



Prise en charge des patients drépanocytaires en réanimation

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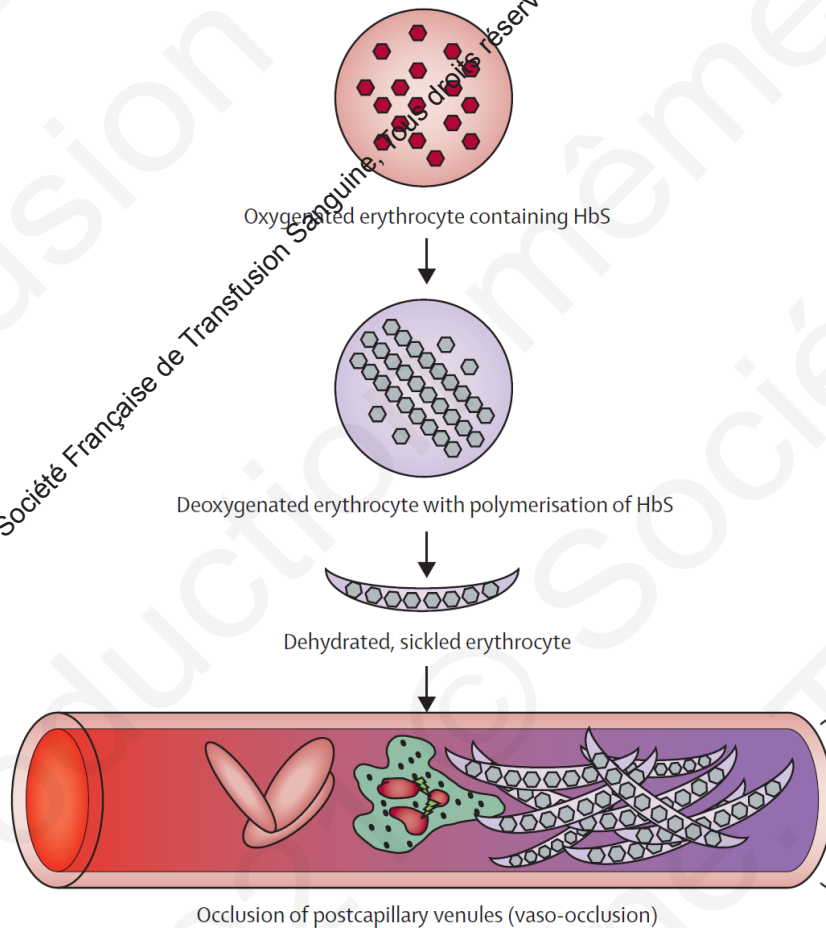
Liens d'intérêt

- Aucun

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Bases moléculaires et classification



Severe sickle-cell disease

HbS/S ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 6\text{Glu} \rightarrow \text{Val}$); sickle-cell anaemia

HbS/ β^0 thalassaemia

Severe HbS/ β^+ thalassaemia

HbS/OArab ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 121\text{Glu} \rightarrow \text{Lys}$)

HbS/D Punjab ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 121\text{Glu} \rightarrow \text{Gln}$)

HbS/C Harlem ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 6\text{Glu} \rightarrow \text{Val} / \beta 73\text{Asp} \rightarrow \text{Asn}$)

HbC/S Antilles ($\beta 6\text{Glu} \rightarrow \text{Lys} / \beta 6\text{Glu} \rightarrow \text{Val}, \beta 23\text{Val} \rightarrow \text{Ile}$)

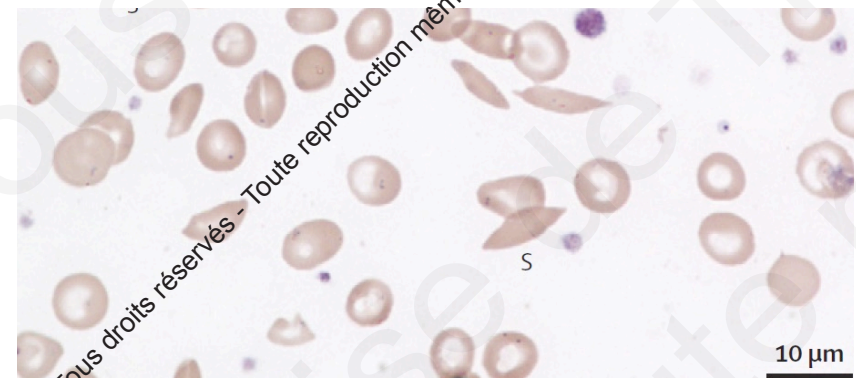
HbS/Quebec-CHORI ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 87\text{Thr} \rightarrow \text{Ile}$)

Moderate sickle-cell disease

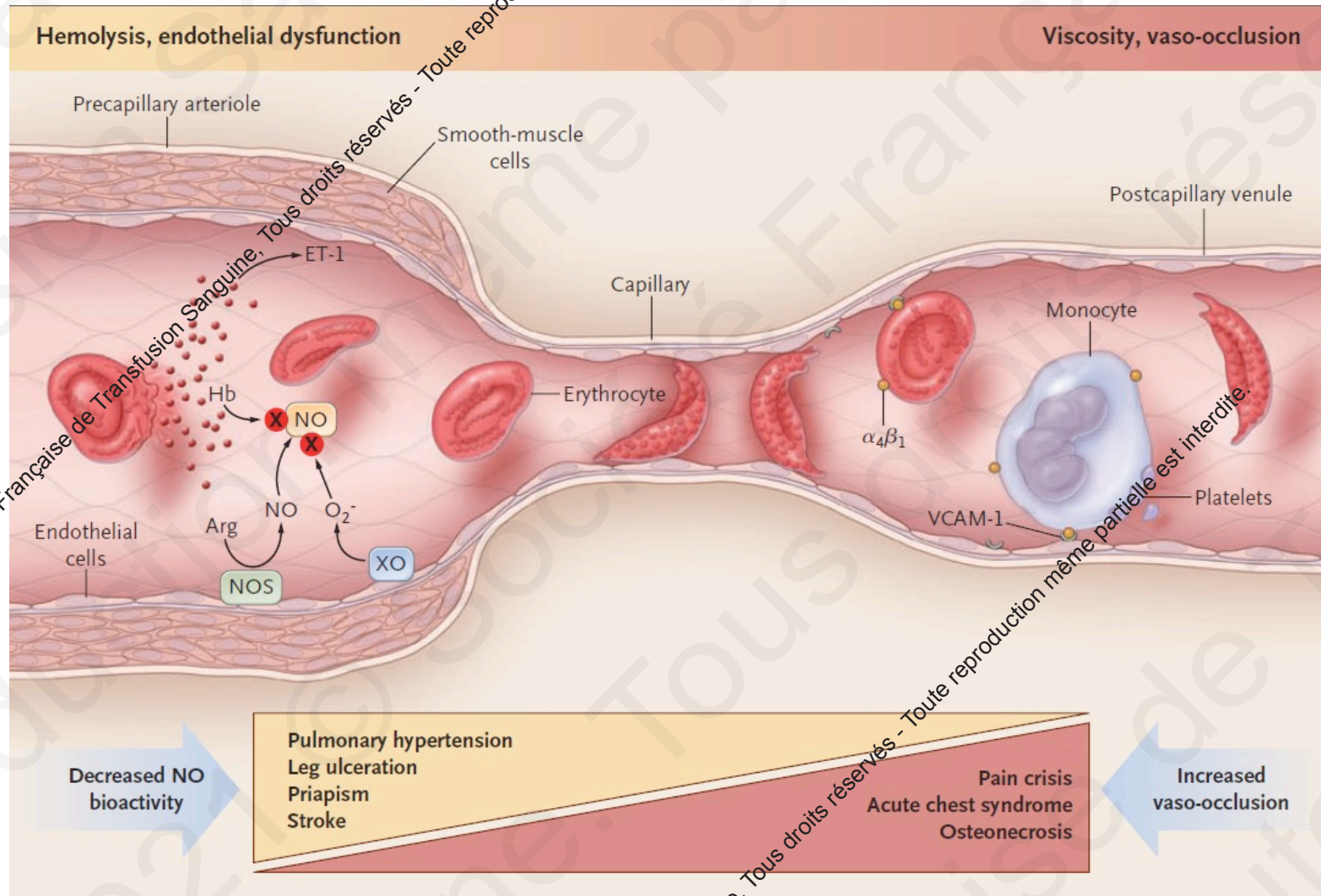
HbS/C ($\beta 6\text{Glu} \rightarrow \text{Val} / \beta 6\text{Glu} \rightarrow \text{Lys}$)

Moderate HbS/ β^+ thalassaemia

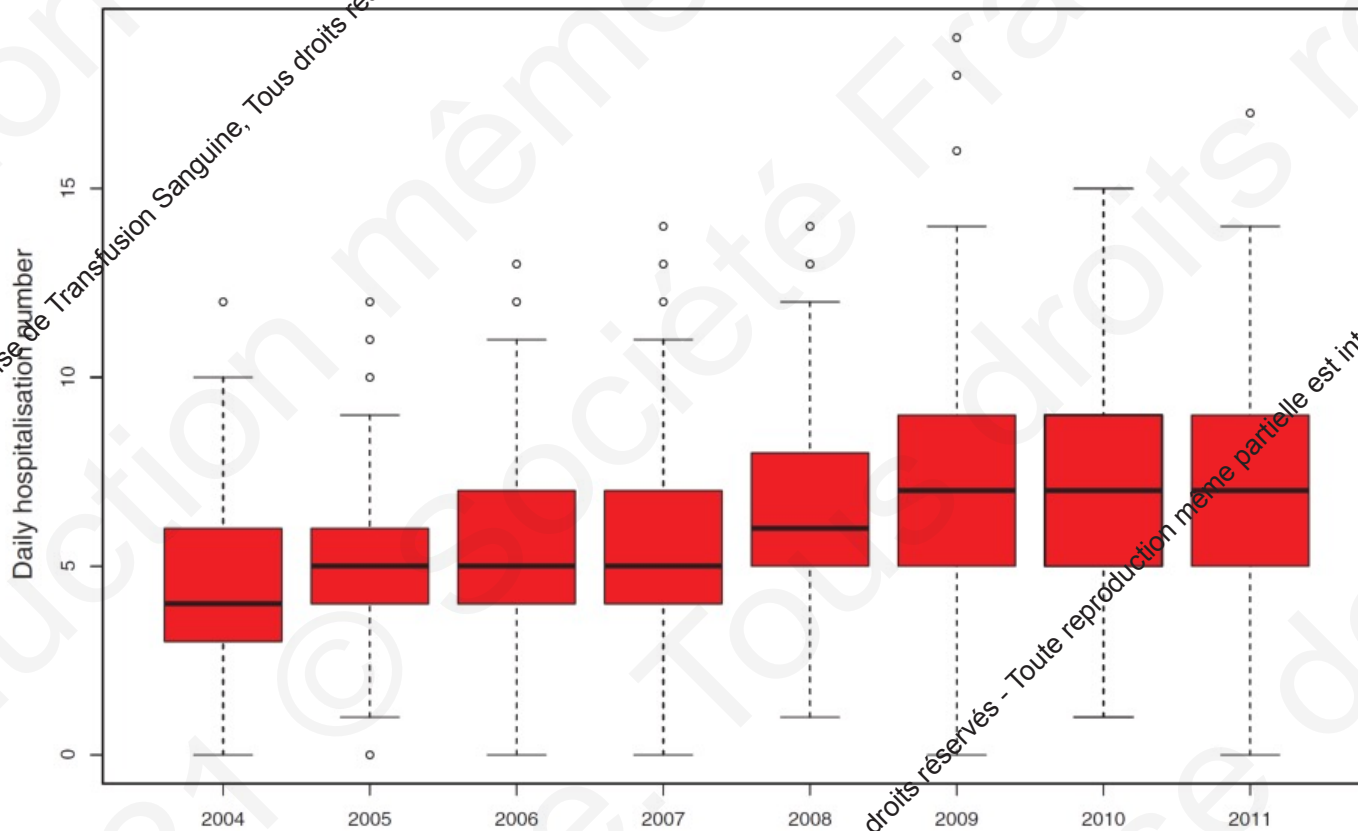
HbA/S Oman ($\beta^+ / \beta 6\text{Glu} \rightarrow \text{Val}, \beta 121\text{Glu} \rightarrow \text{Lys}$)



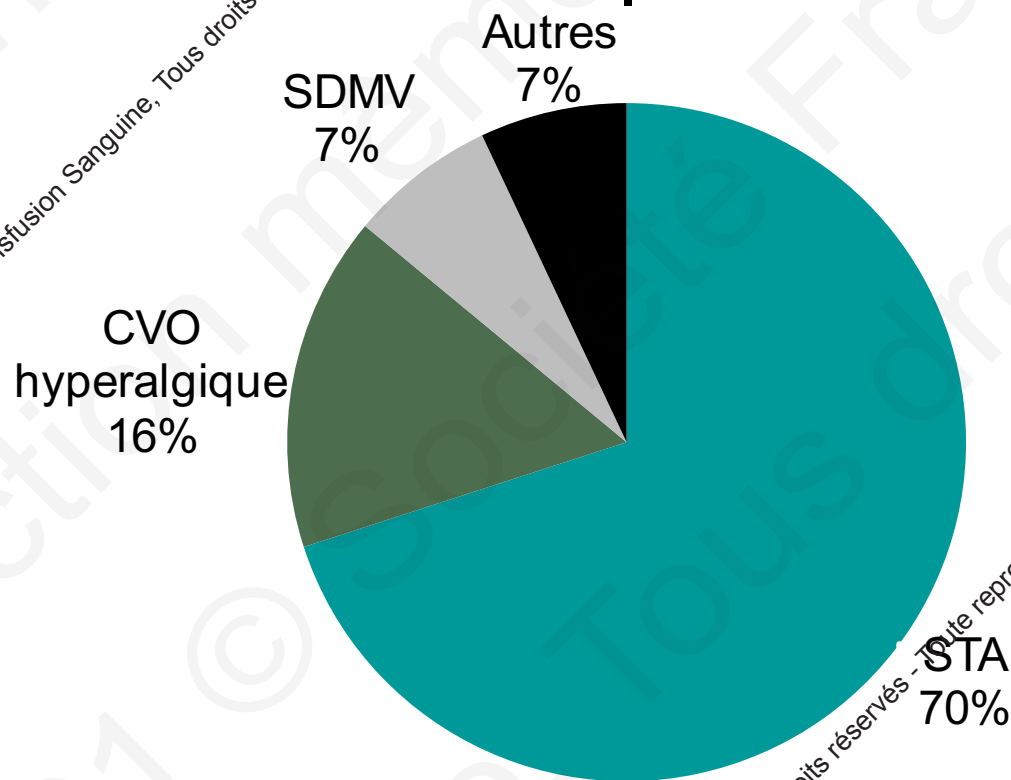
Phénotypes cliniques



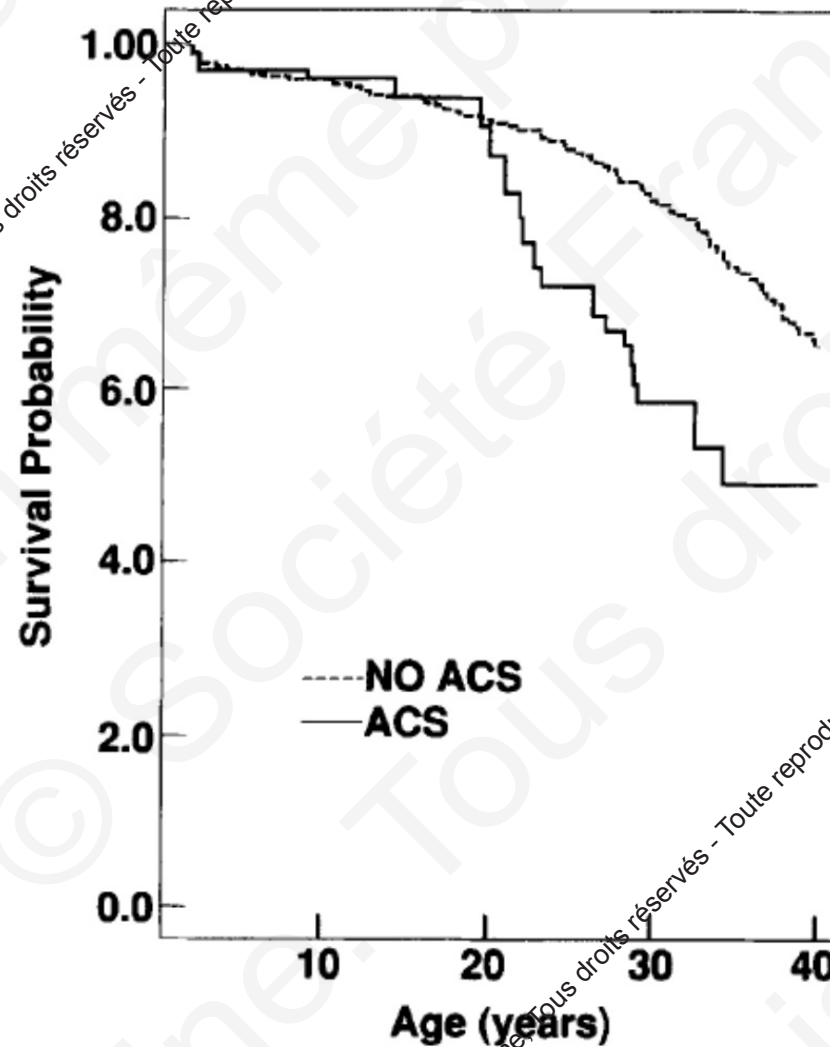
Incidence croissante des complications aiguës graves



Motifs d'admission en réanimation

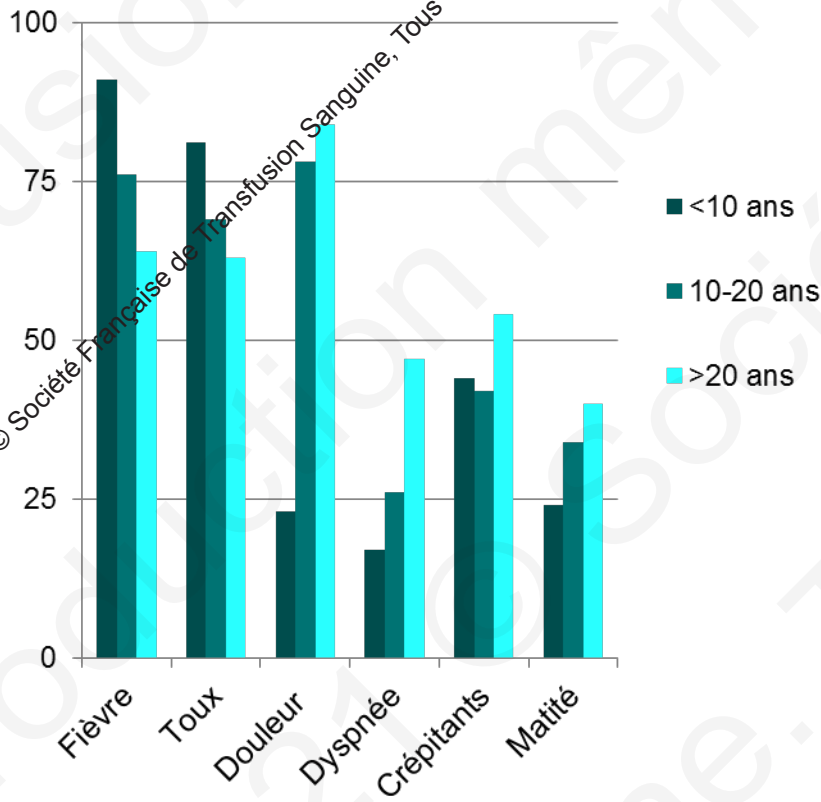


Pronostic si STA



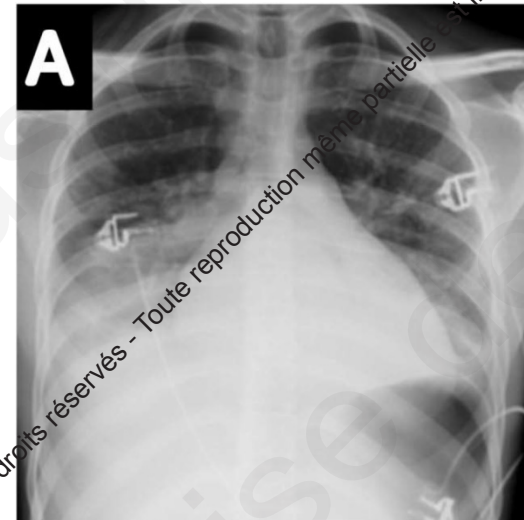
STA: regroupe les complications pulmonaires aiguës de la drépanocytose

SIGNE CLINIQUE



NOUVEL INFILTRAT RADIOLOGIQUE

- Consolidation
 - $\geq$ segmentaire
 - $\neq$ atélectasie

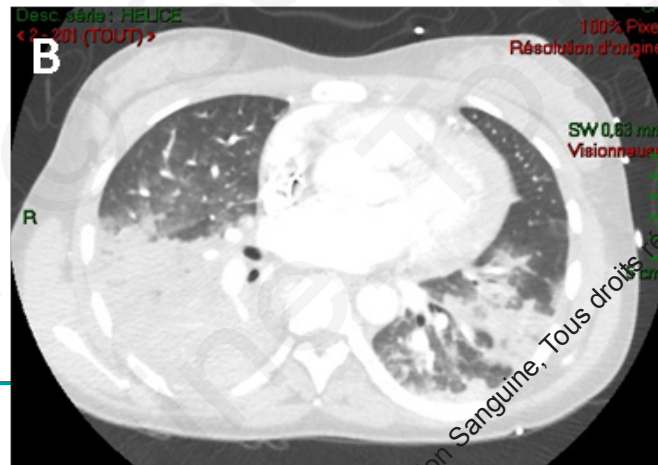
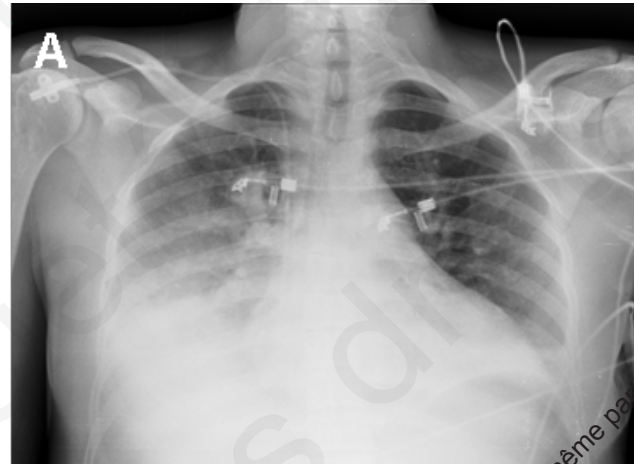


Vichinsky, NEJM 2000
Gladwin, NEJM 2008

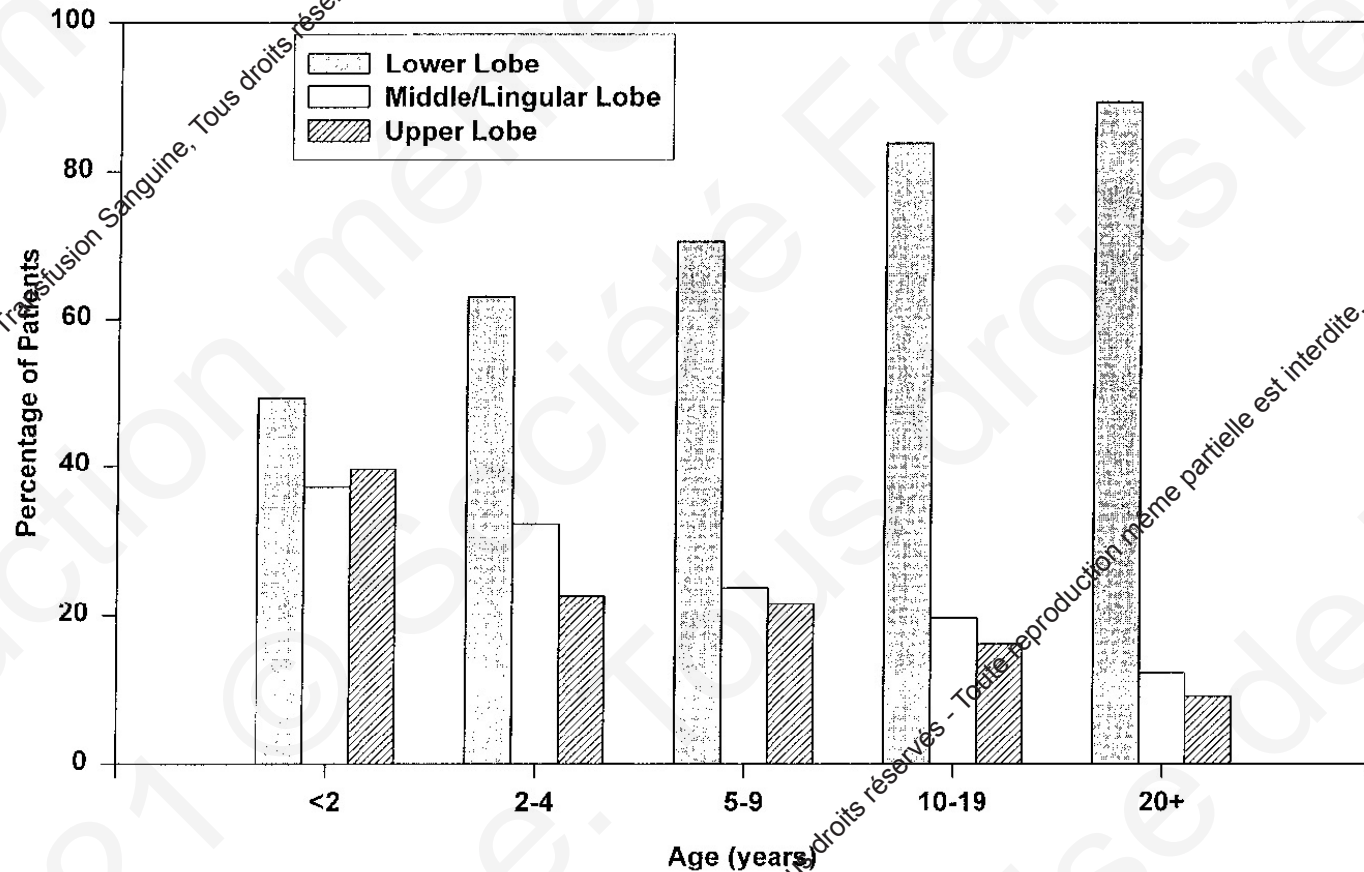
Vichinsky, Blood 1997
Mekontso Dessap, Thorax 2013

STA: prédominance basale

- Epanchement pleural dans $\frac{1}{4}$ des cas
- Atteinte lobe inférieur dans $\rightarrow 95\%$ des cas
 - Son absence élimine le diagnostic chez l'adulte

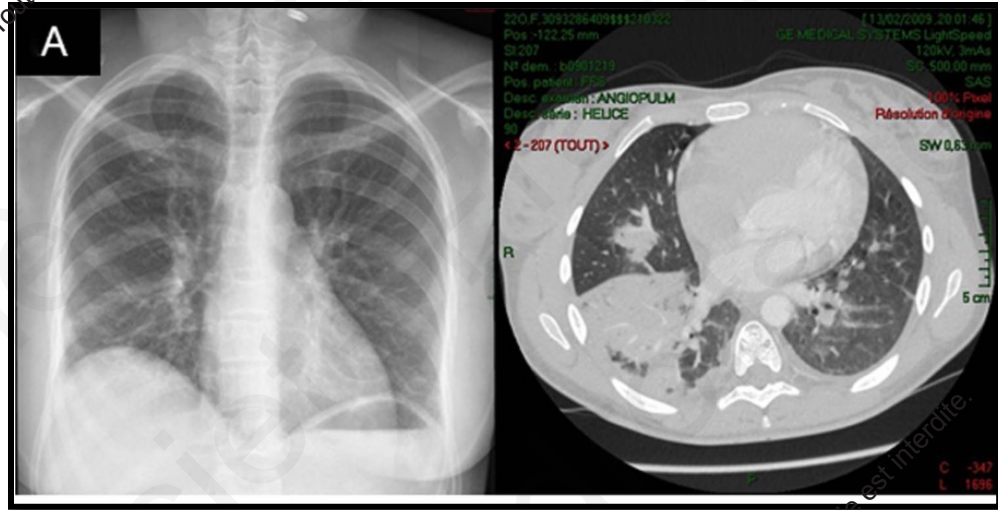


Aspect radiologique STA: effet de l'âge

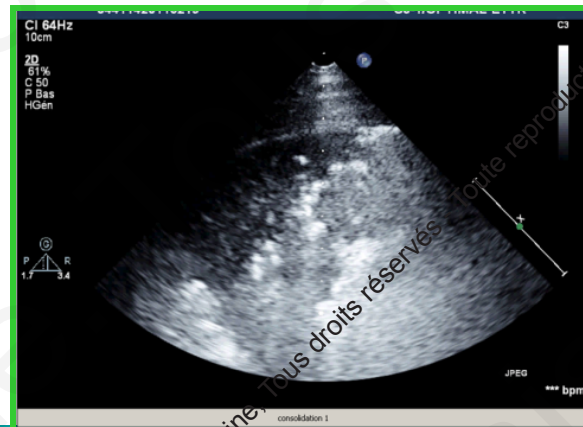


Diagnostic radiologique STA

■ Radio au lit

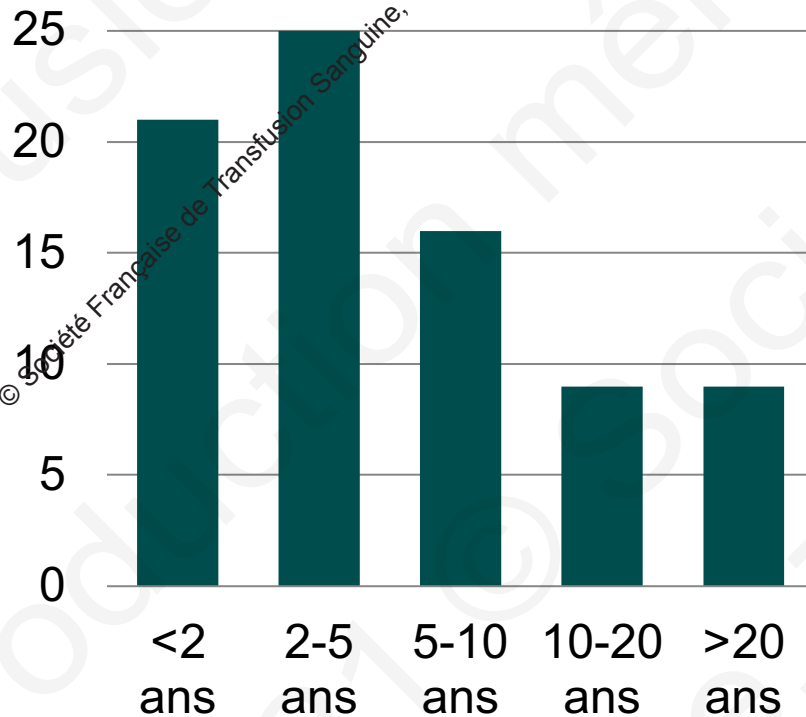


■ Echographie pulmonaire



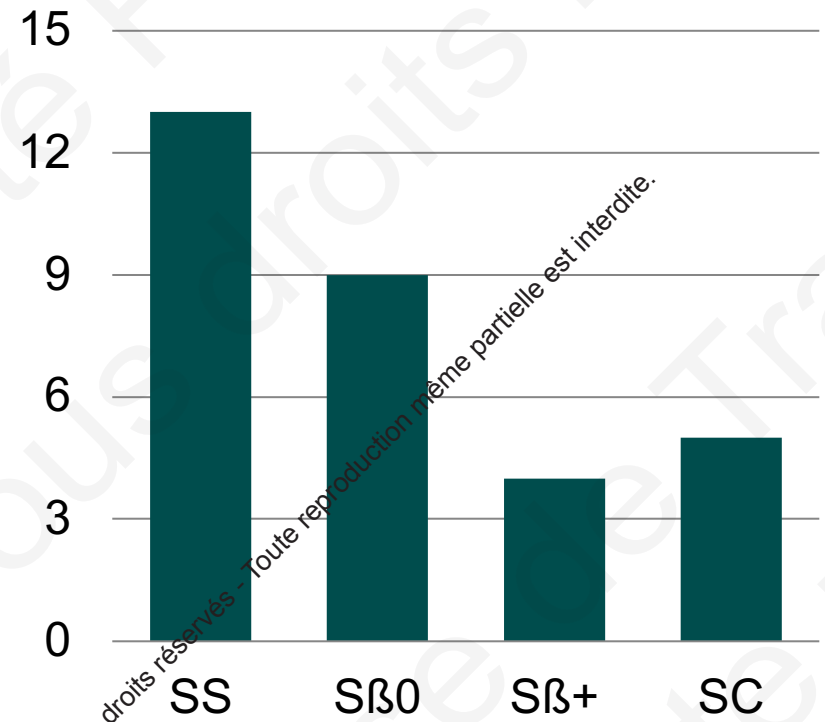
Facteurs de risque CVO/STA

Jeune âge



■ Incidence (/100 patients-années)

Génotype SS

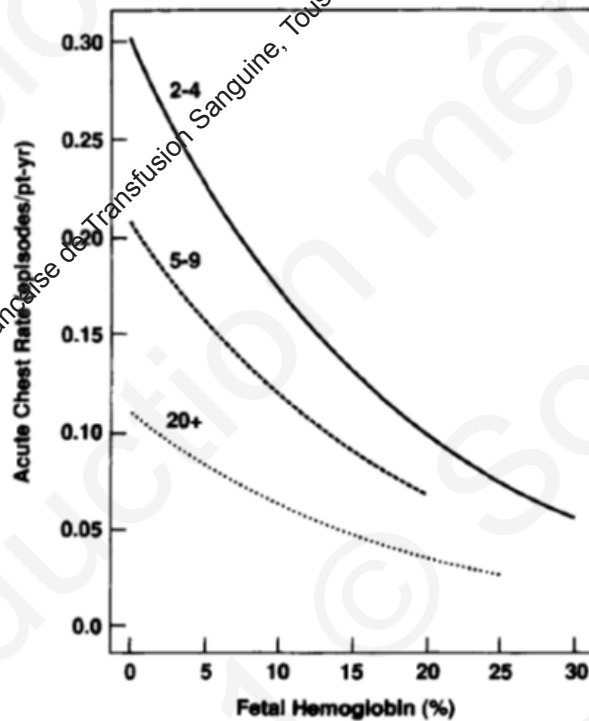


■ Incidence (/100 patients-années)

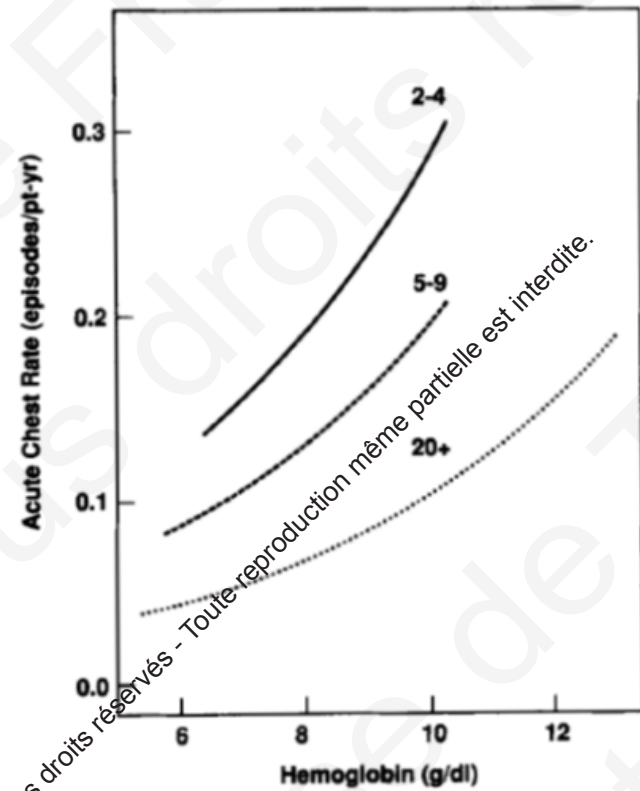
Castro, Blood 1994

Facteurs de risque CVO/STA

↓ **Hb F**



↑ **Hb totale et leucocytes**



Facteurs déclenchants CVO/STA

- Le STA peut inaugurer la maladie drépanocytaire
- Près de la moitié des patients avec STA sont admis pour une autre raison

■ Facteurs déclenchants classiques

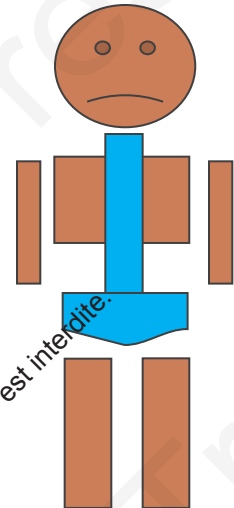
- Grossesse, postpartum
- Chirurgie
- CVO
- Environnement

CVO: score PRESEV

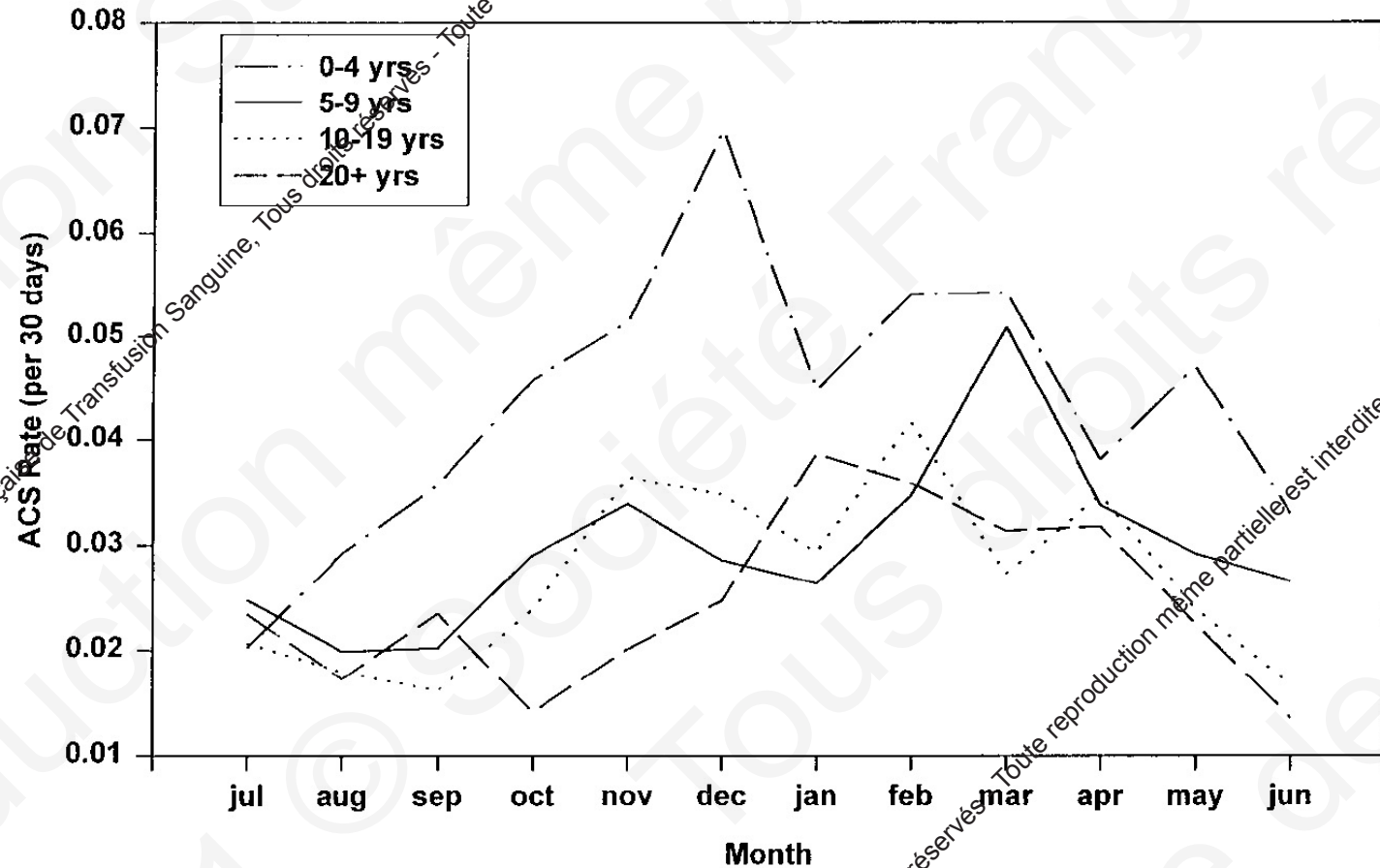
Table 3

ACS-predictive model derived from the multivariate analysis.

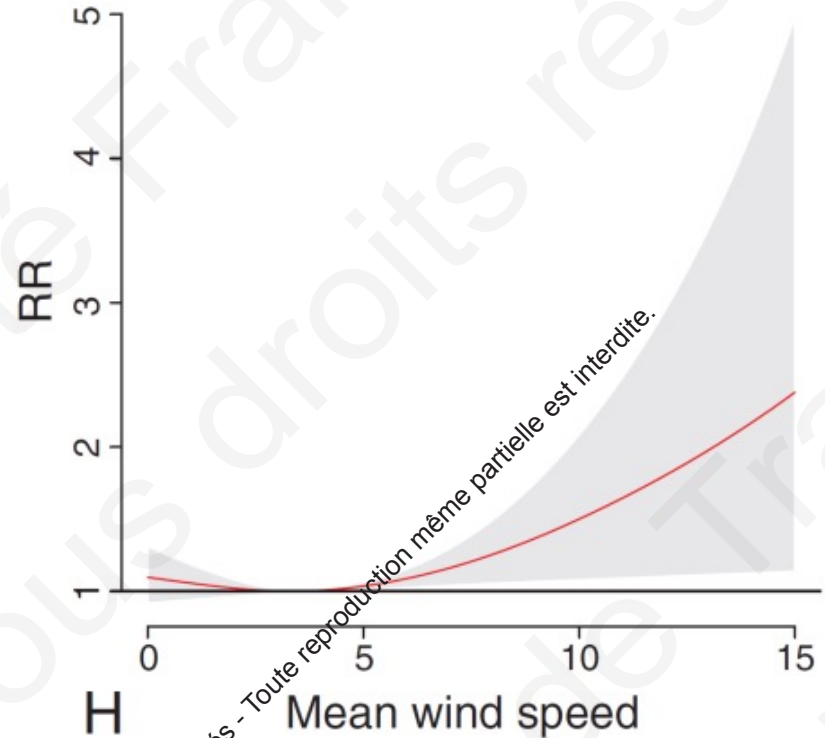
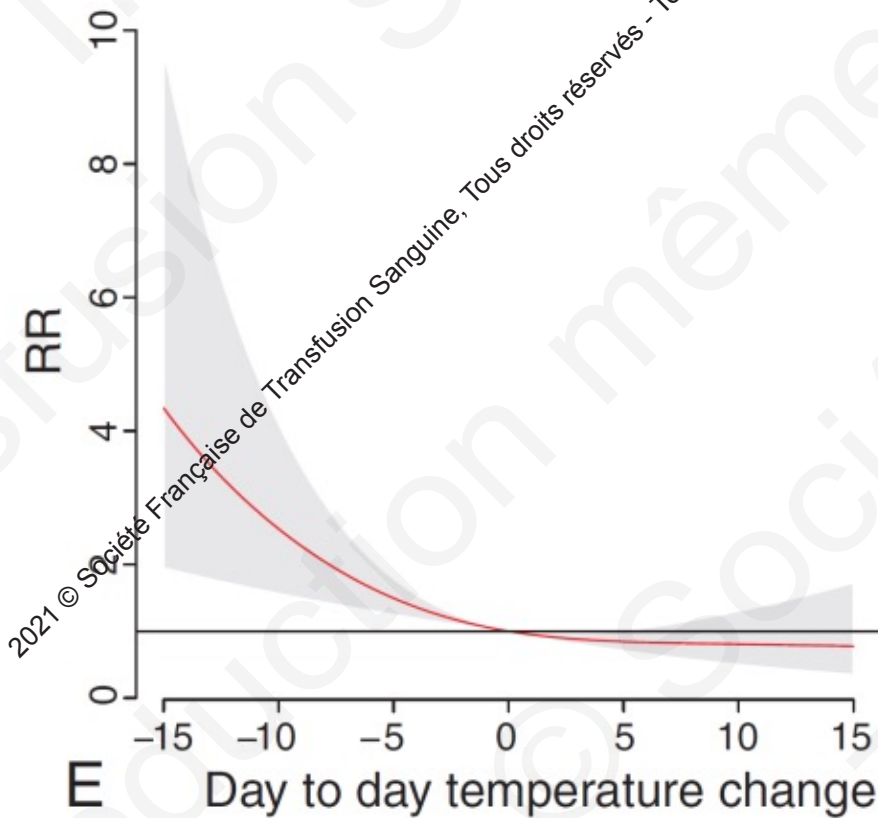
Day-1 variable	β -Coefficient	aOR [95% CI]	p	Points ^a
Reticulocytes ($10^9/L$)				
≤216	0	1		0
>216	2.153	8.613 [3.01–24.69]	<0.001	6
Spine and/or pelvis CPS				0
0 or 1	0	1		
2	1.401	4.060 [1.46–11.26]	0.007	4
3	1.852	6.371 [2.37–17.15]	<0.001	6
Leukocytes ($10^9/L$)				
≤11	0	1		0
>11	1.160	3.190 [1.17–8.72]	0.024	3
Hemoglobin (g/dL) ^b				
>9	0	1		0
≤9	0.246	1.279 [0.55–2.96]	0.567	1
Predictive model performance on the study population				
Predictive score ^c	ACSs	VOCs	Total	Risk
≥11	21	26	47	PPV = 44.7% High
6–10	15	75	90	NPV = 98.9% Intermediate
≤5	1	88	89	Low
Total	37	189	226	



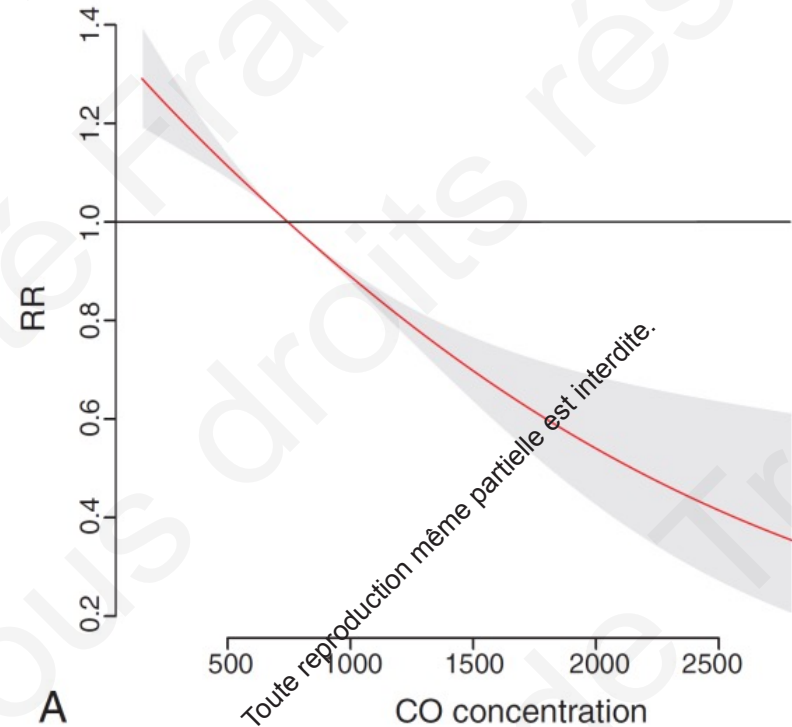
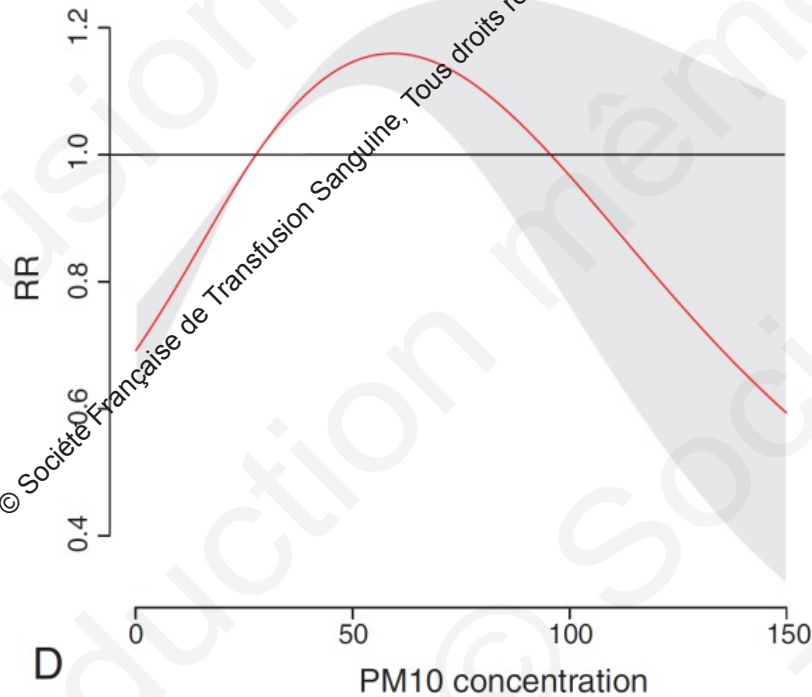
Saisonnalité CVO/STA



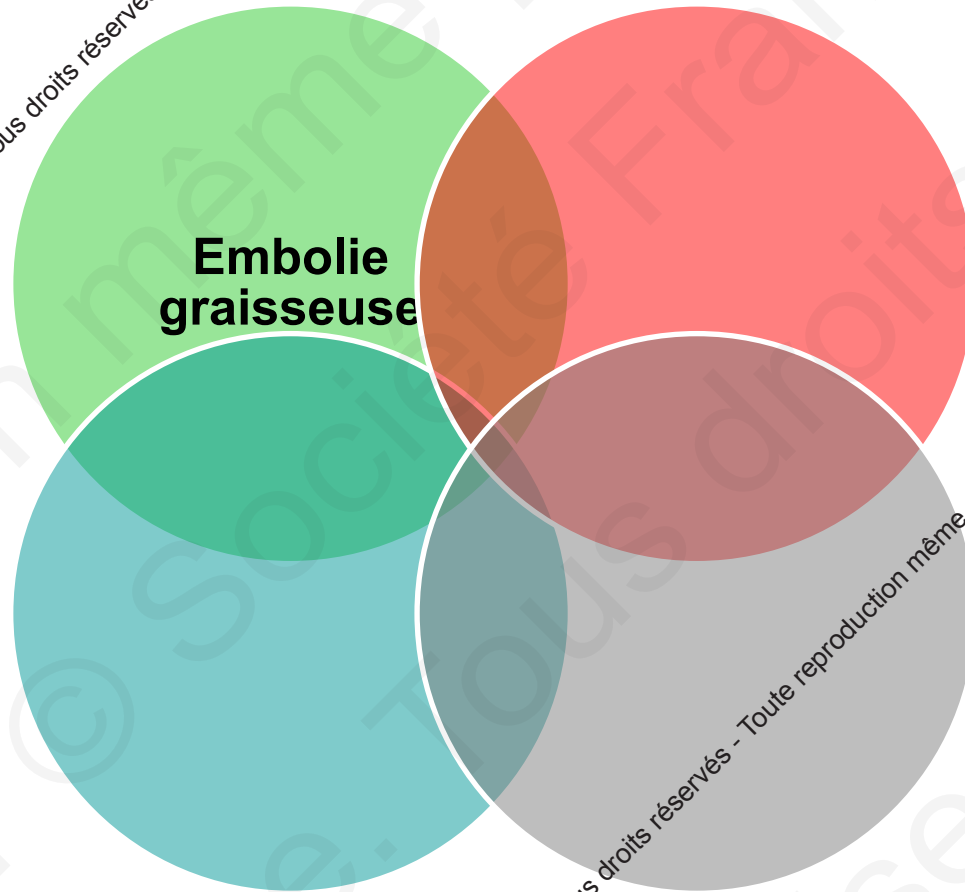
CVO/STA et environnement



CVO/STA et environnement



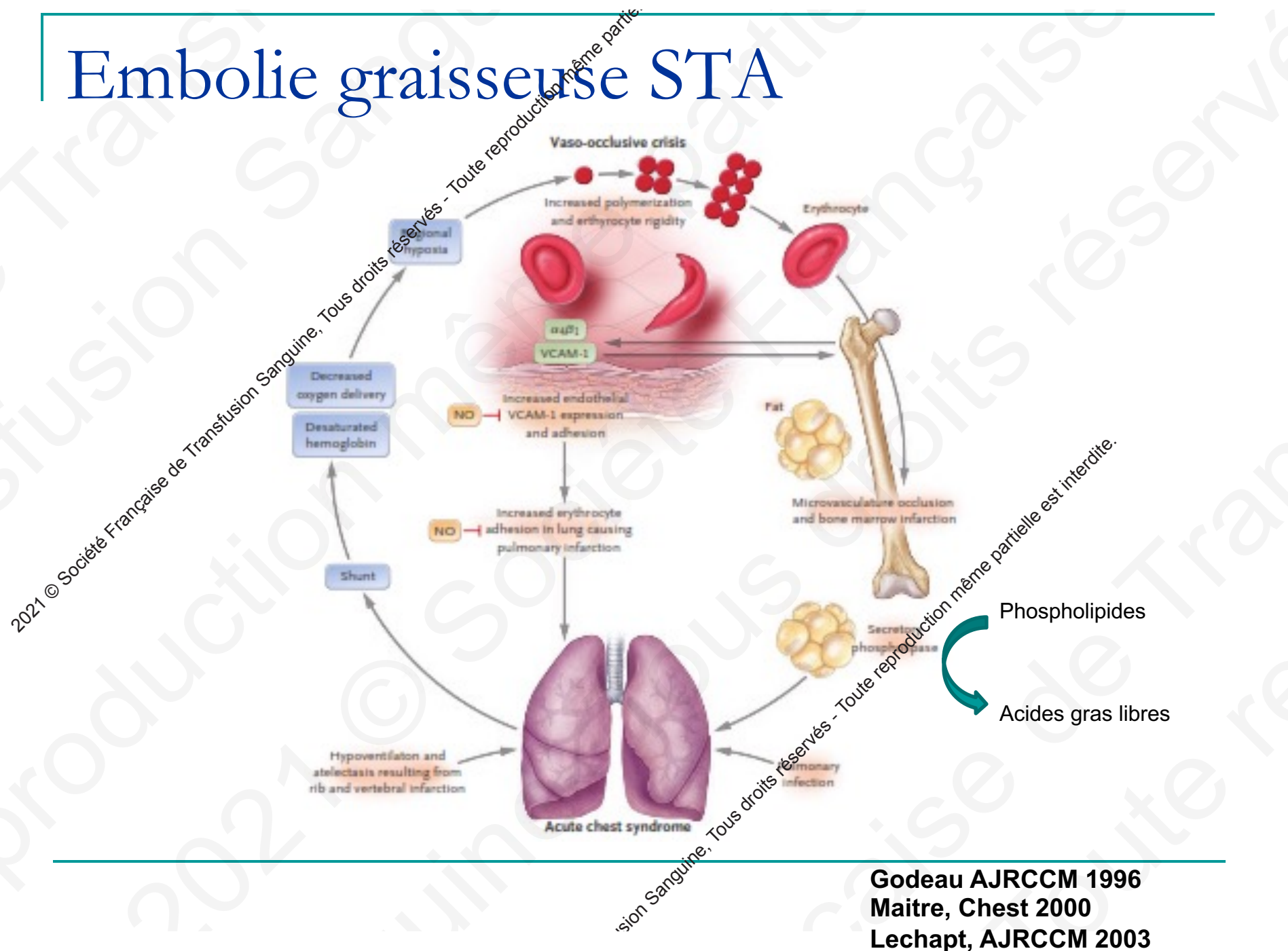
Physiopathologie STA



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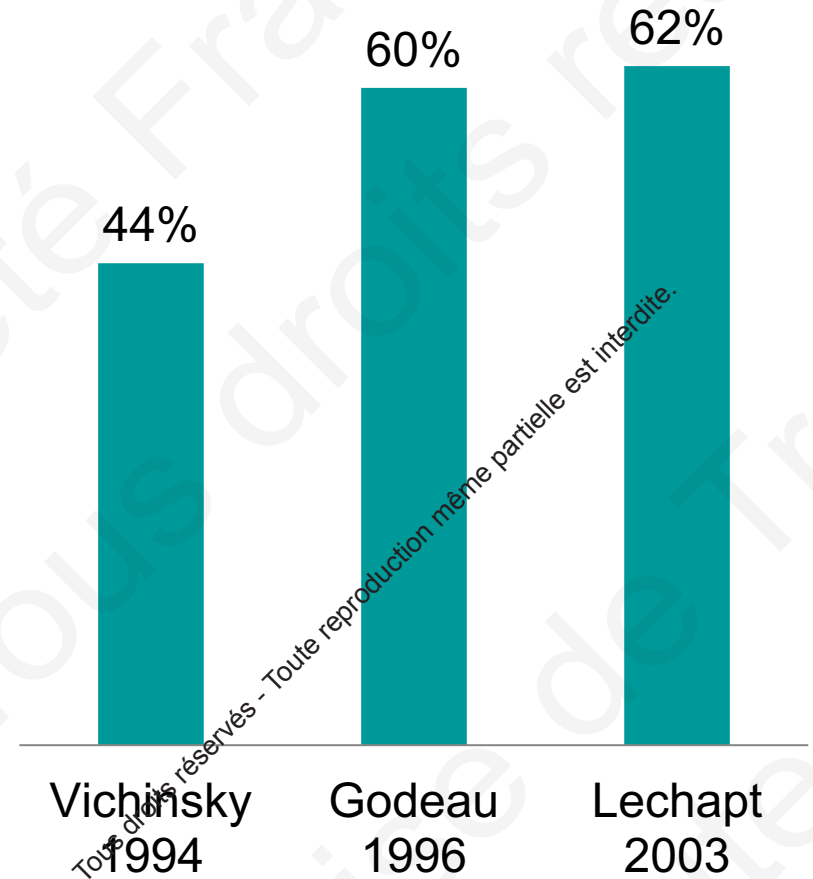
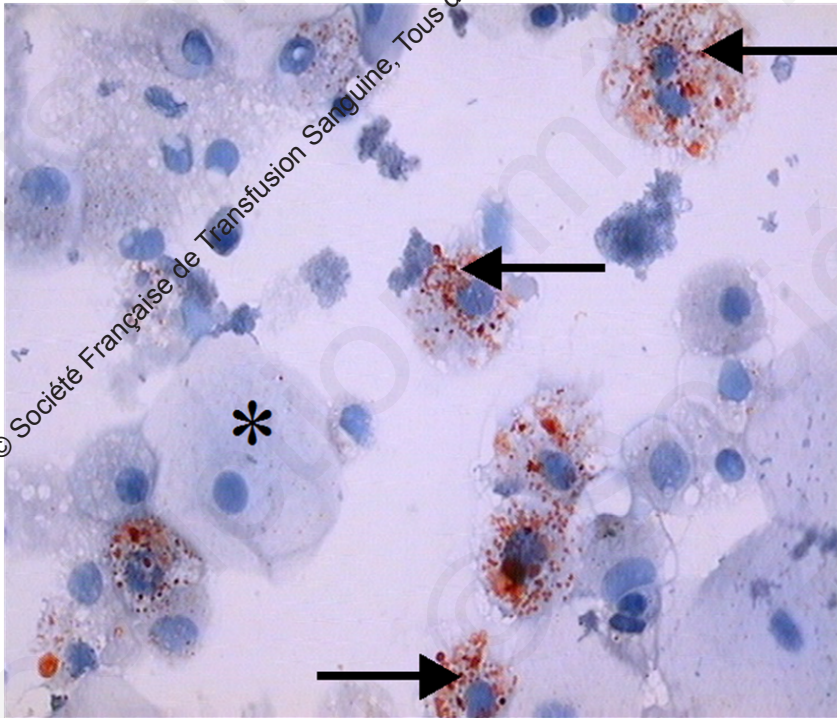
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Embolie graisseuse STA



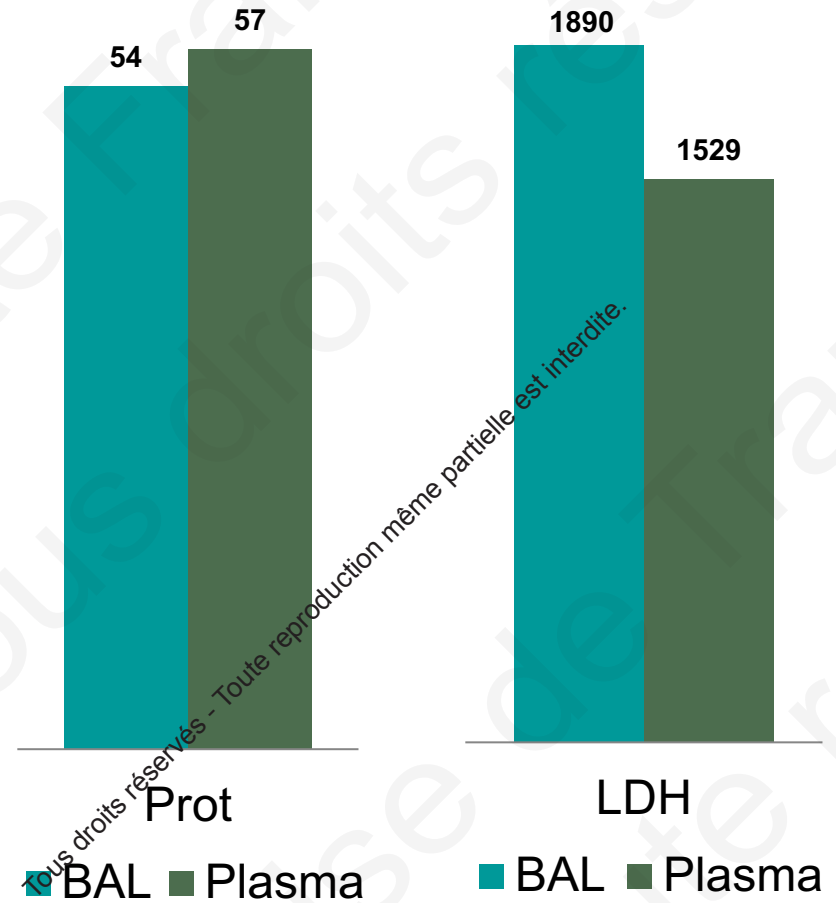
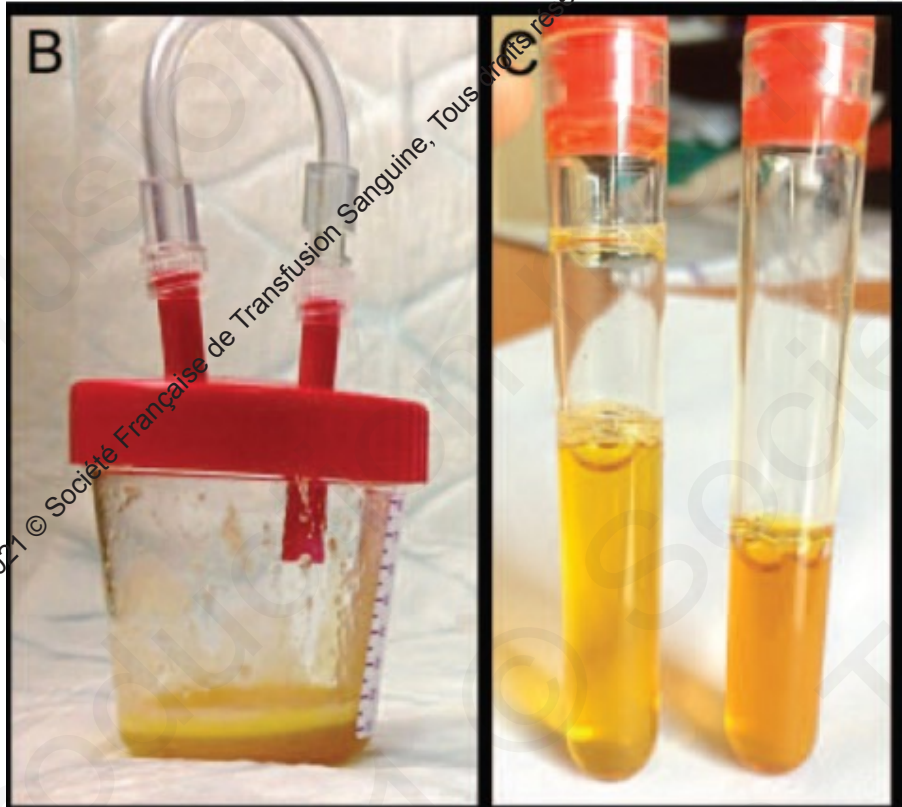
Godeau AJRCCM 1996
Maitre, Chest 2000
Lechapt, AJRCCM 2003

Embolie graisseuse STA

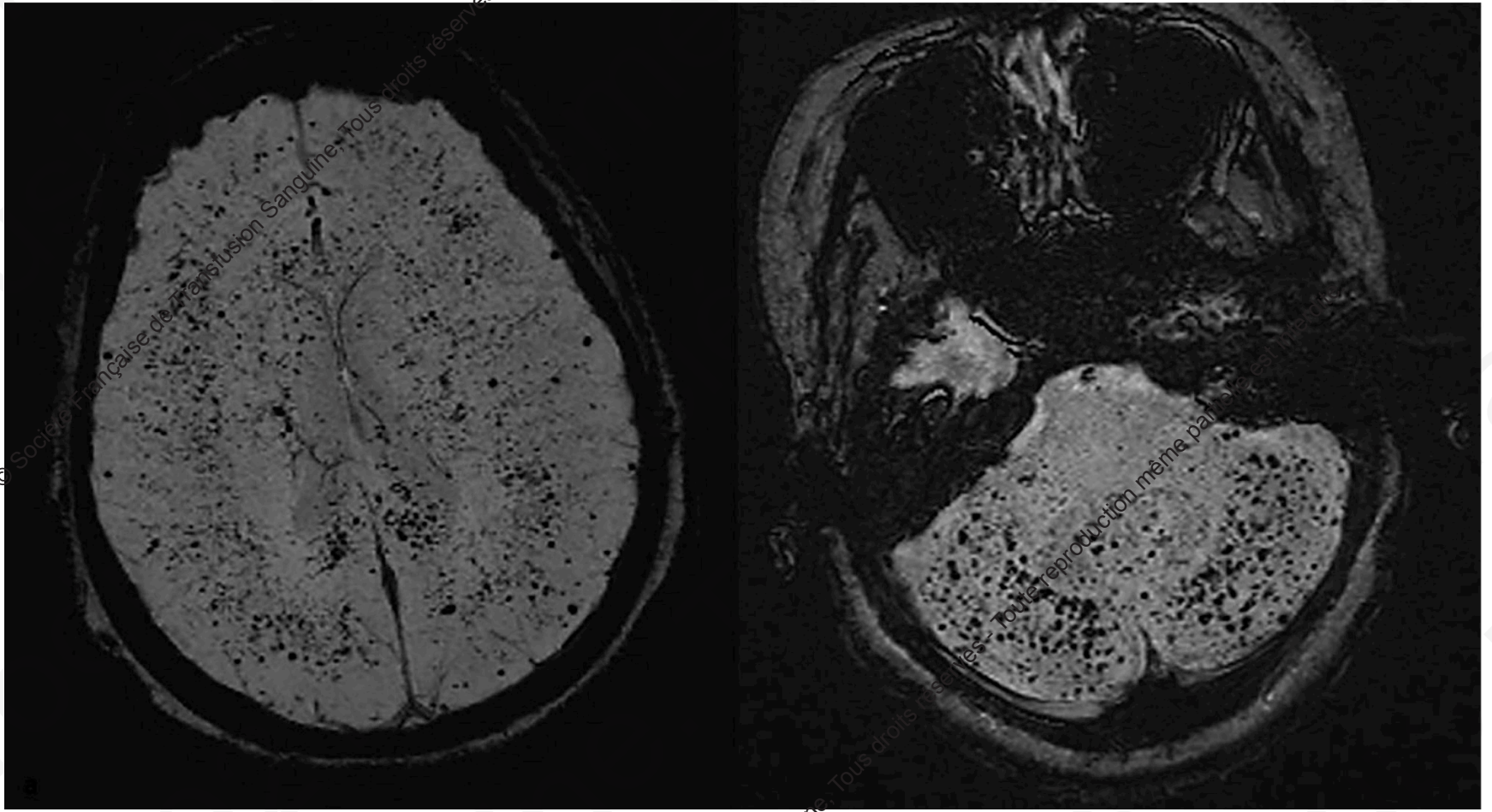


Maitre et al, Chest 2000
Lechapt, AJRCCM 2003

Expectoration jaune d'or

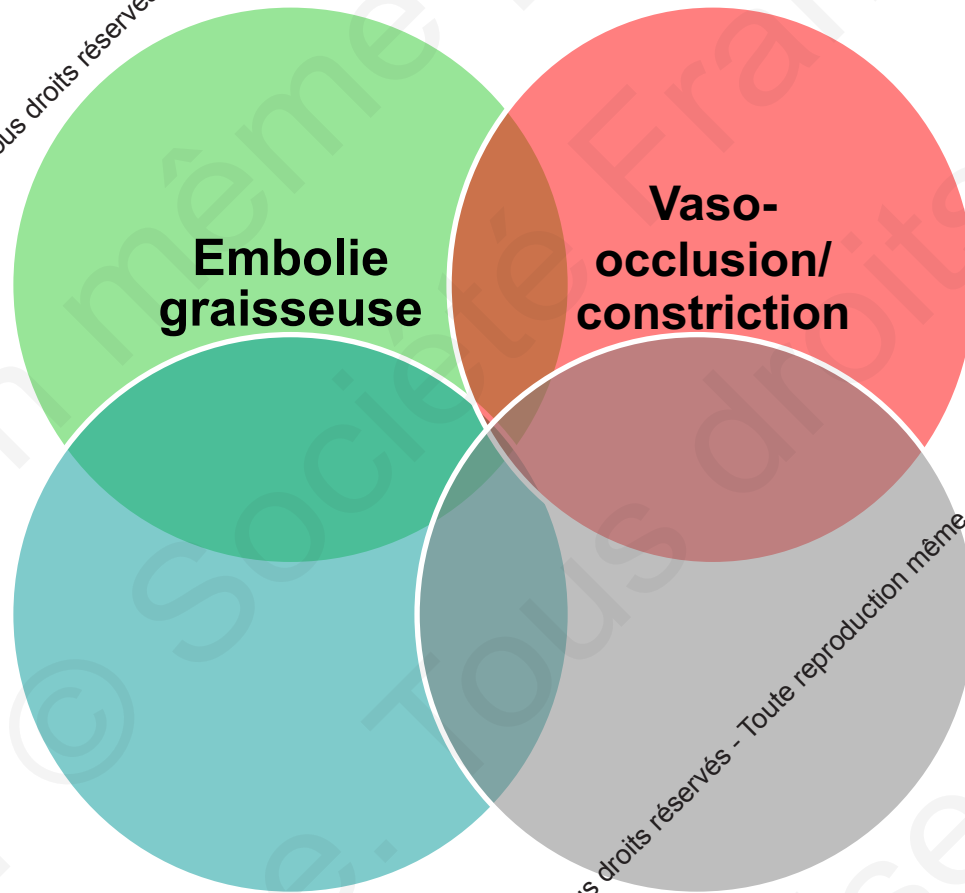


Embolie graisseuse systémique

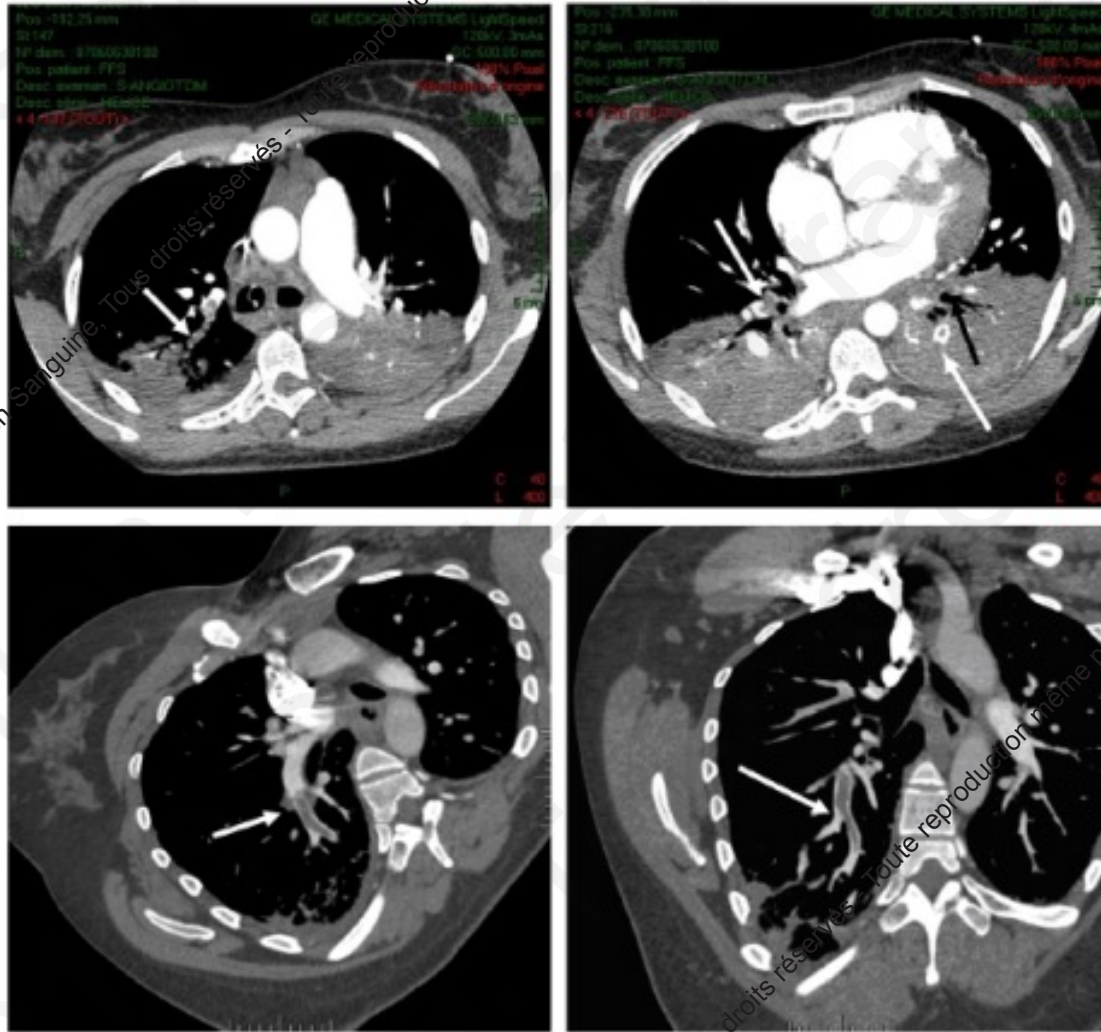


Intérêt SWI phase mapping ?

Physiopathologie STA



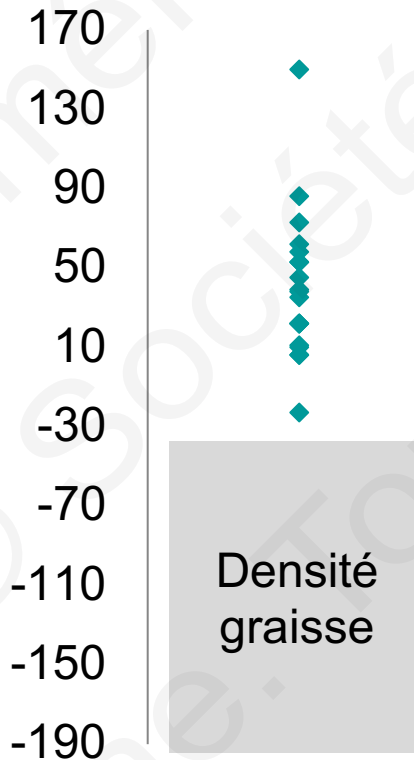
Thrombose artérielle pulmonaire



■ 17% des STA

Thrombose artérielle pulmonaire non graisseuse

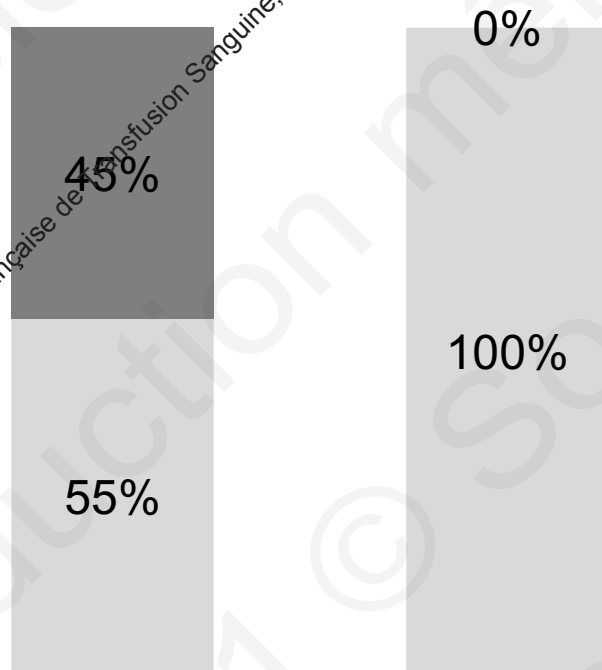
**Densité
cruorique**



MTE classique ?

Sans TVP

■ Absence TVP ■ Présence TVP



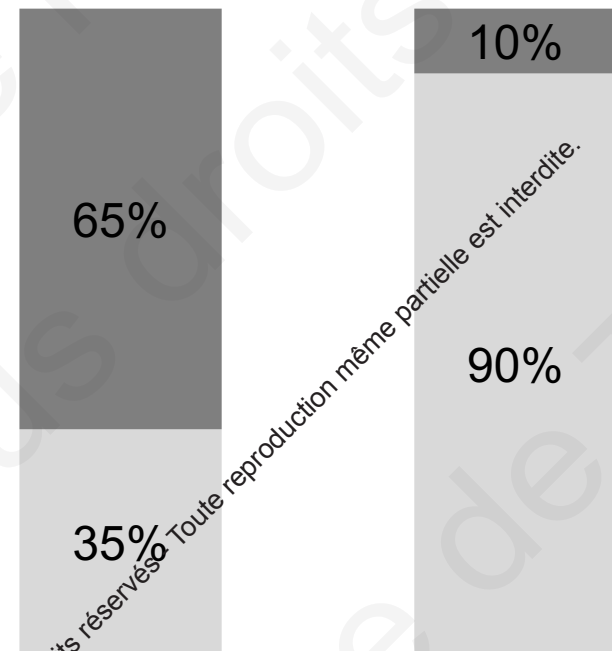
MTE classique

TAP du STA

Girard, Chest 2005

In situ

■ SS/S ■ L/T



MTE classique

TAP du STA

Righini, Lancet 2008

Score de risque de thrombose pulmonaire

FACTEURS DE RISQUE

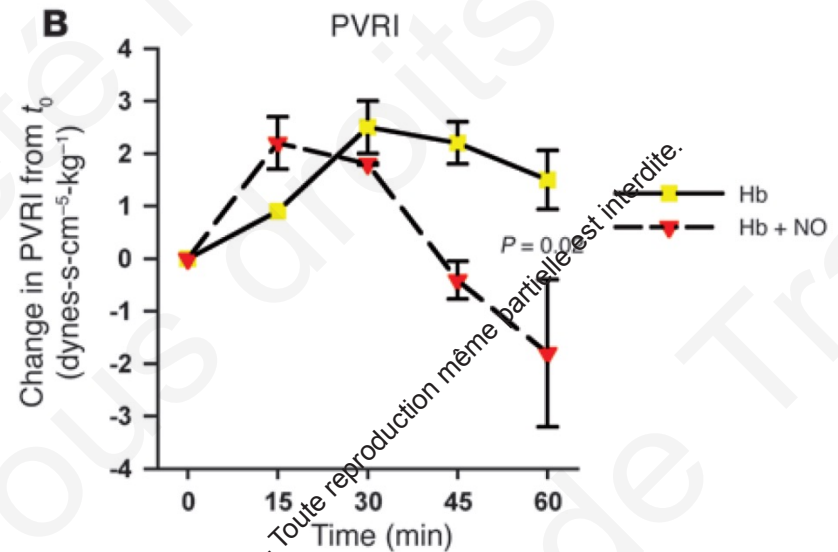
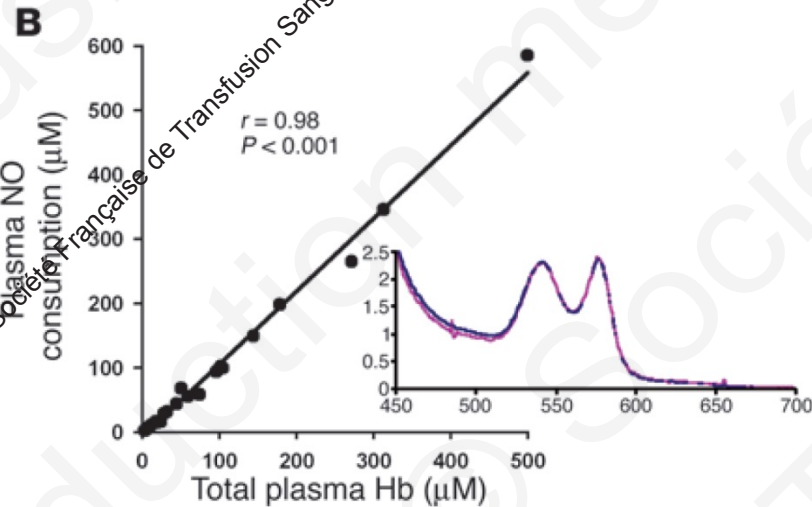
Hb de base >82 g/L

Pas de facteur déclenchant identifié de STA

Numération plaquettaire >440 G/L

$\text{PaCO}_2 <38$ mmHg au diagnostic de STA

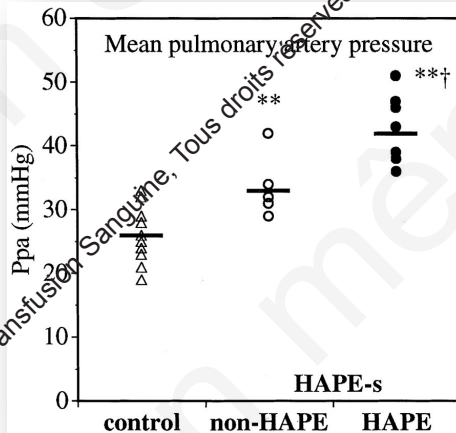
Vasoconstriction pulmonaire



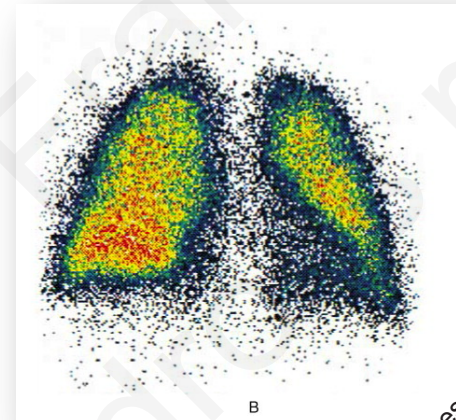
Œdème pulmonaire d'altitude

Vasoconstriction pulmonaire hypoxique

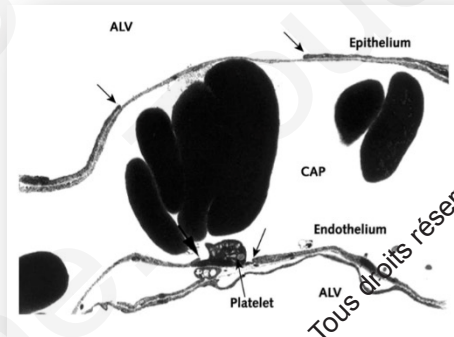
Excessive



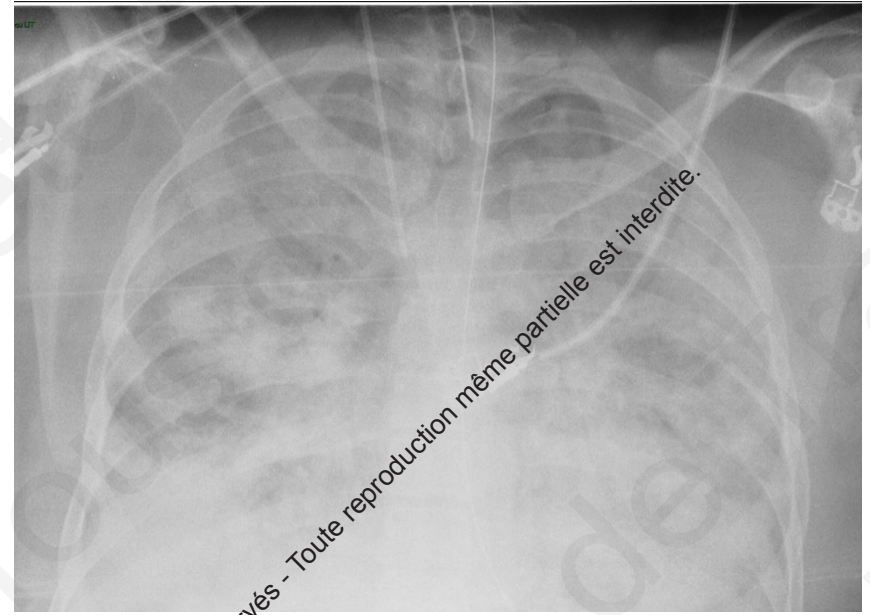
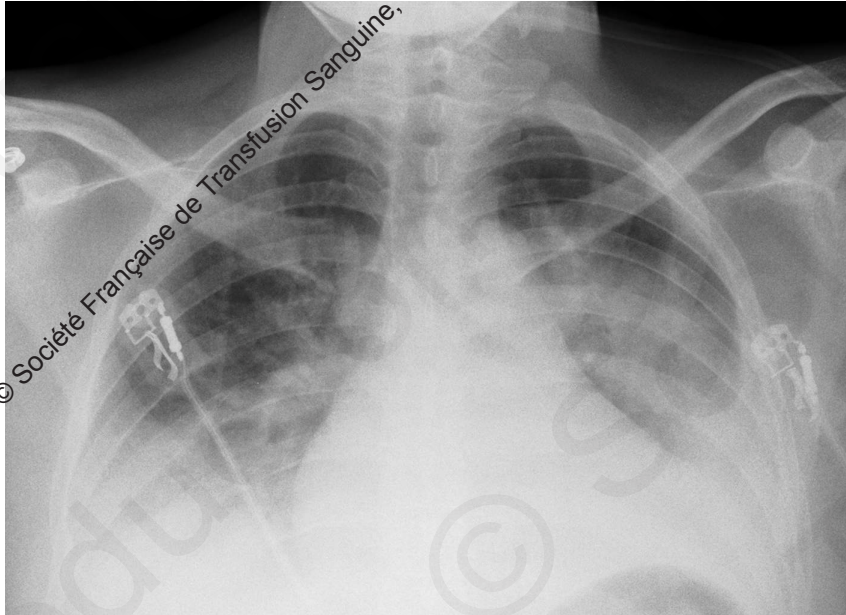
Inhomogène



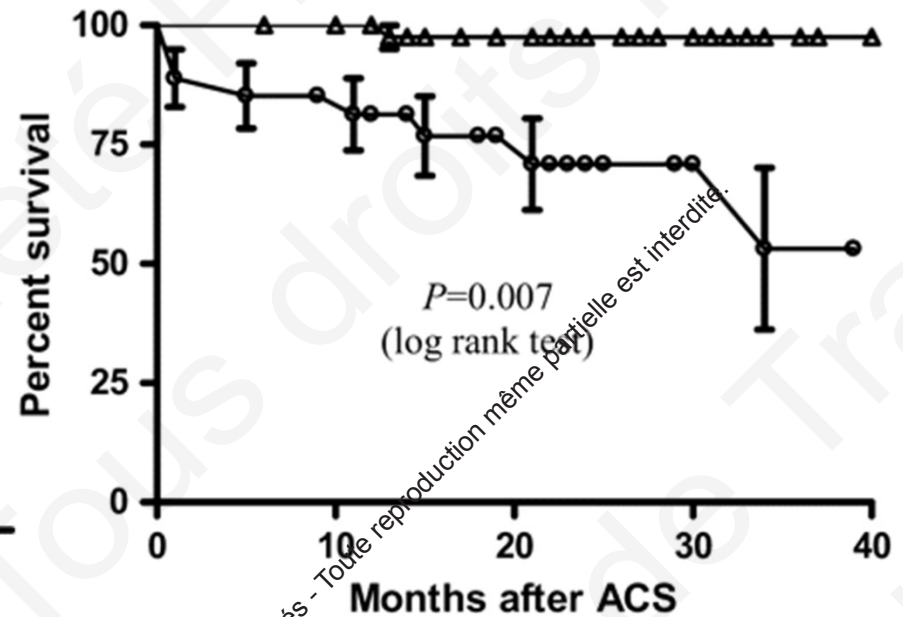
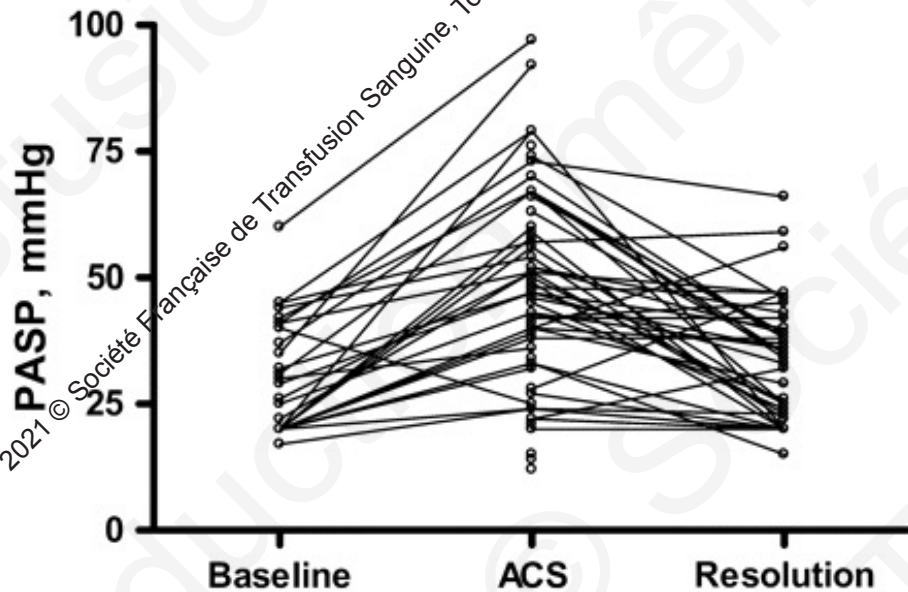
Hyper-perfusion régionale et rupture membrane alvéolo-capillaire



SDRA drépanocytaire

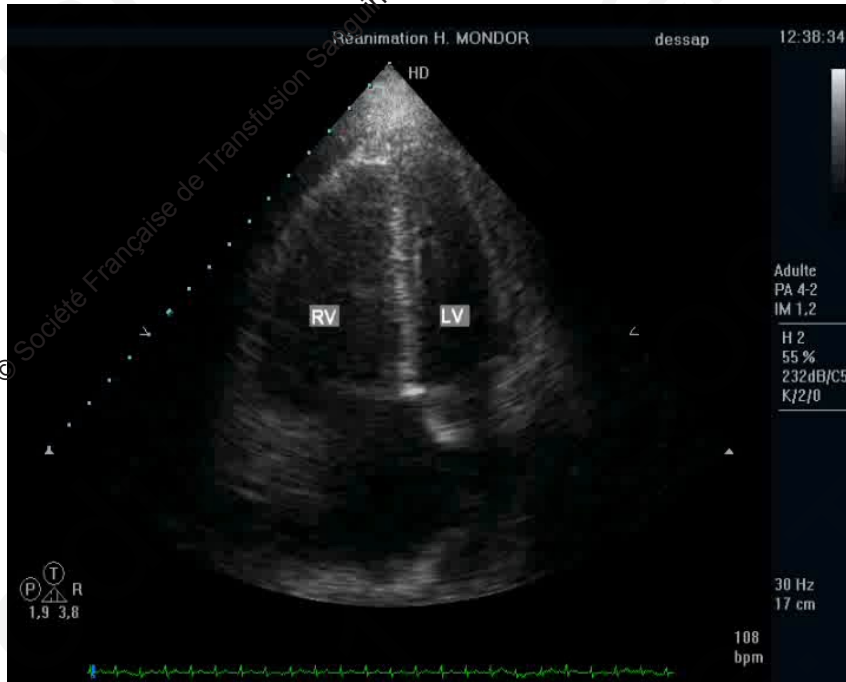


HTP aigue du STA

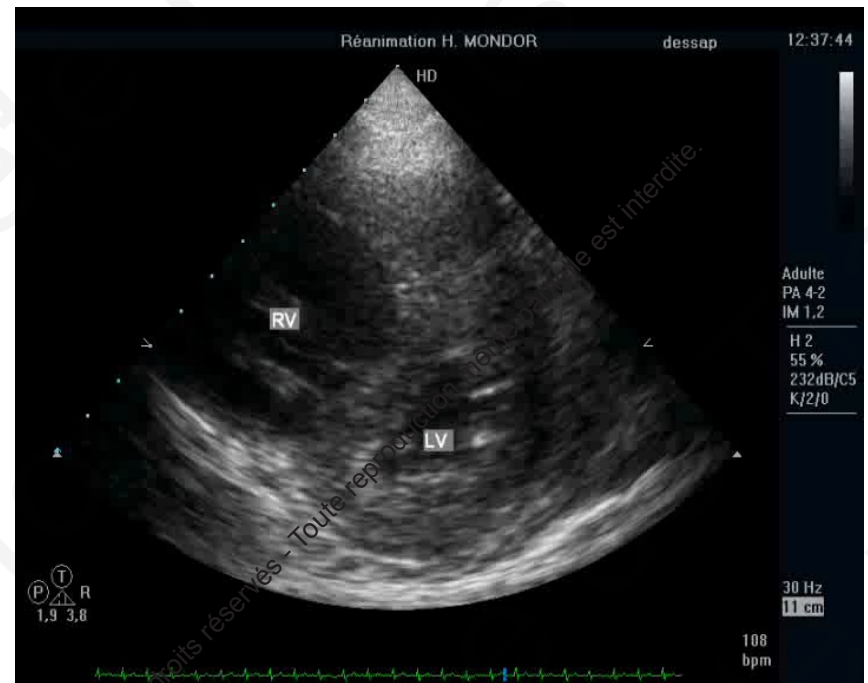


Coeur pulmonaire aigu

Dilatation VD



Septum paradoxal



Défaillances d'organe (IRA)

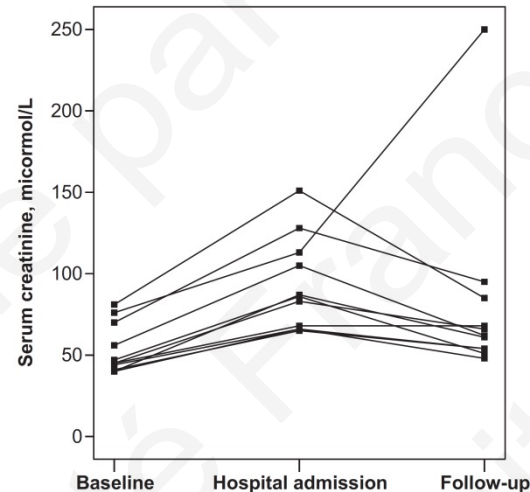
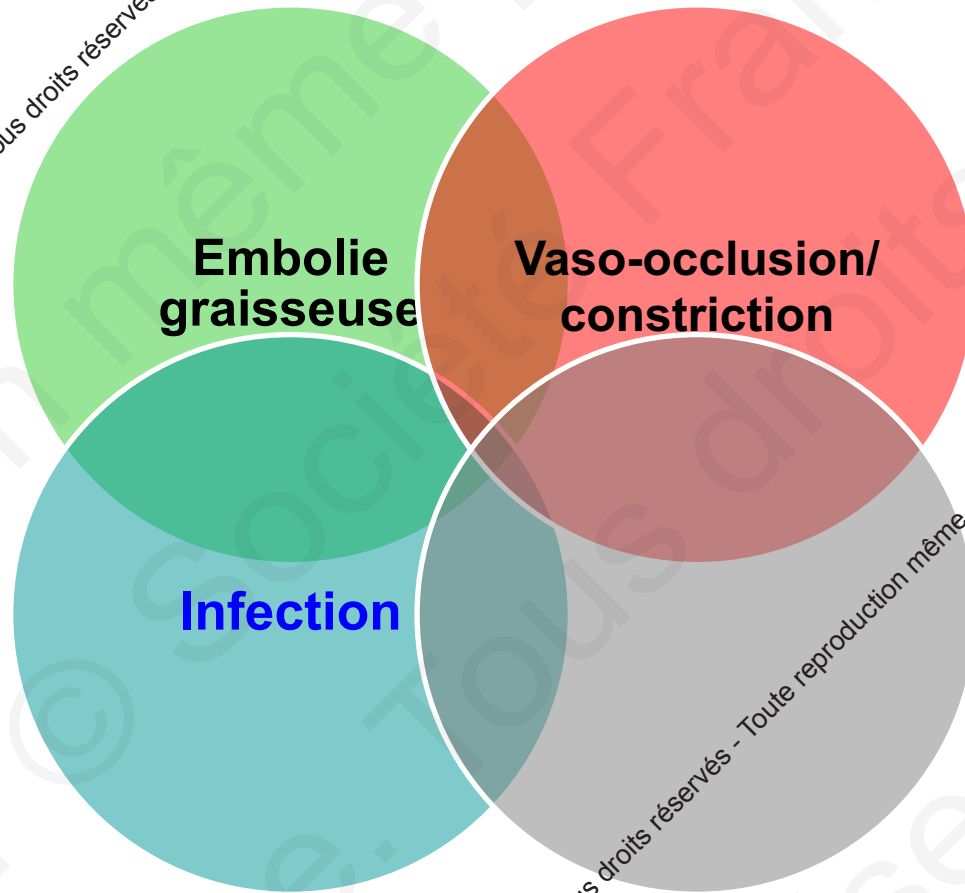


Fig. 1. Serum creatinine values at baseline, at hospital admission and at follow-up in patients with AKI during vaso-occlusive complications ($n = 11$ patients).

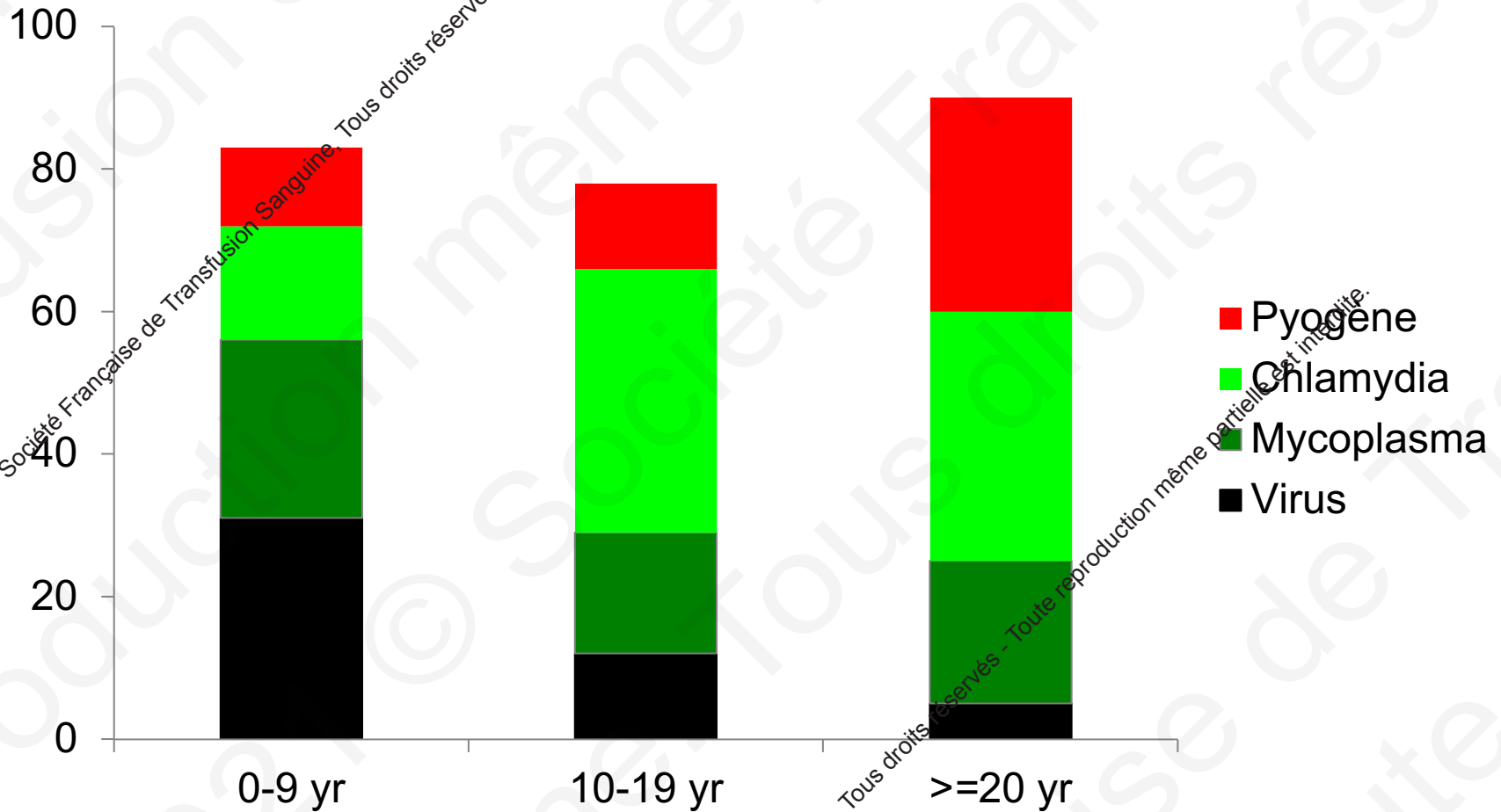
Table 1. Echocardiography data of patients with severe ACS at ICU admission in relation to whether they experienced AKI ($n = 65$ episodes)

Parameter	AKI during severe ACS		P-value
	No ($n = 59$)	Yes ($n = 6$)	
LVEF, %	55 (50–60)	55 (46–65)	0.96
E/A ratio	1.38 (1.10–1.74)	1.40 (0.85–2.49)	0.79
IVC collapse, %	16 (3–38)	0 (0–6)	0.02
Tricuspid regurgitant jet velocity, m/s	2.8 (1.8–3.2)	3.6 (3.1–3.9)	0.01
Systolic pulmonary artery pressure, mmHg	46 (28–54)	67 (54–74)	0.01
Cardiac index, L/min/m ²	3.5 (2.8–4.4)	3.5 (2.6–4.0)	0.73
Stroke index, mL/m ²	38 (33–43)	38 (23–45)	0.70
Cor pulmonale, ^a n (%)	5 (8.5%)	4 (66.7%)	<0.01

Physiopathologie STA

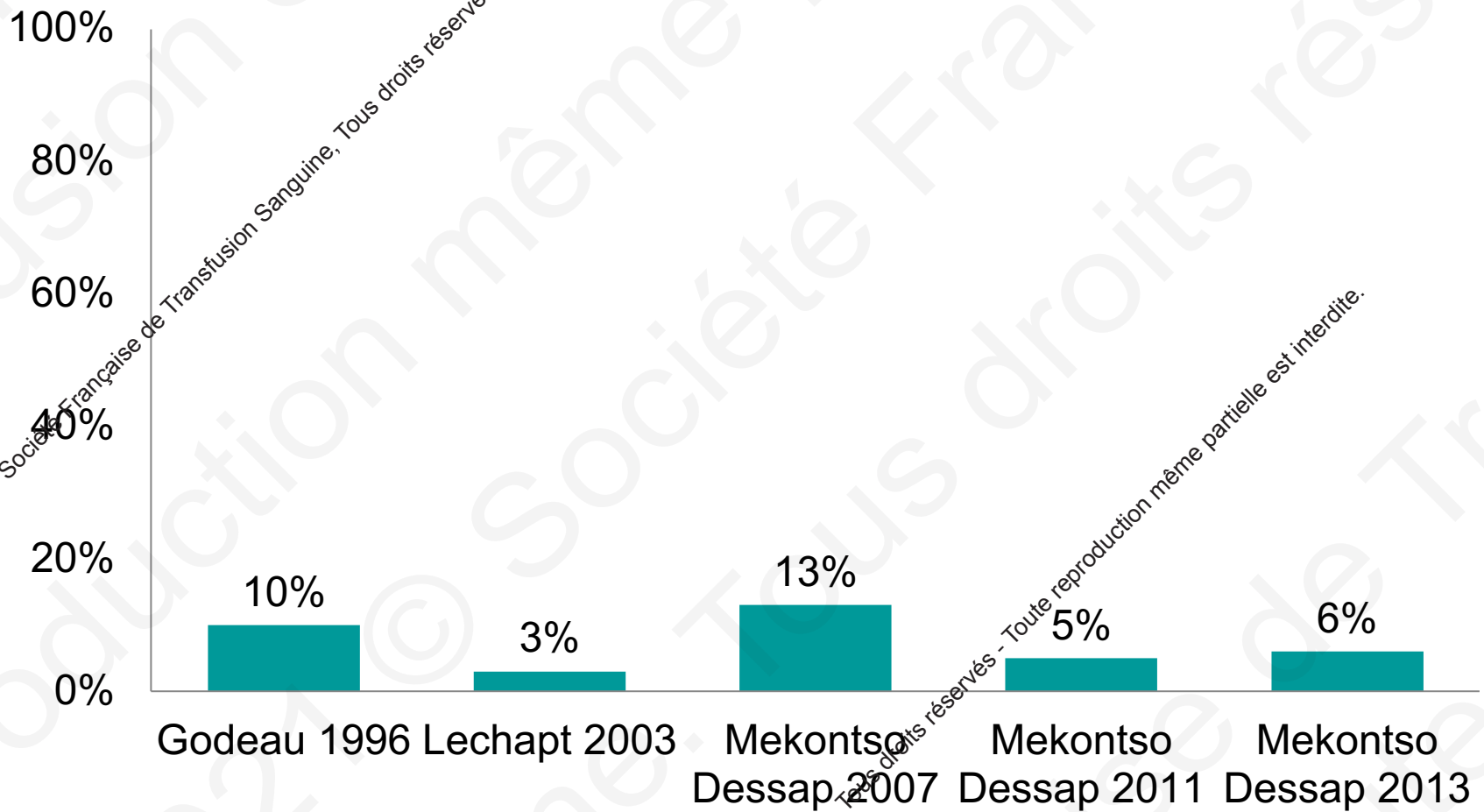


Infection et STA

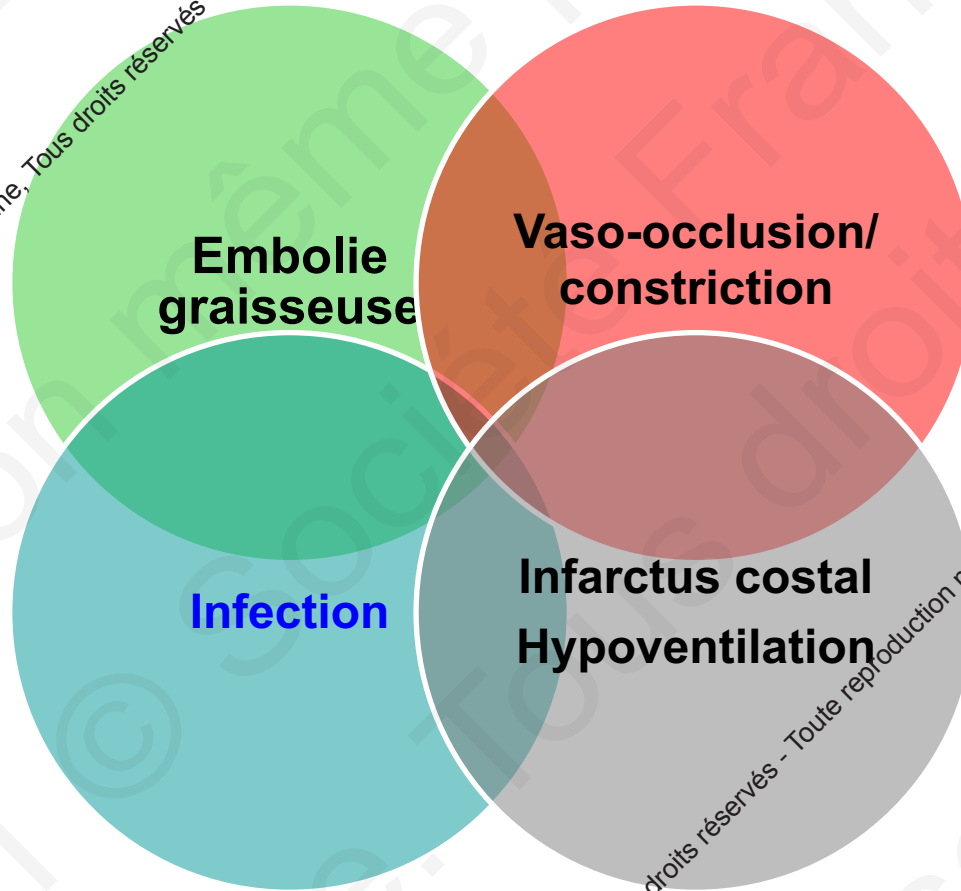


Vichinsky, NEJM 2000

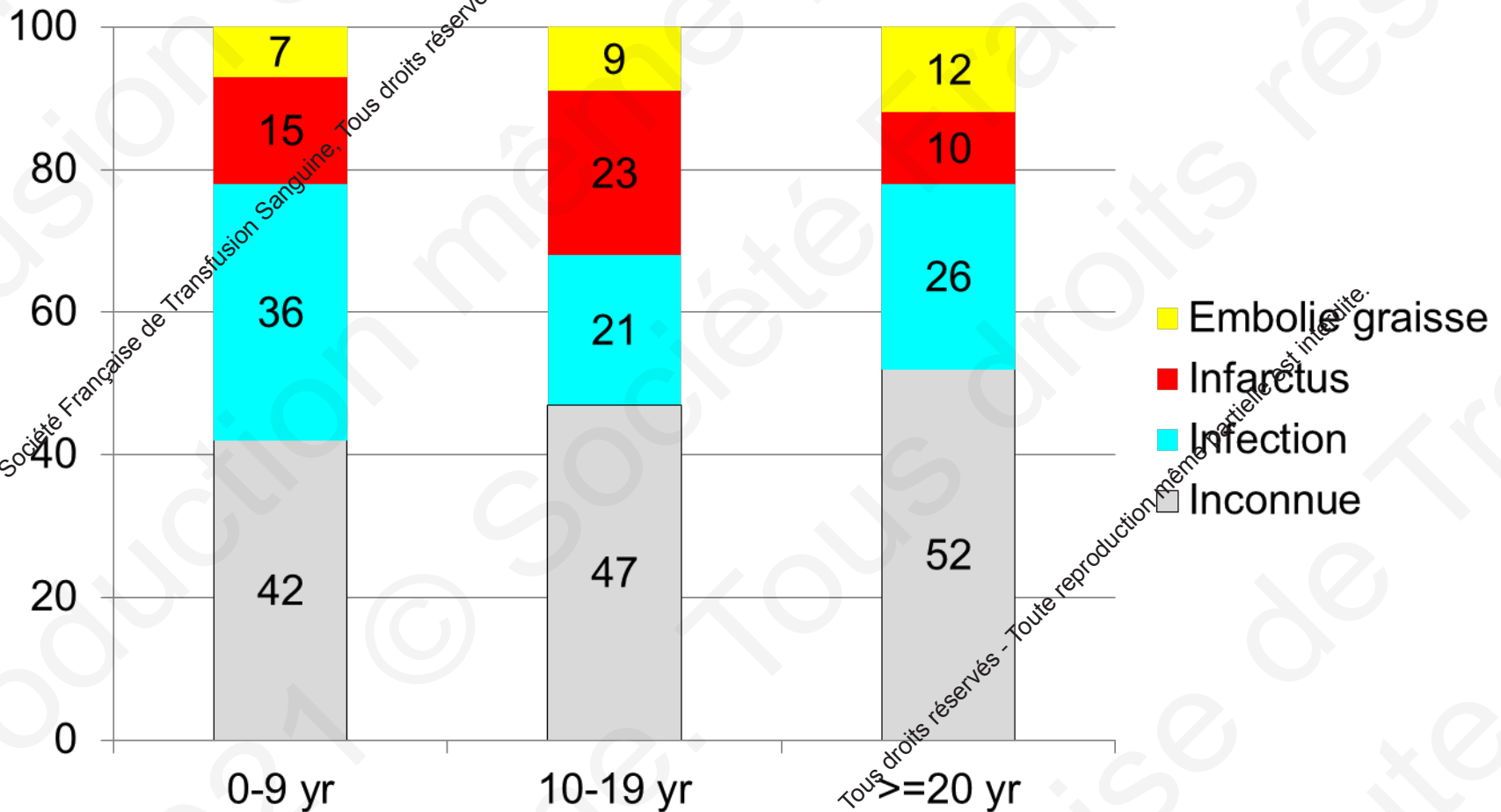
Infection et STA



Physiopathologie STA



Mécanismes du STA



*Ni graisse ni infection
Vichinsky, NEJM 2000

STA: Biologie

LDH

Leucocytes

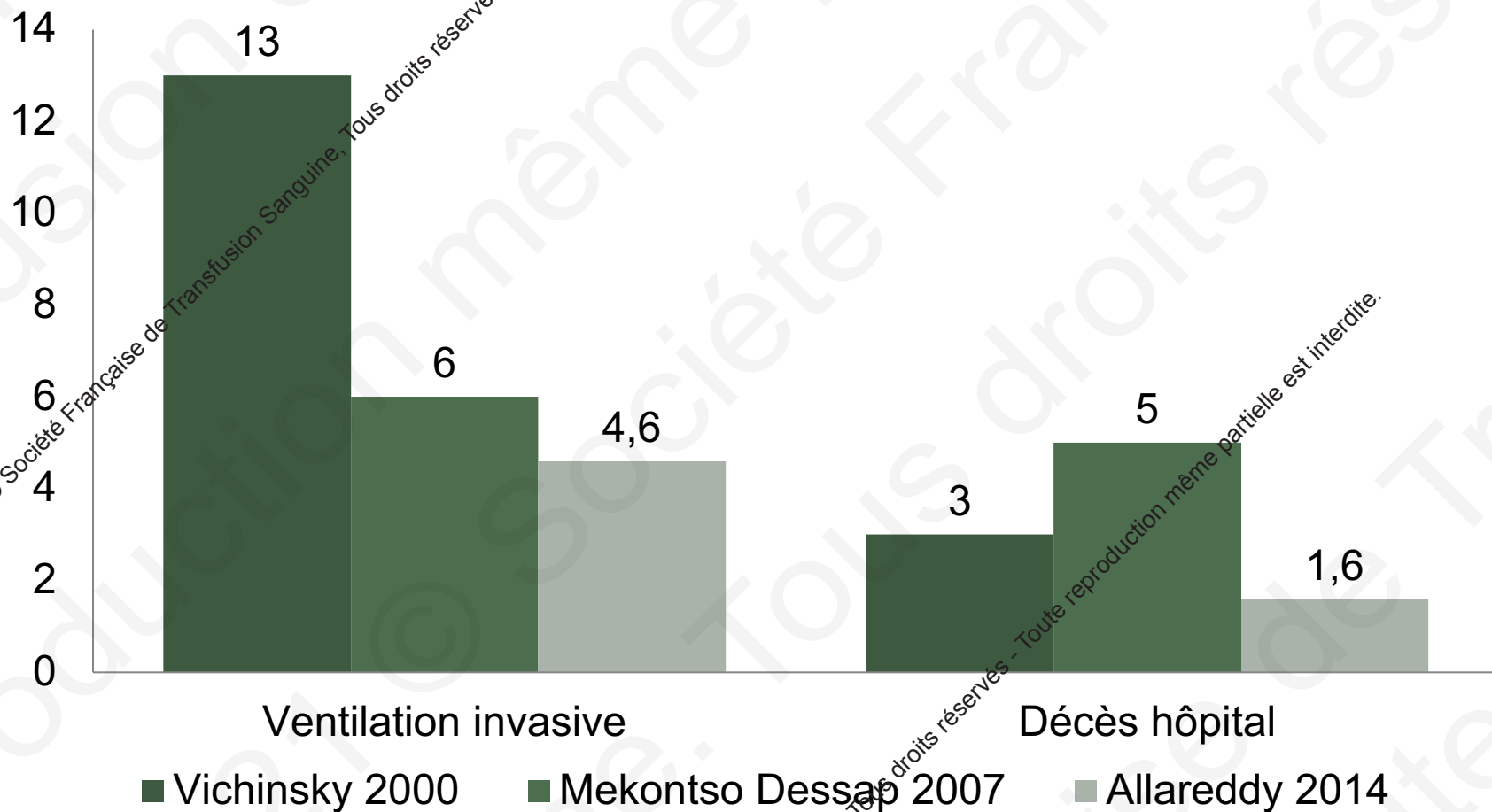
Plaquettes

PaCO₂

Hb

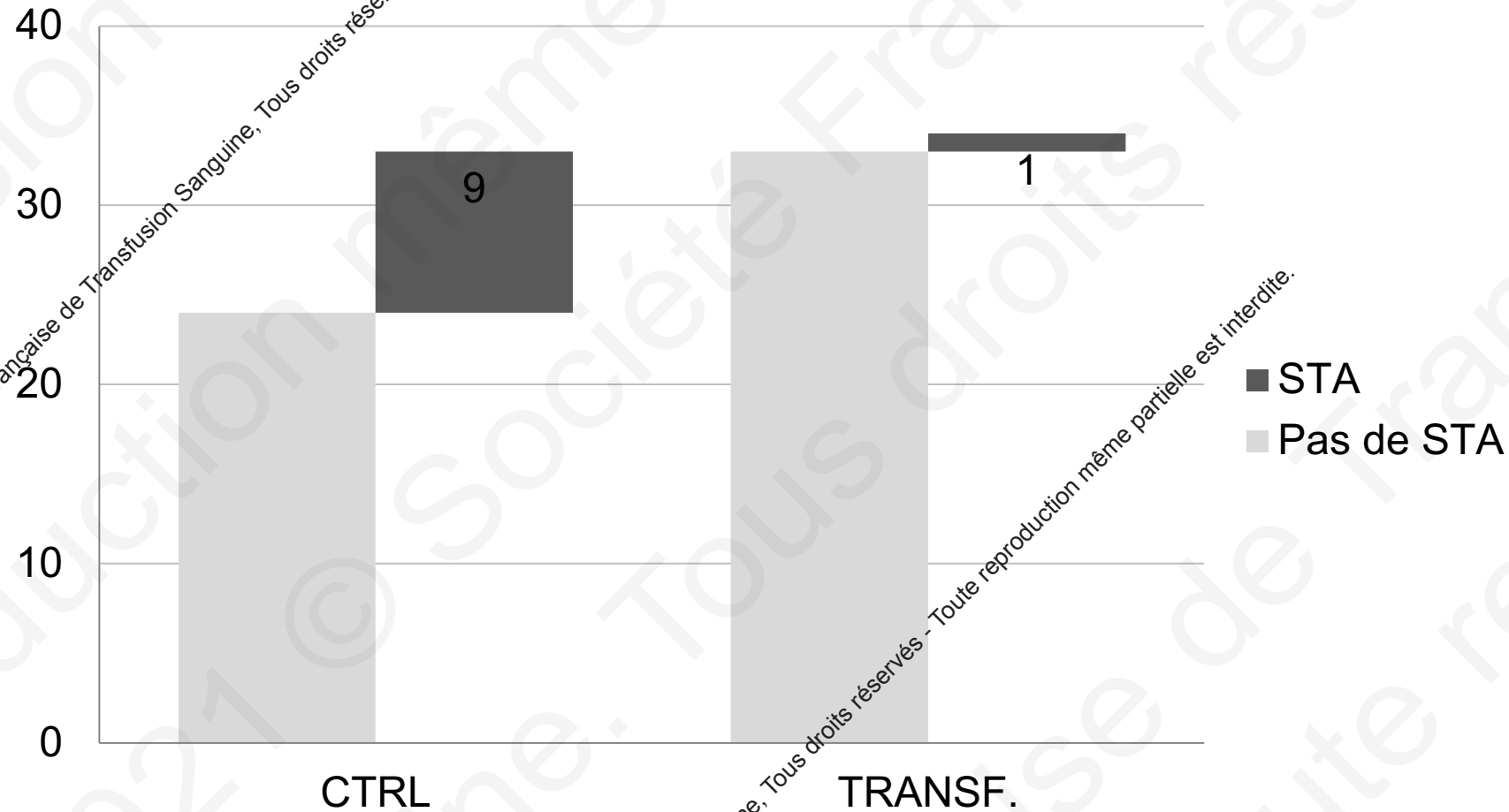
PaO₂

Pronostic STA



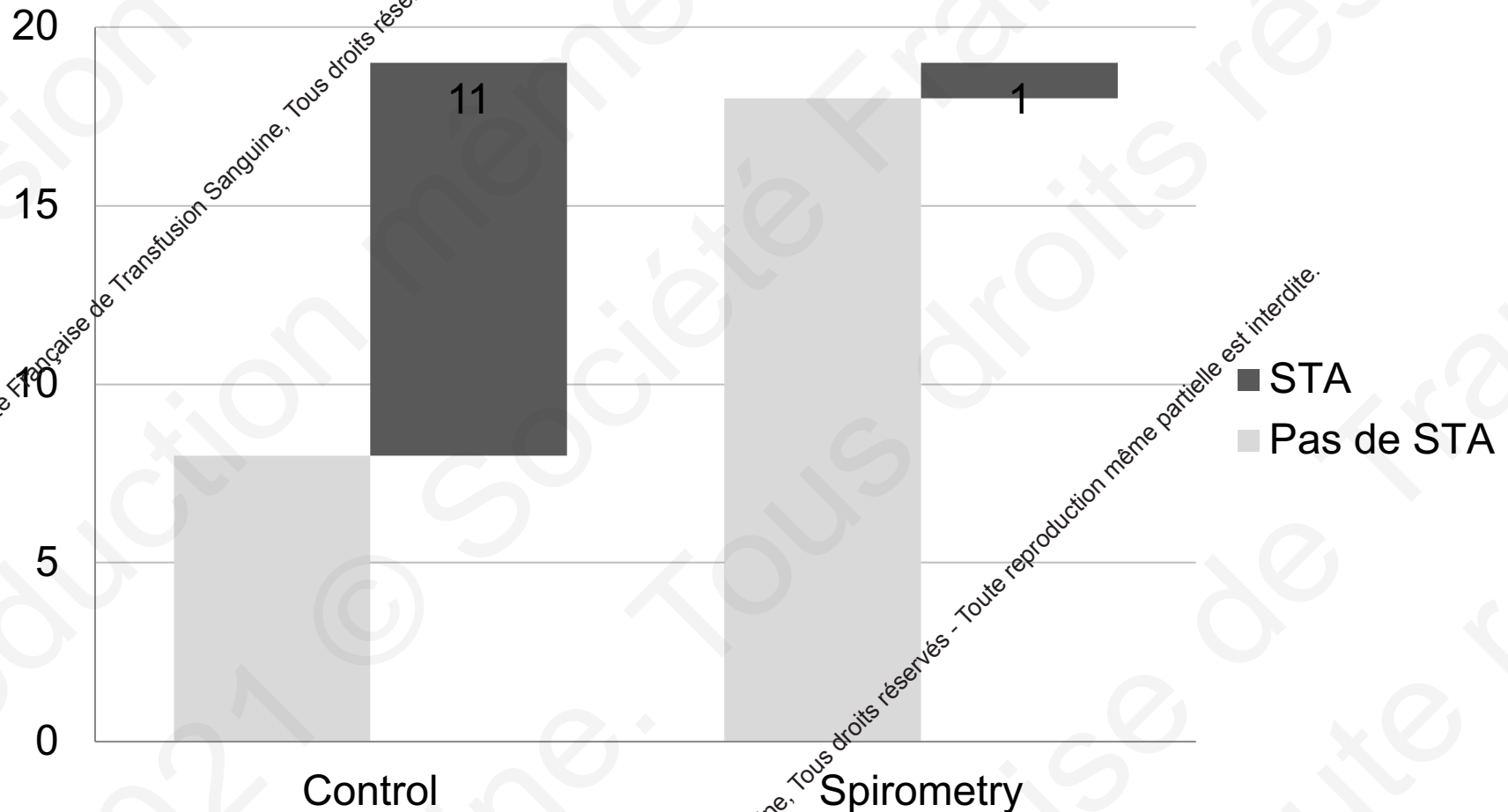
Prévention CVO/STA

Transfusion pré-opératoire



Prévention STA

Spirométrie incitative (CVO)



Bellet, NEJM 1995

Traitement STA

SYMPTOMATIQUE

- Hydratation
- Analgésie
- Oxygène/VNI/OHD
- Transfusion
- Stéroïdes ?
- iNO ?

ETIOLOGIQUE

- Antibiotiques
- Anticoagulants
 - Thrombose pulmonaire

Patient intubé -SDRA

- Mesures de protection vasculaire pulmonaire
 - Limitation volumes et pressions
 - Limitation hypercapnie (espace mort instrumental)
 - Décubitus ventral ++
 - Vasodilatateurs pulmonaires

Analgésie multimodale

■ Morphine

□ Titration

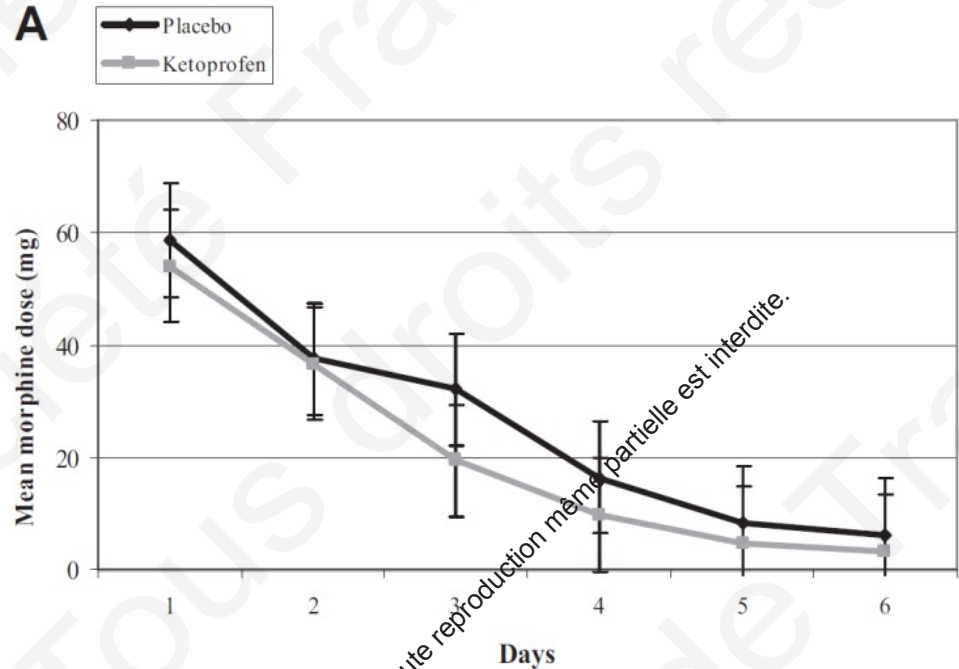
□ PCA

■ Paracétamol

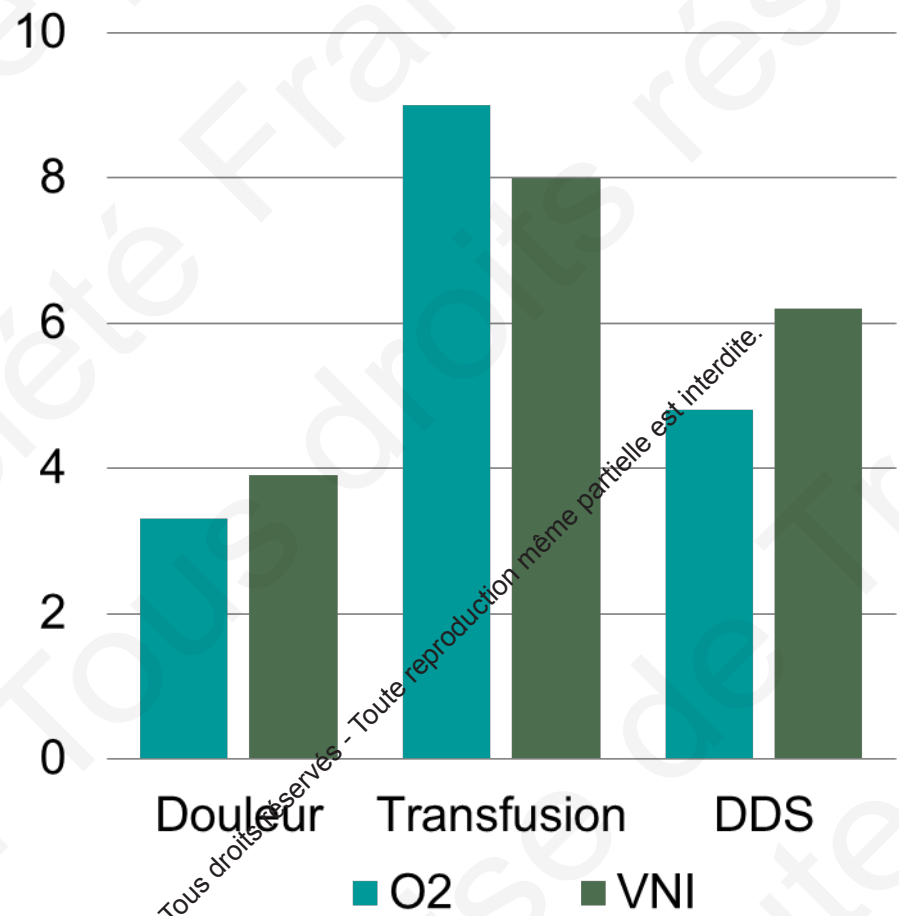
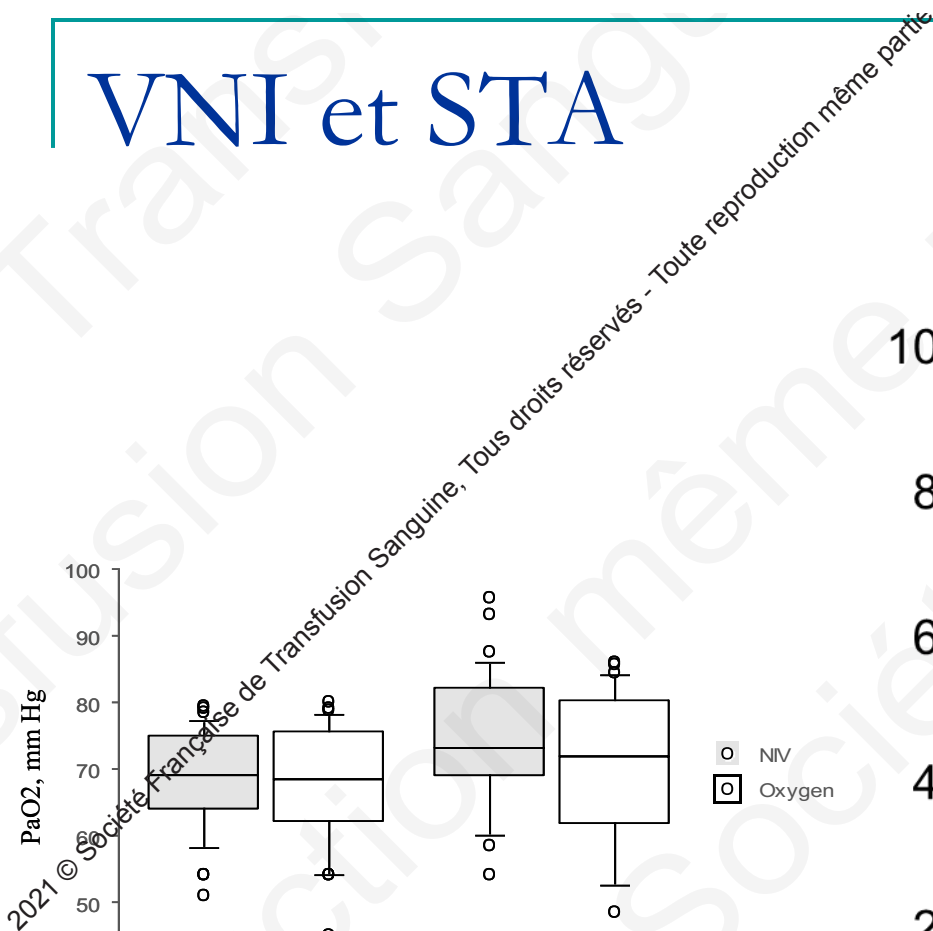
■ Nefopam

■ ± Kétamine

■ ± Protoxyde d'azote



VNI et STA



Transfusion

■ Rationnel:

- ↓ HbS, falciformation et vaso-occlusion
- ↑ TaO₂ et oxygénation tissulaire

Transfusion

- Objectif: Hb de base (<10 g/dL); HbS $< 30\%$ dans cas sévères

Transfusion

■ Indications principales

□ Terrain:

- Programme transfusionnel chronique
- Grossesse, post-partum,
- Postopératoire

□ Sévérité clinique

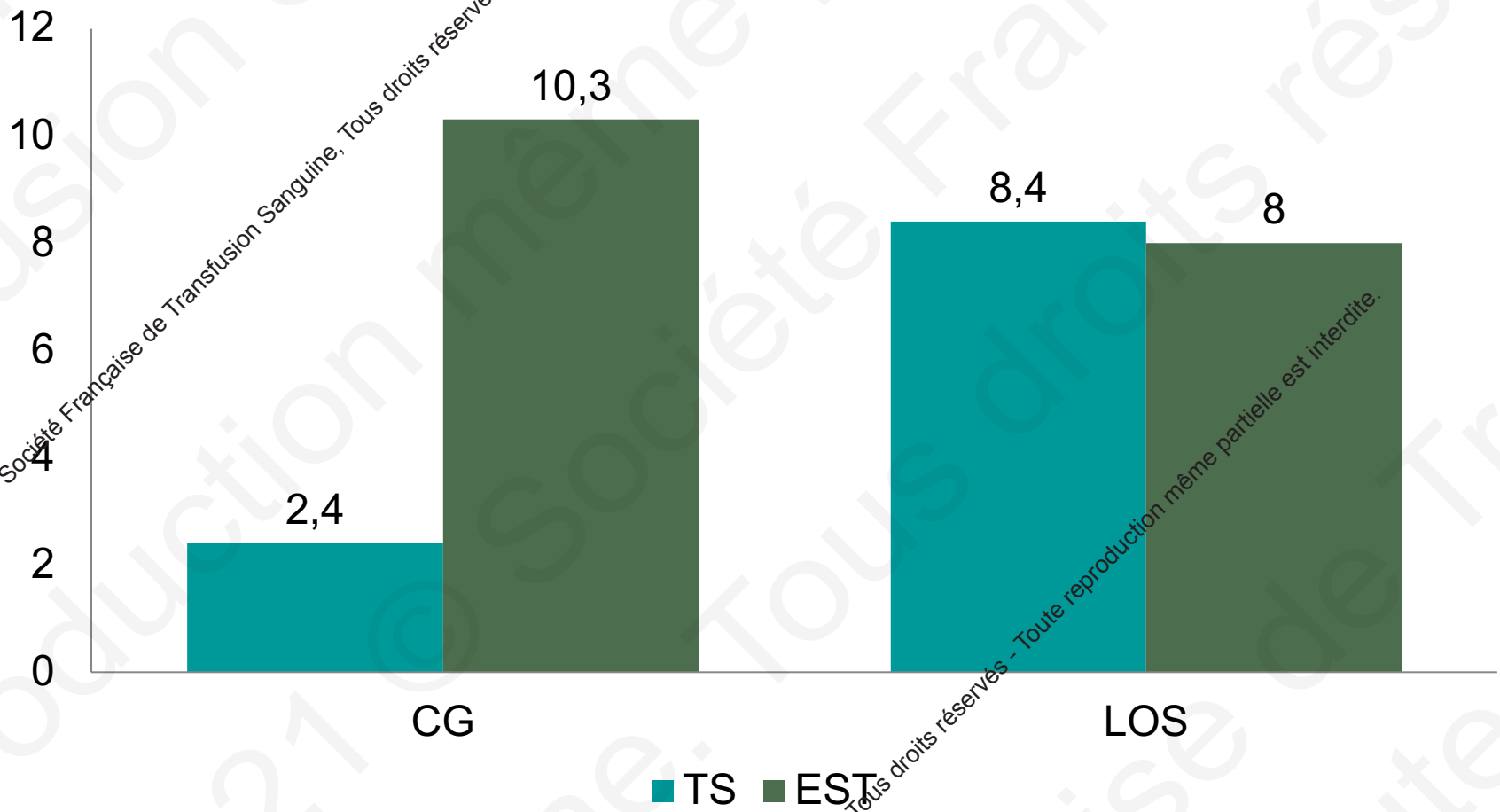
- Détresse respiratoire
- Troubles de la conscience
- IVD
- Sepsis sévère

□ Sévérité paraclinique

- Hb < 6g/dl, atteinte Rx étendue

□ Absence amélioration après 72h

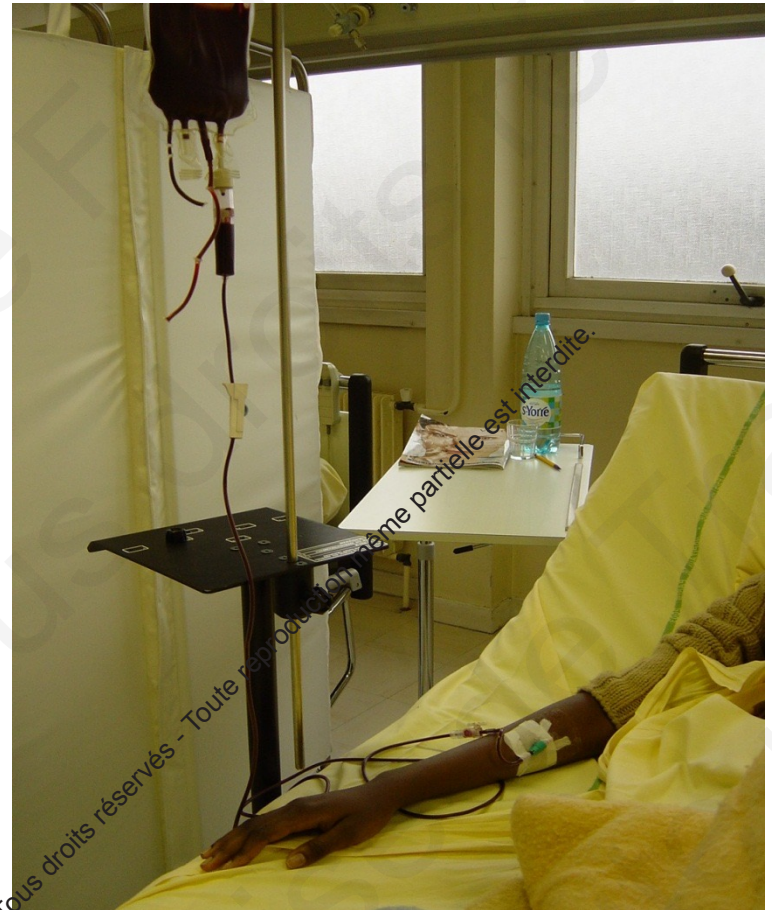
Transfusion simple ou EST ?



Modalités transfusion

Taux d'Hb	Volume de la 1 ^{re} saignée	volume du 2 ^{ème} saignée	Transfusion
< 7 g/dl	0	0	2 à 3 CG
7.5	0	150 ml	3 CG
8	0	200 ml	2 CG
8.5	0	250 ml	2 CG
9	200 ml	200 ml	2 CG
9.5	200 ml	250 ml	2 CG
10	250 ml	300 ml	2 CG
10.5	300 ml	300 ml	2 CG
11	300 ml	350 ml	2 CG
11.5	350 ml	350 ml	2 CG
12	350 ml	400 ml +/- 1 saignée le lendemain	2 CG

Echange transfusionnel manuel



L'échange transfusionnel sur machine



Les avantages

- Isovolémie
- Prélèvement sélectif et rapide (60 à 90min)
- Manipulation automatisée
- Bonne tolérance clinique
- Pas d'hyperviscosité ni de surcharge martiale (Hte constant)

Les contraintes

- La qualité des abords veineux
- La disponibilité du séparateur de cellules
- Le coût

Les complications

- Surcharge en fer : Programme Tf au long cours ou Tf à répétition lors des hospitalisations
- Alloimmunisation
- Hémolyse post Transfusionnelles : rare mais grave
- Trali
- Réactions frissons et fièvre en cours de la transfusion
- Décompensation cardiaque
- Difficultés des voies d'abord

Hémolyse retardée post transfusionnelle

PRESENTATION

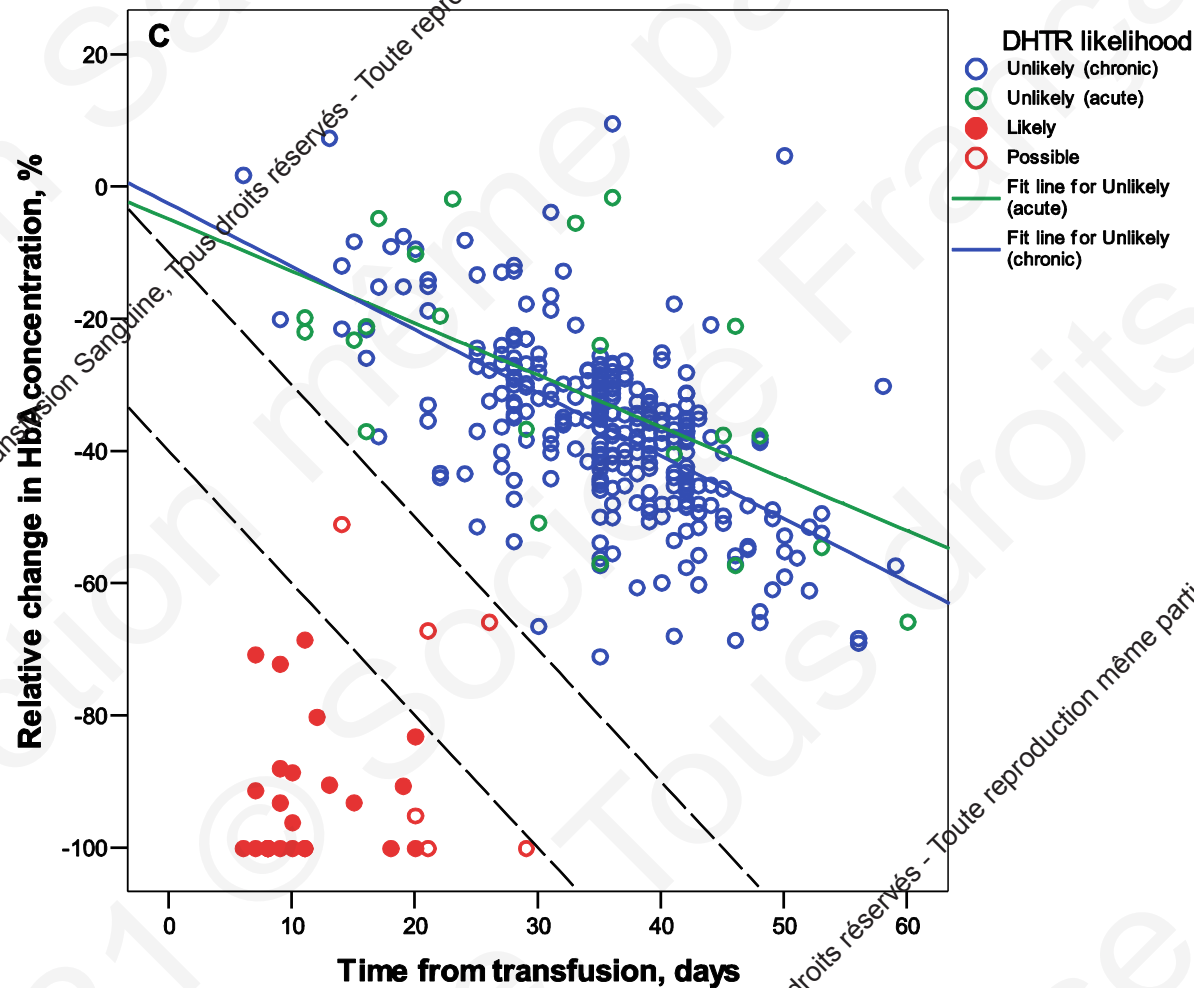
- >J3 transfusion
- CVO±STA



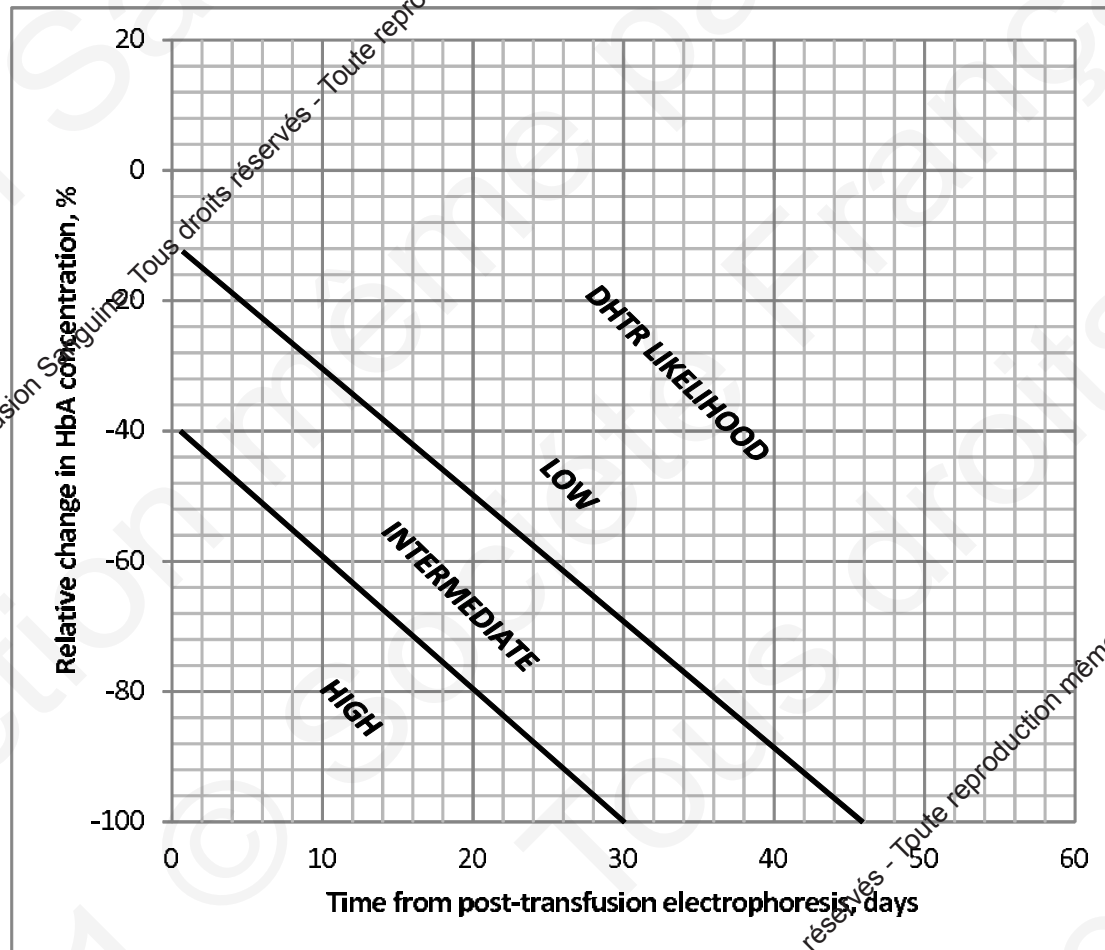
TRAITEMENT

- **Eviter nouvelle transfusion**
- EPO si reticulocytopénie
- Immunomodulation?
 - Ig
 - Rituximab (anti CD20)
 - Eculizimab (anti C5b-9)

DHTR nomogramme



DHTR nomogramme



<http://www.reamondor.aphp.fr/nomogram.php>

Risque de DHTR

Figure 2

PRESCRIPTION OF AN OCCASIONAL TRANSFUSION

Predictive score

- Historical significant Abs 6
- Historical non significant Abs and/or Rh/K 5
- Previous transfused units <12 8
- History of DHTR 5

Immunization status
of the patient

Score < 8

Score ≥ 8 : transfusion maintained

Immunization status of the patient	Score < 8	Score ≥ 8 : transfusion maintained
No previous immunization or only RH/K Abs	Rh/K matched RBCs	Rh/K and extended matched RBCs (Fy, Jk, MNS)
Significant Abs	Rh/K and matched to Ab specificity + if possible extended matched (Fy, Jk, MNS)	Rh/K and extended match (Fy, Jk, MNS) + Rituximab treatment

Antibiotiques et STA

■ Rationnel

- ↑ risque infectieux (asplénie)
- STA non discernable de la pneumonie
- Causes infectieuses rapportées, même si rares en routine clinique
 - Kirkpatrick Am J Med 1991

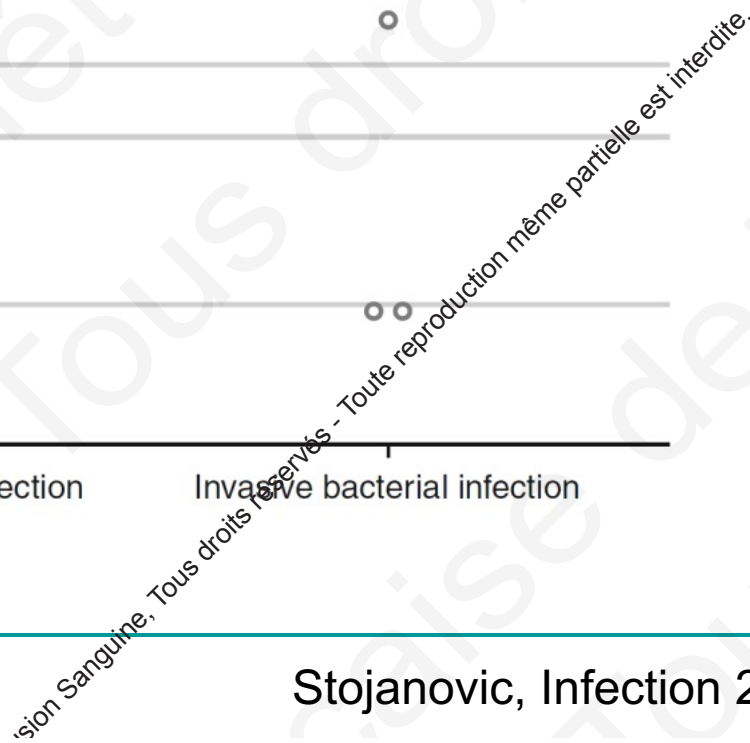
■ Indication

- Quasi-systématique, notamment si fièvre
- *S. pneumoniae* et intracellulaires
- Exemple: amoxicilline+macrolide; telithromycine

■ Documentation

- ECBC, antigénuries, sérologies atypiques

PCT et infection dr



PCT séquentielle

Guidelines for continuing or stopping antibiotics during acute chest syndrome

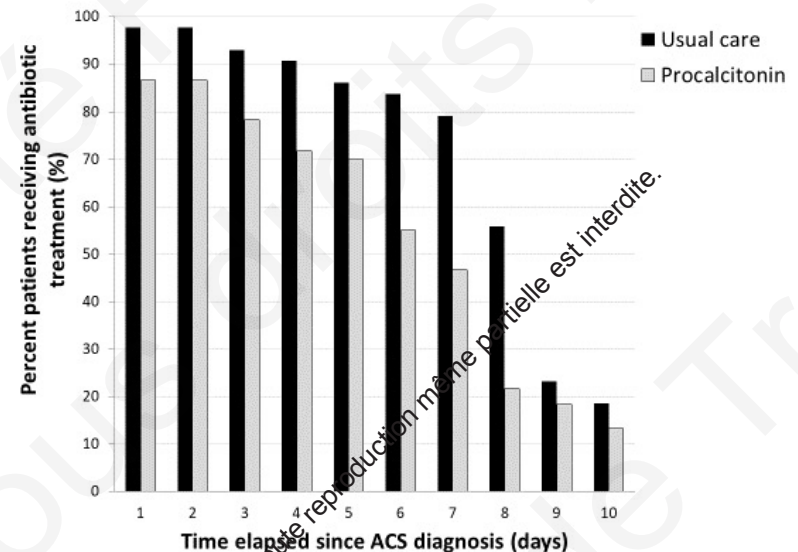
PCT concentration
at day1 < 0,5µg/L
and at day2 < 0,25µg/L

PCT concentration
at day1, day 2 and day 3
< 0,5µg/L

PCT concentration
at day1, day 2 and
day 3 > 0,5µg/L

Stopping antibiotics encouraged

Continuing antibiotics
encouraged for a total
of 7 days



Hyperfiltration glomérulaire

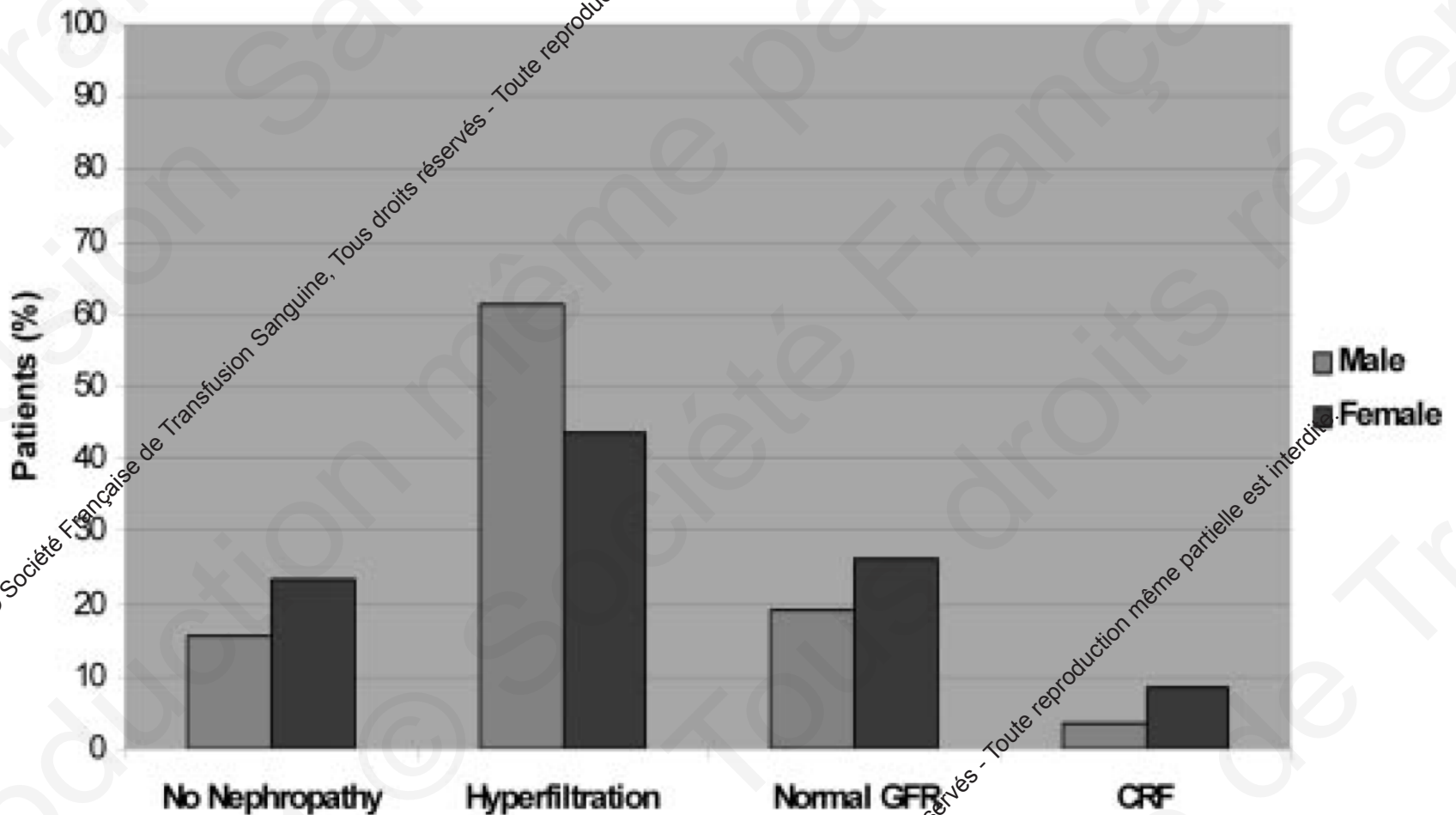
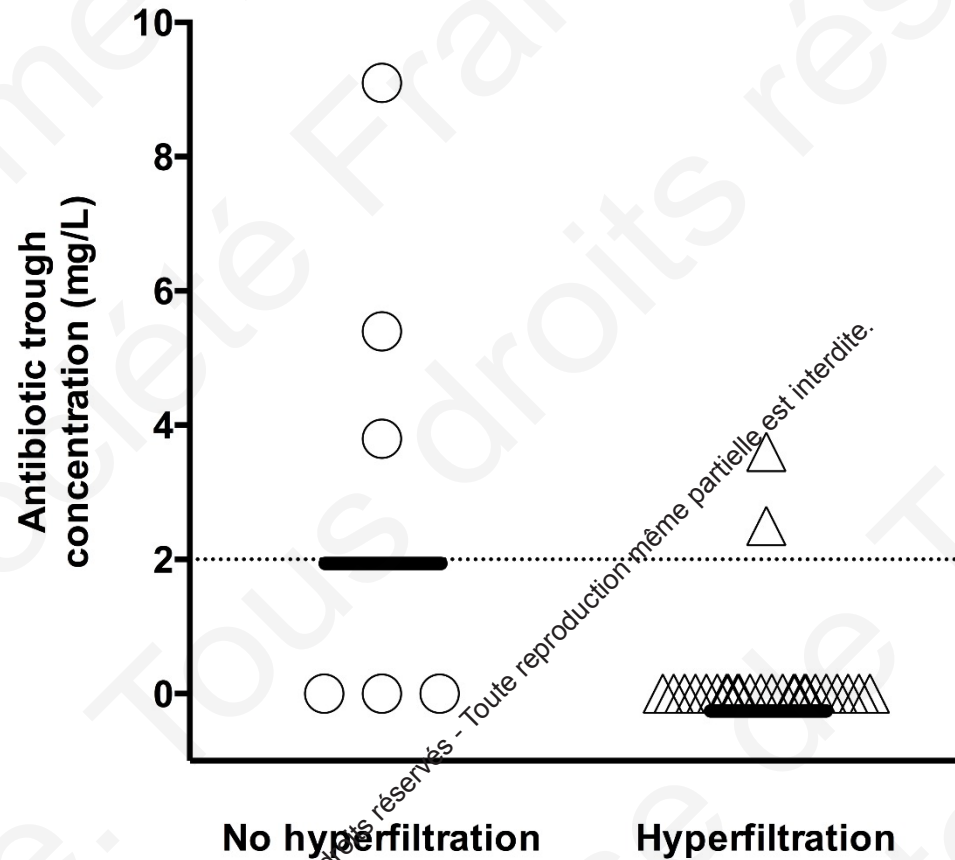


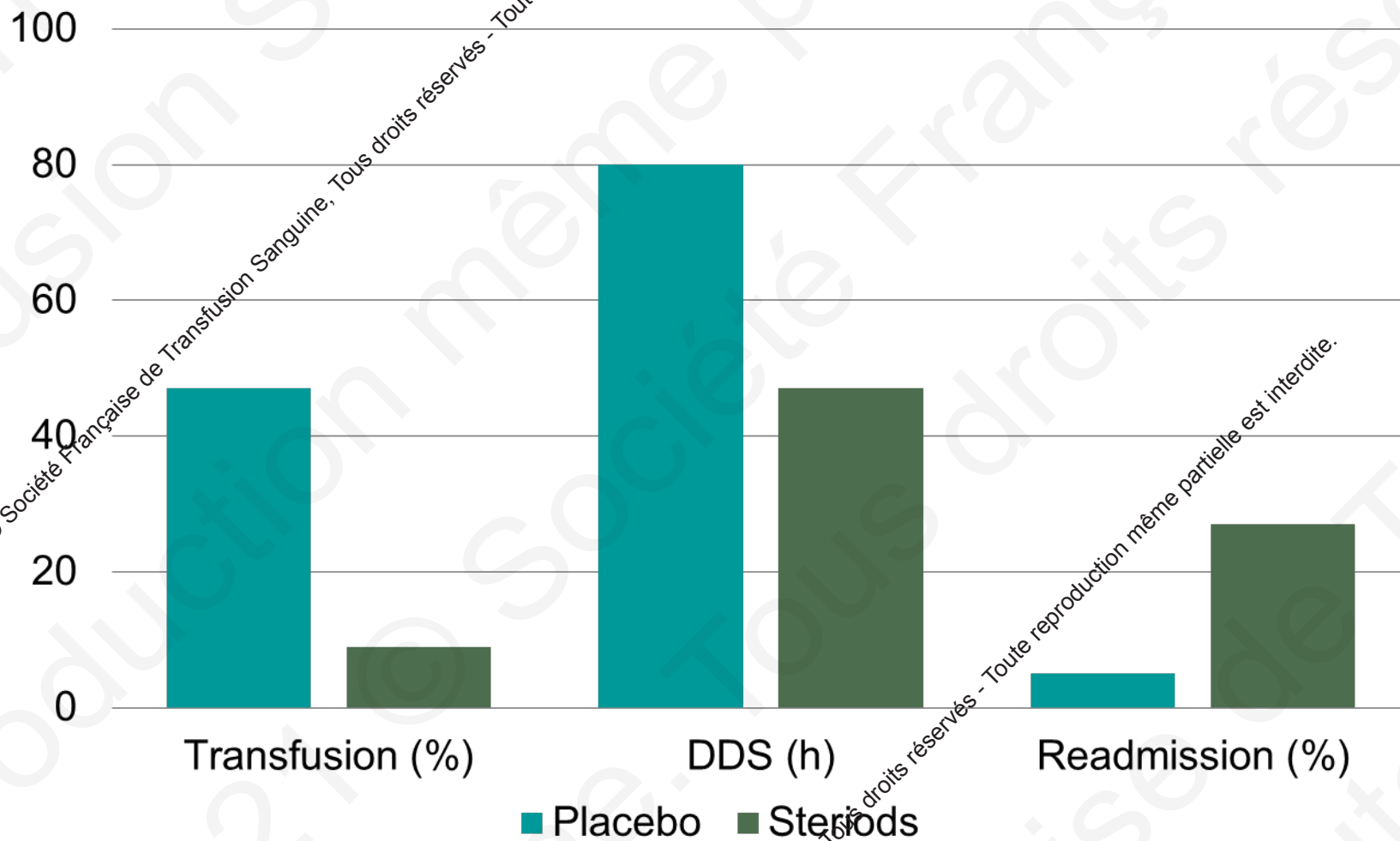
Figure 1. Distribution of patients with SS disease according to GFR.

Dosage antibiotiques

84% des patients ont une concentration d'antibiotique **indéetectable** dans le sang !



Corticoïdes



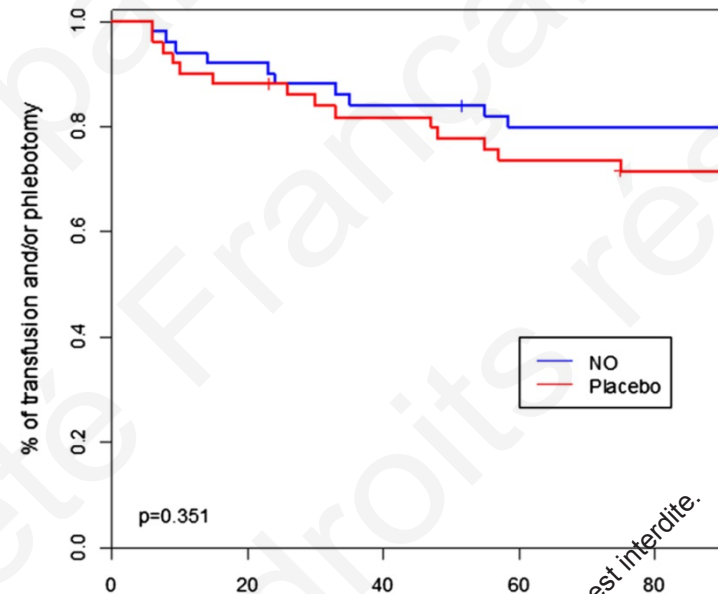
INOSTA

Intensive Care Med
DOI 10.1007/s00134-015-4060-2

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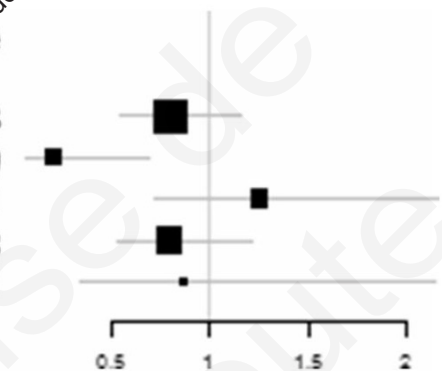


NO 80 ppm



# at risk	0	20	40	60	80
NO	50	46	42	39	39
Placebo	50	44	40	36	34

	iNO (N)	Placebo (N)	Risk Ratio (95% CI)	P-value
All patients	23/50 (46%)	29/50 (58%)	0.8 (0.54-1.16)	0.23
Hypoxemia	7/21 (33.3%)	18/25 (72%)	0.19 (0.06-0.68)	0.009
No hypoxemia	15/25 (60%)	11/25 (44%)	1.25 (0.72-2.17)	0.41
SS genotype	17/36 (47.2%)	25/42 (59.5%)	0.79 (0.52-1.21)	0.28
SC/SB genotype	6/14 (42.8%)	4/8 (50%)	0.86 (0.34-2.15)	1



Anémie selon réticulocytes

ELEVES

- Hémolyse

- CVO
- Post transfusionnelle
- Paludisme
- AHAI

- Séquestration

- splénique
- hépatique

- Hémorragie

BAS

- Carences (fer, folates)
- Inflammation
- Insuffisance rénale
- Toxicité OH-urée
- Nécrose médullaire
- Crise aplastique

NECROSE MEDULLAIRE

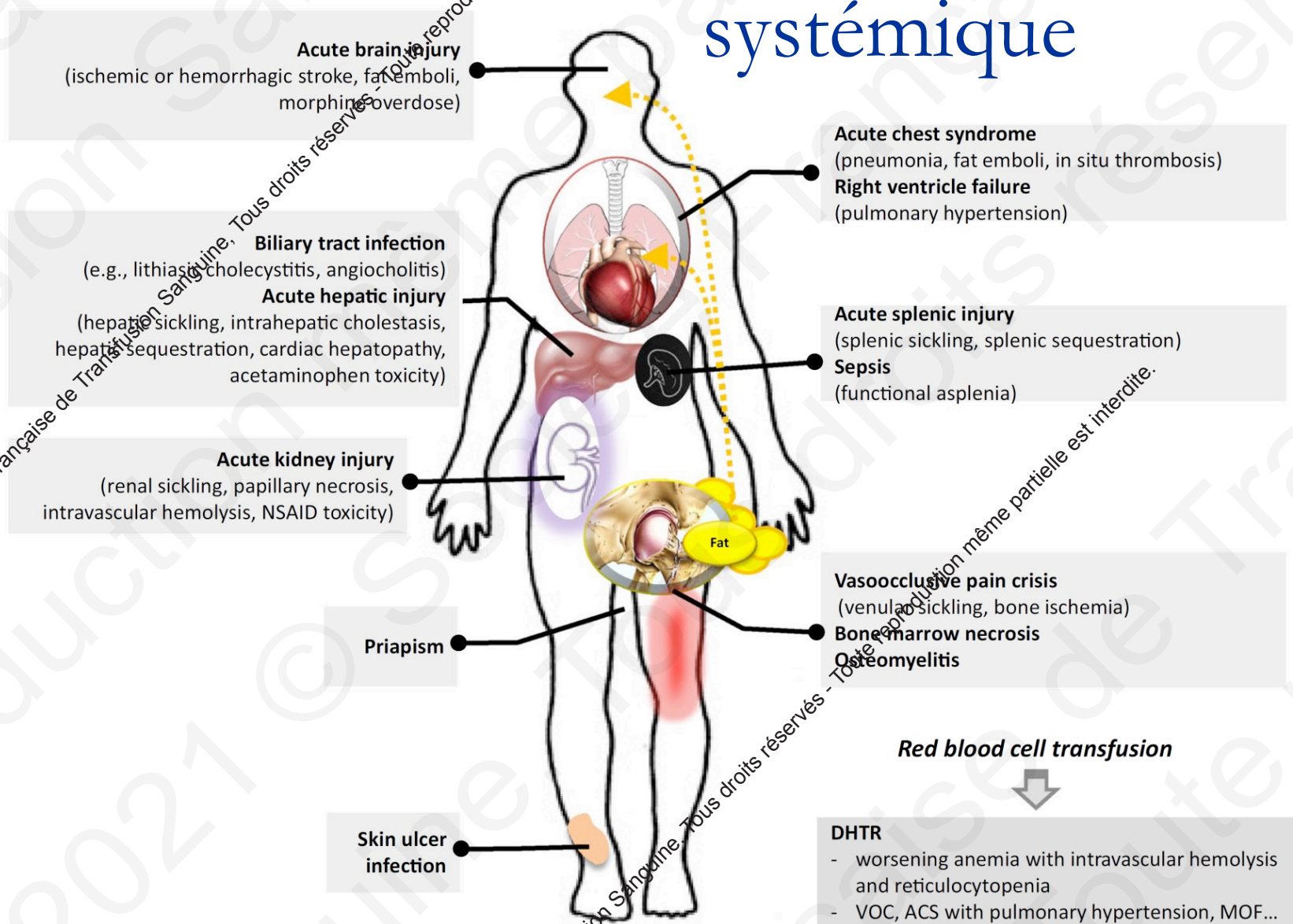
- CVO médullaire extensive
- Fièvre, embolies graisseuse pulmonaire (STA) et systémique, SDM
- $\uparrow$ LDH
- Erythromyélocytose puis pancytopenie
- Scinti os (hyper) + moelle (hypo)
- Myélo: nécrose
- Transfusion $\pm$ EPO

CRISE APLASTIQUE

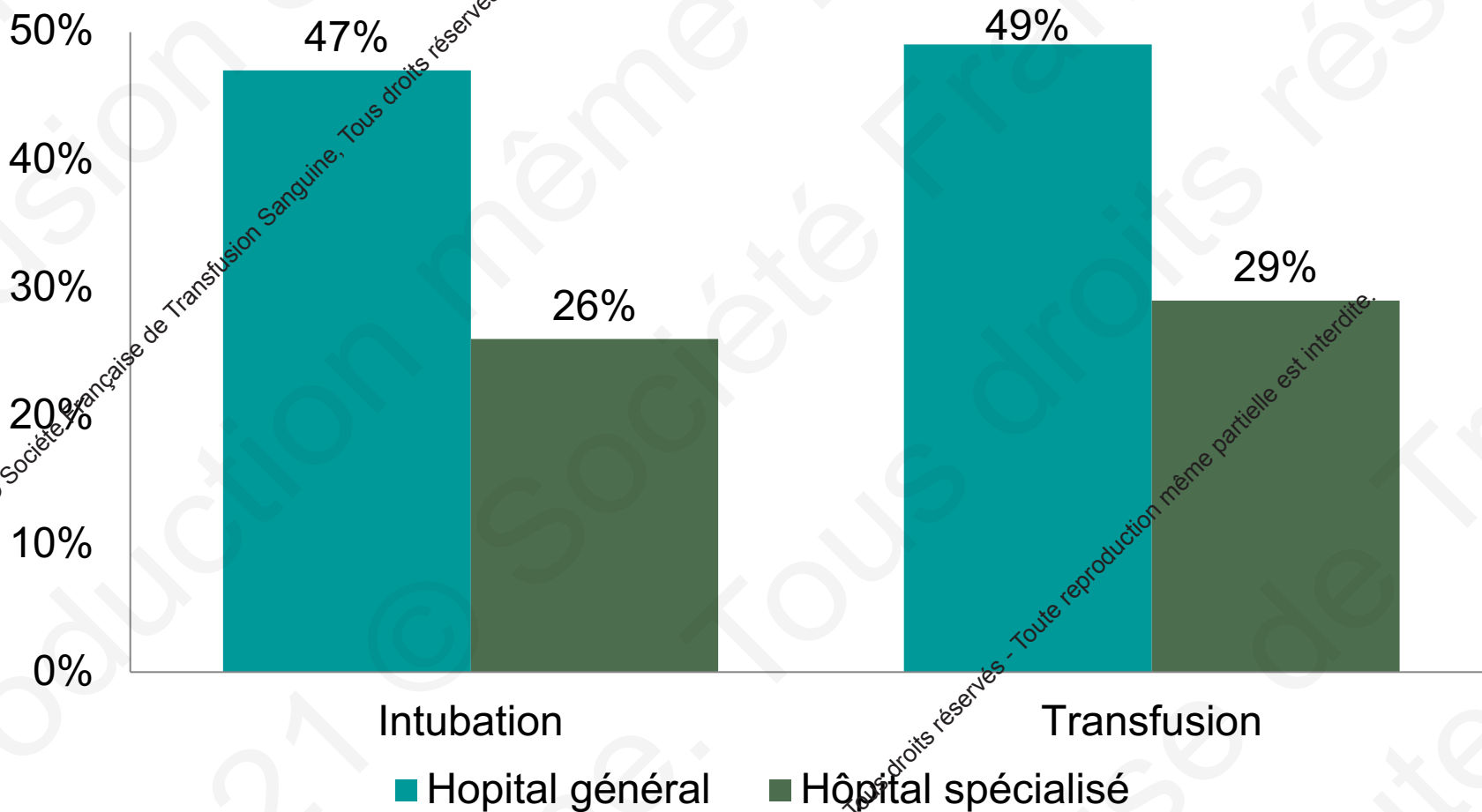
- Parvo B19
- Fièvre, rash, arthrite, STA, myocardite, glomérulonephrite
- Sérologie, PCR
- Myélo: érythroblastopénie $\pm$ nécrose
- Transfusion $\pm$ EPO, Ig

AU TOTAL:

Maladie vasculaire systémique



Effet centre



Points clés

- Physiopathologie complexe
- Discussion multidisciplinaire: réanimateur, UMGGR, EFS
- Evolution parfois rapide
 - ❑ SDMV avec SDRA et défaillance cardiaque droite
 - ❑ Surveillance clinique signes de sévérité
 - ❑ Echographie pulmonaire et cardiaque+++