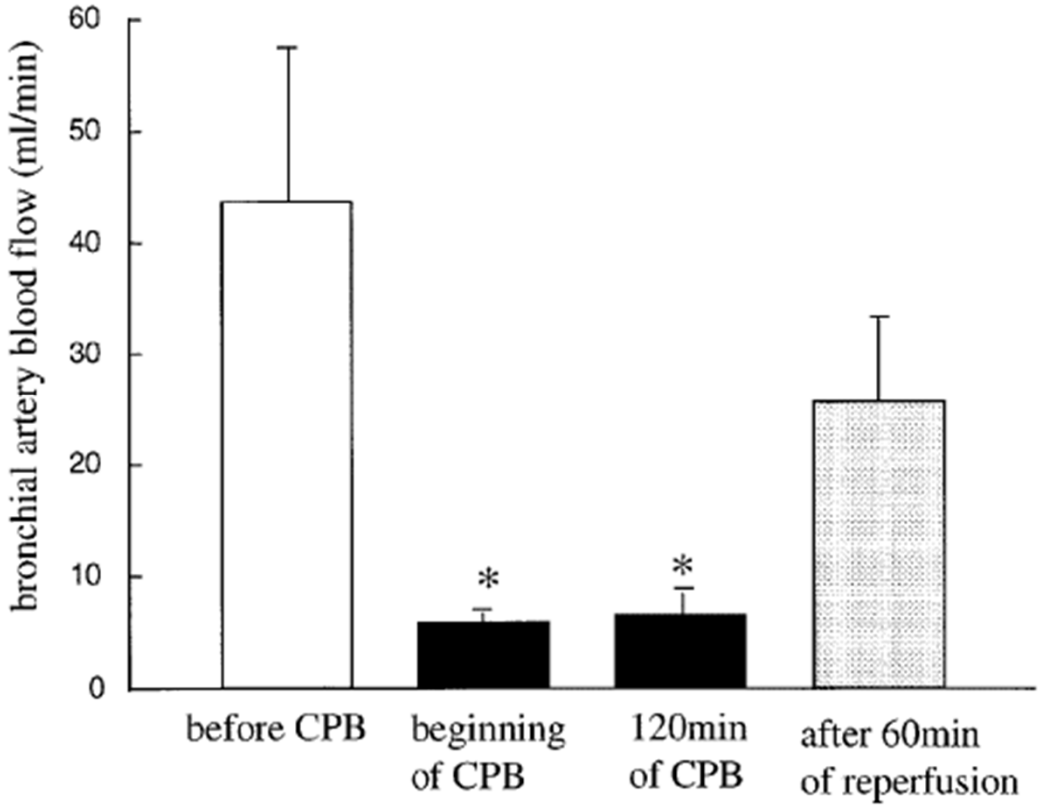


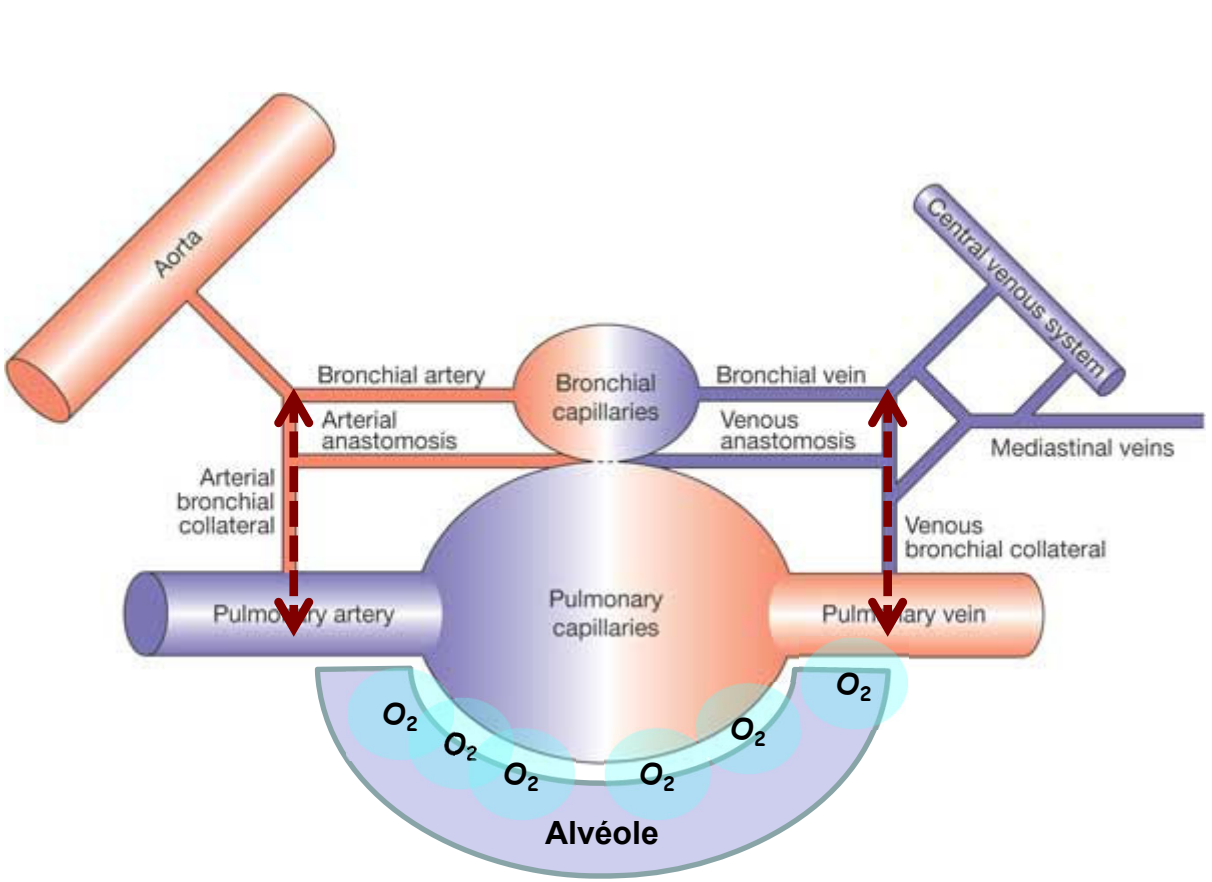


Bronchial artery perfusion during cardiopulmonary bypass does not prevent ischemia of the lung in piglets: assessment of bronchial artery blood flow with fluorescent microspheres☆

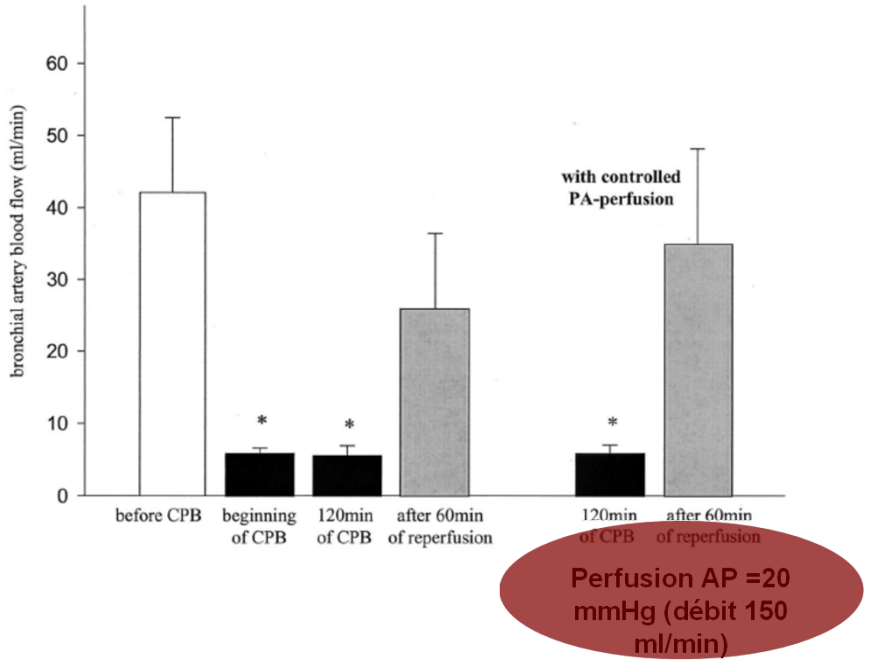
Schlensak C et al. Eur J Cardioth Surg 2001; 19:329-32

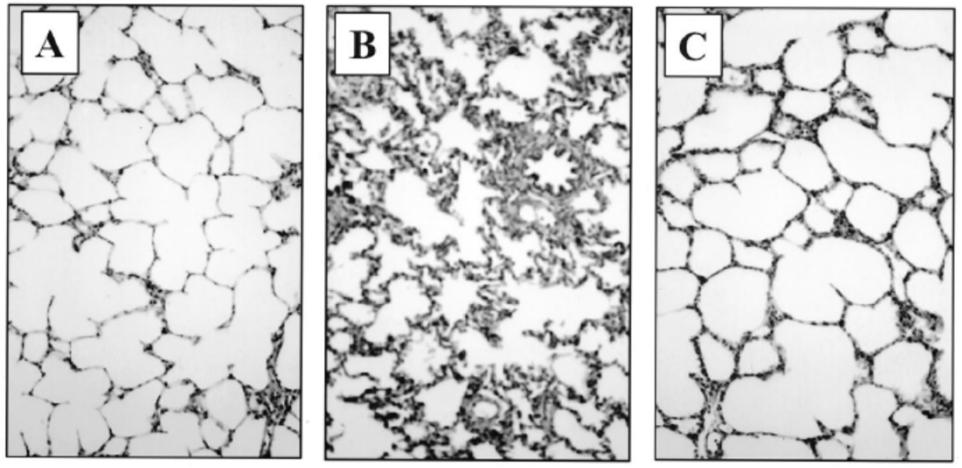






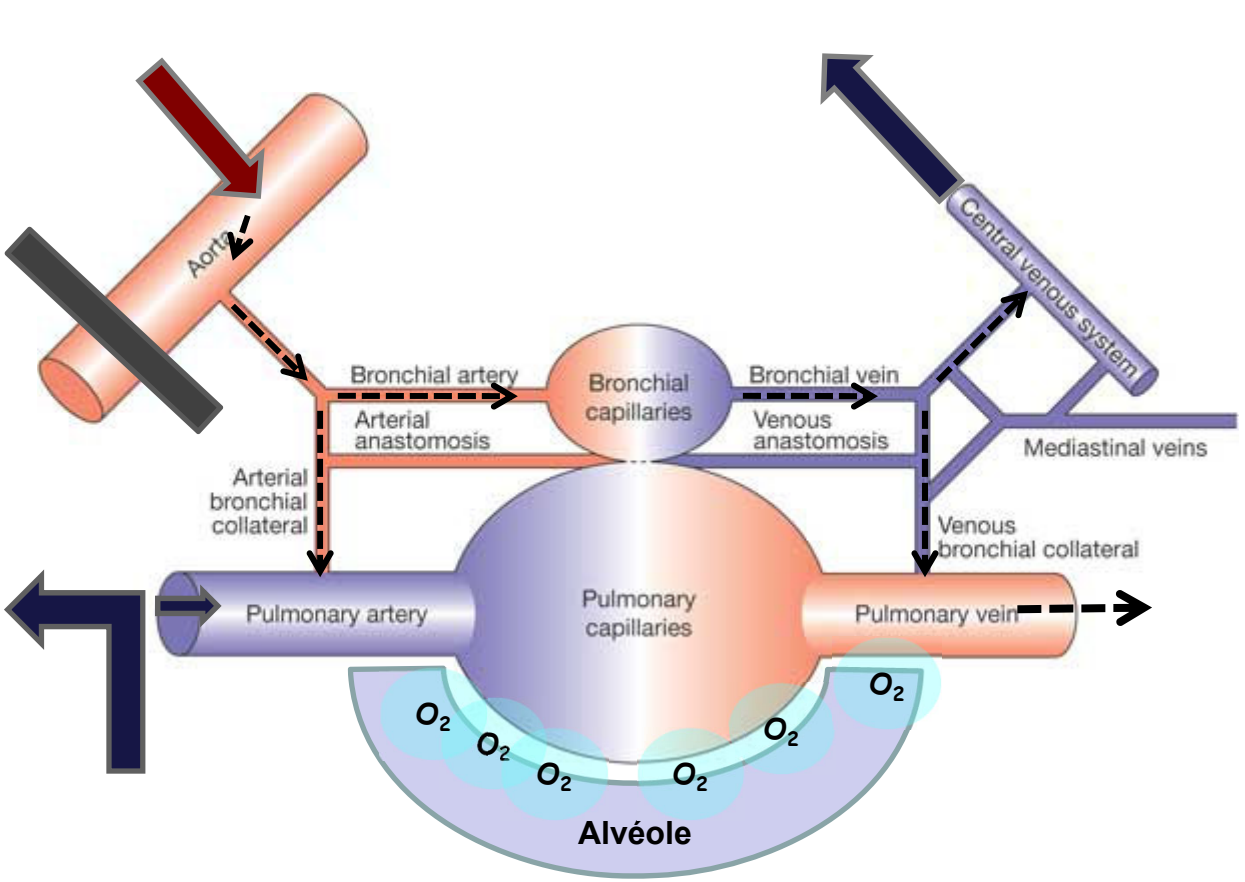
de Leval MR. The circulation of the lung
Nature Clinical Practice Cardiovascular Medicine (2005) 2, 202-8





BL PAP - PAP +

Schlensak C et al. J Thorac Vasc Surg 2002;123:1199-205



de Leval MR. The circulation of the lung
Nature Clinical Practice Cardiovascular Medicine (2005) 2, 202-8

Cardiac surgery/ Cardiopulmonary Bypass

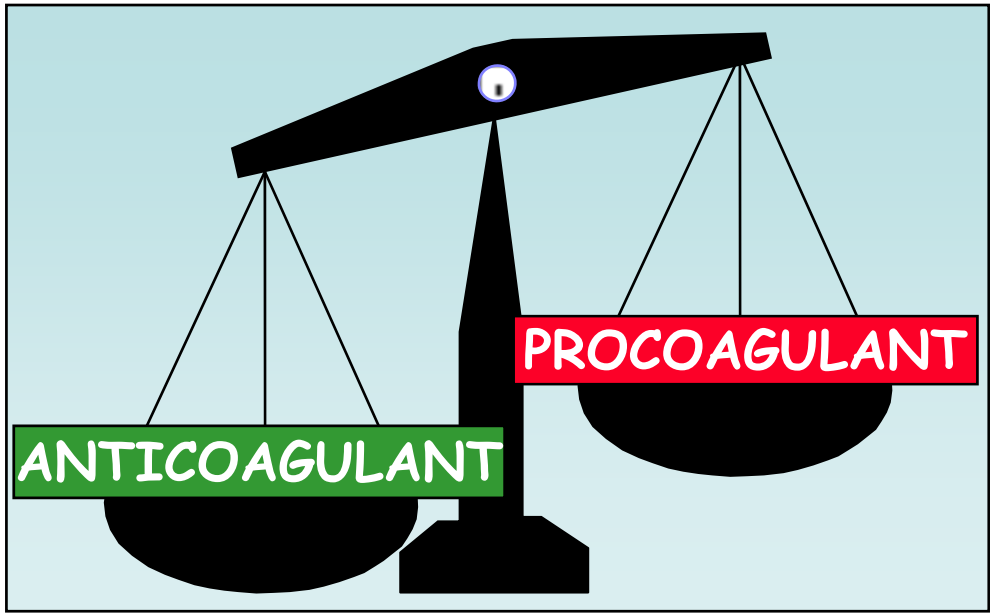
Initiating Factors
- Contact Activation
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

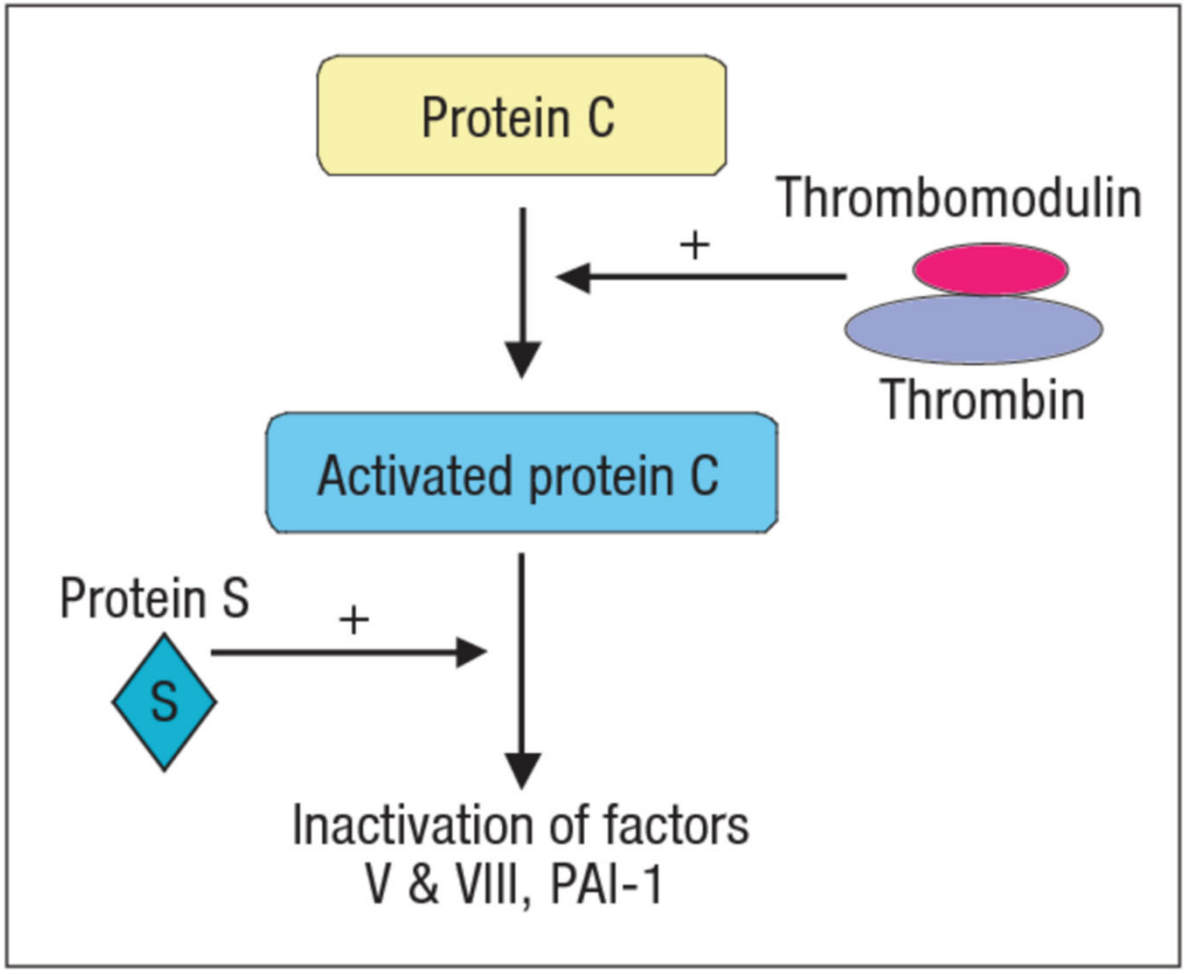
Immune System Activation
- Coagulation/fibrinolysis
- Complement
- Cytokines
- Endothelium
- Cellular Immune System

SIRS

Conditions physiologiques : Surface endovasculaire endothéliale anti-thrombogénique

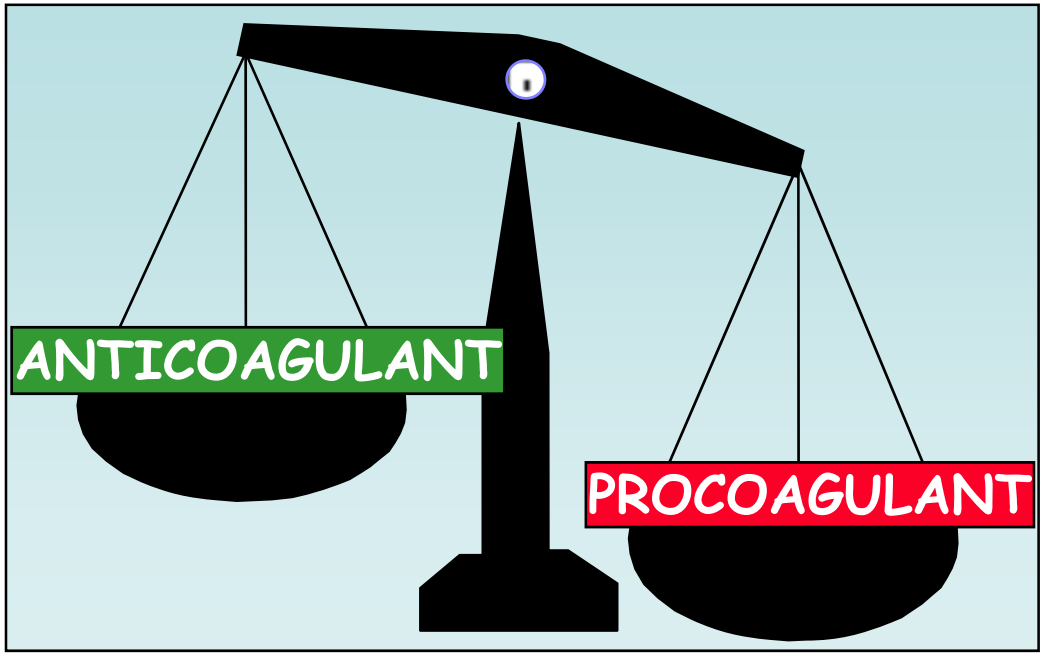
- Synthèse de facteurs antiplaquettaires: PGI_2, NO
- Expression à la surface des cellules endothéliales de la thrombomoduline (anti-coagulante)
- Libération de protéines fibrinolytiques (t-PA)

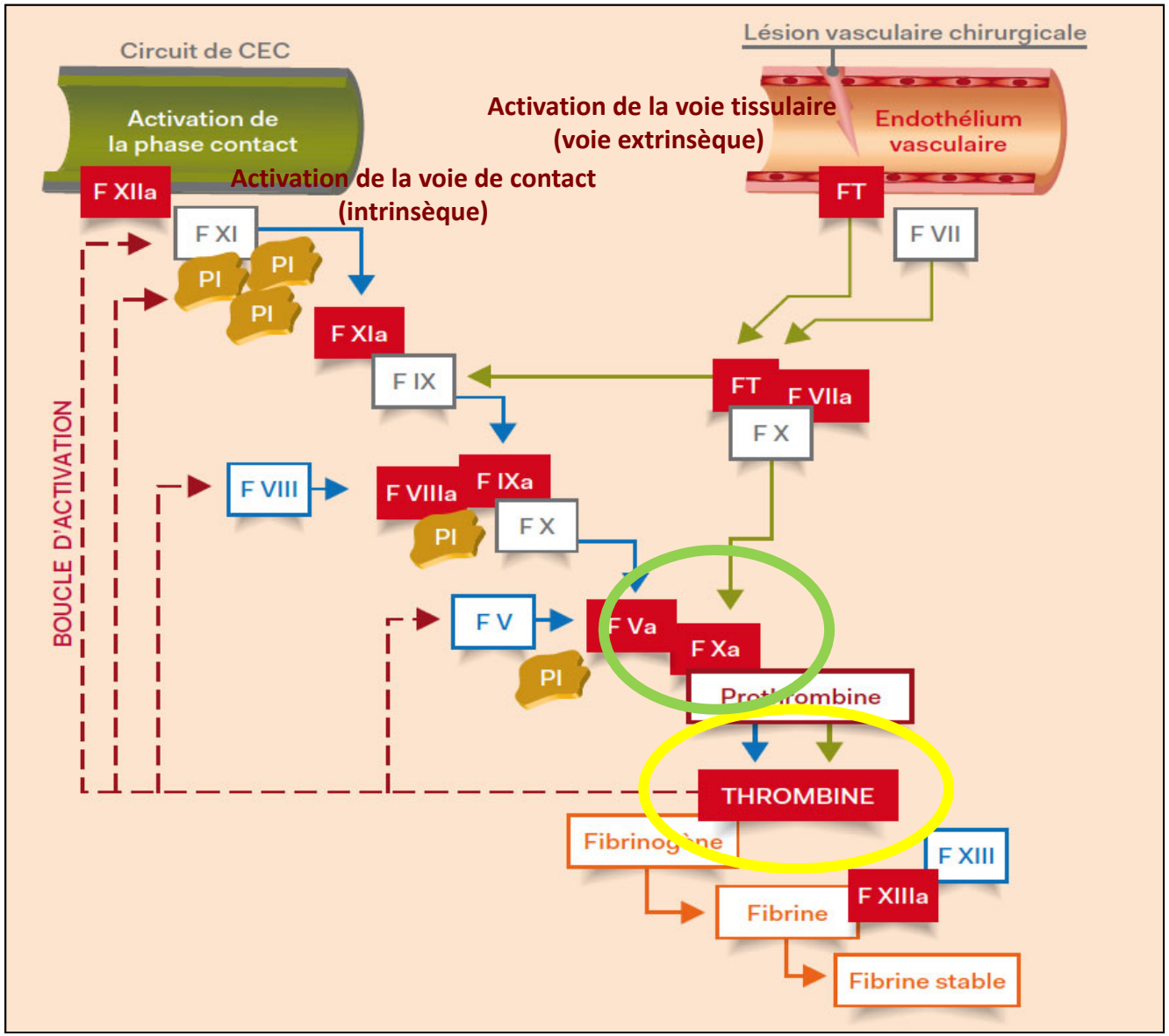



Protein C
Thrombomodulin
+
Thrombin
Activated protein C
Protein S
+
S
Inactivation of factors
V & VIII, PAI-1

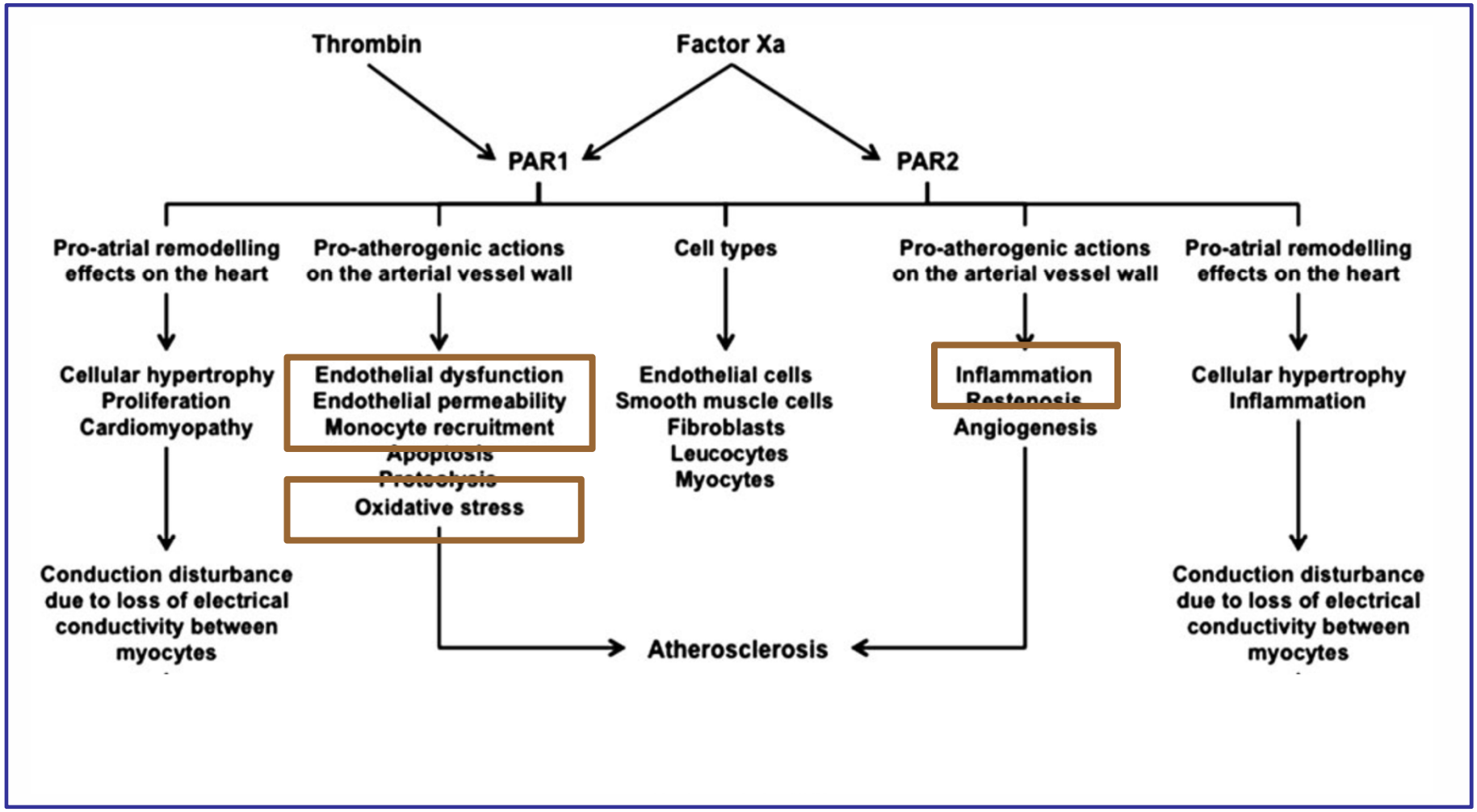
Au cours de l'inflammation…état procoagulant

Surexpression du Facteur tissulaire (FT), Plaminogen activator inhibitor (PAI)-1 et von Willebrand Factor (vWF)



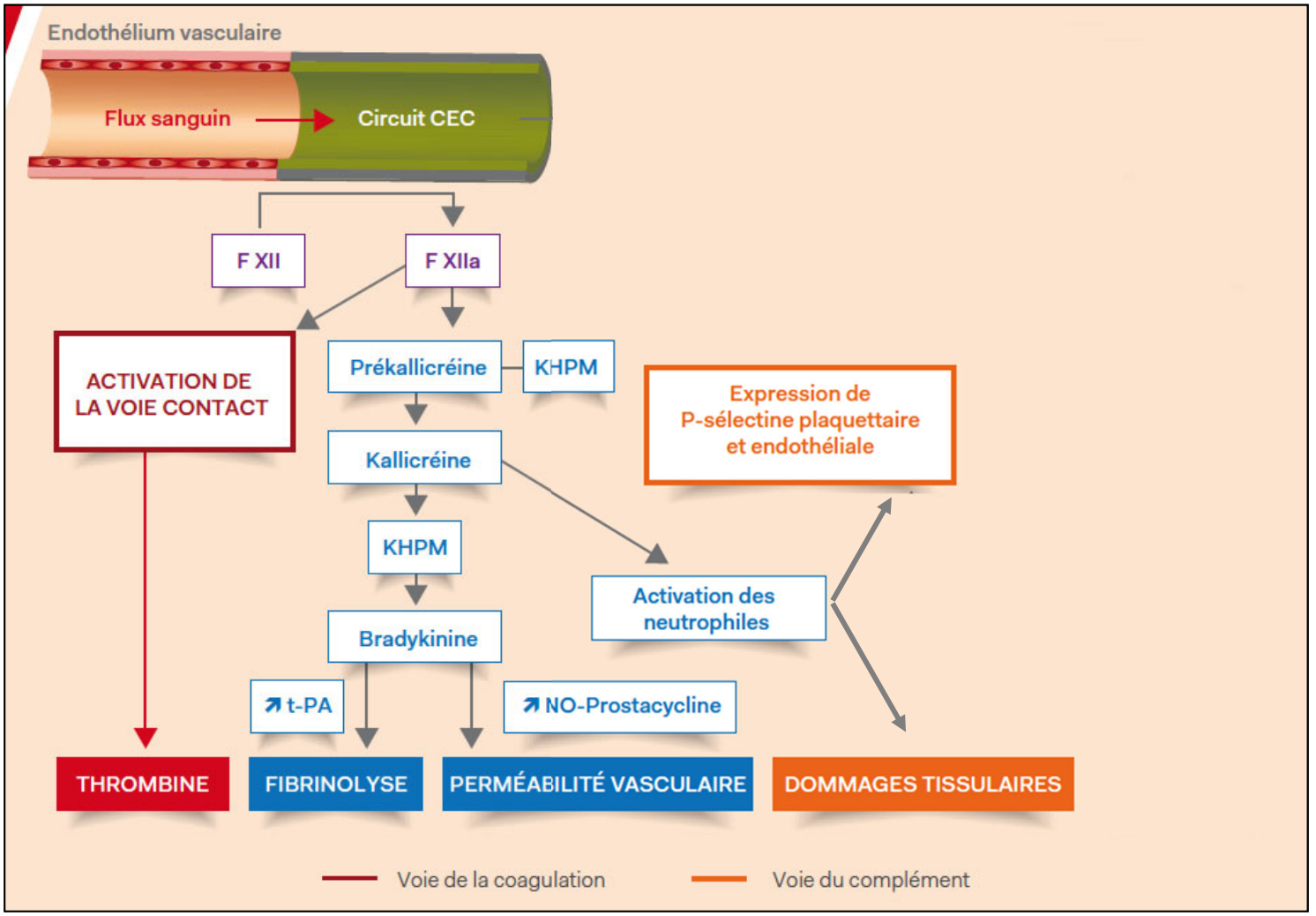

Circuit de CEC
Activation de la phase contact
Activation de la voie de contact (intrinsèque)
Lésion vasculaire chirurgicale
Activation de la voie tissulaire (voie extrinsèque)
Endothélium vasculaire
F XIIa
F XI
PI
PI
PI
F XIa
F IX
FT
F VII
FT
F VIIa
F X
F VIII
F VIIIa
F IXa
PI
F X
F V
F Va
F Xa
PI
Prothrombine
THROMBINE
Fibrinogène
F XIII
Fibrine
F XIIIa
Fibrine stable
BOUCLE D'ACTIVATION

Pleiotropic effects of thrombin and Factor Xa



PAR = protease-activated receptor

Interaction coagulation et syndrome inflammatoire



KHPM=kininogène de haut poids moléculaire (sérine protéase)

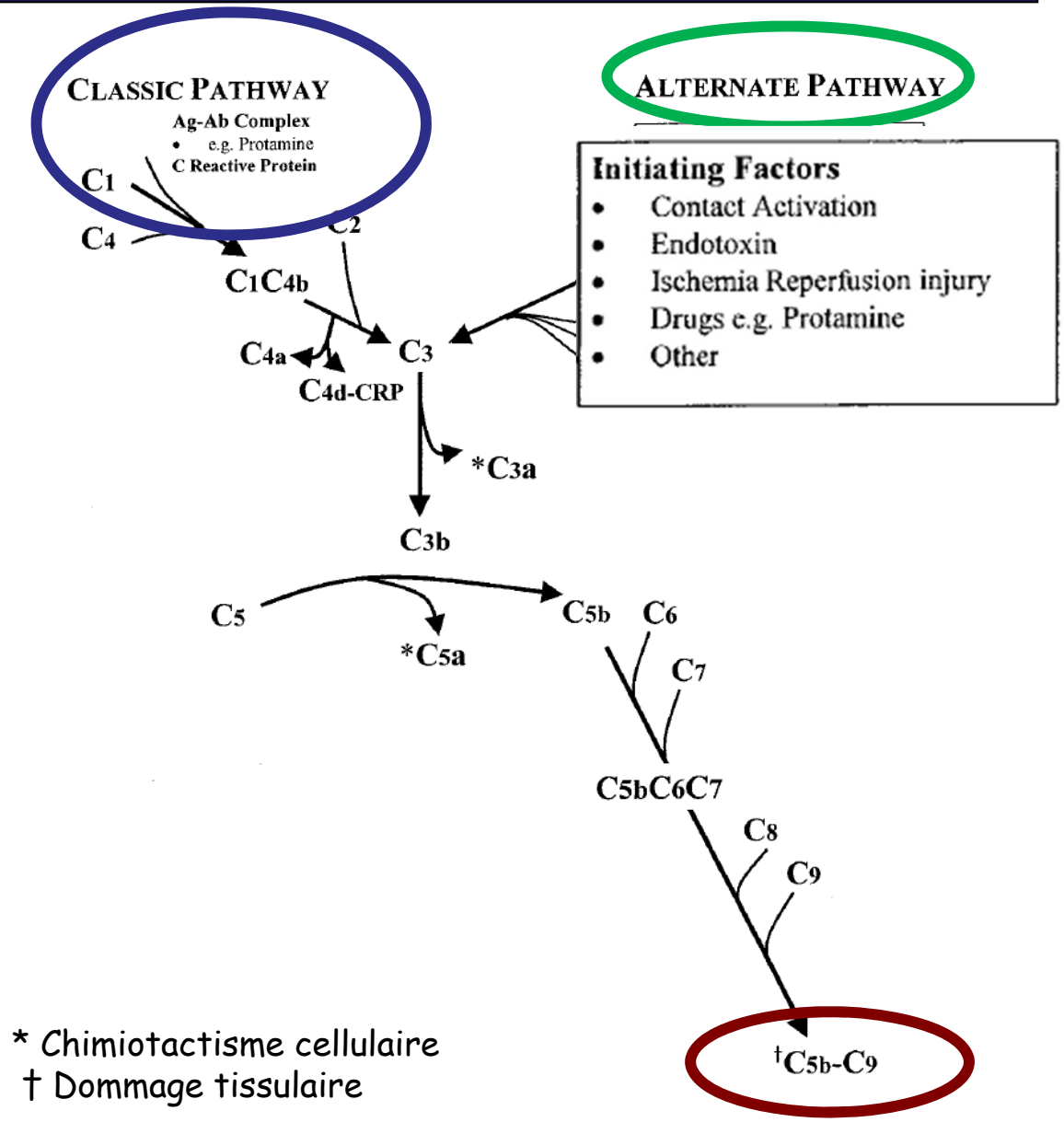
Cardiac surgery/ Cardiopulmonary Bypass

Initiating Factors
- Tissular injury
- Contact Activation
- Blood-air interface
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

Immune System Activation
- Coagulation/fibrinolysis
- Complement
- Cytokines
- Endothelium
- Cellular Immune System

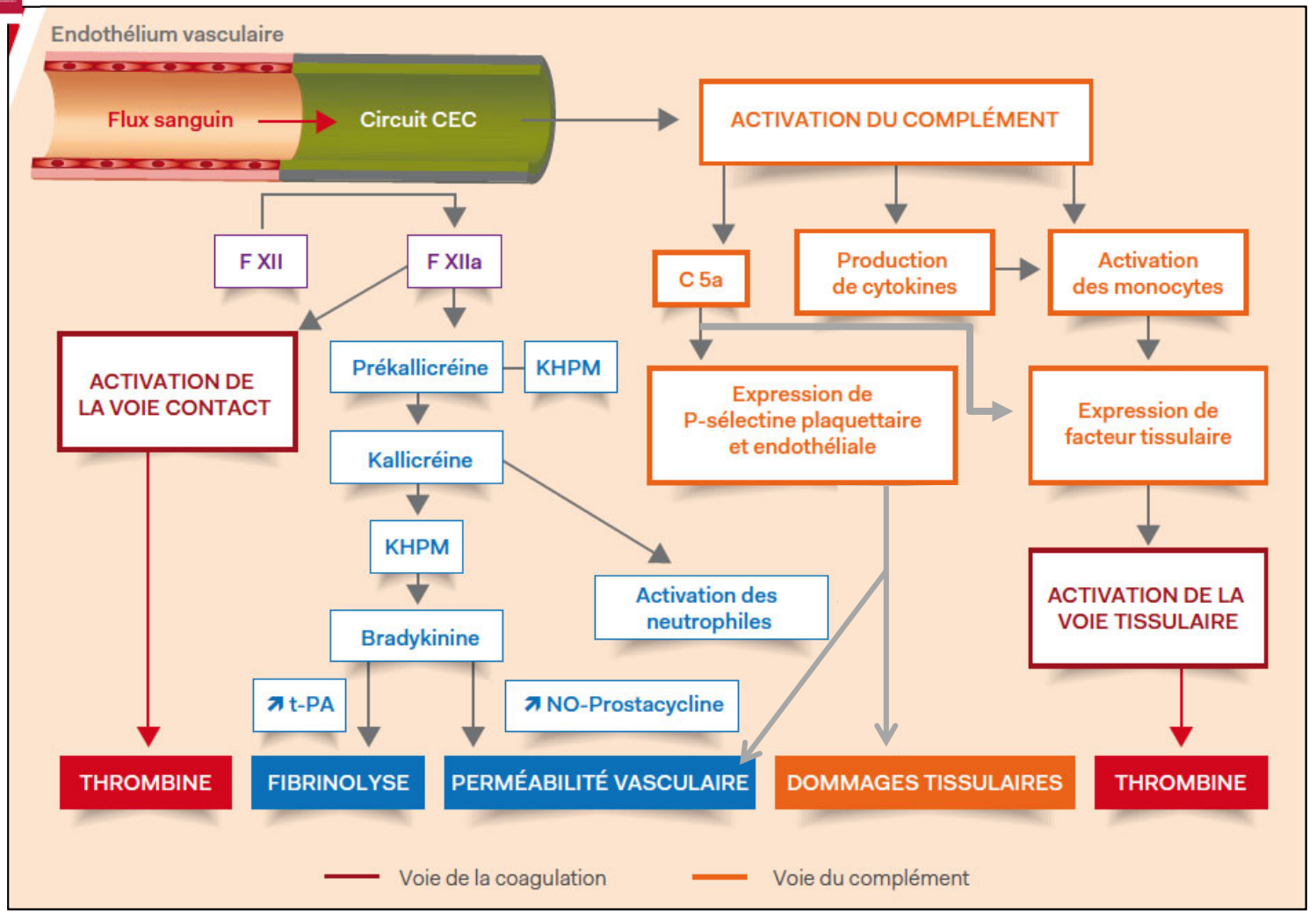
SIRS

Activation de la voie du complément



* Chimiotactisme cellulaire
† Dommage tissulaire

Interaction activation coagulation et syndrome inflammatoire



Interaction forte hémostase/inflammation+++

KHPM=kininogène de haut poids moléculaire

Rinder CS, Rinder HM, Johnson K, et al. Role of C3 cleavage in monocyte activation during extracorporeal circulation. Circulation 1999; 100: 553-8

Park KW, Tofukuji M, Metais C, et al. Attenuation of endothelium-dependent d[illegible] of pig pulmonary arterioles after cardiopulmonary bypass is prevented by monoclonal [illegible]C5a. Anesth Analg 1999; 89: 42-8

Tofukuji M, Stahl GL, Agah A, et al. Anti-C5a monoclo[illegible]reduces cardiopulmonary bypass and cardioplegia-induced coronary endothelial dysf[illegible]orac Cardiovasc Surg 1998; 116: 1060-8

Tofukuji M, Stahl GL, Metais C, et[illegible]ic dysfunction after cardiopulmonary bypass: Role of complement C5a. Ann Thor[illegible], 69: 799-807

Gupta-Bansal R, R[illegible]unden KR. Inhibition of complement alternative pathway function with anti-properdi[illegible]nal antibodies. Mol Immunol 2000; 37: 191-201

Larsson R, Elgue G, Larsson A, et al. Inhibition of complement activation by soluble recombinant CR1 under conditions resembling those in a cardiopulmonary bypass circuit: Reduced upregulation of CD11b and complete abrogation of binding of PMNs to the biomaterial surface. Immunopharmacology 1997; 38: 119-27

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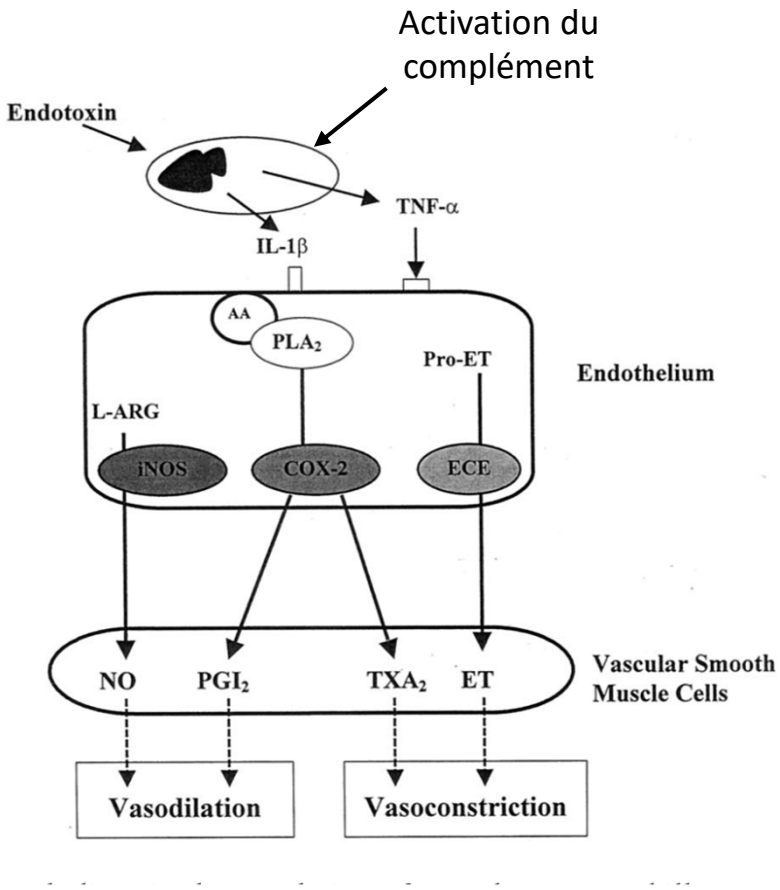
SIRS

Cytokines en chirurgie cardiaque

- Polypeptides solubles
- Messagers paracrines du système immunitaire
- Monocytes activés, macrophages tissulaires, lymphocytes, cellules endothéliales…
- Effet pro-inflammatoire (TNFα, IL-6) et anti-inflammatoire (IL-10)
- Rôle majeur dans homéostasie immunologique
- Produite en réponse à des stimuli physiologiques et/ou pathologiques (endotoxines, activation complément +++)
- Association statistique: taux élevé de cytokines et morbidité postopératoire (IL-6 et mortalité en chirurgie cardiaque congénitale)
- Relation de causalité entre cytokines et morbi-mortalité postopératoire (???)



INFLAMMATORY SIGNALING

- Danger signals
- Interaction between exogenous molecules as Microbial- or Damage-Associated Molecular Patterns (MAMPs or DAMPs) and Pattern Recognition receptors (PRR) on surface or in the cytosol of immune cells (macrophages, monocytes, granulocytes, Natural Killer Cell, dendritic cells...)
- Transcription, maturation and secretion of pro and anti-inflammatory cytokines

MAMPs (surfaces molecules)

- Endotoxin (LPS)
- Lipoproteins
- Flagellin, Fimbrae
- Peptidoglycan,
- Beta-D-glucan…

DAMPs (internal motifs, alarmins)

- Heat shock proteins
- Mitochondrial DNA
- ATP
- High Mobility Group Box (HMGB) 1
- S100 protein

PRR (internal motifs)

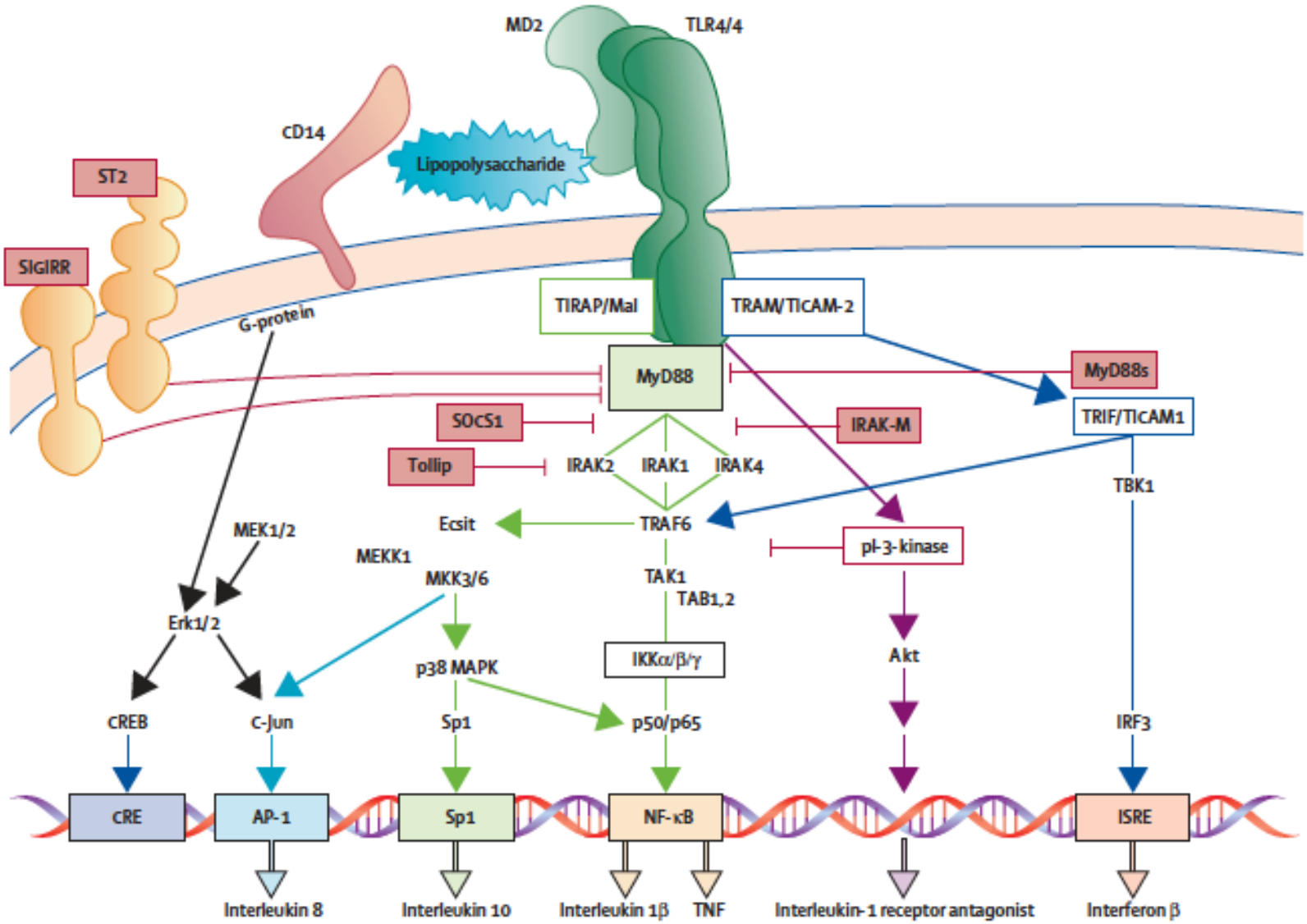
Surface

- Toll-like receptors (+++)
- C-type lectin receptors

Cytosol

- Nod1 and 2 receptors
- RIG-I-Like receptors

Annane D et al. Lancet 2005;365:63-78



AP= activator protein
ISRE Interferon sensitive response element

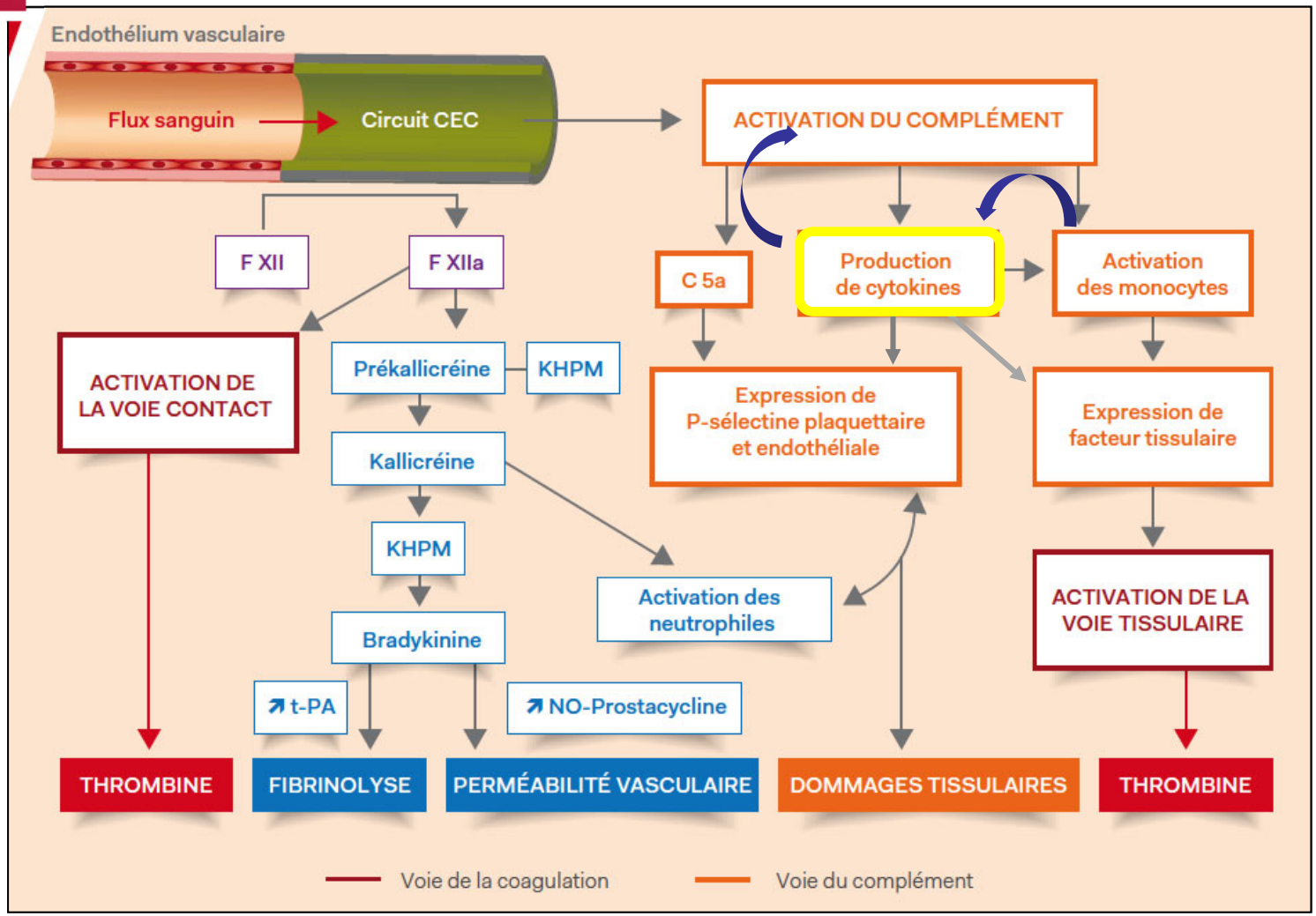
Lancet 2005;365:63-78

Proinflammatory cytokines

- Auto-amplification phenomenon by increasing numbers, lifespan, and activation state of innate immune cells
- Activation of endothelial cells by increasing the expression of adhesion molecule and chemokine
- Cause the release of microparticles (by activated platelets, endothelial cells, and leukocytes) that contain inflammatory, pro-oxidant, and pro-coagulant lipids and proteins (platelet-activating factor, thromboxan, tissue factor, plasminogen activator inhibitor-1, von Willebrand factor multimers…)
- Upregulate intravascular Tissue Factor expression by blood monocytes
- Induce hepatic production of acute phase proteins such as complement, fibrinogen or C-reactive protein (stimulation of chemotaxis, coagulation, vascular permeability) and thus exacerbate inflammatory response

Gotts JE et al. BMJ 2016;353:i1585

Interaction activation coagulation et syndrome inflammatoire

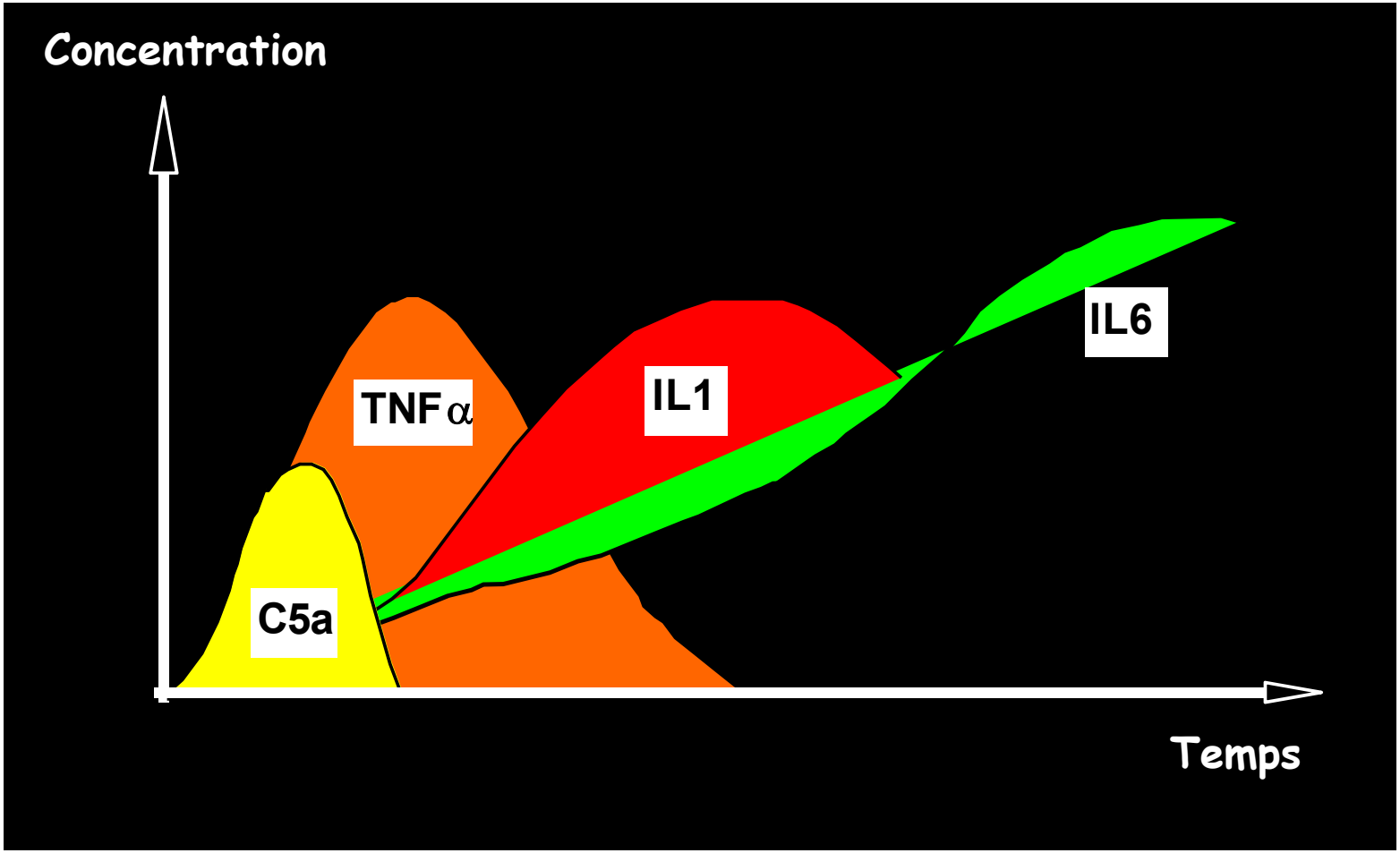


Interaction forte hémostase/inflammation+++

KHPM=kininogène de haut poids moléculaire

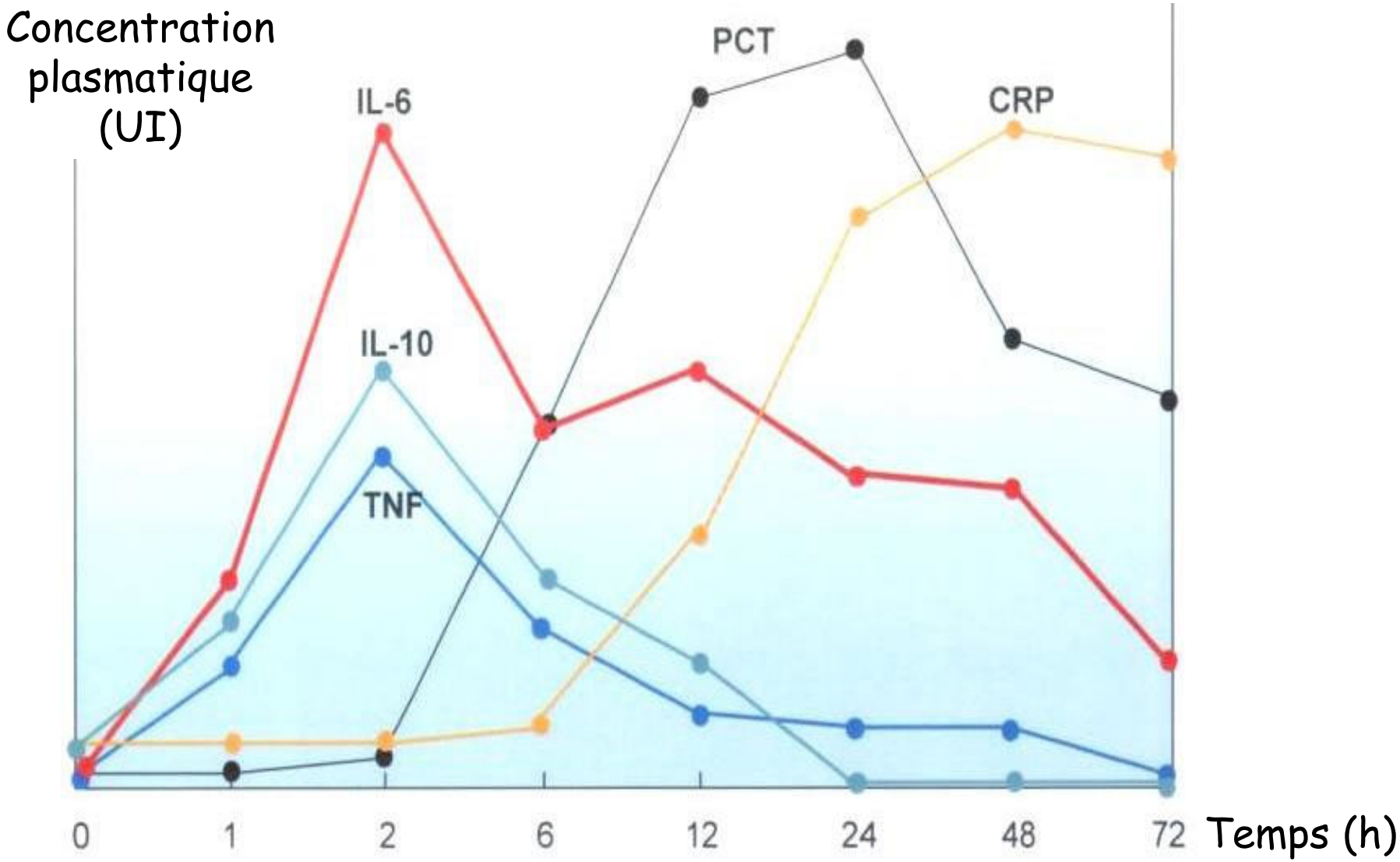
Libération de cytokines après chirurgie cardiaque cardiaque

Pro-inflammatoire		Anti-inflammatoire
TNFα	Précoce	IL-10
IL-1β		TGF b
IL6	Tardive	IL-1ra
IL8		TNFsr 1 et 2


Concentration
TNFα
IL1
IL6
C5a
Temps

Valeurs normales des paramètres en période postopératoire

Meisner et al. J Lab Med 1999



« Effets anti-inflammatoires indirects »

- IL-10 est un puissant inhibiteur de la production de cytokines pro-inflammatoires (TNF-α, IL-1β, IL-6 et IL-8)

  Auto-limitation du syndrome inflammatoire

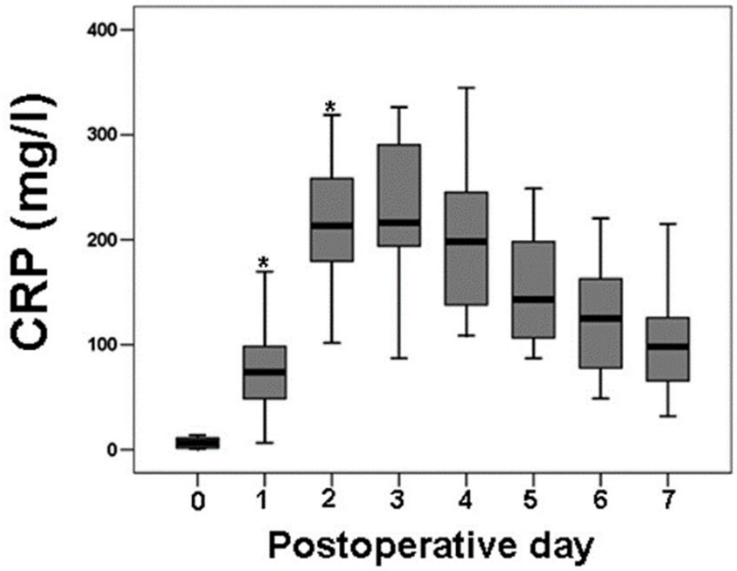
Resolution pathways

Auto-limitation of inflammatory process

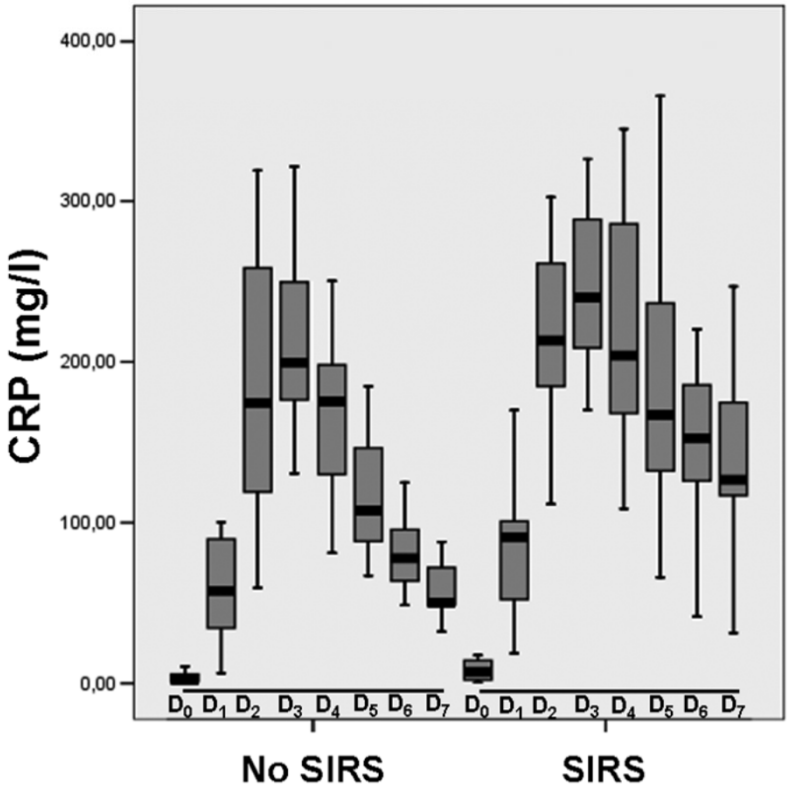
- IL-10 produced by leucocytes suppress IL-6 production
- IL-10 activates production of soluble TNF receptor (ligand function for TNF alpha) and IL-1 receptor antagonist
- Autophagy process to eliminate MAMPs (lysosomal degradation)

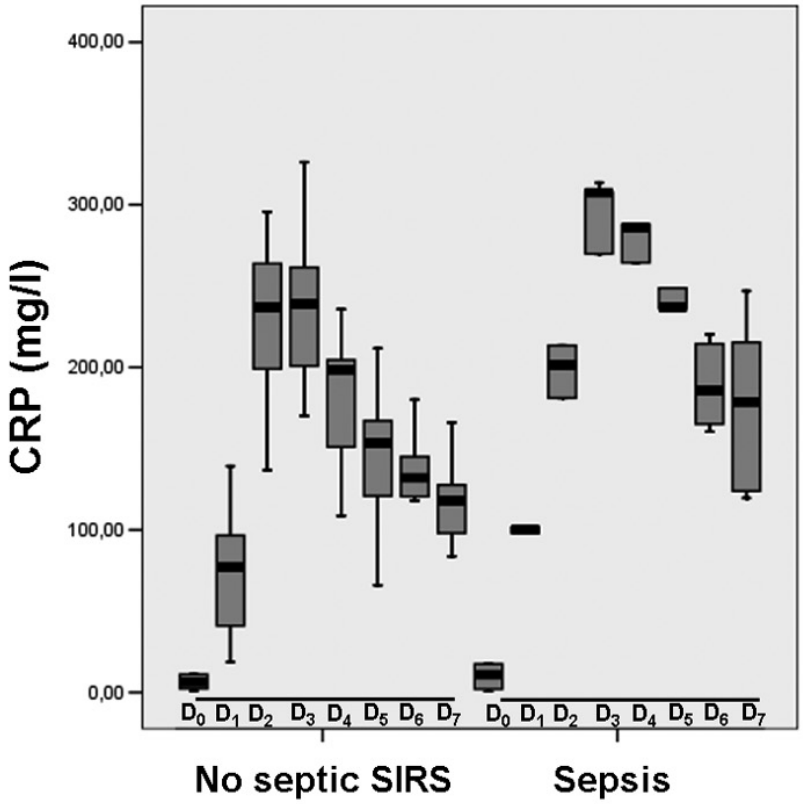
Resolution of inflammation

- Damaged cells and infiltrating leucocytes undergo apoptosis and engulfed by macrophages
- Role of bioactive lipids to reduce ROS production, endothelial permeability and leucocyte recruitment
- Regulatory T cells (Tregs) and myeloid derived suppressor cells play a role in elimination of cytotoxic cells and productions of anti-inflammatory cytokines
- Cholinergic stimulation (inhibition of inflammatory cytokines production)



Delannoy B et al. Crit Care. 2009;13(6):R180



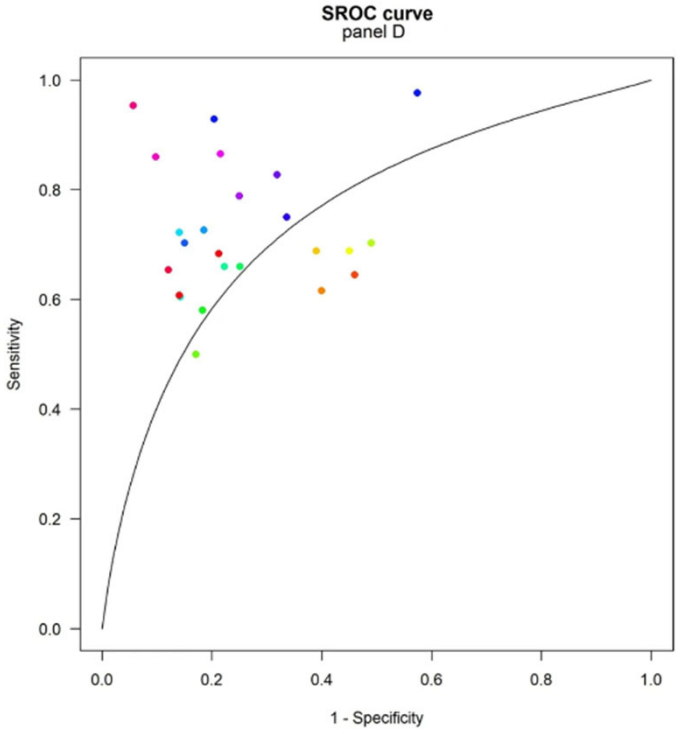


RESEARCH Open Access

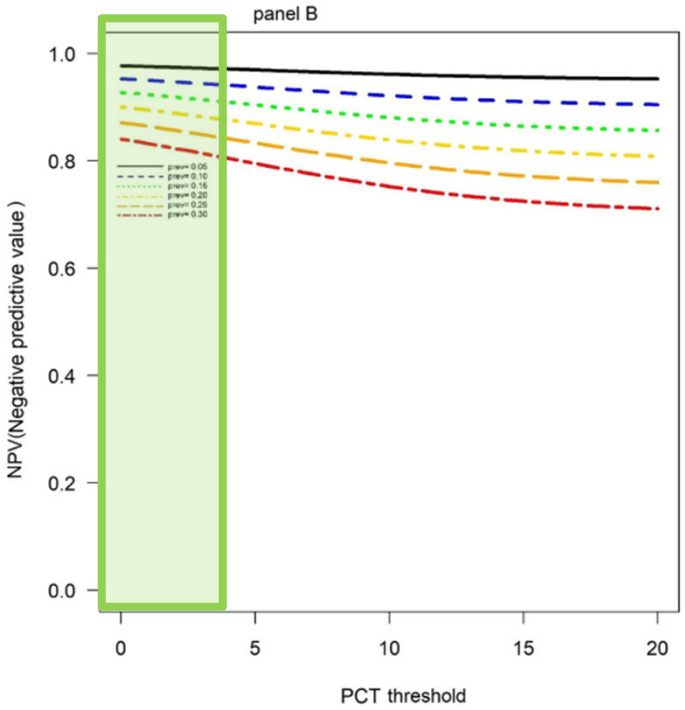
Procalcitonin for the diagnosis of postoperative bacterial infection after adult cardiac surgery: a systematic review and meta-analysis

Davide Nicolotti[1], Silvia Grossi[1], Valeria Palermo[1], Federico Pontone[1], Giuseppe Maglietta[2*], Francesca Diodati[2], Matteo Puntoni[2], Sandra Rossi[1†] and Caterina Caminiti[2†]

Critical Care 2024; 28:44



Pour une valeur seuil de 3 ng/ml,
Se_m 67% et Sp_m 73%



Une valeur < 3 ng/ml
à J2 = VPN > 90%

Cardiac surgery/ Cardiopulmonary Bypass

Initiating Factors
- Contact Activation
- Blood-air interface
- Complexe héparine-protamine
- Ischemia-Reperfusion
- Endotoxemia (hypoperfusion)

Immune System Activation
- Coagulation/fibrinolysis
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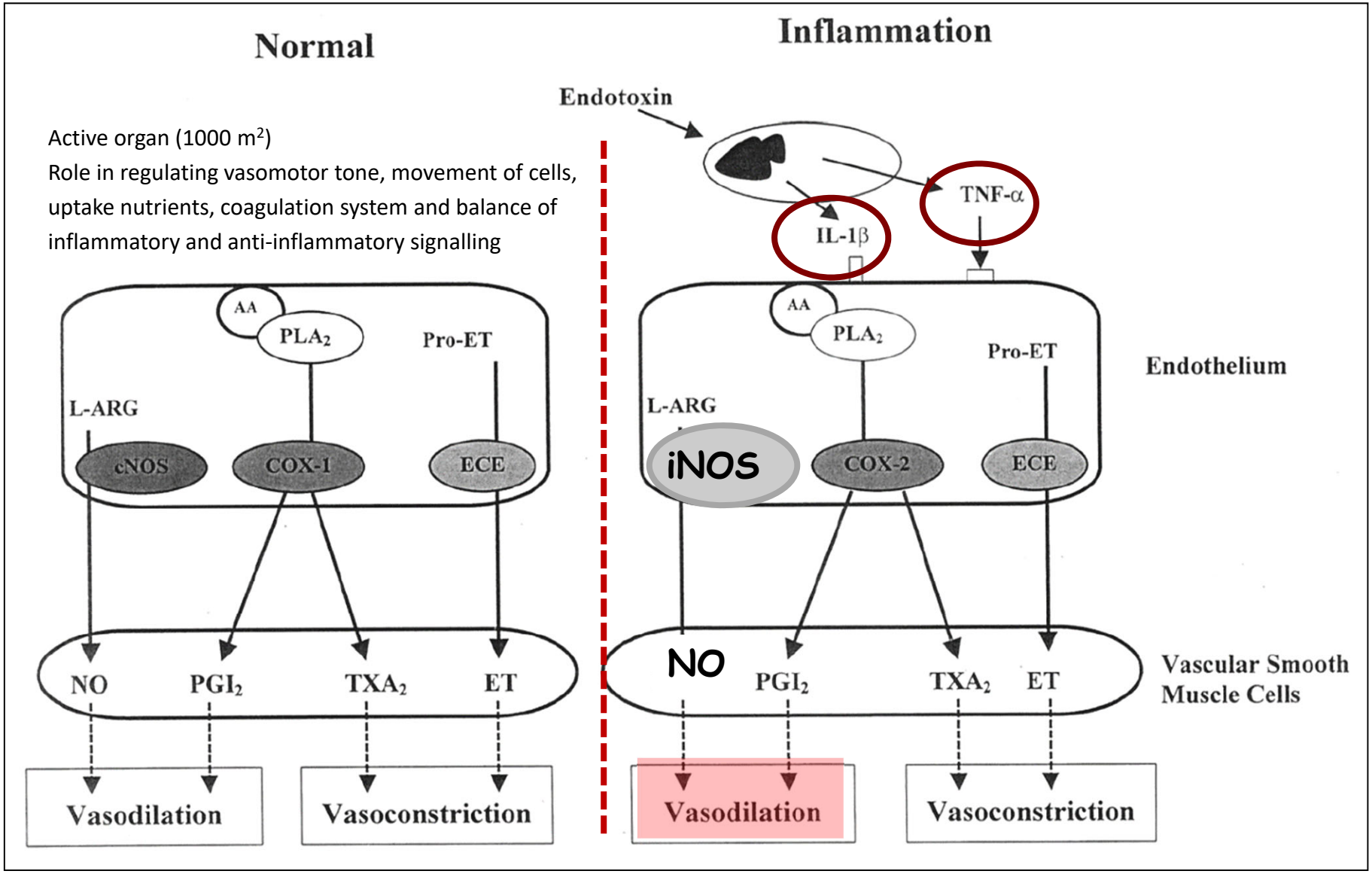
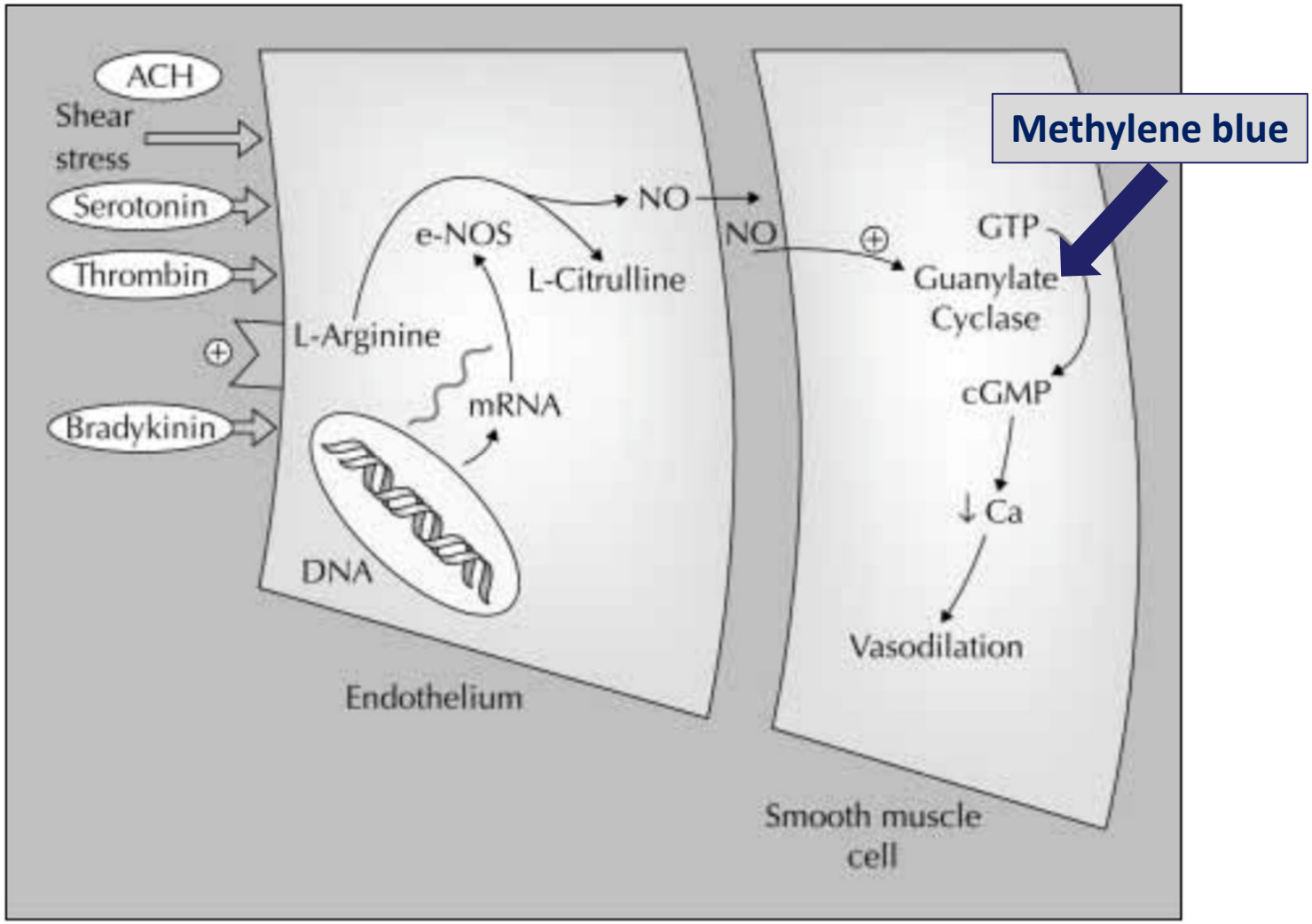
SIRS

Endothélium et syndrome inflammatoire



Mode d'action du monoxyde d'azote



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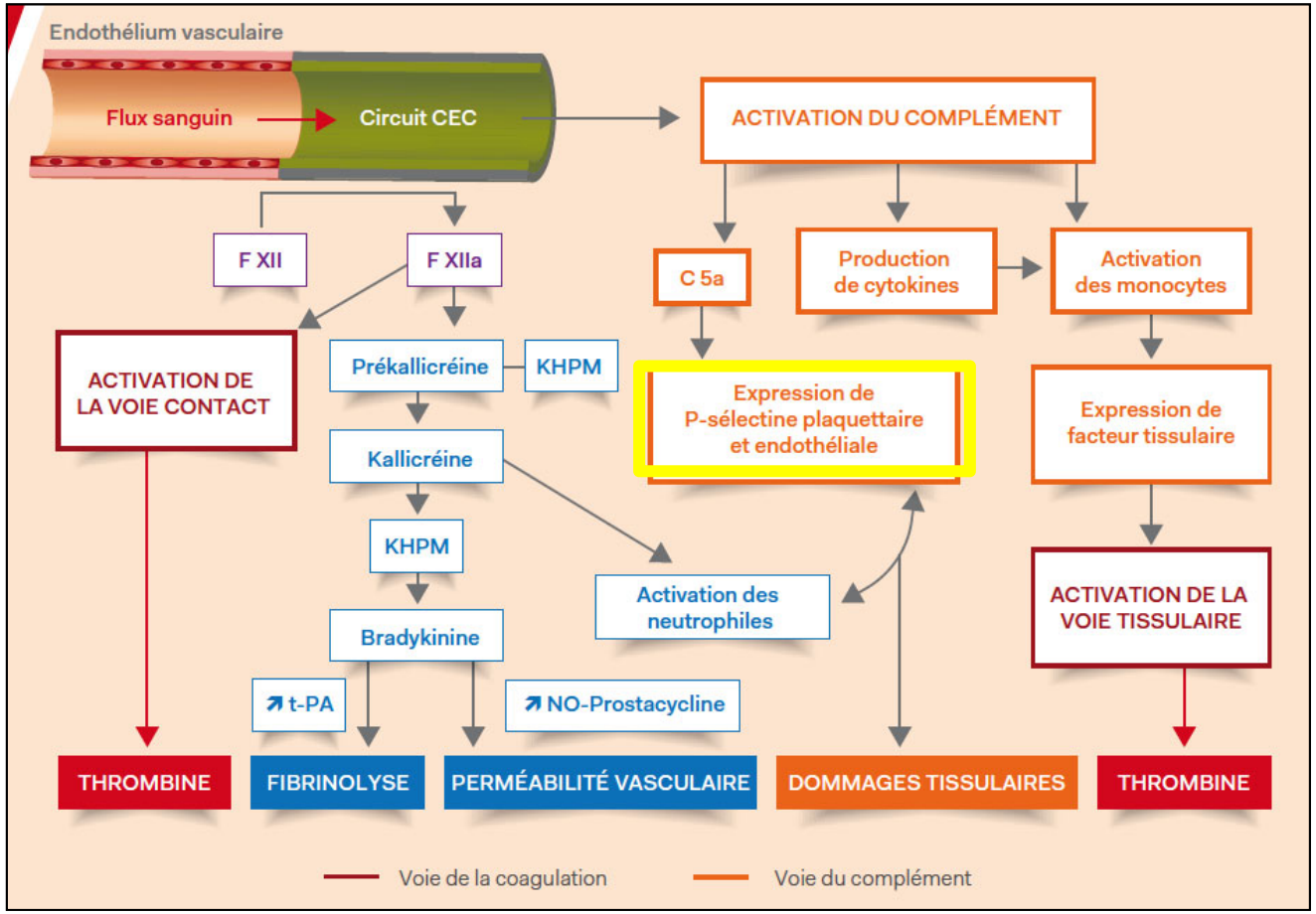
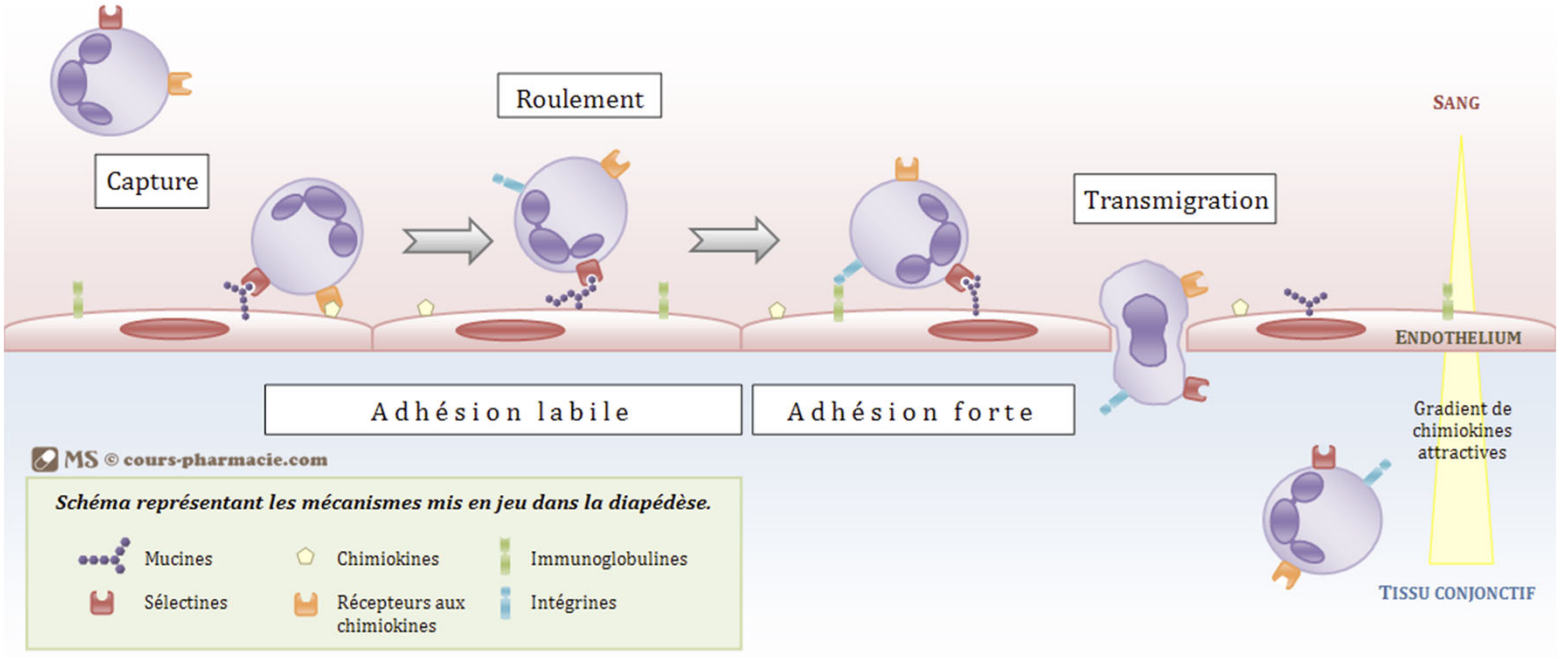
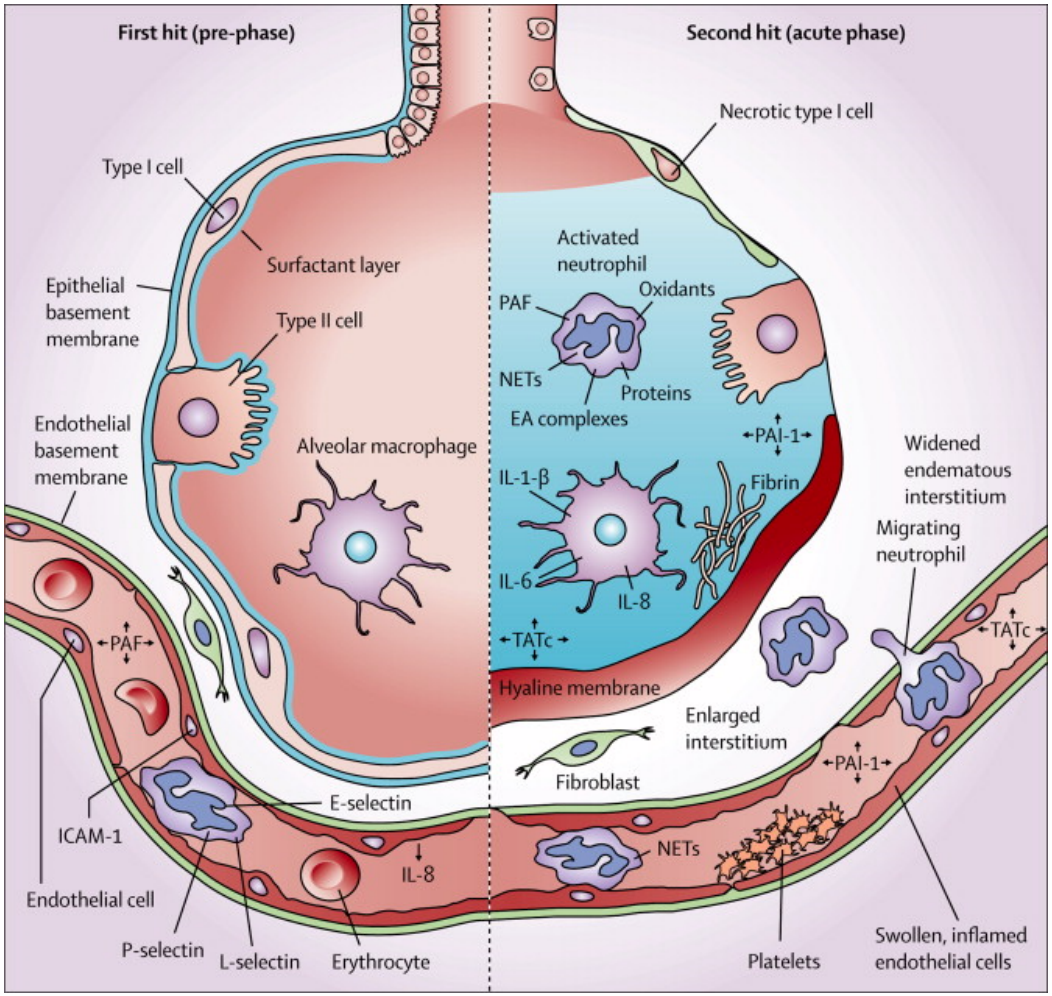

Endothélium vasculaire
Flux sanguin
Circuit CEC
ACTIVATION DU COMPLÉMENT
F XII
F XIIa
C 5a
Production de cytokines
Activation des monocytes
ACTIVATION DE LA VOIE CONTACT
Prékallicréine
KHPM
Kallicréine
KHPM
Bradykinine
Expression de P-sélectine plaquettaire et endothéliale
Expression de facteur tissulaire
Activation des neutrophiles
ACTIVATION DE LA VOIE TISSULAIRE
↗ t-PA
↗ NO-Prostacycline
THROMBINE
FIBRINOLYSE
PERMÉABILITÉ VASCULAIRE
DOMMAGES TISSULAIRES
THROMBINE
Voie de la coagulation
Voie du complément

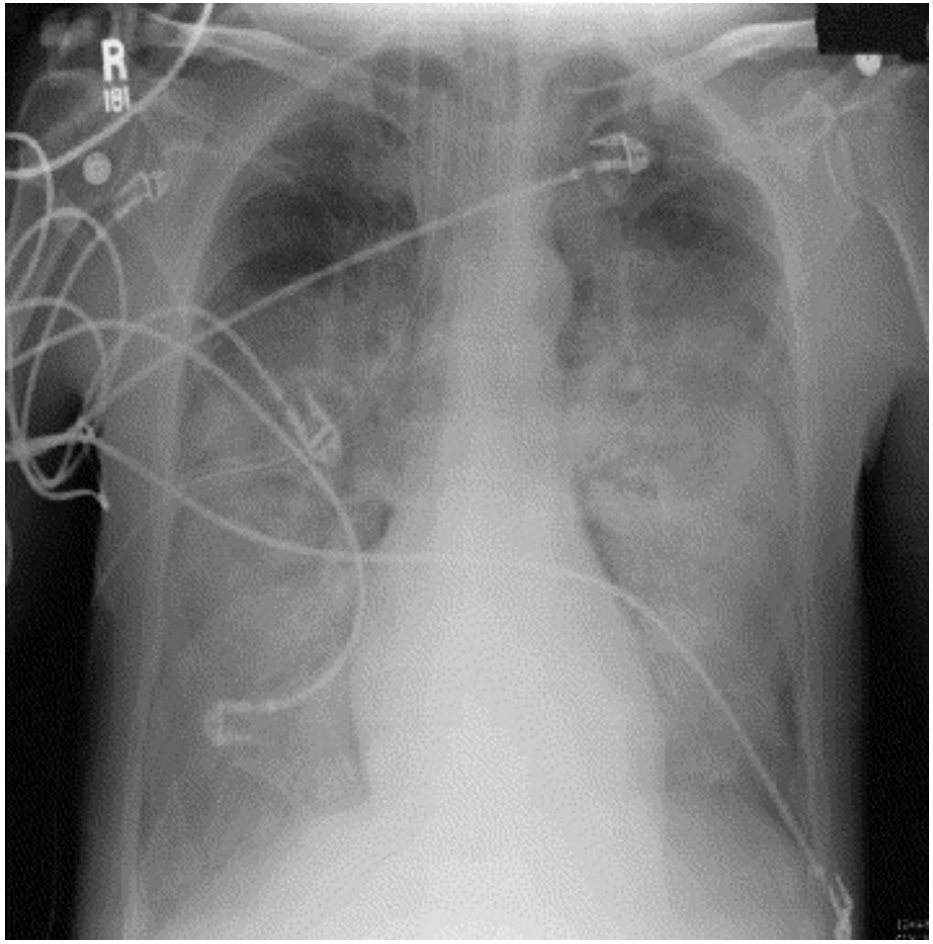
Réponse immunitaire cellulaire
Interaction Leucocytes / endothélium



- Sur-expression de P-selectine endothéliale
- Séquestration pulmonaire +++

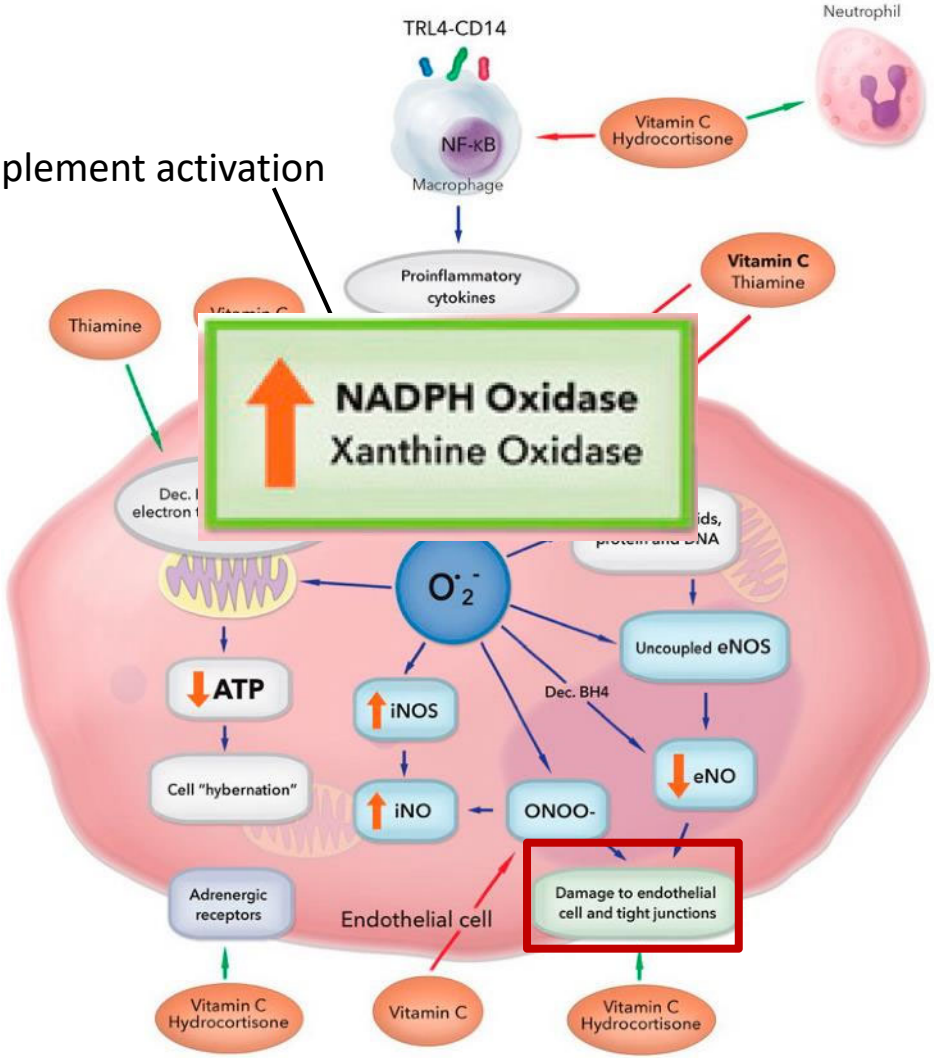


Alexander P J Vlaar APJ et al. Lancet 2013; 382: 984–94


R

Stress oxydatif
Production de radicaux libre de l'oxygène

Complement activation



O2° anion superoxyde
ONOO° peroxyntrite
OH° radical hydroxyle

Cellules endothéliales et immunocompétentes (monocytes…)

Wang W et al. Am J Resp Crit Care Med 1994;150:1449-52

Oxidative stress during extracorporeal circulation

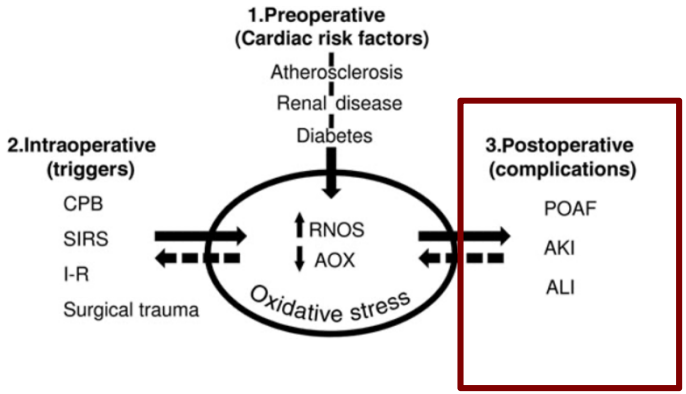
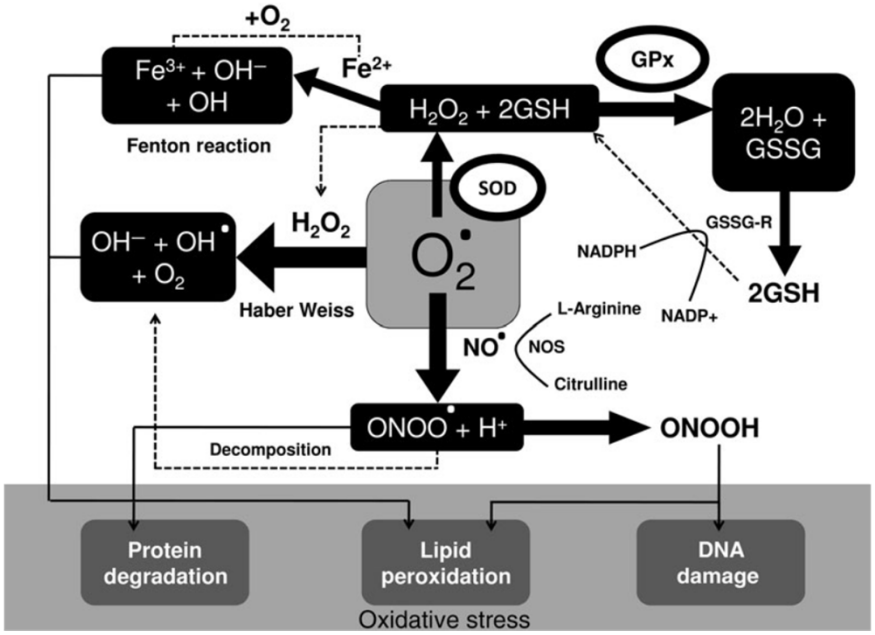
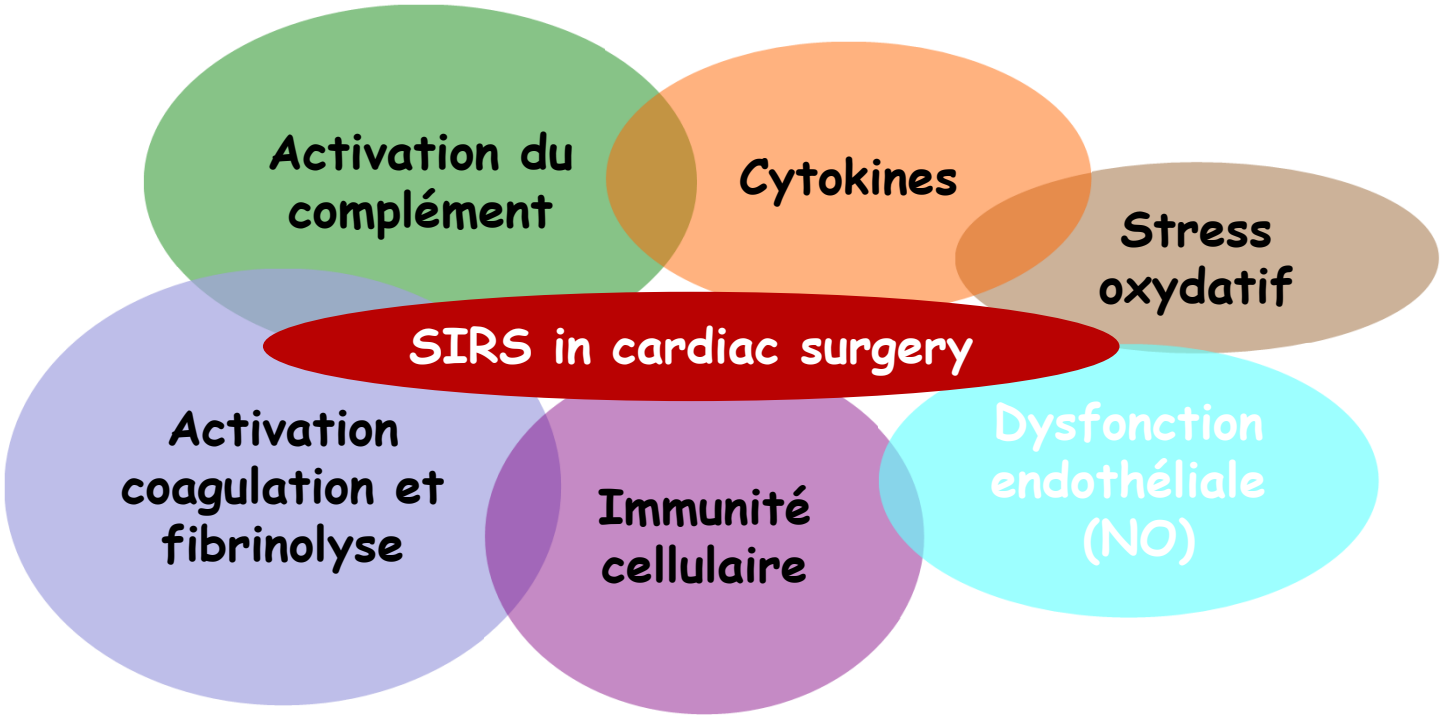


Table 1: Potential triggers for increased RNOS generation during ECMO

Potential triggers for increased RNOS generation during ECMO
Exposure to ECC (ECMO circuits [42], dialysis [5])
SIRS syndrome [43]
Acute respiratory distress syndrome [16]
Hyperoxia [26]
Mechanical ventilation [44]
Sepsis [45]
Ischaemia-reperfusion [46]
Transfusion [27, 28]
Sequestration of antioxidant trace elements by the ECMO circuit [19]



Mc Donald CI et al. Eur J Cardiothorac Surg 2014;46:937-43


Activation du complément
Cytokines
Stress oxydatif
SIRS in cardiac surgery
Activation coagulation et fibrinolyse
Immunité cellulaire
Dysfonction endothéliale (NO)

Réaction inflammatoire systémique et chirurgie cardiaque

Constante!

Expression biologique et clinique variables…

(CRP, hyperleucocytose, hyperfibrinogénémie, vasoplégie, SDMV…)

Réponses individuelles variables

- Contexte de la chirurgie (urgence, hémorragique, CEC longue…)
- Episodes d'hypoperfusion d'organes (conduite optimale+++)
- Prédisposition génétique (???)

Polymorphisme génétique et CEC

Balance Pro- & Anti-inflammatoire

Polymorphisme du gène pour fraction du complément

1. **Chirurgie des cardiopathies congénitales**
2. **Syndrome de fuite capillaire post-CEC accentué chez enfants homozygotes C4A00**

Zhang S, Anesthesiology 2004; 100: 944-9

Polymorphisme génétique et CEC

Balance Pro-& Anti-inflammatoire

Polymorphisme du gène du TNFα

1.1. Génotypes :

- **Forme commune : TNF1**
- **Forme plus rare : TNF2 (surproduction+++)**

1.2. Majoration production TNF

- **Augmentation de lactatémie**

Ryan T, Ann Thorac Surg 2002; 73: 1905-9

- **Fréquence accrue des dysfonctions VG**
- **Fréquence des défaillances pulmonaires postopératoires**

Tomasdottir H, Anesth Analg 2003; 97: 944-9

Polymorphisme des gènes de la famille des interleukines (IL)

1. **Libération accrue IL10 en post-CEC**

Galley HF, Br J Anaesth 2003; 91 :424-6

2. **ACFA après chirurgie cardiaque sous CEC**

Gaudino M, Circulation 2003; 108 Suppl 1: II 195-9

Quelle(s) mesure(s) pour limiter le syndrome inflammatoire au cours de la chirurgie cardiaque?

Facteurs influençant la réponse inflammatoire

- Altération de la fonction ventriculaire gauche
- Patient diabétique
- Instabilité hémodynamique (via hypoperfusion mésentérique)
- Relation entre hypoperfusion splanchnique et SDRA postopératoire
- pH gastrique intra-muqueux prédictif de complication postopératoire
- Effet bénéfique péridurale
- Stratégie ventilatoire perioperatoire

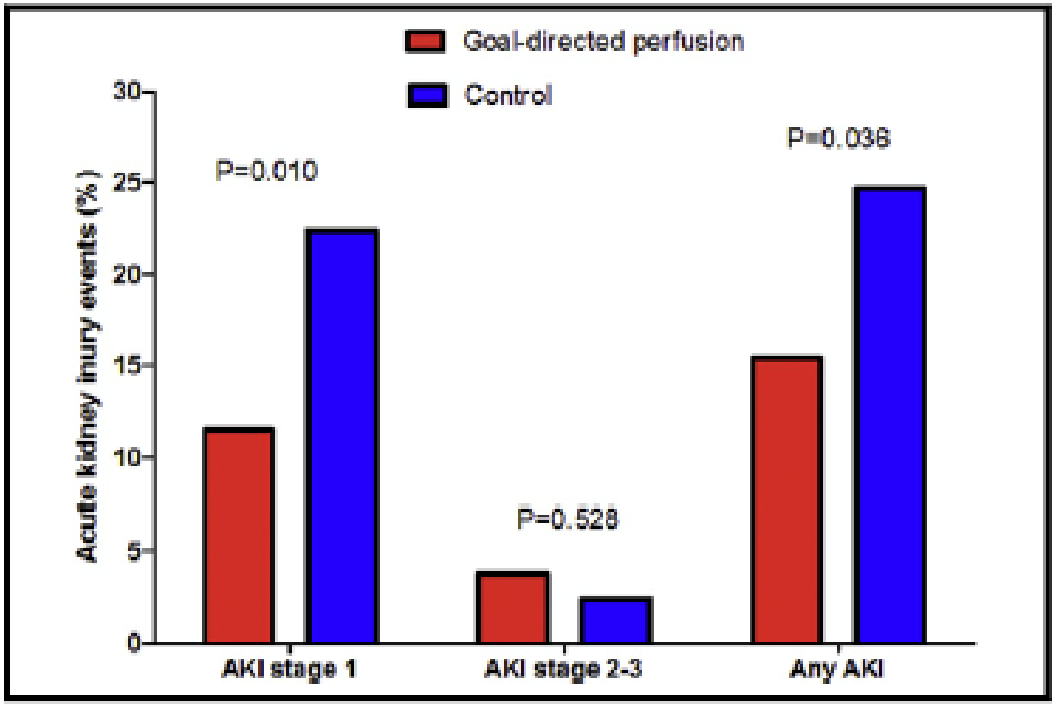
Loick HM et al. Anesth Analg 1999;88:701-9

Fiddian-Green RG et al. Crit Care Med 1987;15:153-6

Goal-directed perfusion to reduce acute kidney injury: A randomized trial

Ranucci M et al. J Thorac Cardiovasc Surg 2018; 156:1918-27

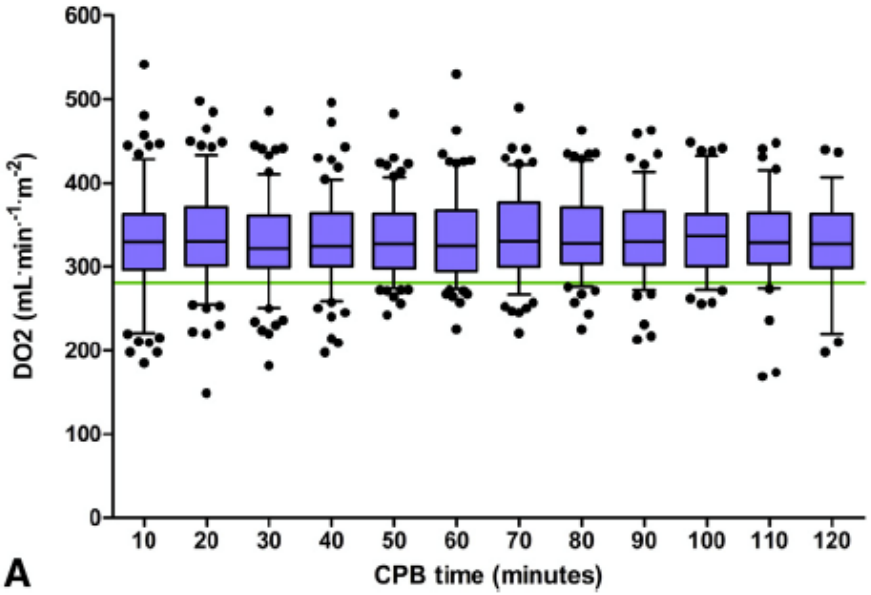
Goal-directed Perfusion was defined as DO_2 > 280 ml.min-1.m-2

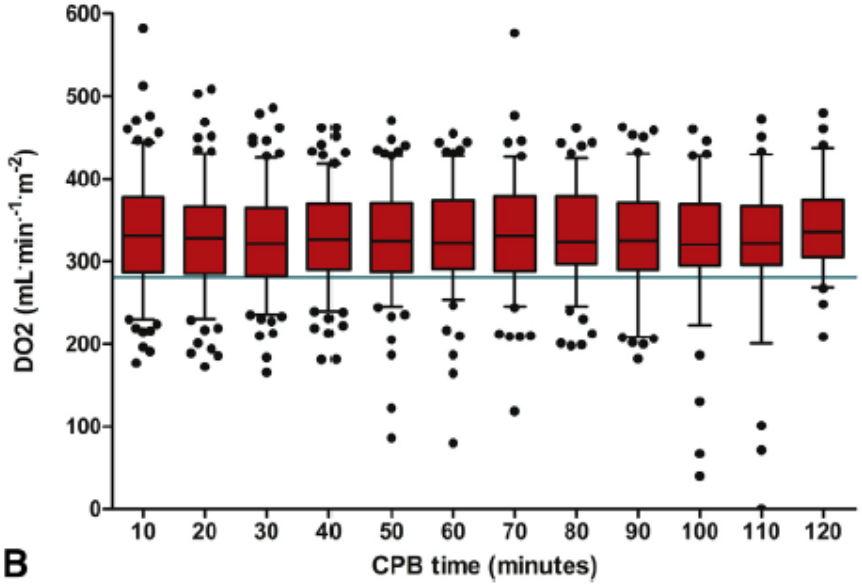


Acute kidney injury in the goal-directed perfusion and control groups.

Goal-directed perfusion to reduce acute kidney injury: A randomized trial

Ranucci M et al. J Thorac Cardiovasc Surg 2018; 156:1918-27





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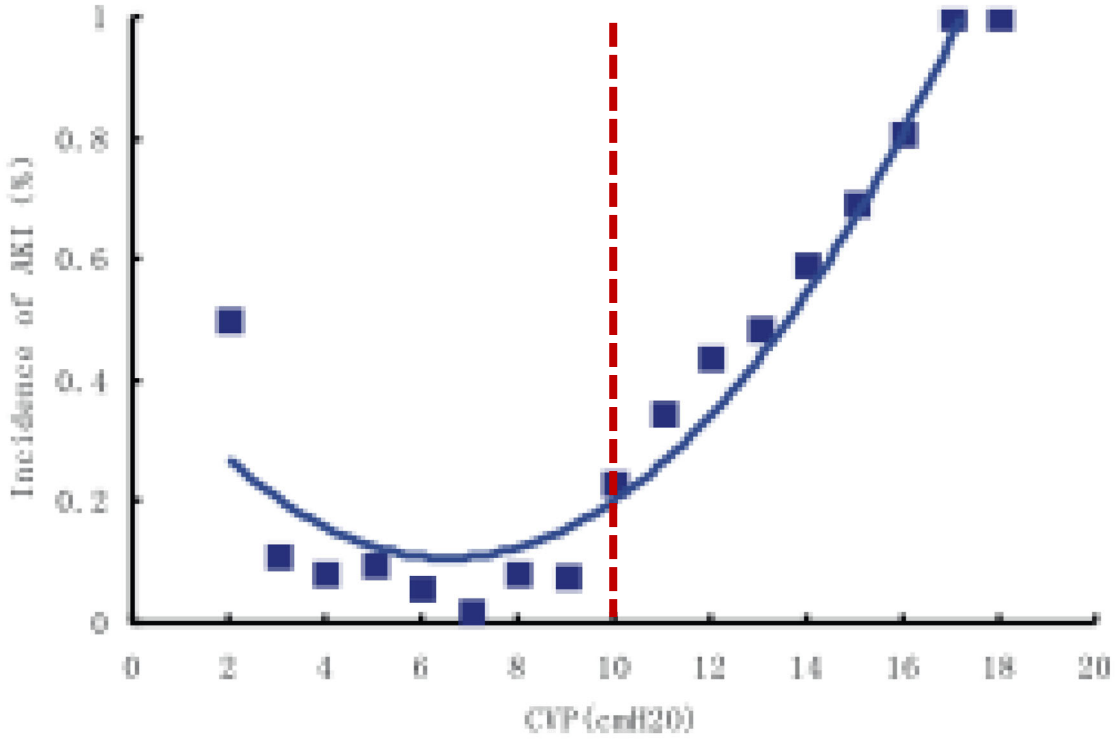
Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

High central venous pressure is associated with acute kidney injury and mortality in patients underwent cardiopulmonary bypass surgery

Yanli Yang *, Jun Ma, Liyun Zhao

Center of Anesethology, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Rd, ChaoYang District, Beijing 100029, China



Yang Y et al. J Crit Care 2018; 48:211-5

Acute Kidney Injury in different CVP groups.

Variables	Low CVP Group (n %) (CVP < 10 cmH_2O)		High CVP Group (n %) (CVP ≥ 10cmH_2O)		p Value
n	1140		801		
Acute Kidney Injury level					
KDIGO stage 1	63	5.526	275	34.332	<0.0001
KDIGO stage 2	11	0.964	46	5.742	<0.0001
KDIGO stage3	12	1.052	26	0.312	<0.0001
Total AKI	86	7.543	347	43.32	<0.0001
CRRT	5	0.438	18	2.247	<0.0001

AKI = Acute Kidney Injury; CRRT = continuous renal replacement therapy; KDIGO = Kidney Disease Improving Global Outcomes; sCR = serum creatinine.

Factors Associated With Mortality in Multivariate Analysis.

Variables	Hazard Ratio (95% CI)	Wald Statistic	P Value
Age	1.016 (1.001–1.035)	2.724	0.009
CVP	1.196 (1.114–1.285)	24.209	<0.0001
CAD	1.050 (1.275–2.325)	8.712	0.003
CPB	1.003 (1.001–1.005)	10.441	0.001
Blood plasma	1.001(1.000–1.003)	56.441	<0.0001

CI = confidence interval; CVP = central venous pressure; CAD = Coronary artery disease; CPB = cardiopulmonary bypass.

Yang Y et al. J Crit Care 2018; 48:211-5

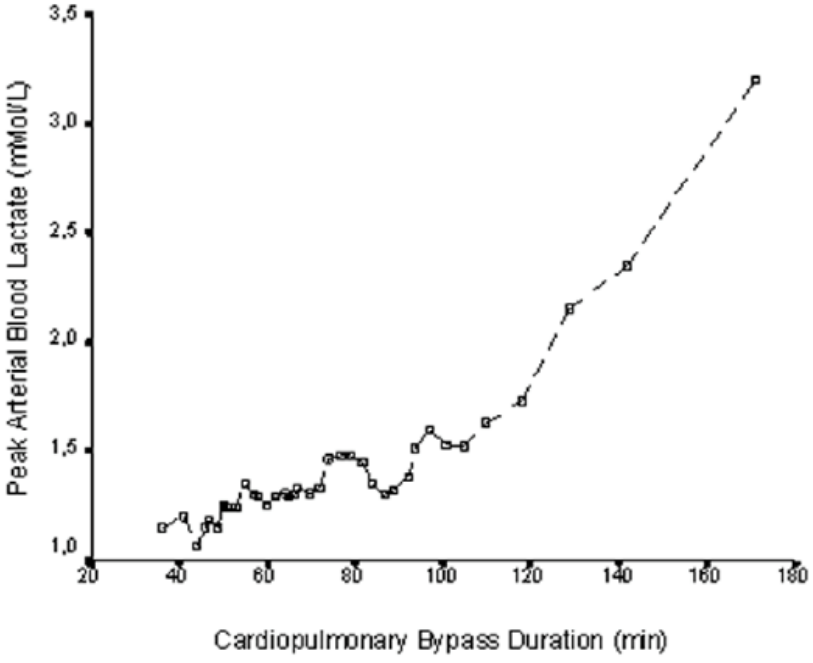
Research

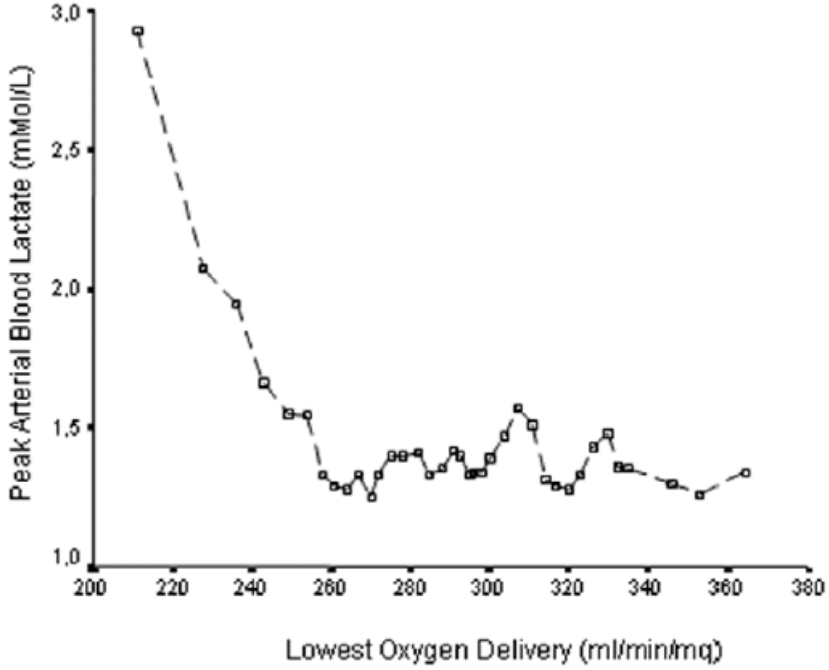
Open Access

Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome

Marco Ranucci, Barbara De Toffol, Giuseppe Isgrò, Federica Romitti, Daniela Conti and Maira Vicentini

Critical Care 2006, **10**:R167 (doi:10.1186/cc5113)



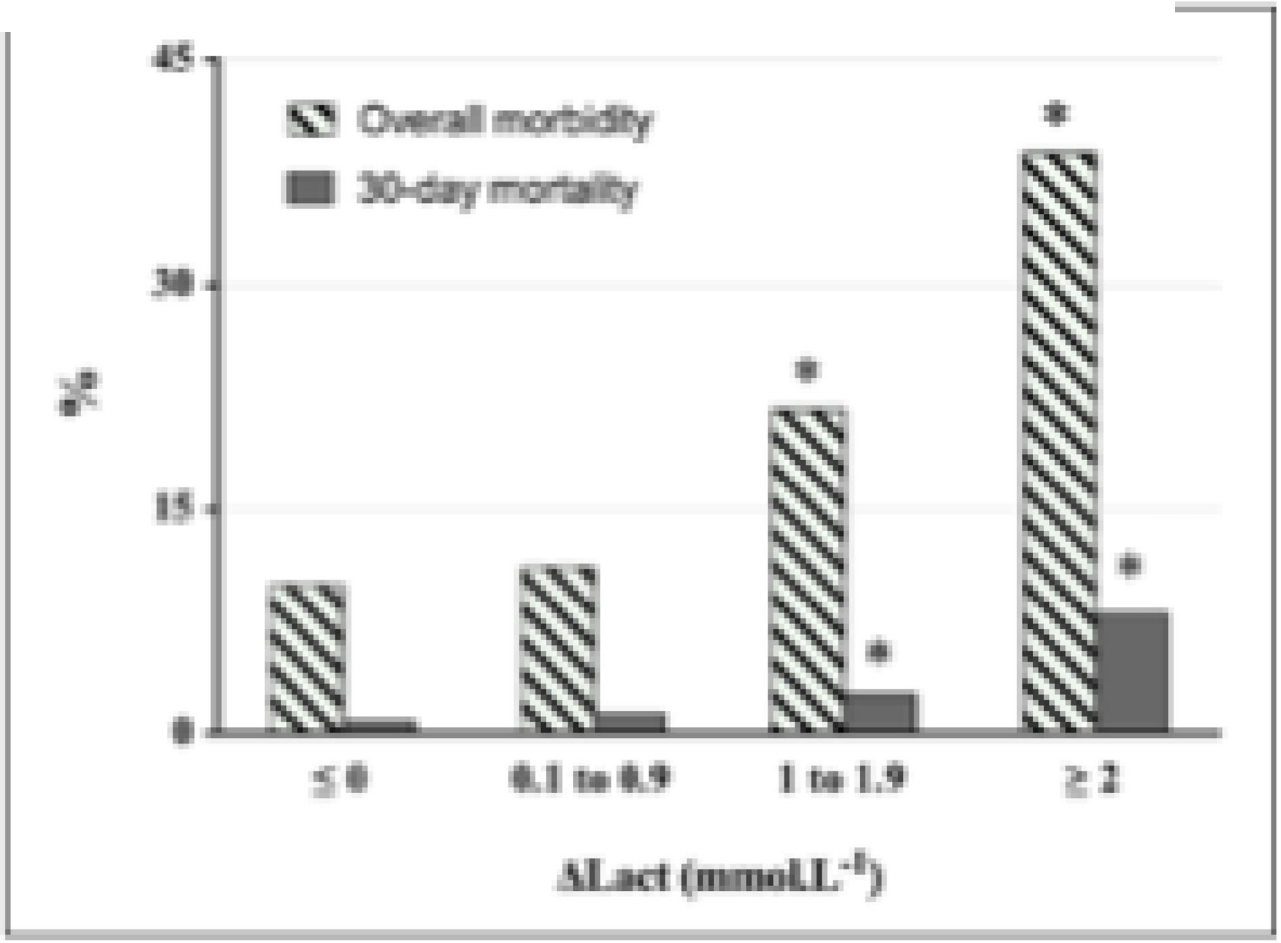


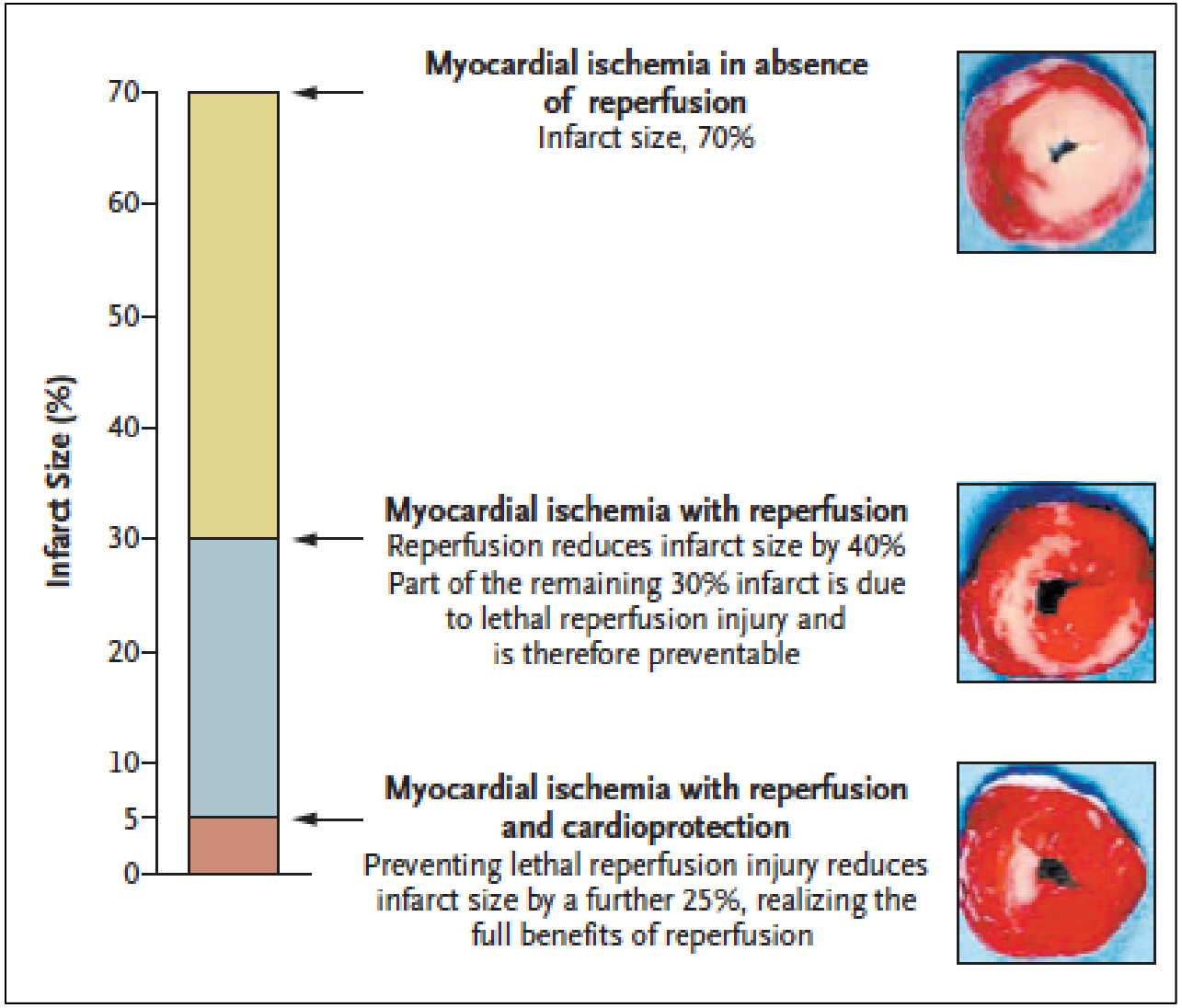
Intraoperative changes in blood lactate levels are associated with worse short-term outcomes after

Perfusion
2019, Vol. 34(8) 640–650

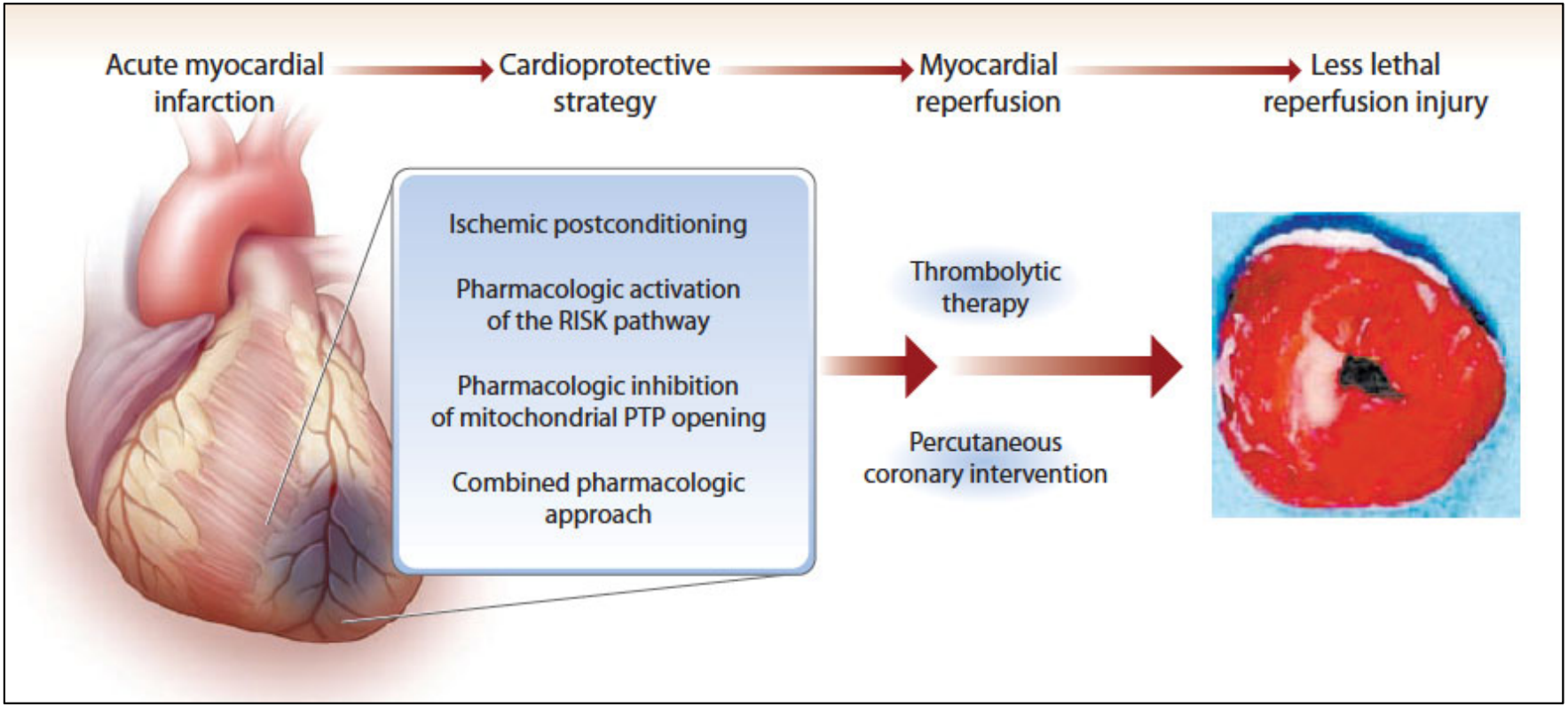
DOI: 10.1177/0267659119855857

Benoit Duval,[1,2] Thibaud Besnard,[1,2] Stefano Mion,[1,2] Sébastien Leuillet,[3] Olivier Jecker,[4] Louis Labrousse,[5] Alain Rémy,[1] Cedrick Zaouter[1] and Alexandre Ouattara[1,2]





Yellon DM et al. N Engl J Med 2007;357:1121-35



Yellon DM et al. N Engl J Med 2007;357:1121-35

Agents médicamenteux et syndrome inflammatoire

- Propofol ↗ IL-10, IL-1ra, ↘ IL-8 (+scavenger des RL)
- Fentanyl ↗ IL-1ra
- Midazolam ↘ accumulation IL-8 extracellulaire
- Kétamine ↗ IL6
- Halogénés ↘ IL-1b, TNF a
- Transfusion homologue ↗
- Xénon (organo-protection)
- Héparine – Protamine : complexe non covalent (C4a, CRP)
- Aprotinine (effet anti-protéase) ↘ cytokines pro-inflammatoires

Circulation extra-corporelle…

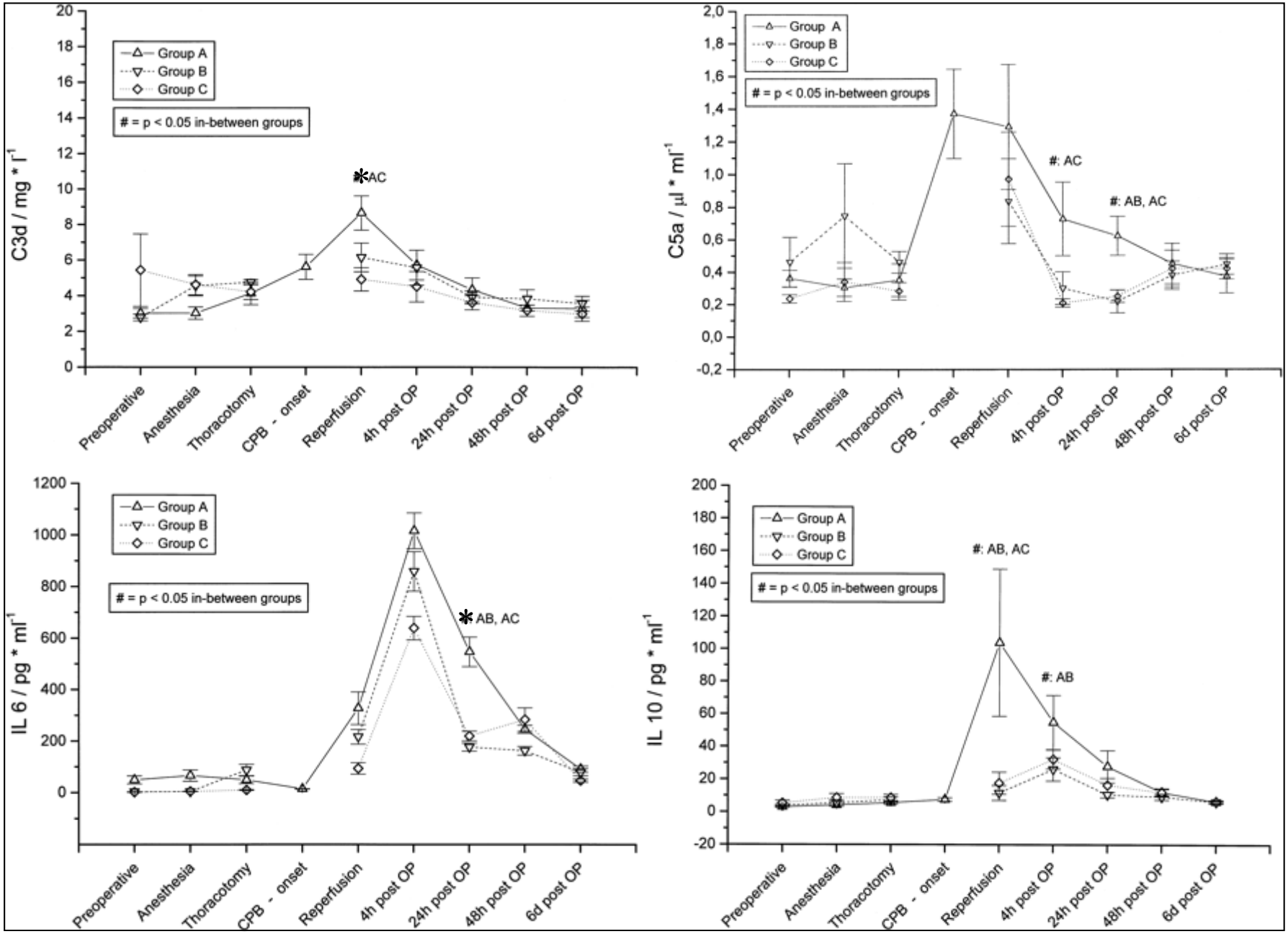
- Sans CEC…(traumatisme chirurgical…)
- Limiter hémodilution
- Iimiter hypoperfusion d'organes (???)
- Circulation extra-corporelle biocompatible
  - Réservoir souple (interface air/sang)
  - Circuit pré-traités (héparine, phosphorylcholine…)
  - Gestion des aspirations
- Pulsatilité?
- Température de perfusion

Humoral Immune Response During Coronary Artery Bypass Grafting. A Comparison of Limited Approach, « Off-Pump » Technique, and Conventional CPB

Pontage aorto-coronaire

- Groupe A: sternotomie + CEC (n = 10)
- Groupe B: sternotomie sans CEC (n = 10)
- Groupe C: mini-thoracotomie sans CEC (n = 10)

Anno Diegeler et al, Circulation 2000; 102:III-95



Anno Diegeler et al, Circulation 2000; 102: III-95

Pulsatile Versus Nonpulsatile Cardiopulonary Bypass Flow: An Evidence-Based Approach

Abdullah A. Alghamdi, M.D, and David A. Latter, M.D
Division of Cardiac Surgery, Department of Surgery, Universitu of Toronto, Toronto, Ontario, Canada *(J Cardio Surg 2006; 21:347-54)*

"Conclusion: The evidence is conflicting and therefore does not support making recommendation for or against routinely providing the PP to reduce the incidence of mortality or MI. The evidence is insufficient to recommend for or against routinely providing the pulsatile profusion to reduce the incidence of stroke or renal failure."

An Evaluation of the Benefits of Pulsatile versus Nonpulsatile Perfusion during Cardiopulmonary Bypass Procedures in Pediatric and Adult Cardiac Patients

Bingyang Ji and Akif Undar *(ASAIO Journal 2006; 52:357–361)*

«These results clearly suggest that pulsatile flow is superior to no pulsatile flow during and after open-heart surgery in paediatric and adult patients »

QUANTIFICATION OF PULSATILITY : ENERGY EQUIVALENT PRESSURE

- Flow is mainly generated by gradient of energy more than pressure gradient
- Pulsatile flow generates hemodynamic energy into vascular system based on flow and pressure at each cycle
- Equivalent Energy Pressure (EEP) expressed in mmHg
- Total hemodynamic energy (THE) transmitted by pump to periphery is the ratio of total work (pressure X flow) in the vascular bed distal in time to volume of blood which passed in the same time (flow)
- In steady blood flow, EEP = MAP
- The difference in EEP and MAP represents the energy in flow secondary to pulsatile property = Surplus Hemodynamic Energy.

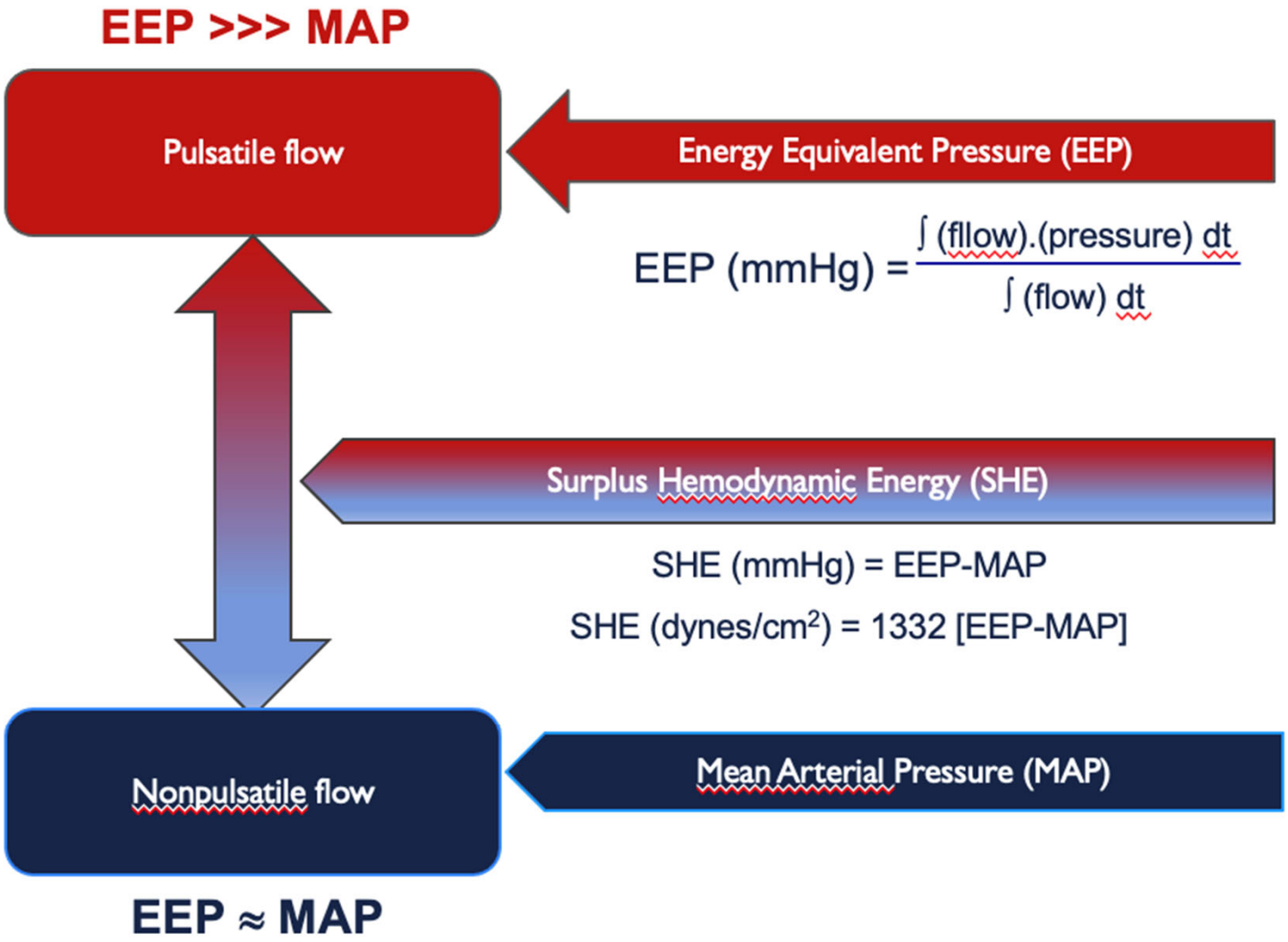
$$EEP\ (mmHg) = \frac{\int (flow).(pressure)\ dt^{*}}{\int (flow)\ dt^{**}}$$

* Area under hemodynamic power curve

**Area under pump flow curve

$$SHE\ (ergs/cm3) = 1332\ X(EEP-MAP)$$

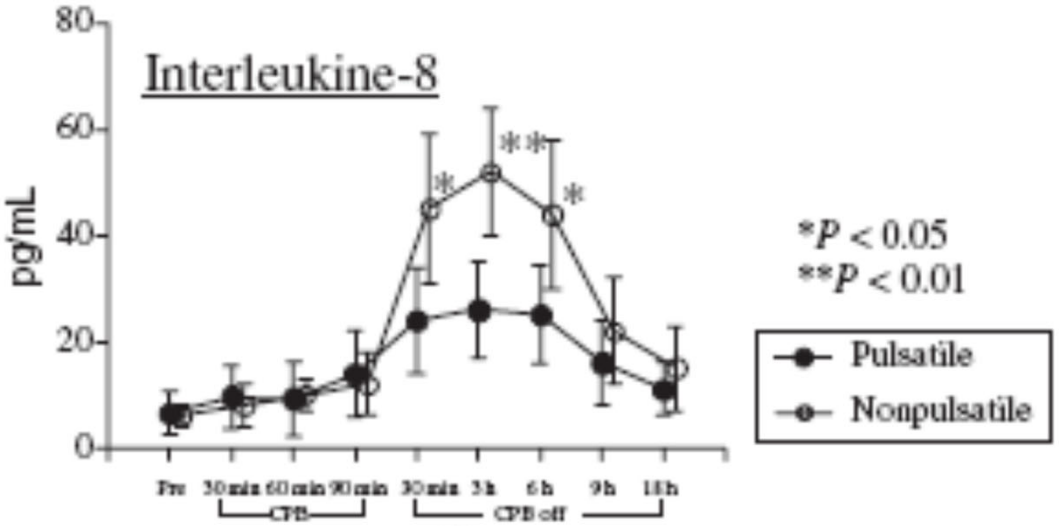
Shepard RB et al. Arch Surg 1966;93:730-40
Wang S et al. JECT 2009;41:P20-P25

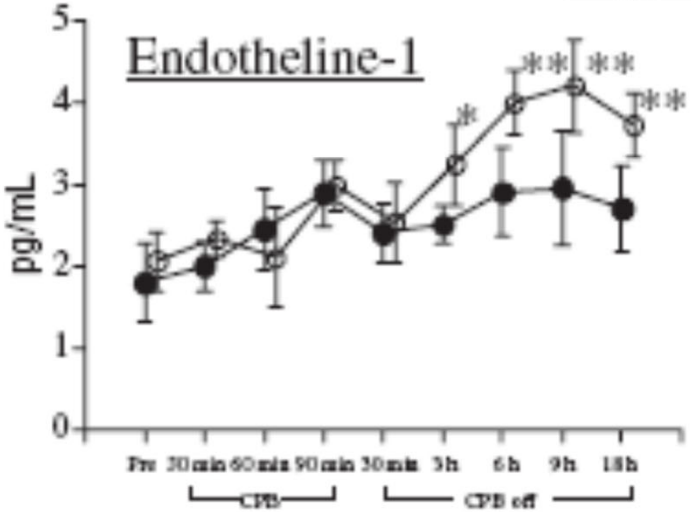

EEP >>> MAP
Pulsatile flow
Energy Equivalent Pressure (EEP)
EEP (mmHg) = ∫ (fllow).(pressure) dt / ∫ (flow) dt
Surplus Hemodynamic Energy (SHE)
SHE (mmHg) = EEP-MAP
SHE (dynes/cm2) = 1332 [EEP-MAP]
Nonpulsatile flow
Mean Arterial Pressure (MAP)
EEP ≈ MAP

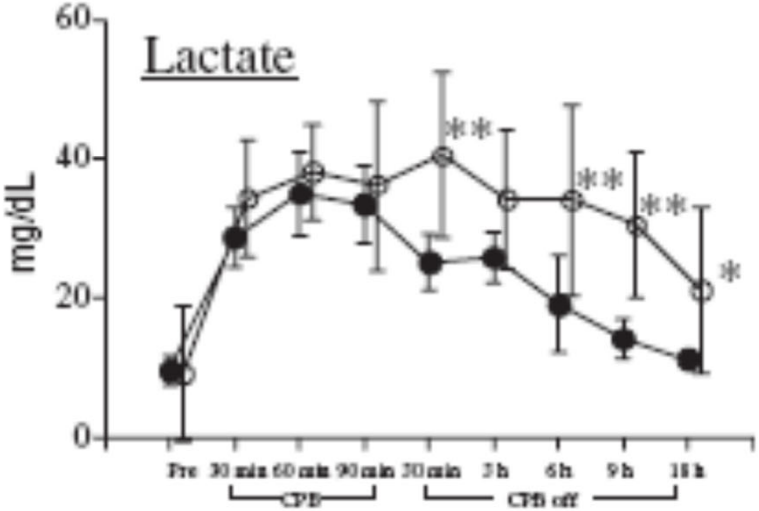
Aspects microcirculatoires
Inflammation et dommage endothélial

Sezai *et al* Artif Organs 2005;29:708

- **Pontages aorto-coronariens**
- **Pas de différence en hémolyse**
- **Amélioration de l'index respiratoire avec CEC pulsatile**

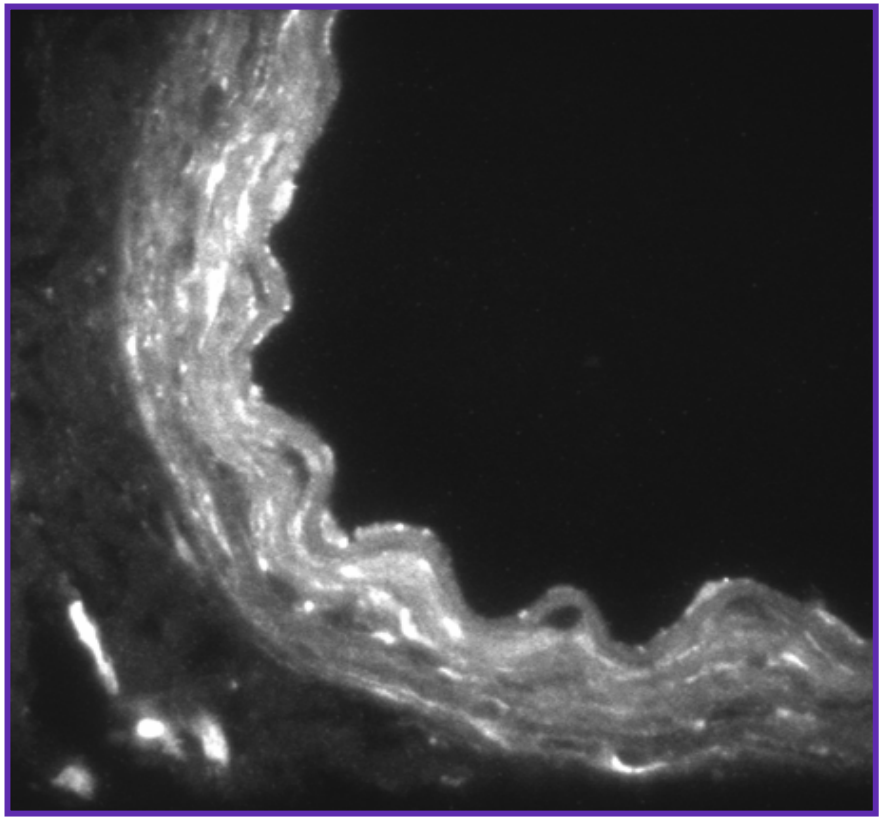






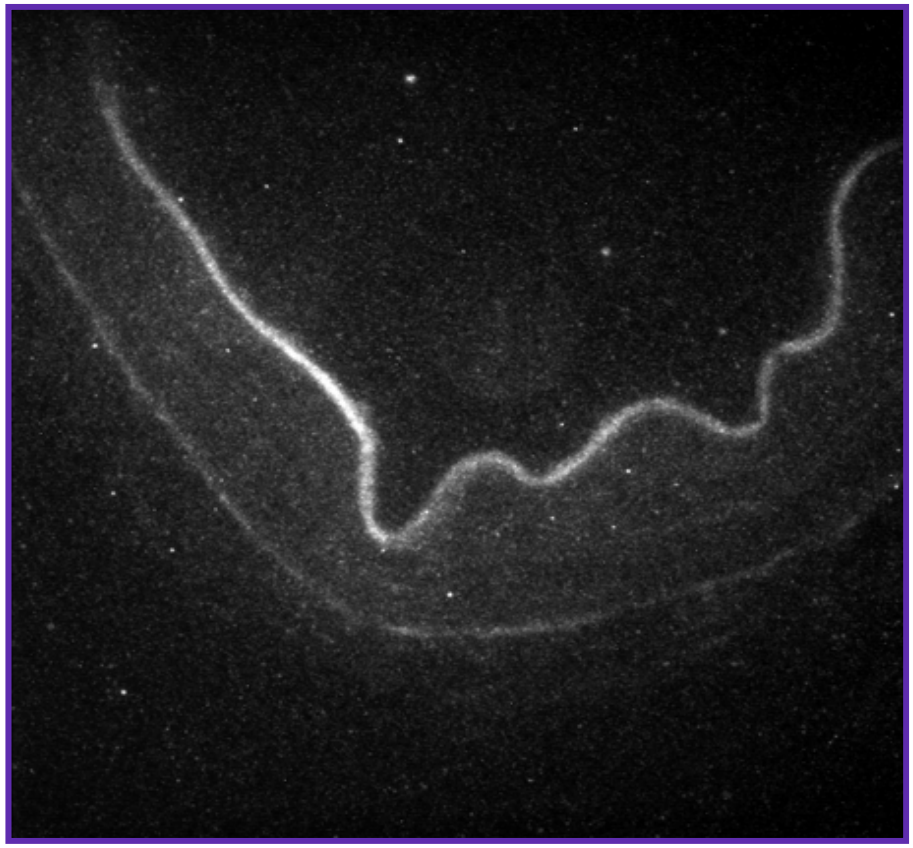
Molécules d'adhésion (MCP-1)

Pulsé

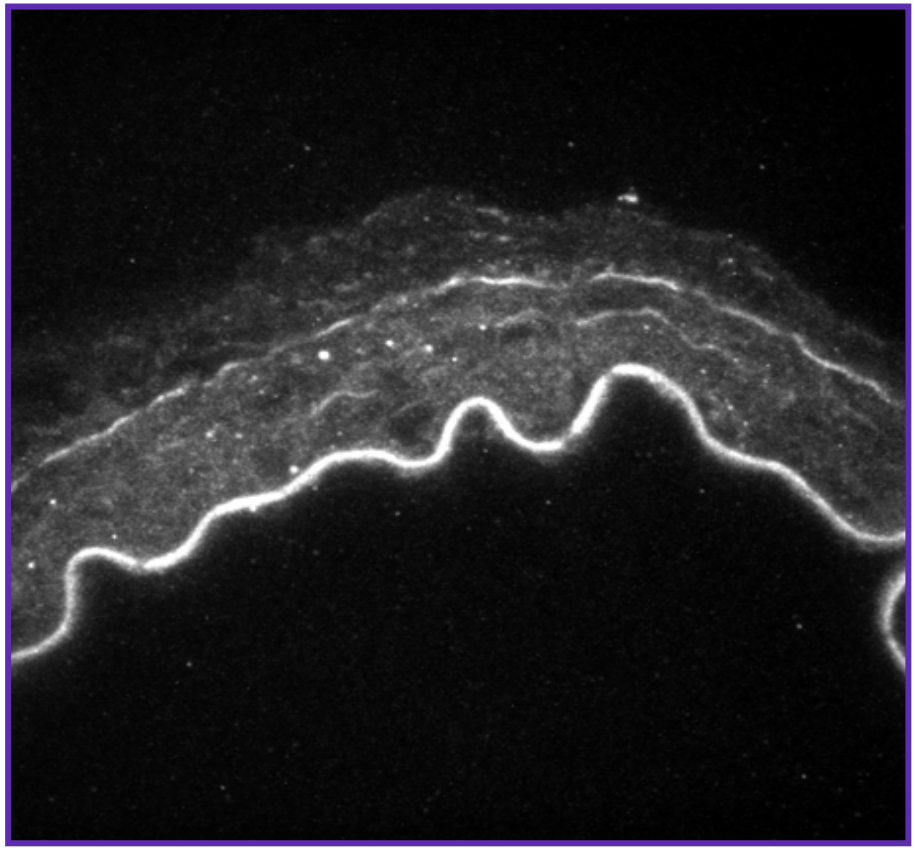


Non Pulsé

iNOS



Pulsé

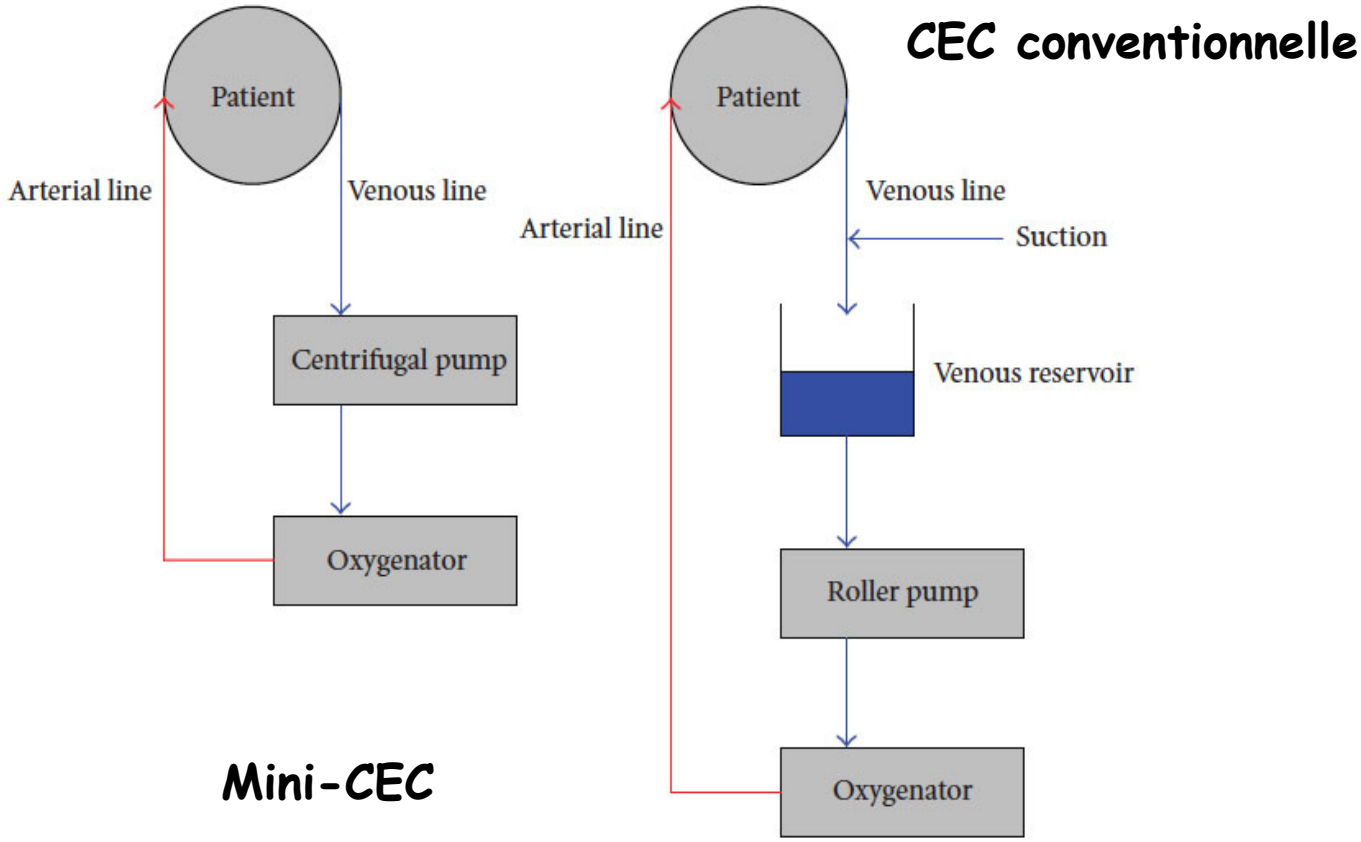


Non Pulsé

Review Article

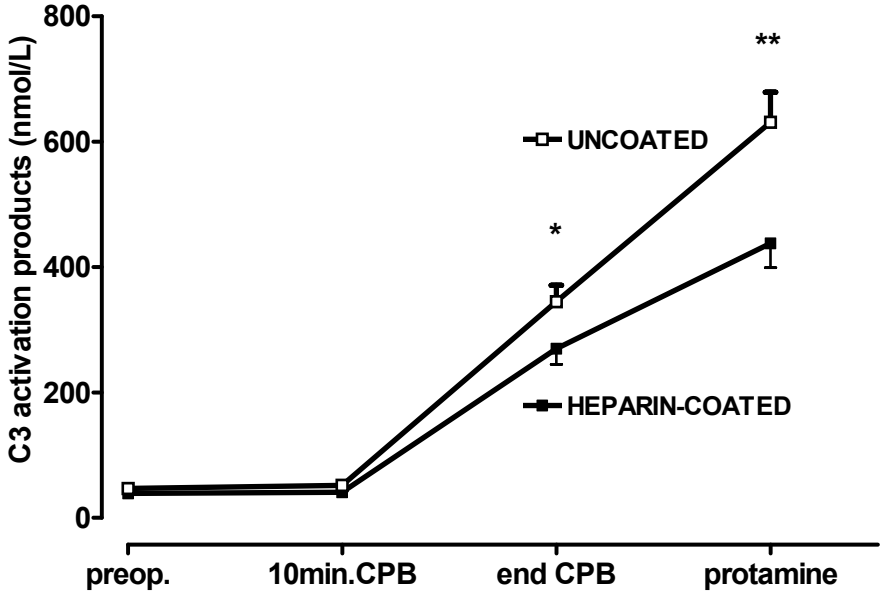
The Inflammatory Response to Miniaturised Extracorporeal Circulation: A Review of the Literature

Hunaid A. Vohra, Robert Whistance, Amit Modi, and Sunil K. Ohri

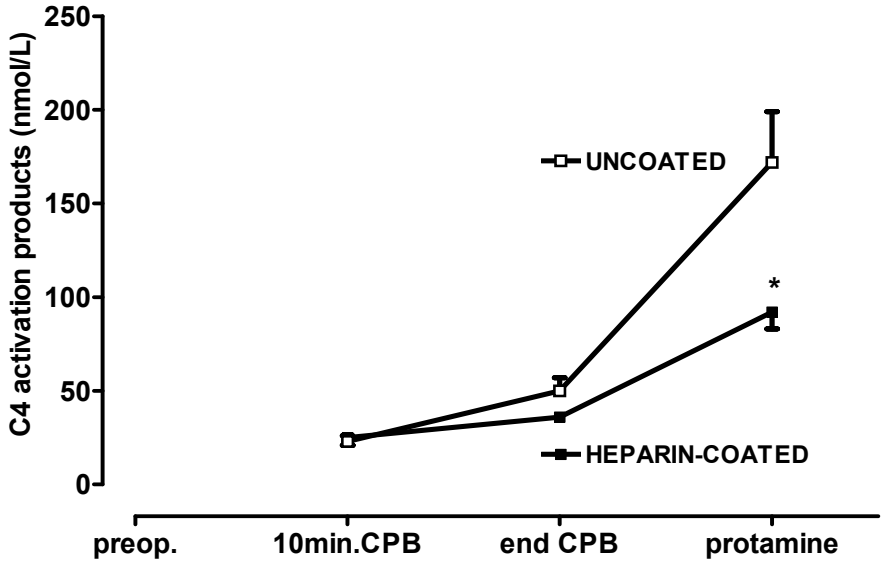


Heparin-coated circuits
preliminary results

Complement activation is reduced by 30 to 50%



Alternative pathway



Classical pathway

Baufreton et al. Ann Thorac Surg 1997;63:50-6.

The Cardiotomy Trial

A Randomized, Double-Blind Study to Assess the Effect of Processing of Shed Blood During Cardiopulmonary Bypass on Transfusion and Neurocognitive Function

Rubens FD et al. Circulation 2007;116 [suppl I]:I-89-97

- Etude prospective randomisée
- Patients bénéficiant d'une chirurgie coronaire isolée non urgente
- CEC à galets (volume d'amorçage 1300 ml) en hypothermie
- Aspirations médiastinales par cell-saver avec retransfusion au travers un filtre à déleucocytation
- Utilisation postopératoire systématique d'un cell-saver jusqu'à H4 (Brat, COBE Cardiovascular Inc)
- Critère de jugement : transfusion de concentrés érythrocytaires et déficit neurocognitive à J5

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

Table 2: Cytokines in cardiotomy suction blood and in the systemic circulation at the same time point ($n = 25$)

	Cardiotomy suction blood	Systemic circulation	*P*-value
IL-1Ra (pg/ml)	312 (88–1534)	82 (32–309)	<0.001
IL-4 (pg/ml)	<2 (<2–7.2)	<2 (<2)	0.43
IL-10 (pg/ml)	19.7 (<2–113)	31 (<2–122)	0.21
IL-6 (pg/ml)	210 (13–2678)	45 (3–1119)	<0.001
TNF-α (pg/ml)	4.3 (<2–40)	2.5 (<2–62)	0.033
IL-6-to-IL-10 ratio	10.2 (1.1–75)	1.7 (0.2–24)	<0.001

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

Table 3: Cytokines in cardiotomy suction blood before and after cell-saver processing (n = 13)

	Before cell salvage	After cell salvage	P-value
IL-1Ra (pg/ml)	260 (88–526)	73 (28–359)	0.002
IL-4 (pg/ml)	<2 (<2)	<2 (<2–3.0)	0.18
IL-10 (pg/ml)	17 (8.4–62)	7 (<2–27)	0.011
IL-6 (pg/ml)	140 (13–2678)	57 (<1–760)	0.10
TNF-α (pg/ml)	4.3 (<2–39)	<2 (<2–15)	0.008

The values represent the median and range.
IL: interleukin; TNF: tumour necrosis factor.

Ann Thorac Surg 2010; 89:1511-7

Cell Saver for On-pump Coronary Operations Reduces Systemic Inflammatory Markers: A Randomized Trial

Sune Damgaard, MD, PhD, Claus H. Nielsen, MD, PhD, Lars W. Andersen, MD, DMSc, Klaus Bendtzen, MD, DMSc, Michael Tvede, MD, and Daniel A. Steinbrüchel, MD, DMSc

Departments of Cardiothoracic Surgery, Anesthesiology, Clinical Microbiology and the Institute for Inflammation Research, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

Table 2. Concentrations of Inflammatory Markers

			Cross-clamp		After Cardiopulmonary Bypass				
Marker	Group	Induction	Before	After	5 Minutes	6 Hours[a]	24 Hours	72 Hours	Interactive
Median (IQR) pg/mL									
IL-6	Cell saver	0 (0–5)	0 (0–6)	13 (4–31)	38 (13–67)	112 (66–168)	89 (45–153)	38 (17–84)	0.021
	Control	0 (0–0)	3 (0–8)	17 (7–59)	51 (29–116)	228 (142–331)	90 (44–190)	44 (29–64)	
IL-8	Cell saver	6 (5–8)	6 (4–11)	15 (7–34)	17 (10–40)	23 (17–36)	17 (11–31)	11 (7–42)	0.058
	Control	7 (3–9)	8 (6–11)	23 (15–38)	28 (24–46)	42 (25–68)	18 (13–31)	18 (10–26)	
IL-10	Cell saver	0 (0–1)	0 (0–2)	6 (0–9)	9 (4–19)	2 (0–2)	0 (0–3)	0 (0–3)	0.530
	Control	0 (0–2)	1 (0–3)	7 (4–12)	10 (8–22)	3 (2–8)	3 (1–5)	2 (1–3)	
Median (IQR) ng/mL									
sTNF-RI	Cell saver	0.9 (0.8–1.8)	0.7 (0.5–1.1)	1.8 (1.5–2.4)	2.1 (1.5–2.8)	1.9 (1.1–2.7)	1.7 (1.2–2.7)	1.8 (1.5–4.4)	0.158
	Control	1.0 (0.8–1.6)	0.9 (0.5–1.2)	1.9 (1.7–2.5)	2.4 (1.8–2.9)	2.6 (1.2–3.8)	2.0 (1.1–2.9)	2.4 (1.8–4.1)	
sTNF-RII	Cell saver	2.5 (1.5–2.9)	1.6 (1.0–2.0)	3.0 (1.6–3.4)	3.0 (2.1–3.8)	3.4 (2.6–4.7)	2.8 (1.6–3.9)	3.1 (2.7–5.8)	0.40
	Control	2.4 (1.6–2.9)	1.5 (1.1–1.9)	2.8 (2.3–3.4)	3.5 (2.7–3.9)	4.4 (2.8–4.9)	3.3 (2.0–4.6)	3.6 (2.7–5.0)	
PCT	Cell saver	0.1 (0.1–0.2)	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.1 (0.1–0.2)	0.2 (0.2–0.6)	0.4 (0.3–1.1)	0.4 (0.2–2.3)	0.472
	Control	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.1 (0.1–0.2)	0.5 (0.3–1.0)	0.7 (0.3–1.4)	0.4 (0.3–0.8)	

Gäbel J et al. Eur J Cardiothorac Surg 2013;44:506-11

IL-6/IL-10

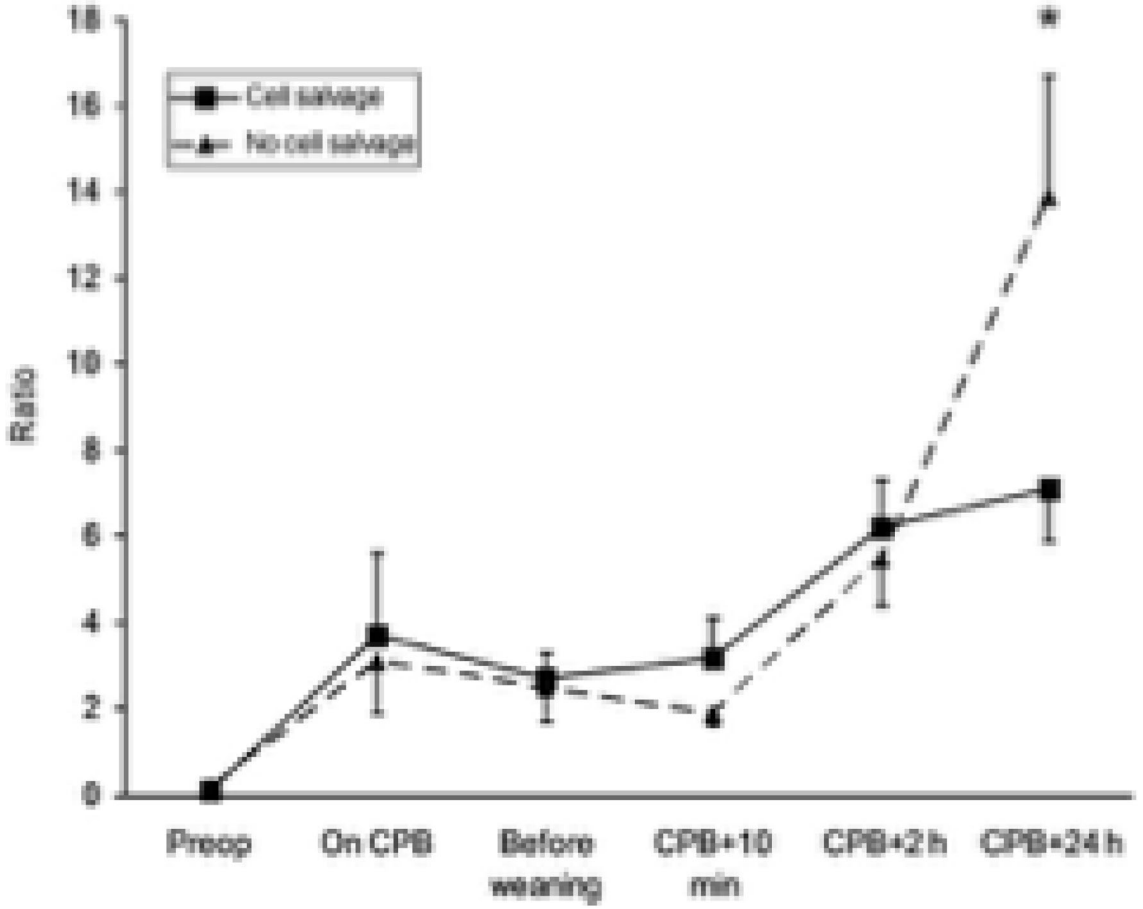


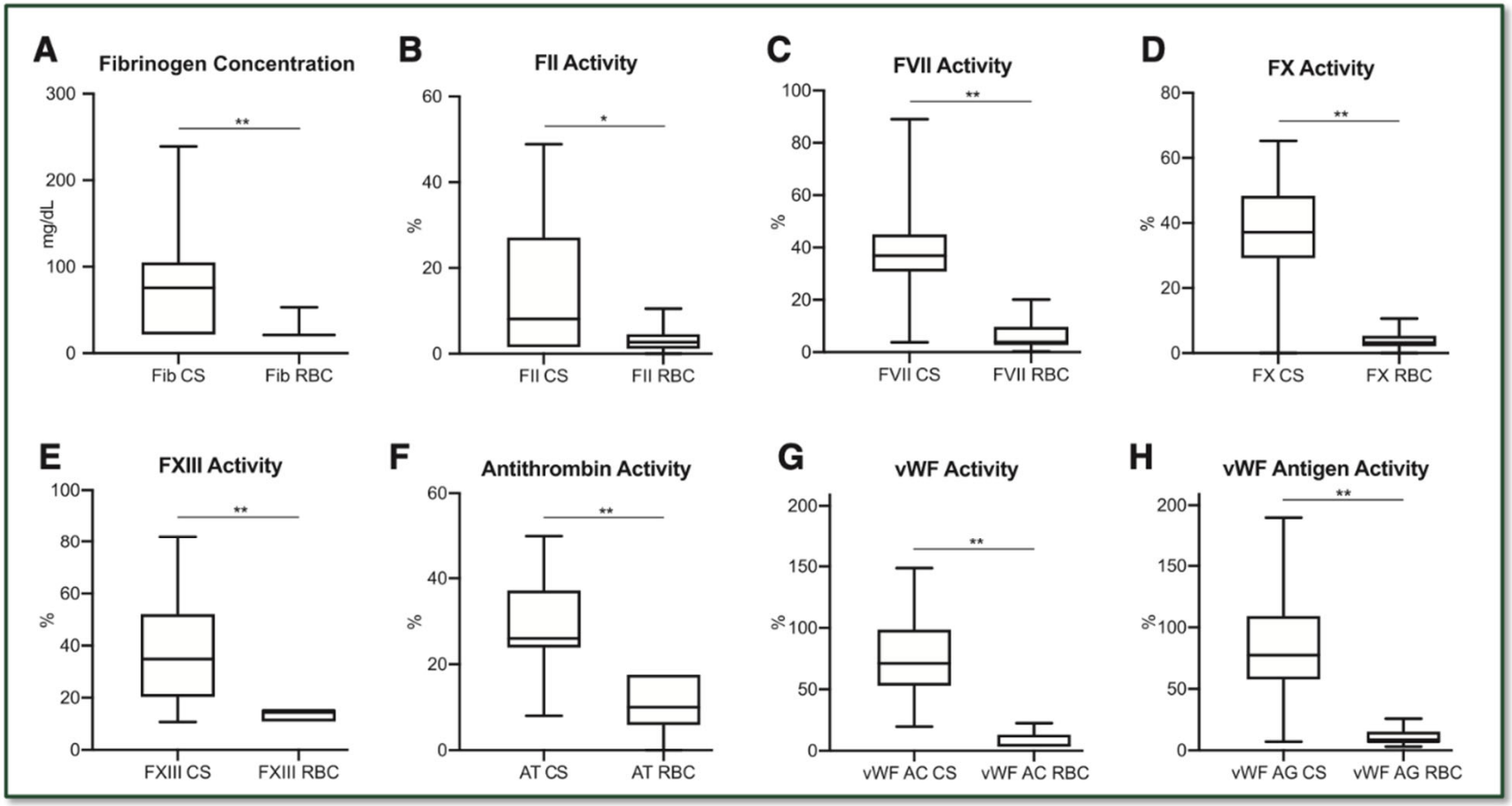
Figure 1: The mean IL-6-to-IL-10 ratio in patients where cardiotomy suction blood was either cell salvaged or not before retransfusion. *$P < 0.05$. The vertical lines represent the standard deviations.

Munoz M et al. Blood Transfus 2011;9:248-61

PERFORMANCES COMPARÉE DES SYSTÈMES

Parameter	Sequestra* (Medtronic)	BRAT 2* (Cobe)	CATS* (Fresenius)	Cell Saver* (Haemonetics)	AUTOLOG* (Medtronic)	OrthoPAT* (Haemonetics)	Colloid ** sedimentation
RBC recovery, %	65 - 76	71 - 93	51 - 87	64 - 94	79	80	90
WBC removal; %	31 - 78	30	45 - 80	22 - 55	78	72	60
PLT removal; %	87 - 93	68	92 - 96	86 - 87	99	88	48
PFHB removal; %	89	63	65 - 95	85 - 93	92	96	53
TP or ALB removal; %	97 - 98	91 - 93	93 - 99	NA	NA	97	76
K^+ removal; %	92	90	90 - 98	91	89	97	NA
Cytokine removal; %	95	95	95	91 - 95	NA	90	70 - 77

Values are minimum – maximum interval. CATS: continuous autotra nsfusion system; RBC: red blood cells; WBC: leucocytes; PLT: platelets; PFHB: plasma free haemoglobin; TP: total protein; ALB: albumin. NA: not assessed. References: * (68-77), ** (51).


A
Fibrinogen Concentration
mg/dL
300
200
100
0
**
Fib CS
Fib RBC
B
FII Activity
%
60
40
20
0
*
FII CS
FII RBC
C
FVII Activity
%
100
80
60
40
20
0
**
FVII CS
FVII RBC
D
FX Activity
%
80
60
40
20
0
**
FX CS
FX RBC
E
FXIII Activity
%
100
80
60
40
20
0
**
FXIII CS
FXIII RBC
F
Antithrombin Activity
%
60
40
20
0
**
AT CS
AT RBC
G
vWF Activity
%
200
150
100
50
0
**
vWF AC CS
vWF AC RBC
H
vWF Antigen Activity
%
200
150
100
50
0
**
vWF AG CS
vWF AG RBC

Best Practice & Research Clinical Anaesthesiology 29 (2015) 381–395

Contents lists available at ScienceDirect

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

Perioperative ventilatory strategies in cardiac surgery

François Lellouche, M.D., Ph.D., Professeur Agrégé [a, *],
Mathieu Delorme, PT, MSc [a, b],
Jean Bussières, MD, FRCPC, DABA, PTEBC, Professeur Agrégé [a],
Alexandre Ouattara, M.D., Ph.D., Professeur Agrégé [b]

IMMUNE DYSFUNCTION AFTER CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS: BENEFICIAL EFFECTS OF MAINTAINING MECHANICAL VENTILATION

Gaudriot B et al. Shock 2015; 44:228-33

Patients de plus de 18 ans

Chirurgie coronaire et/ou valvulaire

Anesthésie (Propofol/sufentanil/atracurium)

Ventilation mécanique pré et post-CEC

(VAC 8 ml.kg^{-1} PIT, FR 10-15 rpm, PEEP 5 cmH_2O, FiO_2 50%)

Ventilation perCEC:

✓Pas de ventilation. Déconnexion du respirateur

✓VAC 2,5 ml.kg^{-1} PIT PEEP 5 cmH_2O FR 8-10 rpm

Critères de jugement

✓PaO2/FiO2 avant et 3 heures après CEC

✓Expression HLA-DR et monocytes CD14+ HLA-DRlo/j

✓TNF alpha et IL-10

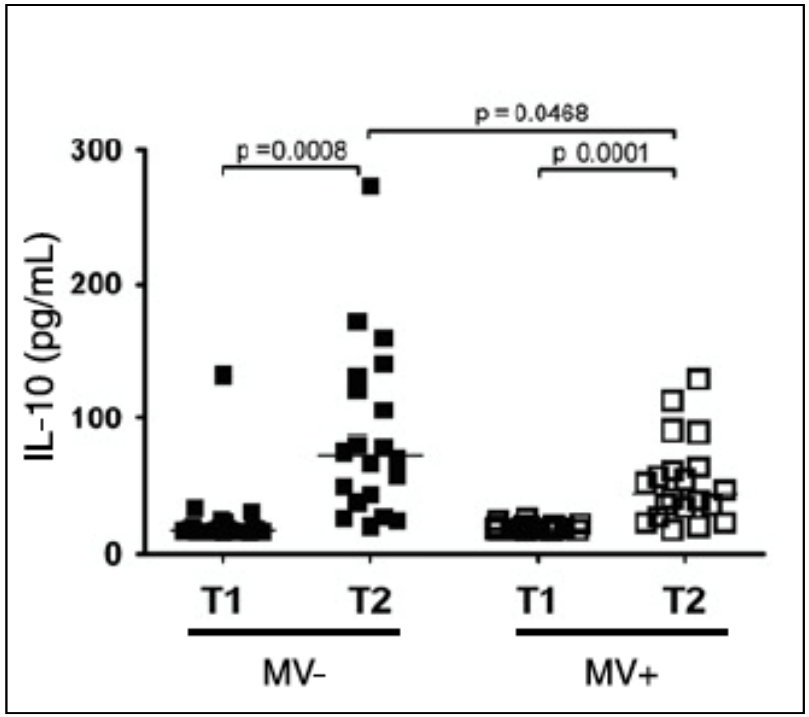
Avant et dans l'heure qui suit l'intervention

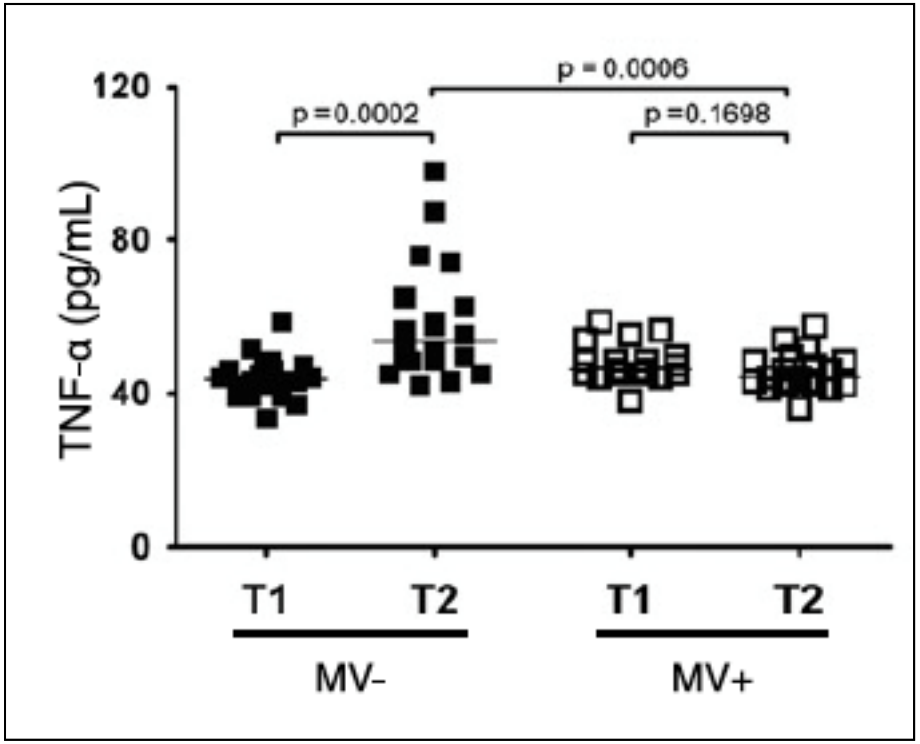
TABLE 1. **Baseline characteristics of patients before CBP**

	MV^- (n = 25)	MV^+ (n = 25)	*P*
Age, y	75 (65–79)	73 (69–80)	0.79
Surgery			
Valvular replacement	17	8	
CABG	5	9	
Mixed (valvular and CABG)	3	8	
BMI, kg/m^2	26 (23–28)	30 (27–33)	0.007
Euroscore II	2.2 (1.4–2.9)	2.3 (1.4–3.3)	0.6
CVP before CPB, mmHg	7 (6–10)	10 (7–12)	0.15
mPAP before CPB, mmHg	23 (20–24)	19 (11–25)	0.28
Pa_{O_2}/F_{IO_2} ratio before CPB	326 (225–381)	240 (173–320)	0.07

TABLE 2. **Effects of MV on outcome and clinical parameters**

	MV^- (n = 25)	MV^+ (n = 25)	*P*
CVP after CPB, mmHg	8 (6–11)	11 (8–12)	0.16
mPAP after CPB, mmHg	19 (18–27)	21 (16–24)	0.74
Pa_{O_2}/F_{IO_2} ratio after CPB	276 (199–360)	242 (211–310)	0.34
CPB duration, min	61 (52–76)	54 (48–68)	0.32
Surgery duration, min	170 (148–210)	150 (139–182)	0.3
ICU stay, d	3 (3–6)	3 (3–5)	0.59
Hospital stay, d	10 (4–16)	10 (4–13)	0.52
Postoperative infections	5 (20%)	2 (8%)	0.5


p = 0.0468
p =0.0008
p 0.0001
300
200
100
0
IL-10 (pg/mL)
T1
T2
T1
T2
MV-
MV+


p = 0.0006
p =0.0002
p =0.1698
120
80
40
0
TNF-α (pg/mL)
T1
T2
T1
T2
MV-
MV+

Reactive oxygen species modulate coronary wall shear stress and endothelial function during hyperglycemia

Stress oxydatif

Eric R. Gross,[1,2,3*] John F. LaDisa, Jr.,[1,3*] Dorothee Weihrauch,[1]
Lars E. Olson,[3] Tobias T. Kress,[1] Douglas A. Hettrick,[1,3]
Paul S. Pagel,[1,3] David C. Warltier,[1,2,3,4] and Judy R. Kersten[1,2]

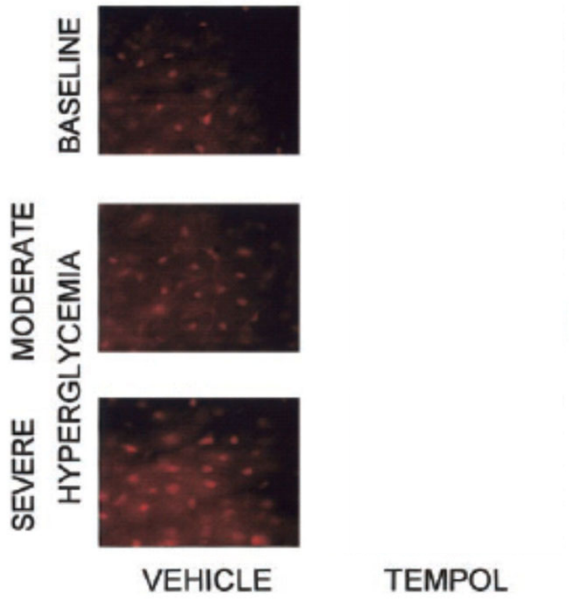
Am J Physiol Heart Circ Physiol 284: H1552–H1559, 2003.

Modèle *in vivo* canin

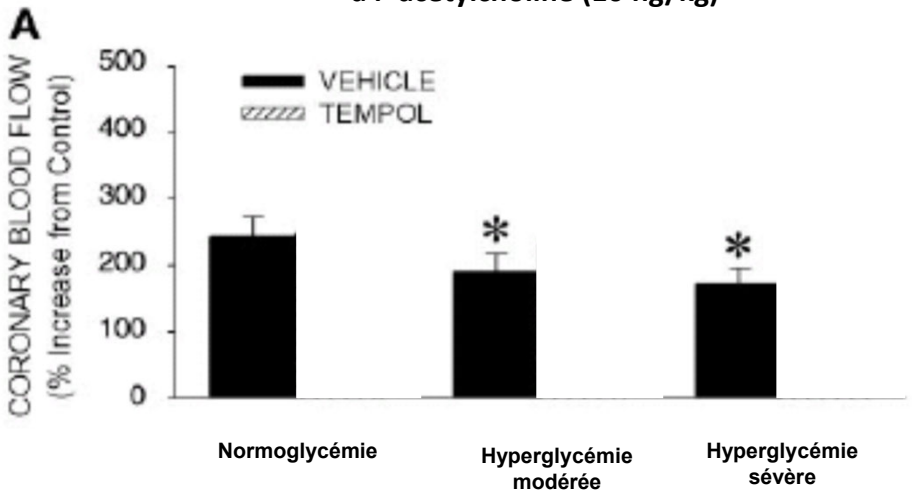
Effets hyperglycémie 350 et 600 mg/dL (Glucose IV) sur production de RL et fonction endothéliale

Antagonisation par le tempol = analogue de la SOD (scavenger des radicaux libres)

Détection par fluorescence des RL dans les biopsies myocardiques



Réponse vasodilatatrice coronaire à l'acétylcholine (10 ng/kg)



Anaesth Crit Care Pain Med 36 (2017) 97–102

SFAR
Société Française d'Anesthésie et de Réanimation

Special article

A special article following the relicence of aprotinin injection in Europe

David Royston [a,*], Stefan De Hert [b], Jan van der Linden [c], Alexandre Ouattara [d,e], Kai Zacharowski [f]

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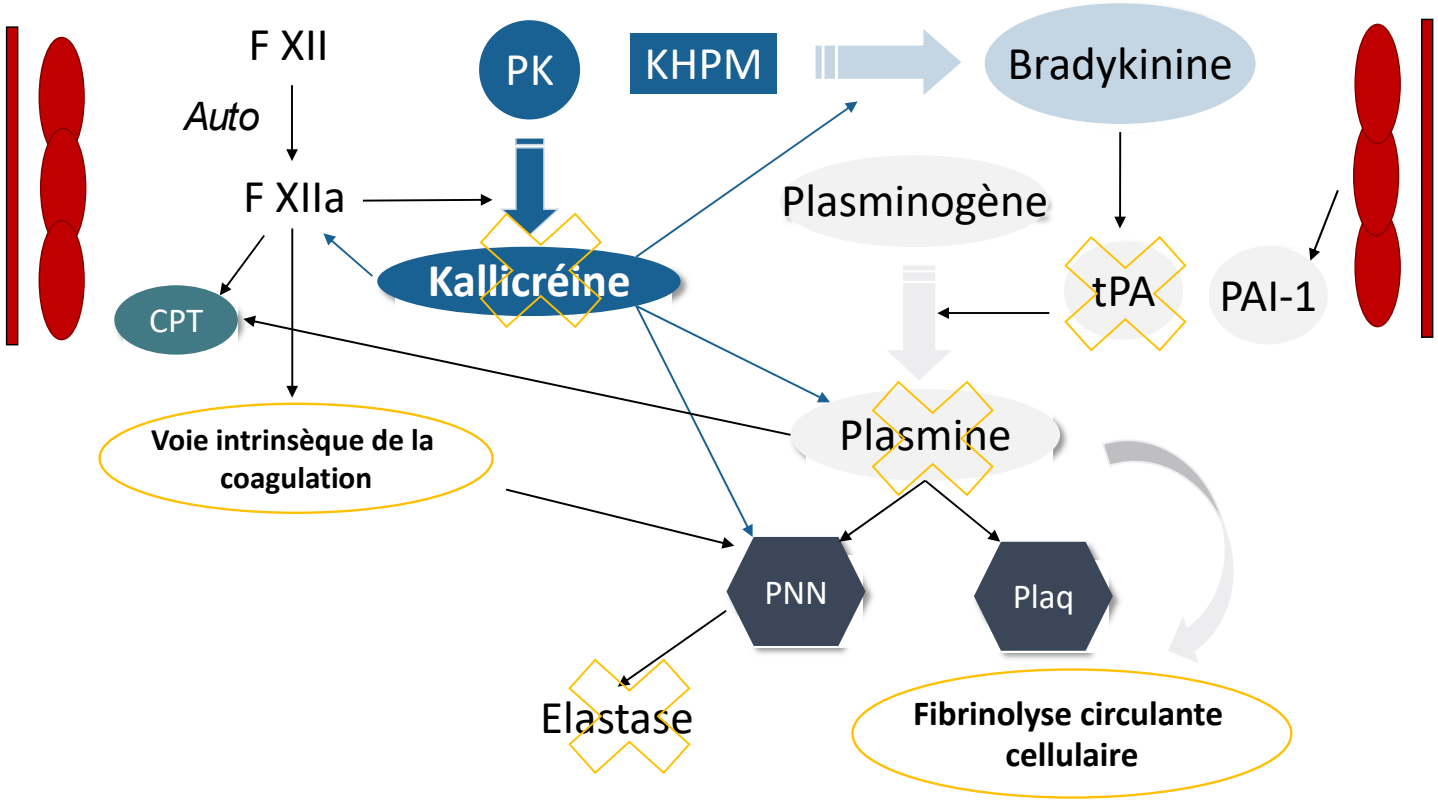
[f] *Klinik für Anästhesiologie, Intensivmedizin und Schmerztherapie, Universitätsklinikum Frankfurt, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany*

Mode d'action de l'aprotinine
(inhibiteur des sérine protéases)



Use of Aprotinin versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE) trial: a multicentre retrospective comparative non-randomized historical study

Eloïse Gallo[a], Philippe Gaudard [b], Sophie Provenchère[c], Fouzia Souab[d], Anaïs Schwab[e], Damien Bedague[f], Hugues de La Barre[g], Christian de Tymowski[c], Laysa Saadi[b], Bertrand Rozec[d], Bernard Cholley[g], Bruno Scherrer[h], Jean-Luc Fellahi[e] and Alexandre Ouattara [a,*], for APACHE investigators

European Journal of Cardio-Thoracic Surgery 2024, 65(2), ezae001

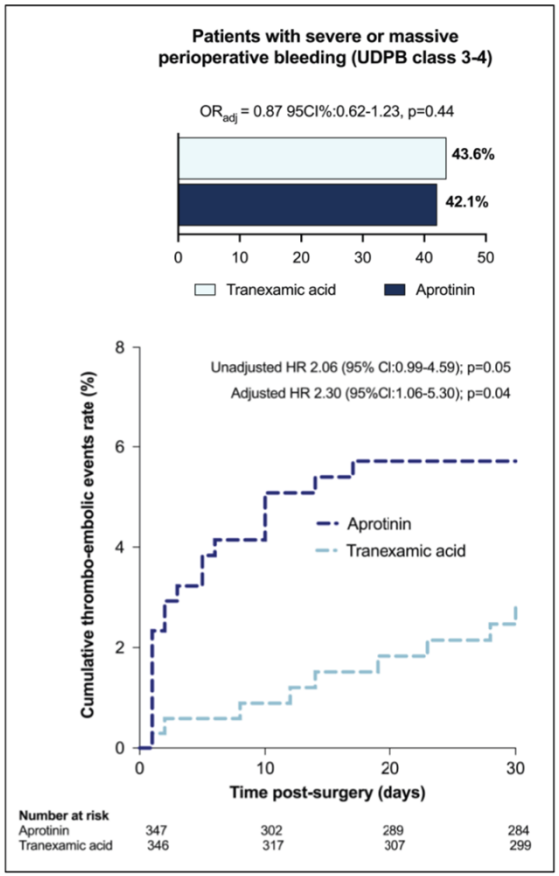
Efficacy and safety of aprotinin compared with tranexamic acid in high-risk cardiac surgery patients

Summary

We tested the hypothesis that the prophylactic use of a half-dose aprotinin regimen instead of a moderate-dose tranexamic acid regimen could significantly reduce severe or massive perioperative bleeding (universal definition of perioperative bleeding class 3-4) in high-risk cardiac surgery patients.

Compared to tranexamic acid, aprotinin did not significantly decrease the occurrence of severe or massive postoperative bleeding. Aprotinin was associated with a significant increase in thromboembolic events with no increase in 30-day all-cause mortality.

Due to the lack of benefit for severe bleeding and a significant increase in thromboembolic adverse events, the use of aprotinin should be considered with caution in high-risk cardiac surgery patients



Intraoperative High-Dose Dexamethasone for Cardiac Surgery

A Randomized Controlled Trial

JAMA. 2012;308(17):1761-1767

Jan M. Dieleman, MD
Arno P. Nierich, MD
Peter M. Rosseel, MD
Joost M. van der Maaten, MD
Jan Hofland, MD
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Karel G. Moons, PhD
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Sandra C. Numan, MSc
Cor J. Kalkman, MD
Diederik van Dijk, MD
for the Dexamethasone for Cardiac Surgery (DECS) Study Group

Etude randomisée multicentrique (n=4494)

DXM (1 mg/Kg à l'induction) versus placebo

Critère de jugement composite

Table 2. Primary Study End Point and Components of the Primary Study End Point in the Dexamethasone and Placebo Groups

	No. (%) of Patients		
	Dexamethasone (n = 2235)	Placebo (n = 2247)	Relative Risk (95% CI)
Primary study end point[a]	157 (7.0)	191 (8.5)	0.83 (0.67-1.01)
Components of the primary study end point			
Death	31 (1.4)	34 (1.5)	0.92 (0.57-1.49)
Myocardial infarction	35 (1.6)	39 (1.7)	0.90 (0.57-1.42)
Stroke	29 (1.3)	32 (1.4)	0.91 (0.55-1.50)
Renal failure	28 (1.3)	40 (1.8)	0.70 (0.44-1.14)
Respiratory failure	67 (3.0)	97 (4.3)	0.69 (0.51-0.94)

[a] Primary study end point was a composite of death, myocardial infarction, stroke, renal failure, or respiratory failure, within 30 days after surgery.

Table 3. Secondary End Points in the Dexamethasone and Placebo Groups

Secondary End Points	Dexamethasone (n = 2235)	Placebo (n = 2247)	Relative Risk (95% CI)	*P* Value[a]
	Median (IQR)			
Duration of postoperative mechanical ventilation, h	7.0 (4.7-10.0)	7.0 (5.0-11.0)	NA	<.001
Length of stay in the ICU, h	22.0 (19.0-24.0)	22.0 (19.0-25.0)	NA	<.001
Length of hospital stay, d	8 (7-13)	9 (7-13)	NA	.009
	Mean (SD)			
Highest serum glucose concentration in the ICU, mg/dL	195 (50)	177 (59)	NA	<.001

Methylprednisolone in patients undergoing cardiopulmonary bypass (SIRS): a randomised, double-blind, placebo-controlled trial

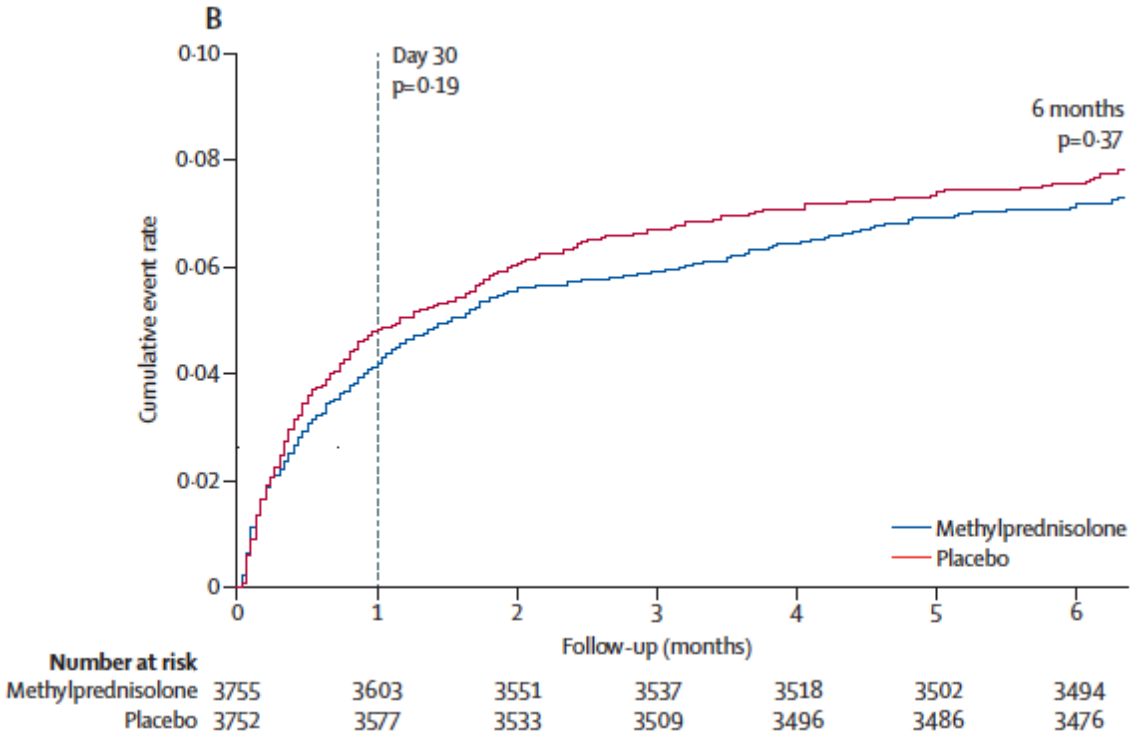
Lancet 2015; 386: 1243–53

*Richard P Whitlock, P J Devereaux, Kevin H Teoh, Andre Lamy, Jessica Vincent, Janice Pogue, Domenico Paparella, Daniel I Sessler, Ganesan Karthikeyan, Juan Carlos Villar, Yunxia Zuo, Álvaro Avezum, Mackenzie Quantz, Georgios I Tagarakis, Pallav J Shah, Seyed Hesameddin Abbasi, Hong Zheng, Shirley Pettit, Susan Chrolavicius, Salim Yusuf, for the SIRS Investigators**

Etude multicentrique (80 hôpitaux au sein de 18 pays) incluant patients avec EuroSCORE ≥ 6

Traitement prophylactique 250 mg prednisolone à l'induction et au départ de la CEC

	Methylprednisolone (n=3755)	Placebo (n=3752)
(Continued from previous column)		
Vitamin K antagonists	319 (8%)	308 (8%)
Dabigatran¶	22 (<1%)	27 (<1%)
H2 antagonist or proton-pump inhibitor	1422 (38%)	1381 (37%)
Insulin	439 (12%)	385 (10%)
Oral hypoglycaemic drugs¶	444 (13%)	469 (13%)
Operative characteristics		
Repeat cardiac surgery	588 (16%)	569 (15%)
Procedure		
Any cardiac valve	2651 (71%)	2724 (73%)
Any coronary artery bypass	1837 (49%)	1796 (48%)
Isolated cardiac valve	1209 (32%)	1228 (33%)
Isolated coronary artery bypass	825 (22%)	762 (20%)
Bypass time (min)	108 (82-144)	110 (84-142)
Cross-clamp time (min)	77 (54-105)	76 (55-104)
Hypothermic arrest	96 (3%)	55 (1%)
Hypothermic arrest time (min)	18 (13–36)	20 (12–39)
Coated circuit	1733 (46%)	1753 (47%)
Antifibrinolytic drugs	2568 (68%)	2617 (70%)
Preoperative inotropes, vasopressors, intra-aortic balloon pump, or ventricular assist device	333 (9%)	353 (9%)
Received at least one dose of study drug or placebo ¶	3364 (96%)	3353 (96%)
Non-study postoperative steroids ¶	75 (2%)	85 (2%)



Prophylactic corticosteroids for cardiopulmonary bypass in adults (Review)

Dieleman JM et al. Cochrane Database Syst Rev 2011:CD005566

Comparison outcome	Number of studies	Participants	Peto OR (Fixed) [95 % CI]	Heterogeneity (I^2%)	Mantel-Haenszel OR (random) [95% CI]
Primary endpoints					
Mortality	49	3213	1.06 [0.58, 1.95]	1	1.00 [0.55, 1.82]
Myocardial complications	26	2103	0.95 [0.57, 1.60]	4	0.95 [0.55, 1.64]
Pulmonary complications	21	1340	0.83 [0.49, 1.40]	5	0.90 [0.51, 1.58]
Atrial fibrillation	17	1399	0.60 [0.46, 0.78]	11	0.61 [0.45, 0.82]
Infections	16	1517	0.86 [0.56, 1.31]	0	0.88[0.57, 1.36]
Time to extubation (min)	23	1351	-1.81 [-11.46, 7.83]	93	-46.87 [-100.25, 6.25]
ICU stay (hours)	25	1215	-2.32 [-2.84, -1.81]	87	-5.47 [-8.13, -2.82]
Hospital stay (days)	15	635	-0.59 [-0.84, -0.34]	96	-0.97 [-2.42, 0.47]

Cardiovascular Surgery

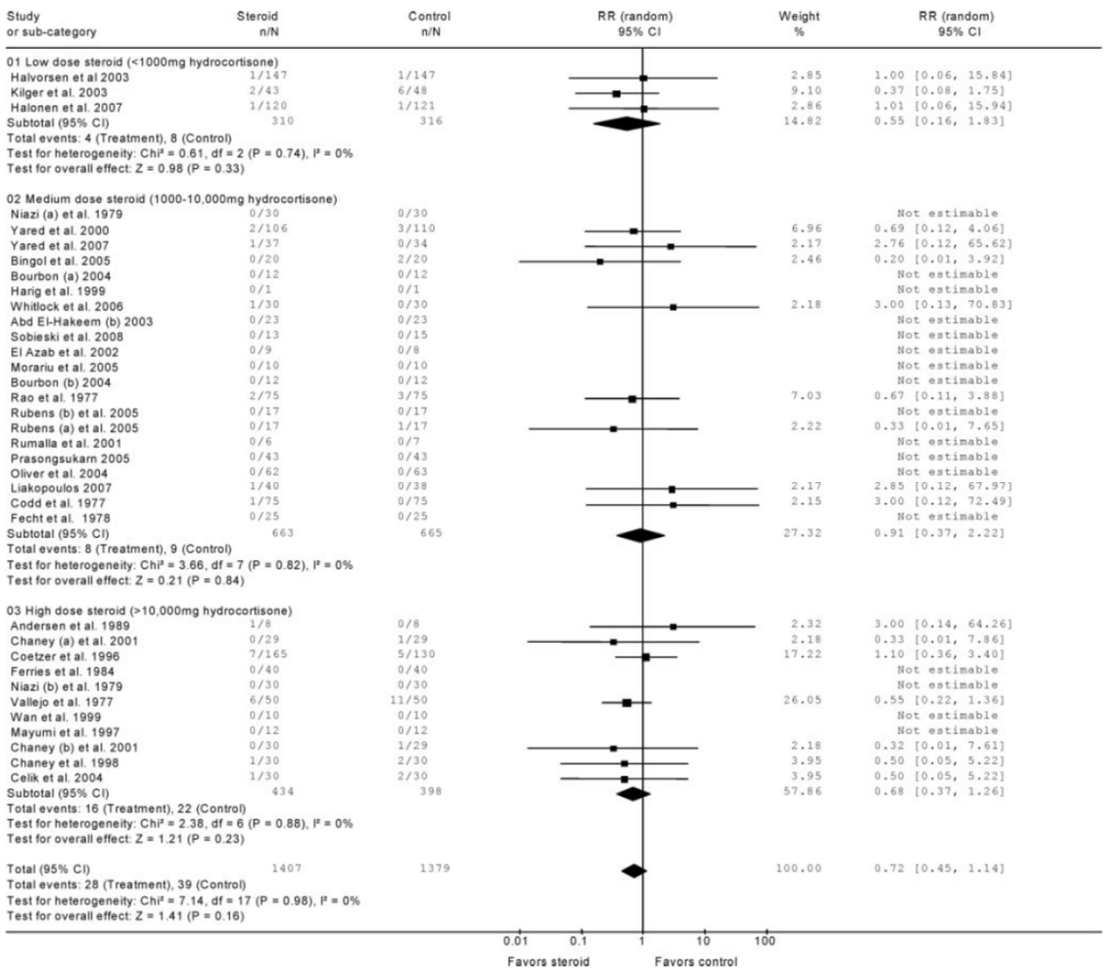
Benefits and Risks of Corticosteroid Prophylaxis in Adult Cardiac Surgery

A Dose-Response Meta-Analysis

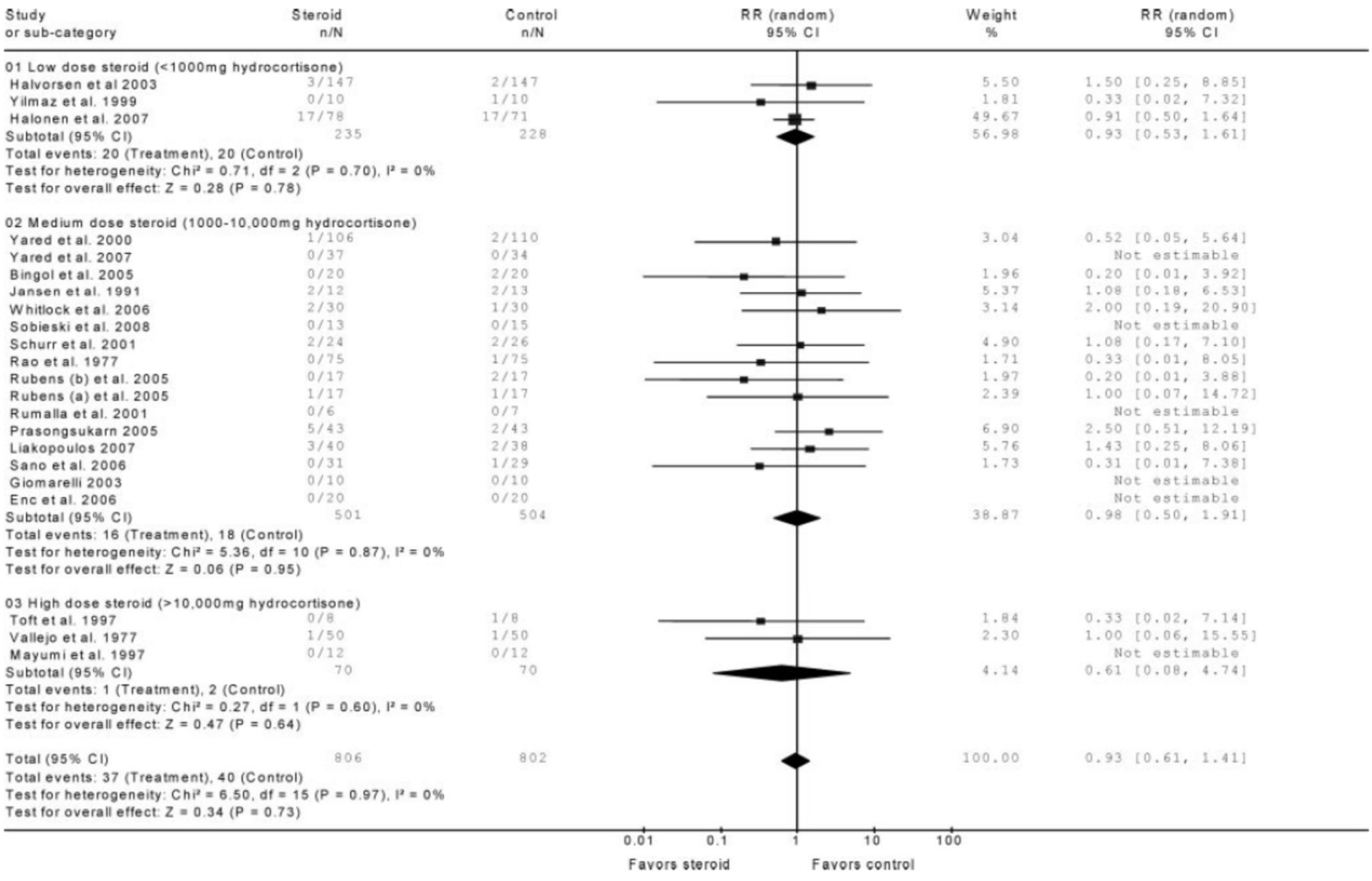
Kwok M. Ho, MPH, PhD, FRCP, FJFICM; Jen Aik Tan, MBBS

Circulation 2009;119:1853-66

Mortality

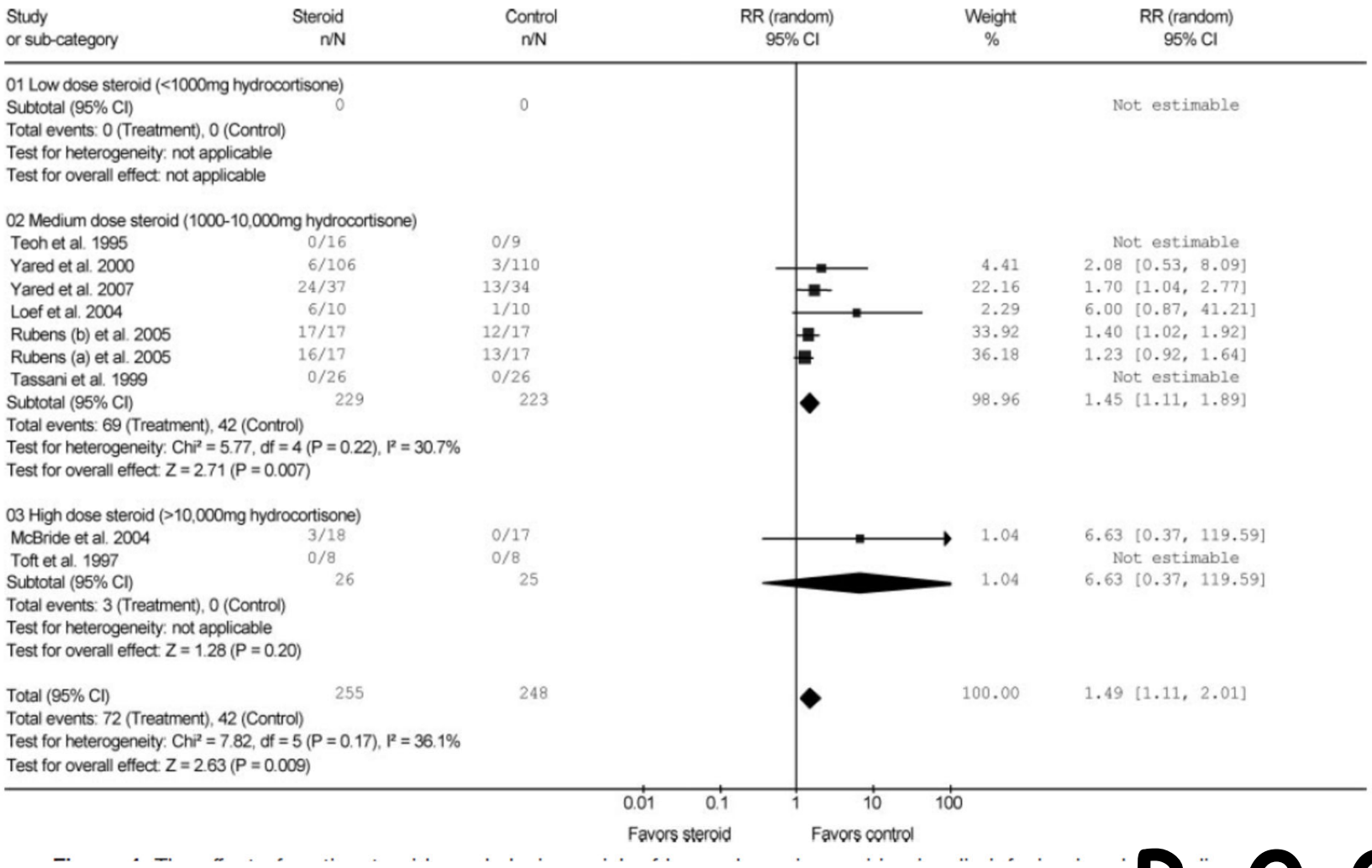


NS



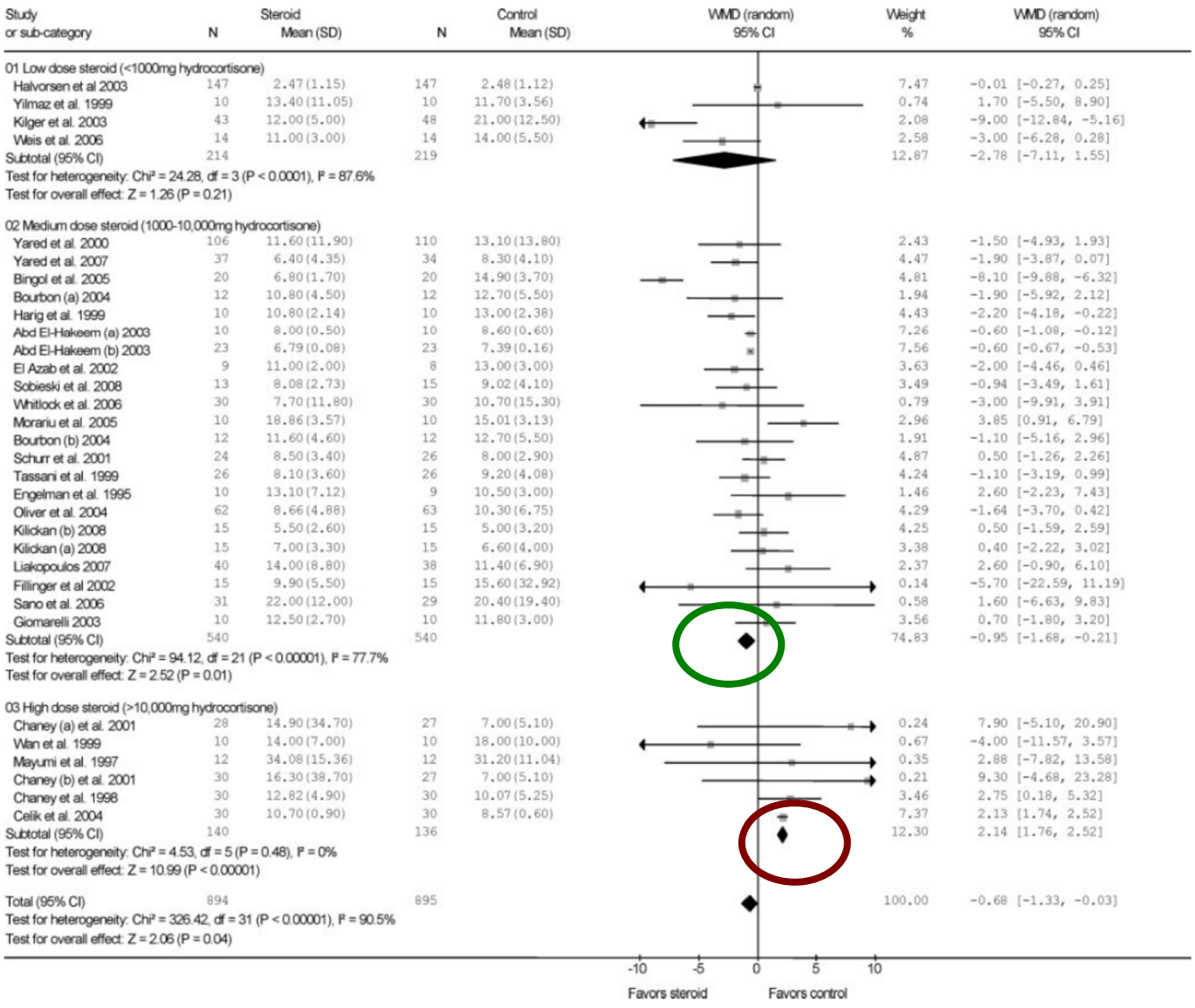
Risk of infection

NS



Risk of hyperglycemia

P<0,05



Risk of atrial fibrillation

Stress doses of hydrocortisone in high-risk patients undergoing cardiac surgery: Effects on interleukin-6 to interleukin-10 ratio and early outcome*

Weiss F et al. Crit Care Med 2009; 37:1685-90

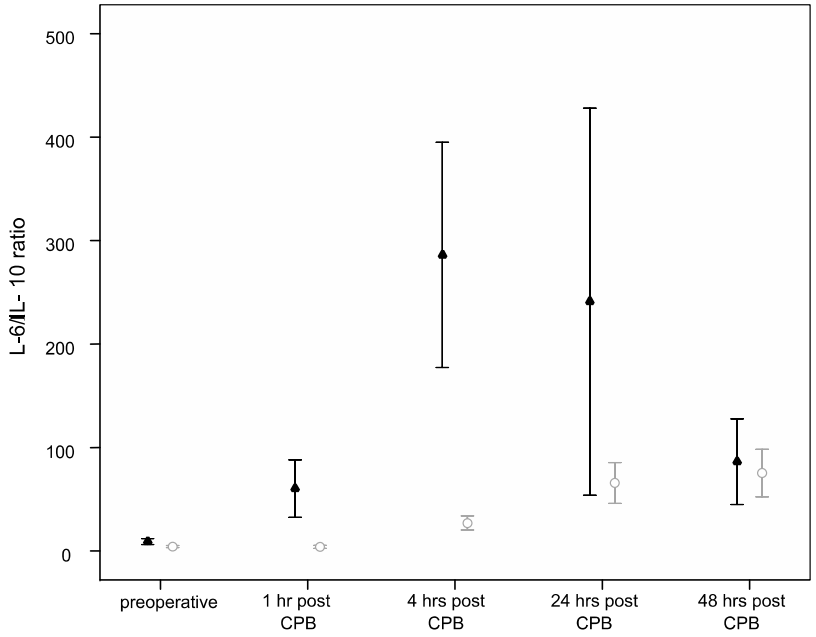
High risk cardiac surgical patients (EF> 40%, combined procedure, CABGX3 or +)

Stress doses of hydrocortisone (IV): Bolus 100 mg before induction and 10 $mg.h^{-1}$ POD_1, 5 $mg.h^{-1}$ POD_2, 30 mg X 3/j IV POD_3, 10 mg X 3/j POD_4

Outcomes: cytokines and early clinical outcomes

Table 1. Comparison of demographic data between the study groups

	Placebo (n = 17)	Hydrocortisone (n = 19)	*p*
Age (yrs)	69 (63/72)	67 (61/78)	n.s.
Sex (f/m)	7/10	8/11	n.s.
EF (%)	31 (21/49)	29 (26/38)	n.s.
BSA (m^2)	1.76 (1.68/1.92)	1.9 (1.75/2.0)	n.s.
ACE inhibitors (n)	13	15	n.s.
COPD (n)	5	7	n.s.
Preop. bilirubine (mg/L)	0.7 (0.5/1.0)	0.7 (0.6/0.9)	n.s.
Preop. creatinine (mg/dL)	1.1 (1/1.4)	1.0 (0.9/1.2)	n.s.
Higgins Score (points)	6 (4/7.5)	6 (4/8)	n.s.
Parsonnet Score (points)	14 (10/20)	15 (12/21)	n.s.
CPB (min)	107 (62/135)	98 (71/154)	n.s.
Clamping (min)	77 (41/112)	58 (45/79)	n.s.



	Placebo (n = 17)	Hydrocortisone (n = 19)	*p*
Pa_{O_2}/Fi_{O_2} 4 hrs post-CPB	373 (287/349)	443 (326/408)	0.06
Pa_{O_2}/Fi_{O_2} on POD 1	285 (232/349)	350 (408)	0.09
Pa_{O_2}/Fi_{O_2} on POD 2	242 (199/309)	330 (263/343)	0.06
Mechanical ventilation (hrs)	14 (7/17.5)	11 (8/14)	n.s
Noninvasive ventilation (n)	7	3	n.s.
Max. dose of norepinephrine (mg/h)	0.6 (0.5/1.6)	0.5 (0.3/1.0)	n.s.
Duration of catecholamine support (d)	4 (2/4.5)	1 (1/2)	<0.01
Intraoperative urine output (mL)	1500 (1150/2100)	1500 (1100/1900)	n.s.
Fluid balance POD 1 (mL)	810 (187/1005)	668 (44/1519)	n.s.
Fluid balance POD 2 (mL)	332 (−162/482)	565 (−91/1267)	n.s.
SOFA-score POD 1 (points)	8 (3/10)	4 (2/9)	n.s.
SOFA score POD 2 (points)	6 (3/9)	4 (2/7.5)	n.s.
Perioperative blood transfusion (n)	3 (1/5)	1 (0/3)	n.s.
Max. level of bilirubine (mg/dL)	0.8 (0.5/1.2)	0.7 (0.5/1.0)	n.s.
Max. level of lactic acid (mg/dL)	2.6 (2.0/4.5)	2.3 (2.0/3.4)	n.s.
Minimal level of cholesterine (mg/dL)	73 (39/84)	69 (57/88)	n.s.
Delirium (%/n)	35/6	16/3	n.s.
SAPS II (points)	36 (31/45)	34 (30/38)	n.s.
IABP support (n)	0	1	n.s.
Mortality within 28 days (%)	0	0	n.s.
Hemofiltration (n)	3	1	n.s.
Postoperative atrial fibrillation (n)	10	5	0.04
Length of stay in the ICU (d)	6 (4/8)	2 (2/3)	<0.01
Length of stay in hospital (d)	11 (8.5/14.5)	13 (11/14)	n.s.

Potential side effects of hydrocortisone (sepsis, sternal wound infection …) were not significantly different between groups

Research

Open Access

Statin prophylaxis and inflammatory mediators following cardiopulmonary bypass: a systematic review

Catherine Morgan[1], Michael Zappitelli[2] and Peter Gill[3]

Critical Care 2009;13:R165

Inflammation, CEC et statines

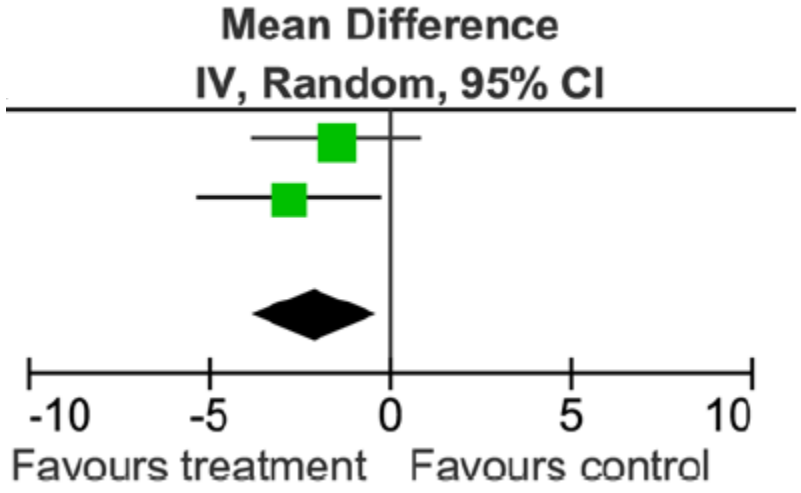
- Méta-analyse
- 8 randomized controlled trials
- CPB open heart surgery adults and children
- Prophylactic statins treatment of inflammation
- Marqueurs de l'inflammation : TNFα, CRP, IL6

Benefit with the use of statin to reduce the post-operative level of TNF-α (WMD -2.10 pg/ml, 95% CI -3.8 to -0.4)

	Statin			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chello 2006	10.4	3.8	20	11.9	3.8	20	54.0%	-1.50 [-3.86, 0.86]
Chello 2007	8.8	3.2	15	11.6	3.9	15	46.0%	-2.80 [-5.35, -0.25]
Total (95% CI)			**35**			**35**	**100.0%**	**-2.10 [-3.83, -0.37]**

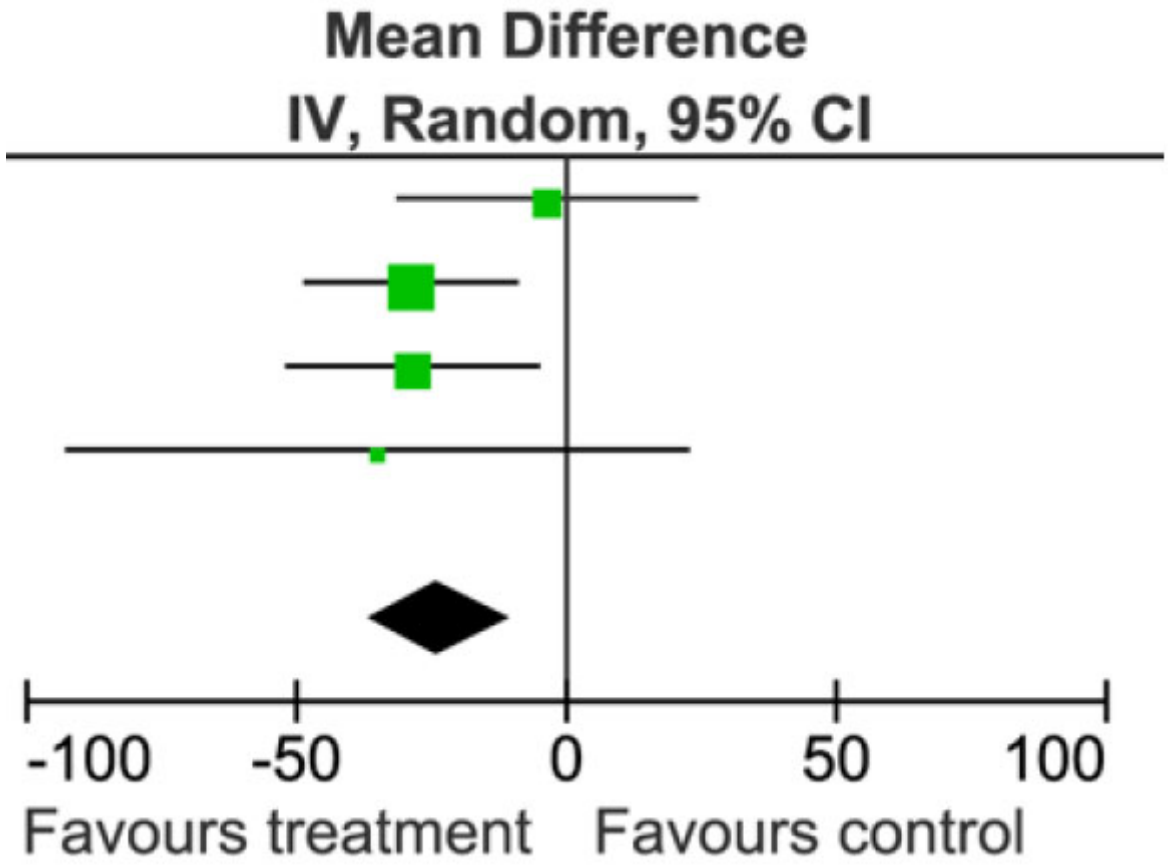
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.54$, df = 1 (P = 0.46); $I^2 = 0\%$

Test for overall effect: Z = 2.38 (P = 0.02)



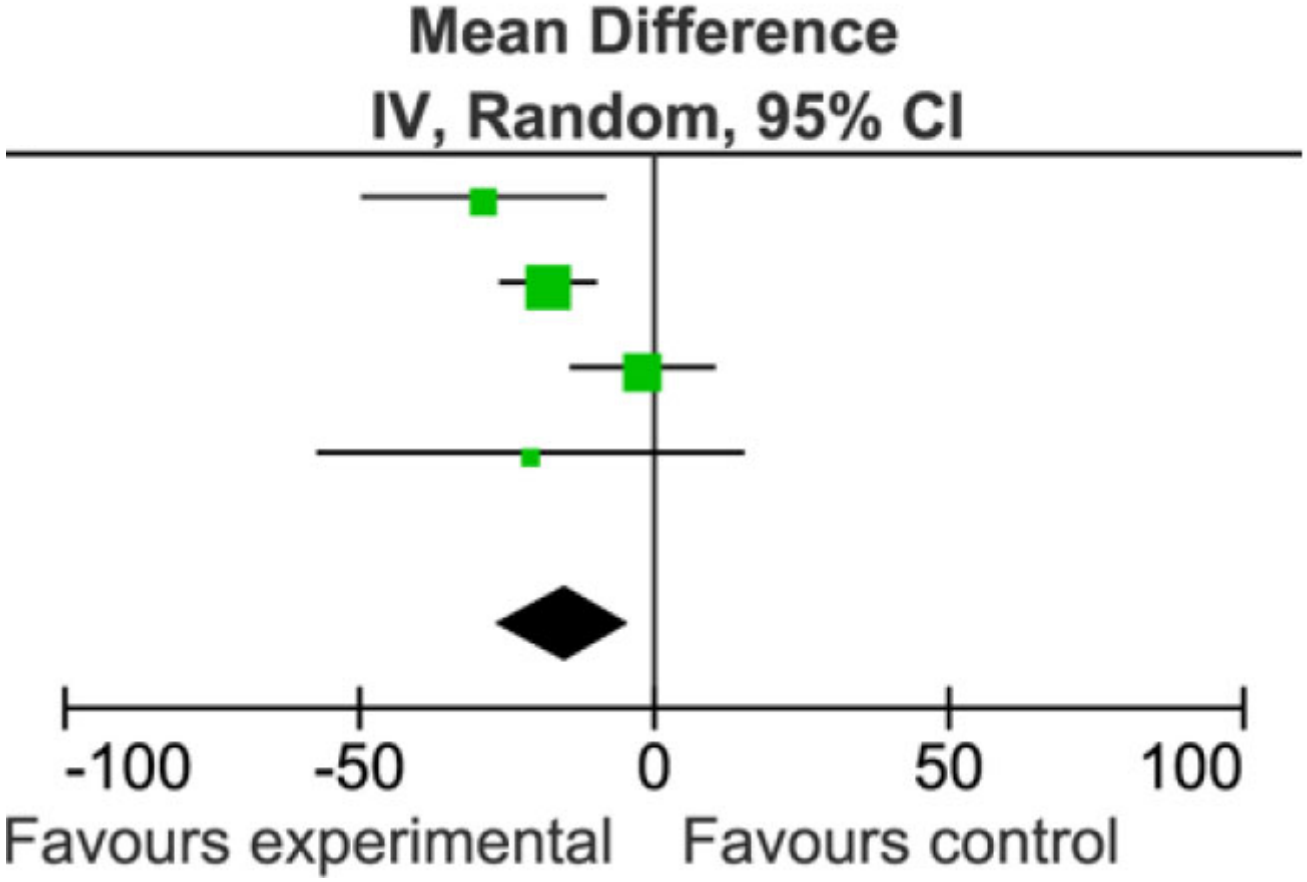
Morgan C. et al. Critical Care 2009, 13: R165

Benefit with the use of statin to reduce the post-operative peak level of IL-6 (WMD -23.5 pg/ml, 95% CI -36.6 to -10.5) measured at four to six hours post-CPB.



Morgan C. et al. Critical Care 2009, 13: R165

Benefit with the use of statin to reduce the post-operative peak level of hsCRP (WMD -15.3 mg/L, 95% CI -26.9 to -3.7).



Morgan C. et al. Critical Care 2009, 13: R165

Randomized Trial of Atorvastatin for Reduction of Postoperative Atrial Fibrillation in Patients Undergoing Cardiac Surgery

Results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) Study

Giuseppe Patti, MD; Massimo Chello, MD; Dario Candura, MD; Vincenzo Pasceri, MD; Andrea D'Ambrosio, MD; Elvio Covino, MD; Germano Di Sciascio, MD

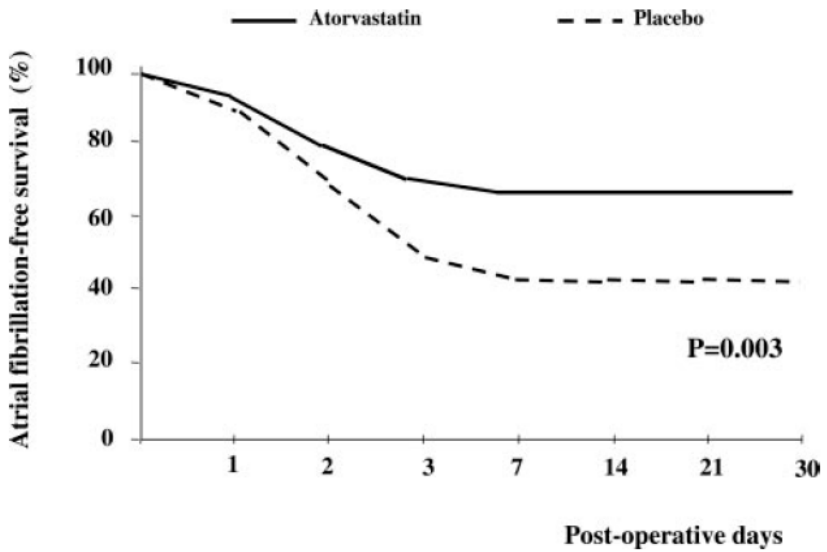
Circulation. 2006;114:1455-1461

Etude prospective, randomisée , double aveugle et placebo control
Chirurgie cardiaque sous CEC (n=200)
Impact Atorvastatine sur ACFA postop (40 mg/j 7j avt intervention)

Incidence ACFA postopératoire
35% vs 57% (P=0,003)

Durée de l'ACFA
24 ±4h vs 24±5 h (NS)

Délai de survenue
51±15h vs 50 ±17 h (NS)



Agents vasopresseurs de recours

Rescue Agents and Relevant Dosing Derived From the Current Literature

Drug	Dose
Vasopressin	0.02-0.1 U/min
Terlipressin*	1-2 μg/kg/h
Methylene blue*	2-3 mg/kg over 10 minutes, followed by 0.5 mg/kg/h for 6 h
Hydroxocobalamin*	5 g infused over 15 min; may repeat once
Angiotensin II (Giapreza)	10-40 ng/kg/min
Vitamin C*	1.5 g intravenously every 6 h
Flurbiprofen (Ropion)*	50-100 mg
Hydrocortisone	50-100 mg once, then 50 mg every 6 h

* Off-label use.

Ortoleva J et al. J Cardiothoracic Vasc Anesth 2020;34:2766-75

ELSEVIER

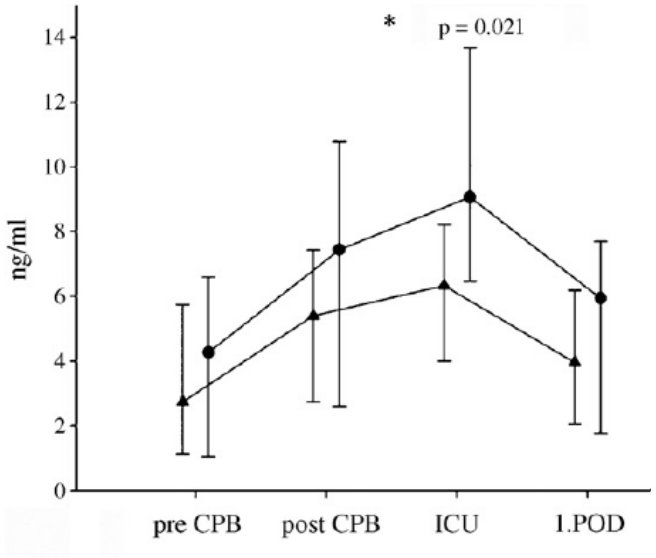
European Journal of Cardio-thoracic Surgery 32 (2007) 83—89

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

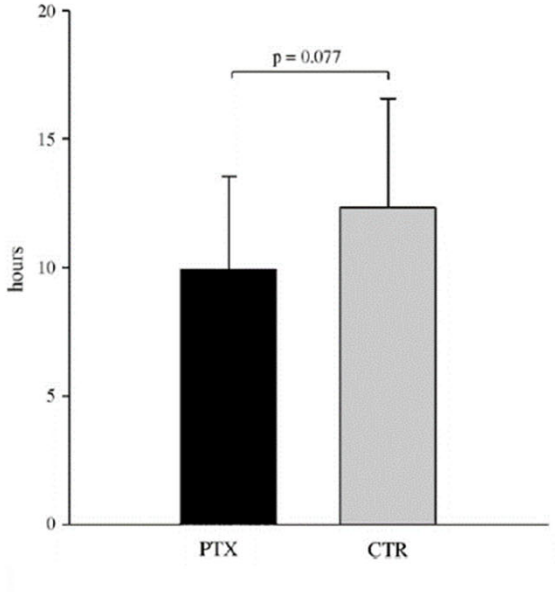
www.elsevier.com/locate/ejcts

A single prophylactic dose of pentoxifylline reduces high dependency unit time in cardiac surgery — a prospective randomized and controlled study☆

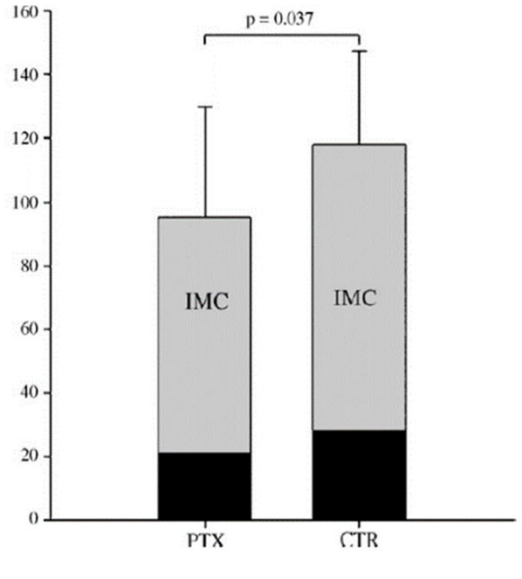
Etude prospective, randomisée, placebo control
PTX (n=20) 5 mg.kg^{-1} après induction anesthésique versus CTRL (n=20) groupe placebo
Anesthésie générale (etomidate/propofol/sufentanil/pancuronium)
CEC conventionelle non pulsée en hypothermie



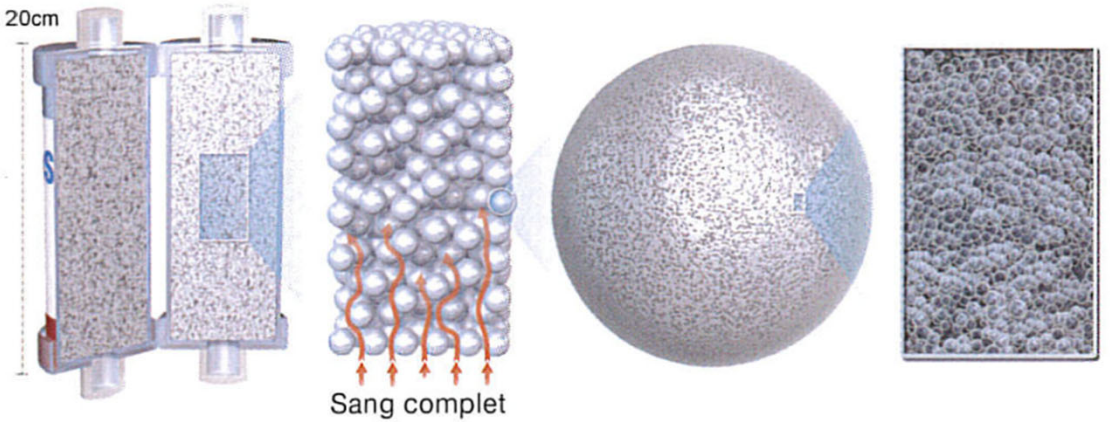
TNFa



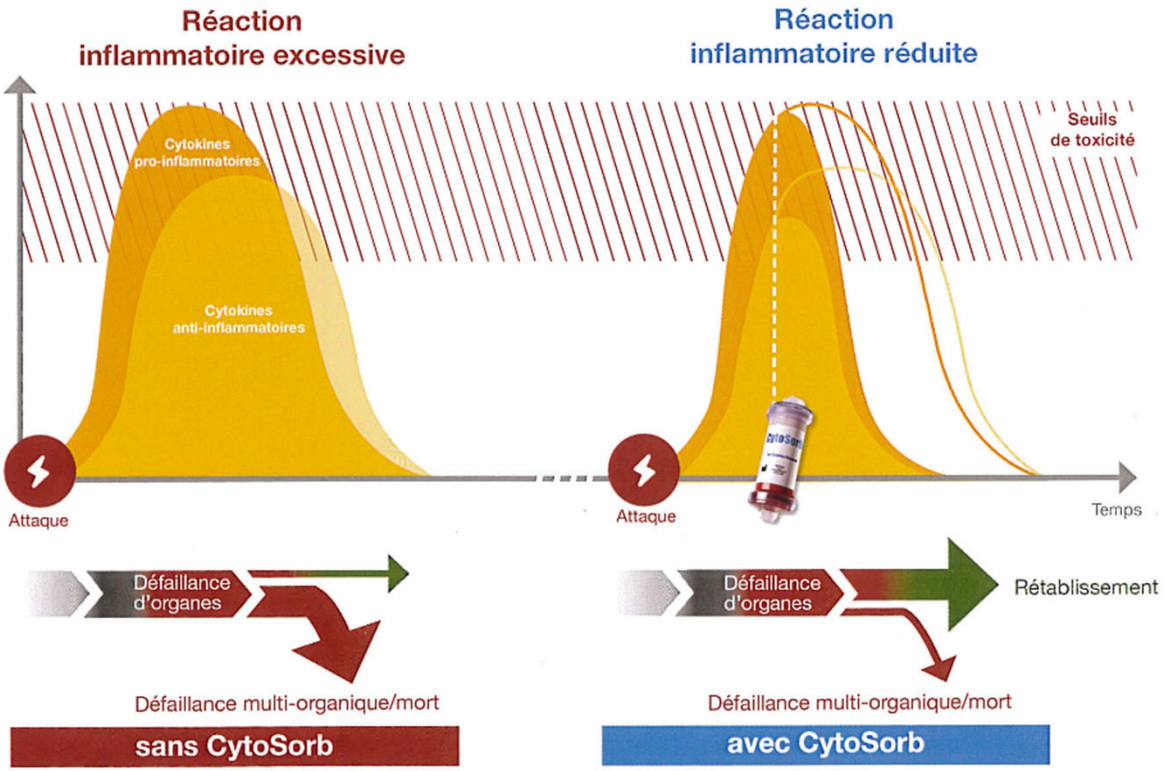
VM



DDS hôpital


20cm
Sang complet
Section de l'adsorbant
Bille d'adsorbant
Structure interne


CytoSorb
For Cytokine Removal


Réaction
inflammatoire excessive
Réaction
inflammatoire réduite
Seuils
de toxicité
Cytokines
pro-inflammatoires
Cytokines
anti-inflammatoires
Attaque
Attaque
Temps
Défaillance
d'organes
Défaillance
d'organes
Rétablissement
Défaillance multi-organique/mort
Défaillance multi-organique/mort
sans CytoSorb
avec CytoSorb

Hemadsorption during cardiopulmonary bypass reduces interleukin 8 and tumor necrosis factor α serum levels in cardiac surgery: a randomized controlled trial

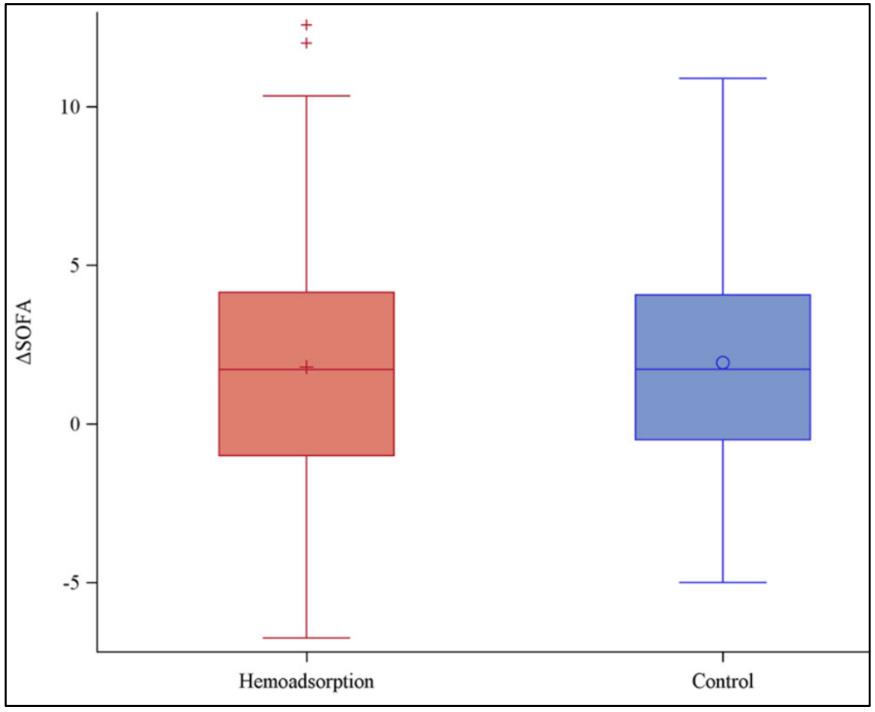
Garau I et al. Minerva Anestesiologica 2019;85:715-23

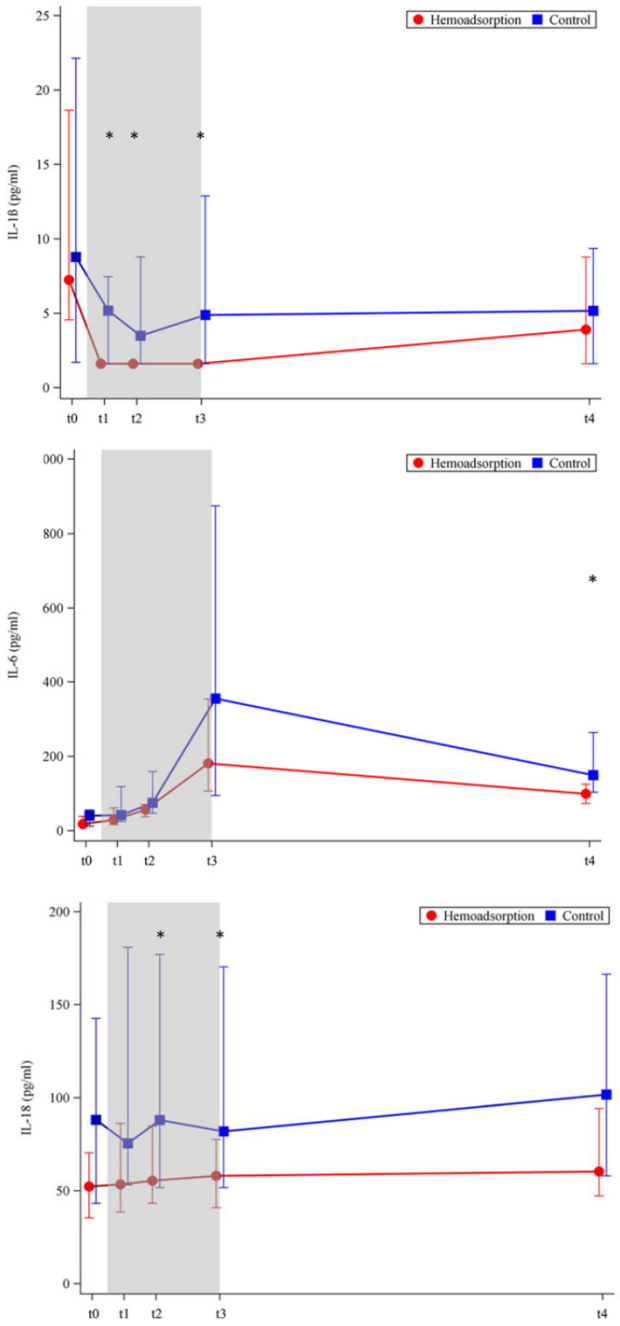
Clinical Study

Extracorporeal Hemadsorption *versus* Glucocorticoids during Cardiopulmonary Bypass: A Prospective, Randomized, Controlled Trial

Stupica GT et al. Cardioavsc Therapeutics 2020

Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial





Diab M et al. Circulation 2022; 145:959-68

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2

Inflammatory response and extracorporeal circulation

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Conclusion

- Réaction inflammatoire constante
- Effets bénéfiques probables
- Effets délétères évidents
- Syndrome de défaillance multiviscérale
- Prédisposition génétique
- Facteurs déclenchant modulables (chirurgie, anesthésie, type de CEC…)
- Appréhender par une prise en charge multimodale périopératoire optimale
- Place des corticoïdes très discutable…


Questions ou commentaires…..?