Session Anesthésie
Transfusion

L'épargne transfusionnelle en post-opératoire et en réanimation

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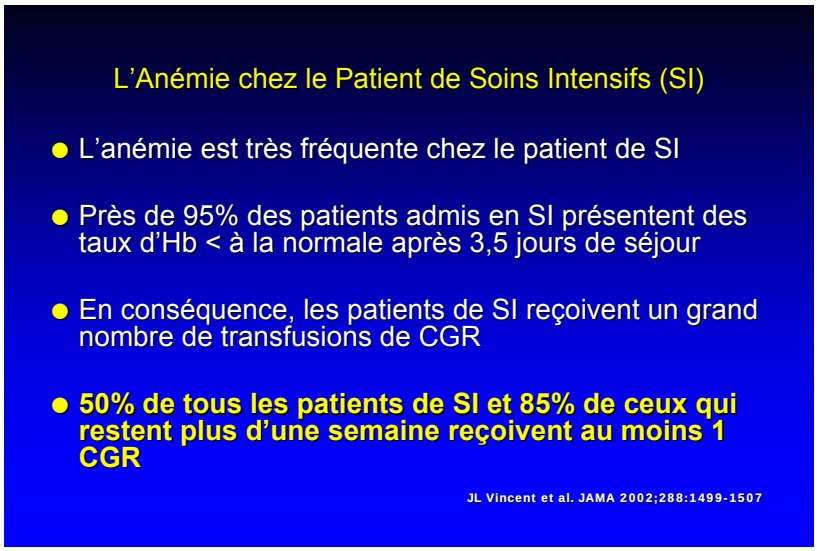
Diapositive 1

Diapositive 2



Diapositive 3

Questions

- Le débat autour des risques transfusionnels des 10 dernières années s'est accompagné d'un examen plus critique des bénéfices liés à la transfusion
- Des critères spécifiques de décision transfusionnelle et la recherche de données illustrant la balance bénéfice/risque de la transfusion sont devenus des objets de recherche intense

Diapositive 4

Questions

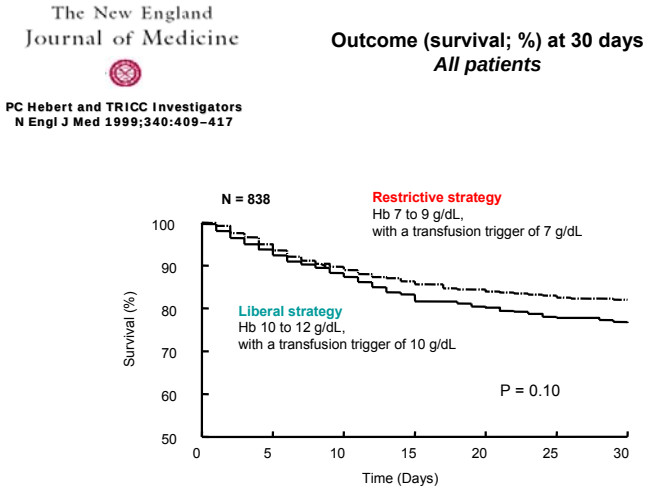
- Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?
- Existe-t-il des méthodes alternatives à la transfusion sanguine ?
- Comment individualiser les besoins transfusionnels ?

Diapositive 5

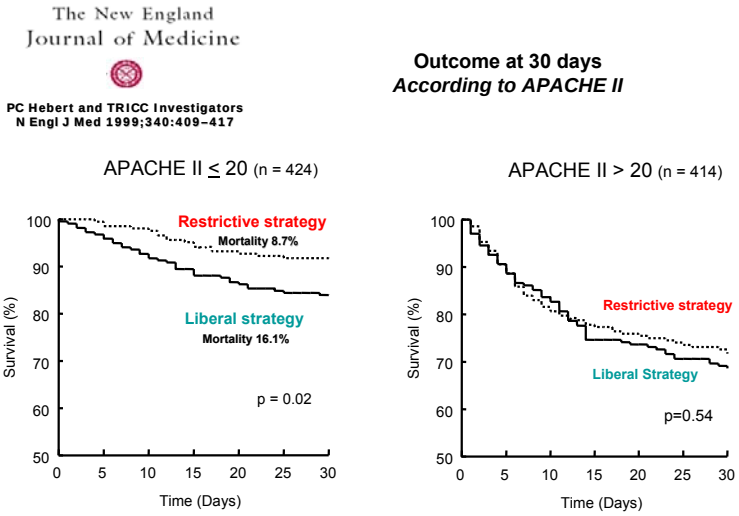
Questions

- Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?
- Existe-t-il des méthodes alternatives à la transfusion sanguine ?
- Comment individualiser les besoins transfusionnels ?

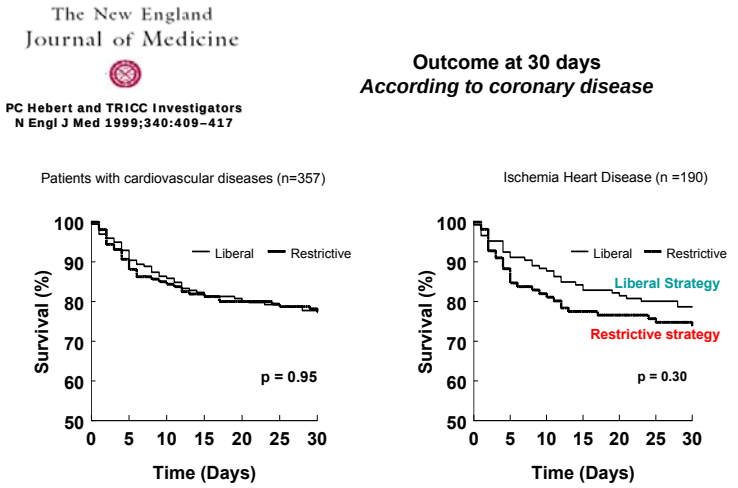
Diapositive 6



Diapositive 7



Diapositive 8



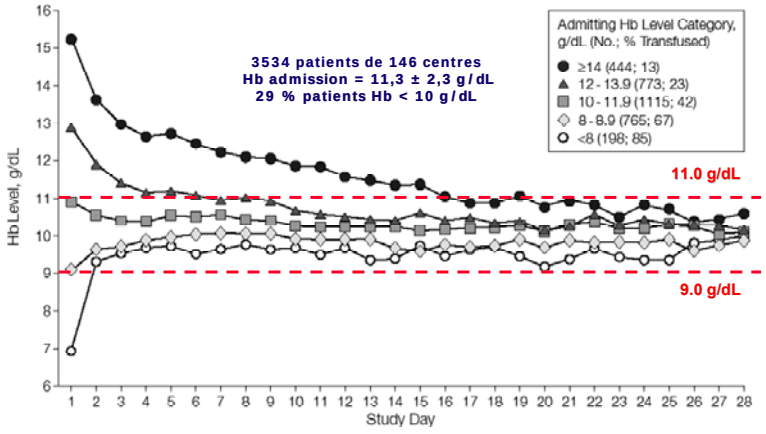
Diapositive 9

JAMA

Anemia and Blood Transfusion in Critically Ill Patients

JL Vincent et al. JAMA 2002;288:1499-1507

ABC Investigators

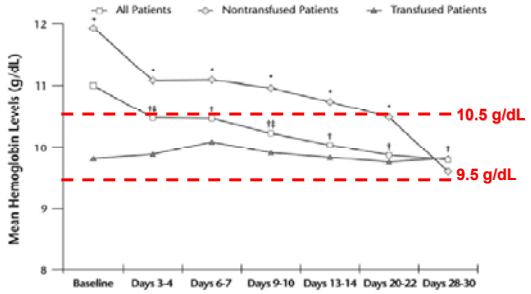


Diapositive 10

The CRIT Study: Anemia and blood transfusion in the critically ill—Current clinical practice in the United States*

HL Corwin et al. Crit Care Med 2004;32:39-52

Conclusions: **Anemia is common in the critically ill and results in a large number of RBC transfusions. Transfusion practice has changed little during the past decade. The number of RBC units transfused is an independent predictor of worse clinical outcome.**



*The difference across groups (transfused vs. nontransfused) is significant at $p<0.007$ (using Bonferonni adjustment).
†The difference is significant at $p<.0045$ (using ANOVA and Bonferonni adjustment) compared with baseline (all patients sample).
‡The difference is significant at $p<.0045$ (using ANOVA and Bonferonni adjustment) compared with previous period (all patients sample).

Diapositive 11

JAMA

Anemia and Blood Transfusion in Critically Ill Patients

JL Vincent et al. JAMA 2002;288:1499-1507

ABC Investigators

Table 4. Summary of Indications for Transfusion*

Indication for Transfusion†	ICU Transfusion (n = 1307) Transfusions, No. (%)	ICU Transfusion (n = 1307) Pretransfusion Hb, Mean (SD), g/dL	Post-ICU Transfusion (n = 326) Transfusions, No. (%)	Post-ICU Transfusion (n = 326) Pretransfusion Hb, Mean (SD), g/dL
Acute bleeding	702 (55.5)	8.4 (1.4)	80 (27.4)	8.4 (1.0)
Inadequate Hb with: Diminished physiological reserves	355 (28.0)	8.4 (1.0)	35 (44.2)	8.3 (1.1)
Altered tissue perfusion	213 (16.8)	8.4 (1.2)	26 (12.0)	8.4 (0.8)
Coronary artery disease	104 (8.2)	8.7 (0.9)	129 (8.9)	8.7 (0.8)
Other indications	142 (11.2)	8.4 (1.2)	47 (16.1)	8.3 (1.0)

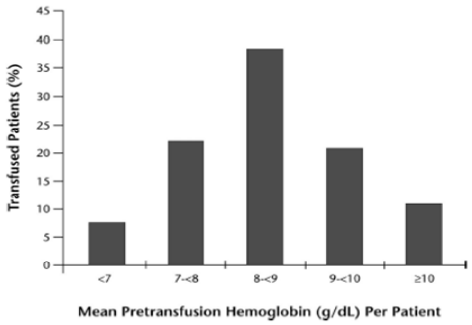
*ICU indicates intensive care unit; Hb, hemoglobin.
†Since many patients were transfused on multiple days, indications for transfusions are not mutually exclusive.

Diapositive 12

The CRIT Study: Anemia and blood transfusion in the critically ill—Current clinical practice in the United States*

HL Corwin et al. Crit Care Med 2004;32:39-52

Measurements and Main Results: The mean hemoglobin level at baseline was 11.0 ± 2.4 g/dL. Hemoglobin level decreased throughout the duration of the study. Overall, 44% of patients received one or more RBC units while in the ICU (mean, 4.6 ± 4.9 units). The mean pretransfusion hemoglobin was 8.6 ± 1.7 g/dL.



Diapositive 13

Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?

- La réponse est évidemment « non »
- Le « phénotype » des patients de SI ne dicte pas la décision transfusionnelle
- La cible thérapeutique du médecin de SI se situe entre 9,5 et 10,5 g/dL
- La décision transfusionnelle (8 g/dL) se fixe les mêmes objectifs en dehors des SI

Diapositive 14

Questions

- Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?
- Existe-t-il des méthodes alternatives à la transfusion sanguine ?
- Comment individualiser les besoins transfusionnels ?

Diapositive 15

Perioperative anaemia management:
consensus statement on the role of i.v. iron
P Beris et al. Br J Anaesth 2008;599-604

- Two prospective randomized trials
  - *K Karkouti et al. Can J Anaest 2006;53:11-9*
  - *SN Madi-Jebara et al. J Cardiothorc Vasc Anesth 2004;18:59-63*
- Three observational studies with control groups
  - *J Bernière et al. Rev Chir Orthop Reparatrice App Mot 1998;84:319-22*
  - *S Hulin et al. Ann Fr Anest Reanim 2005;24:1262-5*
  - *M Munoz Gomez et al. Transfus Med 2006;16:137-42*

Résultats variables en terme d'↑ de l'Hb; 1 seule étude avec ↓ de la transfusion

Diapositive 16

Erythropoietin (EPO) use in critically ill patients: forest and trees
HL Corwin et al. CMAJ 2007;177:747-9

- Failure of circulating EPO to ↑ in response to ↓ Hb
- Several randomized trials:
  - *Corwin HL et al. Crit Care Med 1999;27:2346-50* (n = 160)
  - *Corwin HL et al. JAMA 2002;288:2827-35* (n = 1302)
  - *Corwin HL et al. N Engl J Med 2007;357:965-76* (n = 1460)
- Hb < 12 g/dL: 40,000 units of **rHuEPO** s.c. or a placebo on ICU day 3 and once weekly (3 doses; study days 1, 7 and 14) with oral or i.v. iron when transferrin saturation <20% and ferritin <100 μg/L
- Results:
  - Mortality benefit among trauma patients
  - Increase in hemoglobin concentration
  - No transfusion reduction
  - A significant ↑ in thrombotic events

Diapositive 17

Existe-t-il des méthodes alternatives à la transfusion sanguine ?

- La réponse reste aujourd'hui « non »
- Une partie des échecs des essais cliniques avec l'EPO s'explique par l'absence bon critère de décision transfusionnelle
- En dépit d'une efficacité réelle sur l'augmentation de l'Hb, il n'existe pas de traduction sur l'épargne transfusionnelle

Diapositive 18

Questions

- Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?
- Existe-t-il des méthodes alternatives à la transfusion sanguine ?
- Comment individualiser les besoins transfusionnels ?
  - Recommandations…

Diapositive 19

CHEST Postgraduate Education Corner
CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

Controversies in RBC Transfusion in the Critically Ill*

Hebert, Tinmouth and Corwin Chest 2007;131:1583–90

Table 1—*Transfusion Recommendations*

Variables	Transfusion Trigger, g/L*	Goal, g/L
General critically ill (no acute bleeding)	70	70–90
Critically ill with septic shock (> 6 h)	70	70–90
Critically ill with septic shock (< 6 h)	80–100	100
Critically ill with chronic cardiac disease	70	70–90
Critically ill with acute cardiac disease	80–100	100

*Administer 1 U of RBCs at a time and remeasure hemoglobin concentrations.

Diapositive 20

Questions

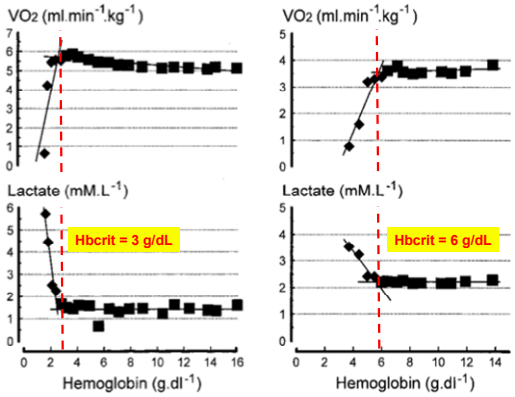
- Existe-t-il un (des) seuil(s) d'Hb clé et universel(s) pour la décision transfusionnelle ?
- Existe-t-il des méthodes alternatives à la transfusion sanguine ?
- Comment individualiser les besoins transfusionnels ?
  - Recommandations…
  - Seuils « physiologiques »

Diapositive 21

Anesthesiology

Tolerance to Acute Isovolemic Hemodilution

P Van Der Linden et al. Anesthesiology 2003;99:97-104



Diapositive 22

Anesthesiology

Electrocardiographic ST-segment Changes during Acute, Severe Isovolemic Hemodilution in Humans

JM Leung et al. Anesthesiology 2000;93:1004-1010

- ✓ Healthy resting humans during acute isovolemic anemia (**5,2 ± 0,5 g/dL**) over 1h
- ✓ Whole body VO_2 did not change
- ✓ HR ↑ (27%; P < 0.0001) from 63 ± 11 to 94 ± 14 beats/min
- ✓ MAP ↓ (13%; P < 0.0001) from 87 ± 10 to 76 ±
- ✓ **ECG (Holter recorder): reversible ST depression in 3 asymptomatic subjects**
- ✓ But in those who had significantly higher maximum HR (110–140 beats/min)

Diapositive 23

Anesthesiology

Oxygen Reverses Deficits of Cognitive Function and Memory and Increased Heart Rate Induced by Acute Severe Isovolemic Anemia

RB Weiskopf et al. Anesthesiology 2002;96:871–7

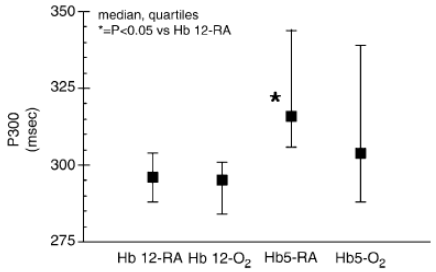
- ✓ Young healthy volunteers acute isovolemic reduction (Hb concentration to **5.7 ± 0.3 g/dL**)
- ✓ Tested with verbal memory and standard, computerized neuropsychologic tests
- ✓ **Reaction time for digit-symbol substitution test (DSST) increased**
- ✓ **Delayed memory was degraded**
- ✓ Increasing PaO_2 to 406 ± 47 mmHg reversed :
  - the DSST result
  - the delayed memory changes to values not different from baseline

Diapositive 24

Acute isovolemic anemia impairs central processing as determined by P300 latency

Richard B. Weiskopf[a,*], Pearl Toy[b], Harriet W. Hopf[c], John Feiner[d], Heather E. Finlay[b], Michelle Takahashi[b], Alan Bostrom[e], Christopher Songster[f], Michael J. Aminoff[f]

Clinical Neurophysiology 116 (2005) 1028–1032



Auditory P300 latencies in nine volunteers at hemoglobin concentration of 12.4 g/dL breathing air (Hb12-Air) or oxygen (Hb12-O_2), and at hemoglobin concentration of 5.1 g/dL breathing air (Hb5-Air) or oxygen (Hb5-O_2). Data are median and quartiles. * P<0.05 versus Hb12-Air

Diapositive 25

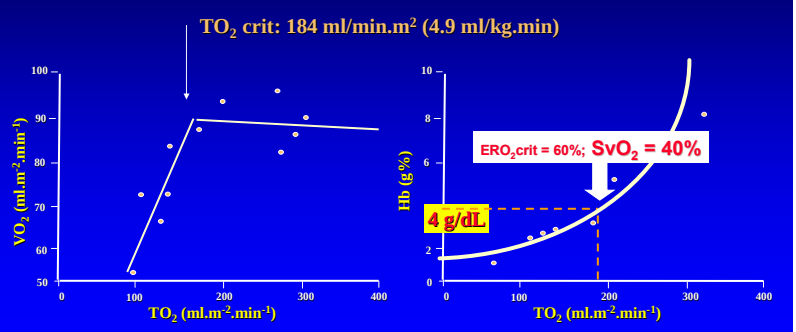
Anemia : a Marker of Risk

- In most individuals, below **7 g/dL** any further ↓ in Hb is associated with an ↑ risk of death
- Cardiac output (fluid infusion) must compensate
- **5 g/dL** is close to be an Hb_{crit} in young healthy adults
- But **isovolemic anemia at 5 g/dL can be associated with spots of ↓ O_2 delivery although global O_2 markers remain adequate**

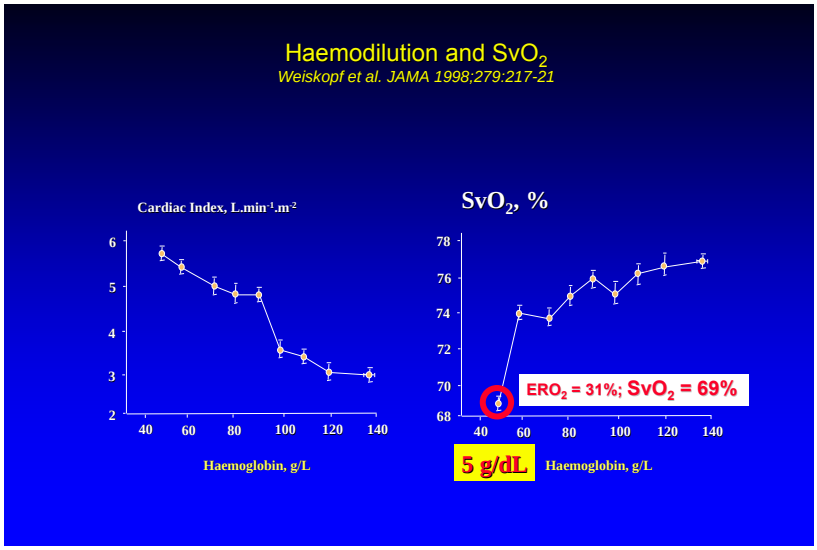
Diapositive 26

Critical Hb and Hemodilution in Human

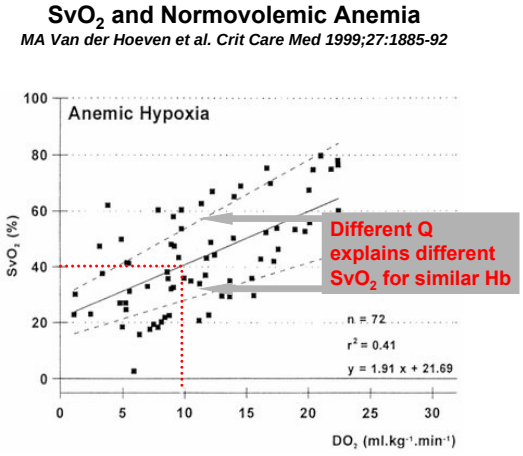
Van Woerkens et al. Anesth Analg 1992;75:818-21



Diapositive 27



Diapositive 28



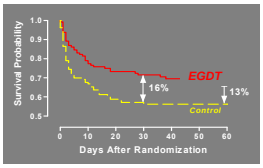
Diapositive 29

The New England Journal of Medicine

E Rivers et al.
N Engl J Med 2001;345:1368–77

"Early Goal-Directed Therapy" (EGDT) and Treatment for Severe Sepsis and Septic Shock

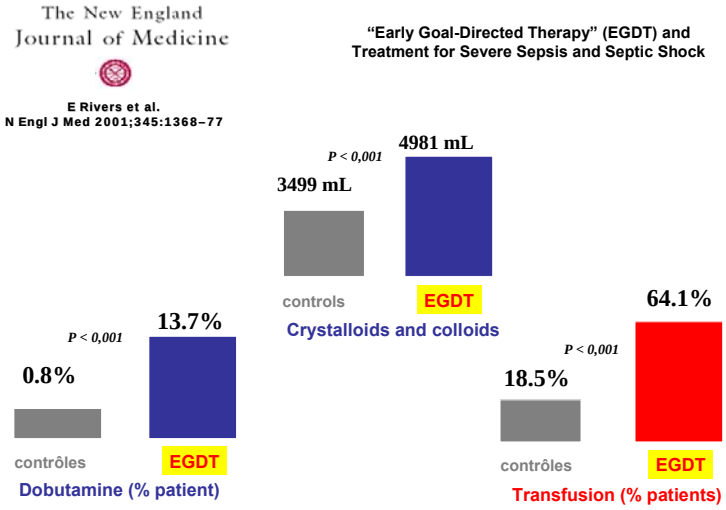
$$ScvO_2 \approx SaO_2 - \frac{VO_2}{Hb \cdot 1.39 \cdot IC}$$



Optimizing $ScvO_2$ (> 70%):

- SaO_2 > 93%
- Hemoglobin > 10 g/dL
- Cardiac index with dobutamine (≤20 µg/kg.min)
  - after fluid loading
- Decreasing VO_2 (MV and sedation)

Diapositive 30



Diapositive 31

Physiologic transfusion triggers

Vallet B, Adamczyk S, Barreau O, Lebuffe G.
Best Pract Res Clin Anaesthesiol. 2007;21:173-81

- Prospective observational study
- 60 high risk surgery patients in whom BT decision was discussed
  - hemodynamically stable
  - equipped with CV catheter
  - blood transfusion decision taken by anesthesiologists in charge (being informed of French recommendations and $ScvO_2$)

Threshold value of Hb (g/dL)	Clinical context
10	Acute coronary syndrome
9	- Ischemic heart disease - Stable heart failure
8	Age >75 Severe sepsis
7	Others

Diapositive 32

Physiologic transfusion triggers

Vallet B, Adamczyk S, Barreau O, Lebuffe G.
Best Pract Res Clin Anaesthesiol. 2007;21:173-81

- 2 blood samples, before and after BT:
  $ScvO_2$ and **Hb**
- Other parameters collected:
  - Age
  - Cardiovascular disease (CVD)
  - Sepsis
  - Blood units transfused
  - Heart rate (HR)
  - Systolic arterial pressure (SAP)

Diapositive 33

Physiologic transfusion triggers

Vallet B, Adamczyk S, Barreau O, Lebuffe G.
Best Pract Res Clin Anaesthesiol. 2007;21:173-81

- Analysis:
  - Patients retrospectively divided in 2 groups
  - $ScvO_2$ < or ≥ 70% *(Rivers et al N Engl J Med 2001)*
  - *, Chi-2, p <0.05

	Global population (n=60)	$ScvO_2$ <70 % (n=29)	$ScvO_2$ ≥70 % (n=31)
Age (years)	66.5 (24-100)	67 (24-92)	66 (24-100)
CVD (n)	17	6	11
Sepsis (n)	12	8	4
Blood units (n)	2 (1-4)	2 (1-4)	2 (0-3)

Diapositive 34

Physiologic transfusion triggers

Vallet B, Adamczyk S, Barreau O, Lebuffe G.
Best Pract Res Clin Anaesthesiol. 2007;21:173-81

- Analysis:
  - In 53 transfused patients (7 non transfused with $ScvO_2$ ≥ 70%)
  - $ScvO_2$ < or ≥ 70%,
  - **AND** Reco + (BT recommended) or – (BT not recommended)
  - *, Chi-2, p <0.05

	$ScvO_2$ <70% (n=26)		$ScvO_2$ ≥70% (n=27)		
Reco	+ (n=14)	- (n=12)	+ (n=13)	- (n=14)	Test (p=0.05)
Age (years)	74.5 [62.2-77.2]	55.5 [46.4-64.4]	69 [59.7-80.3]	46 [30.5-62.9]	ns
Weight (kgs)	74 [67.8-76.8]	73.5 [62.9-96.9]	70 [57.3-72.5]	70 [58.7-86.7]	ns
Blood units (n)	2 [1.8-2.7]	2 [1.7-2.1]	2 [1.6-2.2]	2 [1.8-2.7]	ns

Results given as median [CI 95%]

Diapositive 35

- Analysis before *vs* after BT:
  - Patients retrospectively divided in 2 groups
  - $ScvO_2$ < or ≥ 70% *(Rivers et al N Engl J Med 2001)*
  - *, Wilcoxon test, p <0.05 *vs* preBT

	Global population (n=60)		
$ScvO_2$ preBT	70.1 (36-89.2)		
$ScvO_2$ postBT	71* (40-91.7)		
Hb preBT	7.8 (6.4-9.8)		
Hb postBT	9.8* (7.9-11.9)		

Diapositive 36

- Analysis before *vs* after BT:
  - Patients retrospectively divided in 2 groups
  - $ScvO_2$ < or ≥ 70% *(Rivers et al N Engl J Med 2001)*
  - *, Wilcoxon test, p <0.05 *vs* preBT

	Global population (n=60)	$ScvO_2$ <70 % (n=29)	
$ScvO_2$ preBT	**70.1** (36-89.2)	**58** (36-69.1)	
$ScvO_2$ postBT	**71*** (40-91.7)	**68.7*** (40-80)	
Hb preBT	7.8 (6.4-9.8)	7.5 (6.5-9.3)	
Hb postBT	9.8* (7.9-11.9)	9.6* (7.9-11.6)	

Diapositive 37

- Analysis before *vs* after BT:
  - Patients retrospectively divided in 2 groups
  - $ScvO_2$ < or ≥ 70% *(Rivers et al N Engl J Med 2001)*
  - *, Wilcoxon test, p <0.05 *vs* preBT

	Global population (n=60)	$ScvO_2$ <70 % (n=29)	$ScvO_2$ ≥70 % (n=31)
$ScvO_2$ preBT	**70.1** (36-89.2)	**58** (36-69.1)	**77** (70-89.2)
$ScvO_2$ postBT	**71*** (40-91.7)	**68.7*** (40-80)	**76.7** (63-91.7)
Hb preBT	7.8 (6.4-9.8)	7.5 (6.5-9.3)	8.0 (6.4-9.8)
Hb postBT	9.8* (7.9-11.9)	9.6* (7.9-11.6)	9.9* (8.5-11.9)

Diapositive 38

- Analysis before *vs* after BT:
  - In 53 transfused patients (7 non transfused with $ScvO_2$ ≥ 70%)
  - $ScvO_2$ < or ≥ 70%,
  - **AND** Reco + (BT recommended) or – (BT not recommended)
  - *, Wilcoxon test, p <0.05 *vs* preBT

	$ScvO_2$ <70% (n=26)		$ScvO_2$ ≥70% (n=27)	
Reco	+ (n=14)	- (n=12)	+ (n=13)	- (n=14)
$ScvO_2$ preBT	58.6 [52.2-62.3]	56.5 [49.0-62.9]	75.3 [68.0-79.9]	75.4 [58.5-86.9]
$ScvO_2$ postBT	69.3* [58.8-74.5]	65.4 [55.5-69.7]	77.4 [71.0-80.8]	75.9 [67.7-80.8]

Diapositive 39

- Analysis before *vs* after BT:
  - In 53 transfused patients (7 non transfused with $ScvO_2 \geq 70\%$)
  - $ScvO_2 <$ or $\geq 70\%$,
  - **AND** Reco + (BT recommended) or – (BT not recommended)
  - *, Wilcoxon test, $p < 0.05$ *vs* preBT

	$ScvO_2$ <70% (n=26)		$ScvO_2 \geq 70\%$ (n=27)	
Reco	**+ (n=14)**	**- (n=12)**	**+ (n=13)**	**- (n=14)**
$ScvO_2$ preBT	**58.6** [52.2-62.3]	**56.5** [49.0-62.9]	**75.3** [68.0-79.9]	**75.4** [58.5-86.9]
$ScvO_2$ postBT	**69.3*** [58.8-74.5]	**65.4** [55.5-69.7]	**77.4** [71.0-80.8]	**75.9** [67.7-80.8]

Diapositive 40

	$ScvO_2$ <70%		$ScvO_2 \geq 70\%$		
Reco	**+**	**-**	**+**	**-**	Test
$ScvO_2$ preBT	**58.6** [52,2-62,3]	**56.5** [49.0-62.9]	**75.3** [68.0-79.9]	**75.4** [58,5-86,9]	**p<0.001**
$ScvO_2$ postBT	**69,3*** [58.8-74.5]	**65.4** [55.5-69.7]	**77.4** [71.0-80.8]	**75.9** [67.7-80.8]	**p = 0.002**
Hb preBT	**7.4** [7.2-7.9]	**8.0** [7.6-8.5]	**7.6** [7.2-8.2]	**7.5** [7,3-8,0]	ns
Hb postBT	**9.2*** [8.7-9.8]	**9.9*** [9.4-10.3]	**9.7*** [9.2-10.6]	**10.2*** [9.2-10.7]	ns
HR preBT	**89.0** [84.3-106.1]	**95.5** [90.1-112.9]	**87.5** [75.8-102.6]	**97.0** [86.3-126.6]	ns
HR postBT	**92.0** [86.2-98.9]	**92.0** [82.9-101.1]	**84.0** [78.7-100.4]	**100.0** [84.2-107.5]	ns
SAP preBT	**120.5** [105.7-138.4]	**130.0** [120.7-149.5]	**128.0** [117.1-138.7]	**124.0** [109.6-150.0]	ns
SAP postBT	**122.0** [111.4-138.3]	**120.0** [108.6-146.6]	**140.0*** [131.8-159.2]	**130.0*** [117.9-163.5]	ns

Diapositive 41

Physiologic transfusion triggers

Vallet B, Adamczyk S, Barreau O, Lebuffe G.
Best Pract Res Clin Anaesthesiol. 2007;21:173-81

- 26 patients received BT in spite of recommendations (49%)
- **22.6%** out of these recommendations (Reco -) with an $ScvO_2<70\%$ seem to take benefit from BT (according to the VO_2/TO_2 relationship): "**lack of BT**?"
- According to $ScvO_2$, BT might even be insufficient (n= 2 blood units) in this sub-group
- **24.5%** w/i these recommendations (Reco +) with an $ScvO_2>70\%$ received BT although VO_2/TO_2 might have been adequate: "**excess of BT**?"

$ScvO_2$ appears as an interesting parameter to help BT decision in hemodynamically stable high-risk surgery patients equipped with central venous catheter

Diapositive 42

Comment individualiser les besoins transfusionnels ?

- **La SvO_2 intègre l'adaptation "individuelle" cardiorespiratoire vis-à-vis des besoins en O_2 globaux de l'organisme durant l'anémie**
- La $ScvO_2$ est un succédané (technique simplifiée) pour la SvO_2
- **Les mesures de $ScvO_2$ (prélèvements itératifs ou monitoring) pourrait aider dans la décision (et l'épargne) transfusionnelle (quand $ScvO_2$ < 70%)**

Diapositive 43

Conclusions

- Quand l'Hb↓, l'↑ du Q est l'adaptation essentielle…
- Cette adaptation est une réponse physiologique "individuelle"…
- Comprendre le statut cardiovasculaire du patient pris en charge représente donc une étape clé dans le développement d'une stratégie thérapeutique durant l'anémie
- **La $ScvO_2$ intègre l'adaptation "individuelle" cardiorespiratoire vis-à-vis des besoins en O_2 globaux au cours de l'anémie et pourrait aider dans la décision transfusionnelle**