Patient blood management et seuils transfusionnels

Raisonnment clinique

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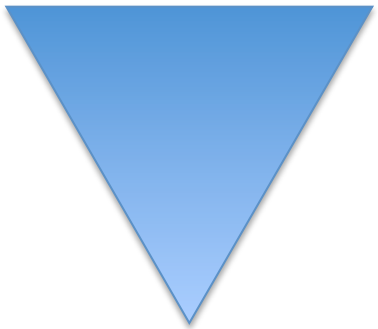
Masterclass ARCHOTOVA, novembre 2019

Objectifs

- Definitions et contenu du PBM
- Transfusion de CGR
  - Seuils transfusionnels
  - Bruit de la mesure de la concentration d'hémoglobine
  - Anémie (normovolémique) d'hémodilution
- Raisonnement médical pour la décision de transfuser des CGR

Anciennement

Anémie



Transfusion
CGR

Seuils transfusionnels
de plus en plus bas (7g/dL)

Le contexte actuel de connaissances/ décisions

PATIENT BLOOD MANAGEMENT

Définition de Patient Blood Management

"*the timely application of evidence based medical and surgical concepts designed to maintain haemoglobin concentration, optimise haemostasis and minimise blood loss in an effort to improve patient outcome*"

"L'application à temps des pratiques médicales/ chirurgicales, fondées sur des preuves, conçues pour maintenir la concentration d'hémoglobine, optimiser l'hémostase et minimiser les pertes sanguines dans un effort d'amélioration des résultats-patient (outcome)"

Society for the Advancement of Blood Management (SABM). http://www.sabm.org. [accessed 06/04/2015].

Contents lists available at SciVerse ScienceDirect

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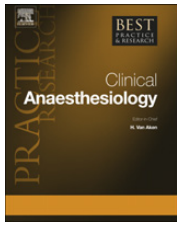
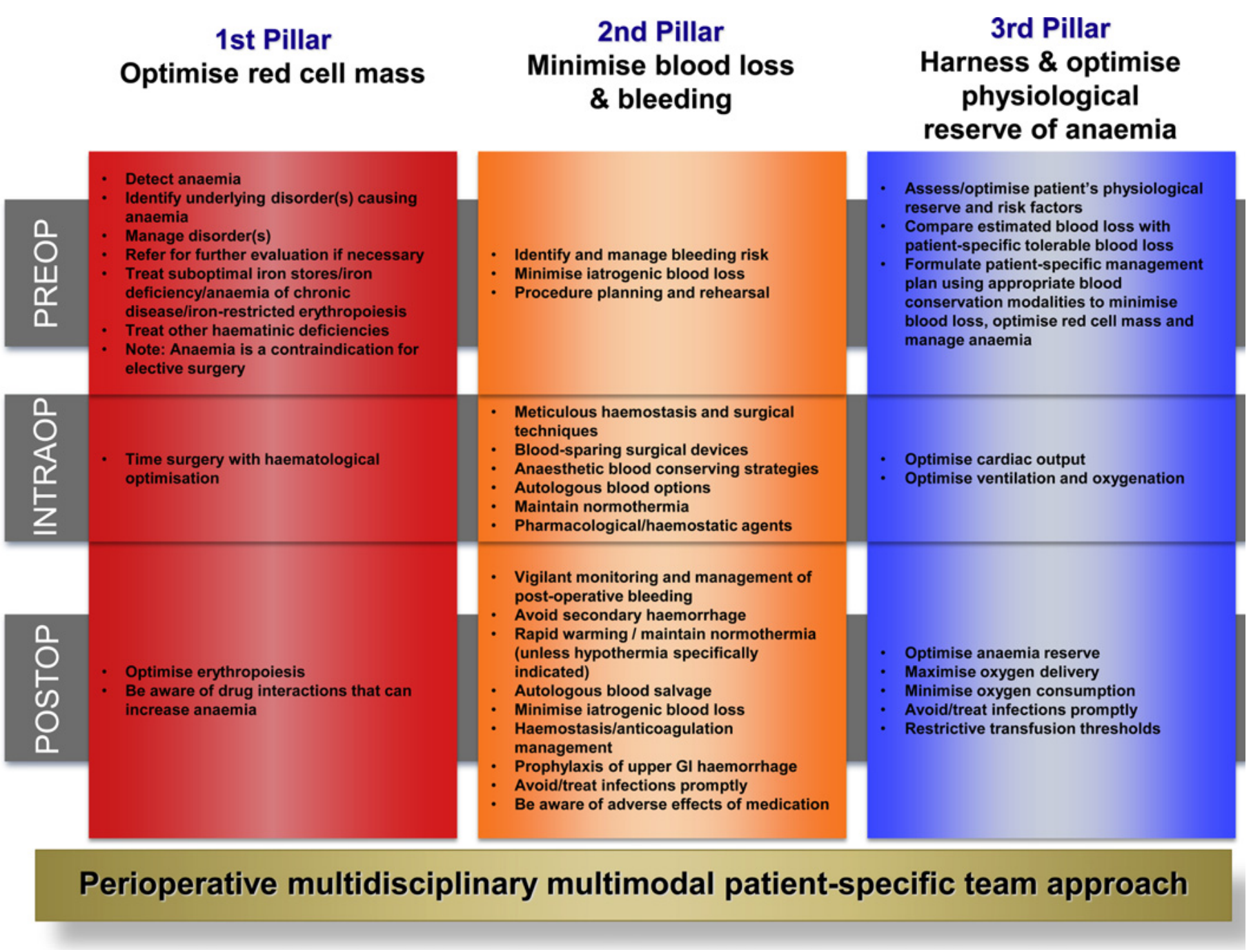
journal homepage: www.elsevier.com/locate/bean

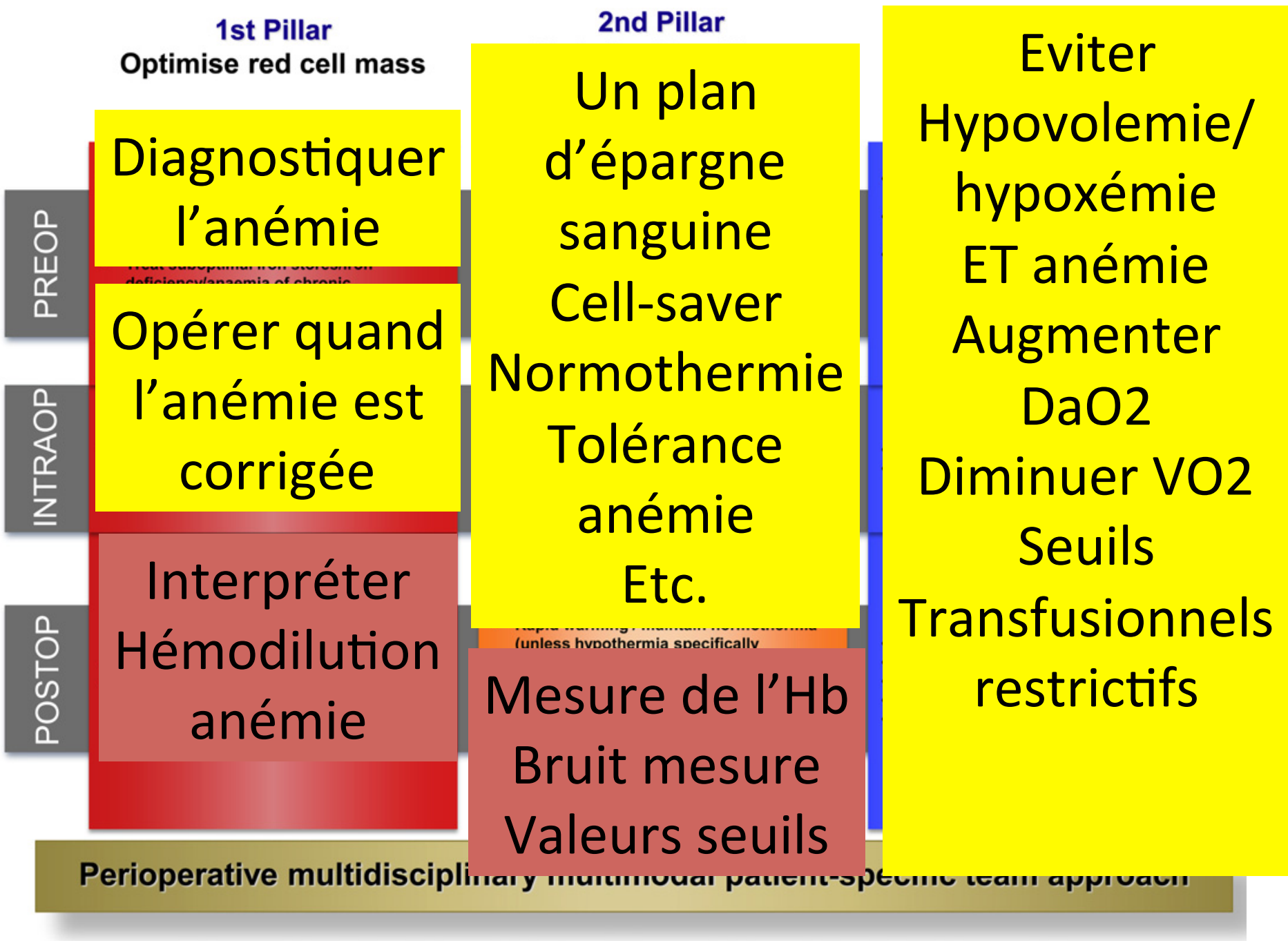


5

Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA)

Shannon L. Farmer, Research Fellow, Consultant, Adjunct Research Fellow, Adjunct Senior Research Fellow [a,b,c,*], Simon C. Towler, FCICM, FANZCA, FAMA, Staff Specialist Intensive Care, Medical Advisor, Adjunct Professor [a,c,d,e,h], Michael F. Leahy, MB ChB, FRACP, FRCP, FRCPath, Clinical Professor, Consultant Haematologist. Director, Clinical Professor in Medicine [a,g,f,i], Axel Hofmann, ME MD, Medical Economist, Consultant, Adjunct Associate Professor, Visiting Professor [a,b,c,j]


1st Pillar
Optimise red cell mass
2nd Pillar
Minimise blood loss & bleeding
3rd Pillar
Harness & optimise physiological reserve of anaemia
PREOP
Detect anaemia
Identify underlying disorder(s) causing anaemia
Manage disorder(s)
Refer for further evaluation if necessary
Treat suboptimal iron stores/iron deficiency/anaemia of chronic disease/iron-restricted erythropoiesis
Treat other haematinic deficiencies
Note: Anaemia is a contraindication for elective surgery
Identify and manage bleeding risk
Minimise iatrogenic blood loss
Procedure planning and rehearsal
Assess/optimise patient's physiological reserve and risk factors
Compare estimated blood loss with patient-specific tolerable blood loss
Formulate patient-specific management plan using appropriate blood conservation modalities to minimise blood loss, optimise red cell mass and manage anaemia
INTRAOP
Time surgery with haematological optimisation
Meticulous haemostasis and surgical techniques
Blood-sparing surgical devices
Anaesthetic blood conserving strategies
Autologous blood options
Maintain normothermia
Pharmacological/haemostatic agents
Optimise cardiac output
Optimise ventilation and oxygenation
POSTOP
Optimise erythropoiesis
Be aware of drug interactions that can increase anaemia
Vigilant monitoring and management of post-operative bleeding
Avoid secondary haemorrhage
Rapid warming / maintain normothermia (unless hypothermia specifically indicated)
Autologous blood salvage
Minimise iatrogenic blood loss
Haemostasis/anticoagulation management
Prophylaxis of upper GI haemorrhage
Avoid/treat infections promptly
Be aware of adverse effects of medication
Optimise anaemia reserve
Maximise oxygen delivery
Minimise oxygen consumption
Avoid/treat infections promptly
Restrictive transfusion thresholds
Perioperative multidisciplinary multimodal patient-specific team approach


1st Pillar
Optimise red cell mass
2nd Pillar
PREOP
INTRAOP
POSTOP
Diagnostiquer l'anémie
Opérer quand l'anémie est corrigée
Interpréter Hémodilution anémie
Un plan d'épargne sanguine
Cell-saver
Normothermie
Tolérance anémie
Etc.
Mesure de l'Hb
Bruit mesure
Valeurs seuils
Eviter Hypovolemie/ hypoxémie ET anémie
Augmenter DaO2
Diminuer VO2
Seuils Transfusionnels restrictifs
Perioperative multidisciplinary

Définitions de l'anémie

	Severity of anaemia (concentrations in g/dL)		
	Minor	Moderate	Severe
Age > 5 yrs			
Males	12-12.9	9-11.9	6-8.9
Females	11-11.9	8-10.9	5-7.9
Preganant	10-10.9	7-9.9	4-6.9
Age < 5 yrs			
Males	11-11.9	8-10.9	5-7.9
Females	11-11.9	8-10.9	5-7.9

Les mécanismes de l'anémie n'interviennent pas dans les définitions

QCM N°1

- Parmi les questions suivantes concernant l'anémie per-opératiore, lesquelles sont vraies (plusieurs réponses correctes possibles)
  - 1. L'anémie, quelle que soit sa sévérité, est associée à une augmentation de la morbi-mortalité post-opératoires
  - 2. Ces seuils de définition de l'anémie sont robustes parce que la concentration d'hémoglobine est une valeur fiable (peu/pas de bruit de la mesure de l'hémoglobine)
  - 3. La transfusion de CGR corrige toujours le risque lié à l'anémie
  - 4. L'anémie hypovolémique est plus dangereuse que l'anémie normovolémique

Prévalence de l'anémie pré-opératoire

38.77O patients (27 pays, 474 hôpitaux)

<u>30,1 % (11.675) de patients anémiques</u>

Anémie mineure (>11 g/dL; 52 %; 6074)

Anémie modérée (> 8 g/dL; 43,9 %; 5124)

Anémie sévère (< 8 g/dL; 4.1 %; 477)

Polycythémie (1,3 %; 500)

British Journal of Anaesthesia, 121 (6): 1227–1235 (2018)

Mortalité J30

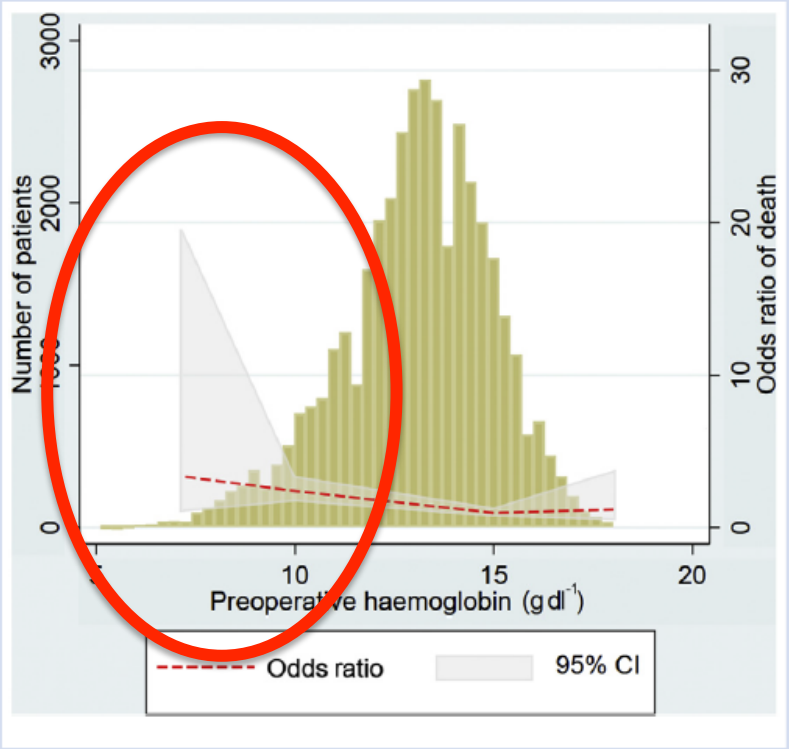


Fig 1. Restricted cubic spline graph of the relationship between haemoglobin and risk of in-hospital death within 30 days of surgery. Number of surgical patients summarised by vertical bars, red line showing odds ratio of death for a given haemoglobin concentration, and 95% confidence interval (CI) in grey.

Complications J30

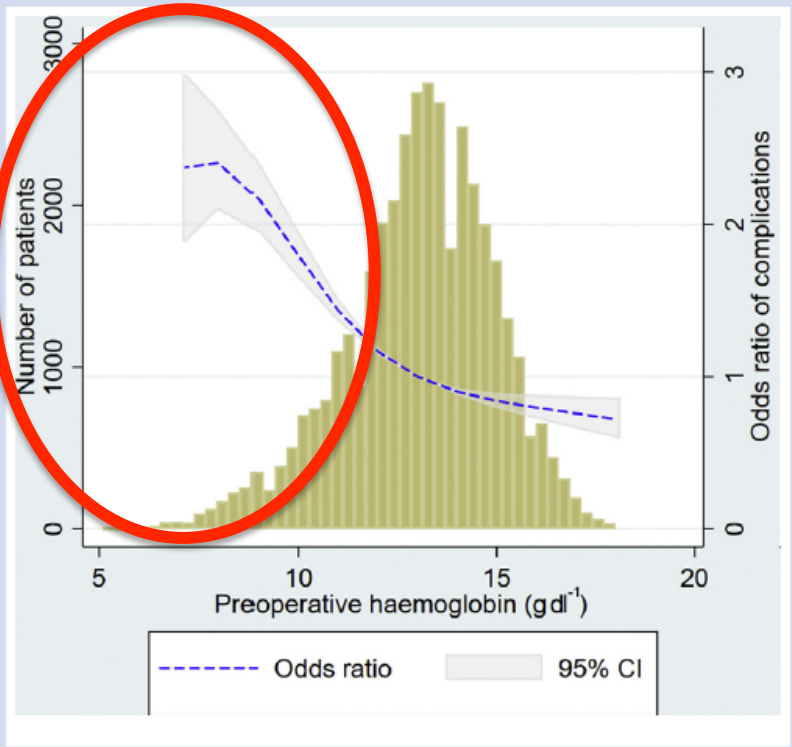


Fig 2. Restricted cubic spline graph of the relationship between haemoglobin and risk of in-hospital complications within 30 days of surgery. Number of surgical patients summarised by vertical bars, blue line showing odds ratio of complications for a given haemoglobin concentration, and 95% confidence interval (CI) in grey.

British Journal of Anaesthesia, 121 (6): 1227–1235 (2018)

	Unadjusted association			Multivariable analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.06	1.05–1.07	<0.01	1.02	1.01–1.04	<0.01
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.57	0.43–0.75	<0.01	0.85	0.61–1.17	0.32
Smoker	1.27	0.90–1.78	0.17	1.47	0.93–2.01	0.12
Anaemia category						
No anaemia	Reference	Reference	Reference	Reference	Reference	Reference
Polycythaemia	2.93	1.07–8.05	0.04	3.22	1.12–9.28	0.03
Mild anaemia	2.04	1.36–3.08	<0.01	1.05	0.68–1.63	0.82
Moderate anaemia	5.54	4.02–7.64	<0.01	2.70	1.88–3.87	<0.01
Severe anaemia	7.78	3.99–15.2	<0.01	4.09	1.90–8.81	<0.01
Grade of surgery						
Minor	Reference	Reference	Reference	Reference	Reference	Reference
Intermediate	1.44	0.79–2.60	0.23	1.51	0.81–2.81	0.20
Major	4.39	2.53–7.62	<0.01	2.64	1.44–4.84	<0.01
ASA physical status						
1	Reference	Reference	Reference	Reference	Reference	Reference
2	16.65	2.28–121.56	<0.01	6.35	0.85–47.30	0.07
3	110.52	15.43–791.75	<0.01	17.60	2.36–131.30	<0.01
4	511.19	70.59–3701.958	<0.01	49.05	6.33–379.79	<0.01

Risque très élevé si : agé; ASA > 3 ou 4; chirurgie majeure; anémie > modérée (Hb > 12 g/dL chez les hommes et 11 g/dL chez les femmes)

British Journal of Anaesthesia, 121 (6): 1227–1235 (2018)

Messages

- L'anémie est fréquente dans la population générale
- L'anémie pré- et post-opératoires
  - Associée de manière indépendante à une augmentation de la morbidité/mortalité, même lorsqu'elle est modérée (au dessus des seuils transfusionnels)
  - Rechecher, diagnostiquer et traiter l'anémie pré- et post-opératoire (même si la valeur d'hémoglobine est >>> au seuils transfusionnels)
  - L'anémie ferriprive (fer IV/PO, EPO, délais)

Message

Le saignement est un facteur de risque de morbi-mortalité post-opératoires

Il faut minimiser le saignement per-opératoire (acide tranexamique, chirurgie, hémostase chirurgicale, normothermie, etc.)

Message

La transfusion (de CGR) est, le plus souvent, délétère. Elle est parfois bénéfique

Problème des seuils transfusionnels

QCM 3

- Parmi les propositions suivantes concernant les seuils transfusionnels, lesquelles vous paraissent vraies ?
  - 1. Le seuil transfusionnel restrictif (indique la transfusion de CGR) est défini par une valeur d'Hb < 7 g/dL
  - 2. Le seuil transfusionnel restrictif (indique la transfusion de CGR) est défini par une valeur d'Hb < 7-8 g/dL
  - 3. Un seuil transfusionnel libéral est défini (indique la transfusion de CGR) si Hb < 10 g/dL
  - 4. Un seuil transfusionnel libéral est défini (indique la transfusion de CGR) si Hb <9- 10 g/dL

QCM 4

- Une transfusion de CGR par excès est définie par le critère suivant (une ou plusieurs réponses correctes possibles)
  - 1. Une valeur d'Hb > 12 g/dL après transfusion de CGR
  - 2. Une valeur d'Hb > 10 g/dL après transfusion de CGR
  - 3. Une valeur d'Hb > 9 g/dL après transfusion de CGR
  - 4. Je ne sais pas

QCM 5

- Les seuils transfusionnels restrictifs ne s'appliquent pas aux patients (plusieurs réponses correctes possibles)
  - 1. Ayant une cardiopathie
  - 2. Ayant un état de choc septique
  - 3. Ayant une coronaropathie stable
  - 4. Ayant une coronaropathie instable

Seuils transfusionnels de CGR

Patients de réanimation/
choc septique

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 9, 2014 VOL. 371 NO. 15

Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock

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This article was published on October 1, 2014, at NEJM.org.

Table 1. Characteristics of the Trial Patients at Baseline.*

Characteristic	Lower Hemoglobin Threshold (N = 502)	Higher Hemoglobin Threshold (N = 496)
Age — yr		
Median	67	67
Interquartile range	57–73	58–75
Male sex — no. (%)	272 (54.2)	259 (52.2)
Chronic cardiovascular disease — no. (%)†	75 (14.9)	66 (13.3)
Chronic lung disease — no. (%)‡	111 (22.1)	102 (20.6)
Hematologic cancer — no. (%)	39 (7.8)	36 (7.3)
Admission to a university hospital — no. (%)	323 (64.3)	324 (65.3)
Surgery during index hospitalization — no. (%)		
Emergency	191 (38.0)	217 (43.8)
Elective	59 (11.8)	53 (10.7)
Source of ICU admittance — no. (%)		
Emergency department	90 (17.9)	79 (15.9)
General ward	268 (53.4)	257 (51.8)
Operating or recovery room	113 (22.5)	121 (24.4)
Other ICU	31 (6.2)	39 (7.9)
Source of sepsis — no. (%)§		
Lungs	267 (53.2)	259 (52.2)
Abdomen	206 (41.0)	198 (39.9)
Urinary tract	58 (11.6)	61 (12.3)
Soft tissue	59 (11.8)	59 (11.9)
Other	50 (10.0)	47 (9.5)
Positive culture from blood or sterile site	188 (37.5)	160 (32.3)
Interval from ICU admission to randomization — hr		
Median	23	20
Interquartile range	7–50	7–43
SAPS II¶		
Median	51	52
Interquartile range	42–62	44–64

This article was published
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Table 1. (Continued.)

Characteristic	Lower Hemoglobin Threshold (N = 502)	Higher Hemoglobin Threshold (N = 496)
SOFA score‖		
Median	10	10
Interquartile range	8–12	8–12
Renal-replacement therapy — no. (%)**	68 (13.5)	53 (10.7)
Mechanical ventilation — no. (%)††	345 (68.7)	350 (70.6)

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on October 1, 2014, at NEJM.org.

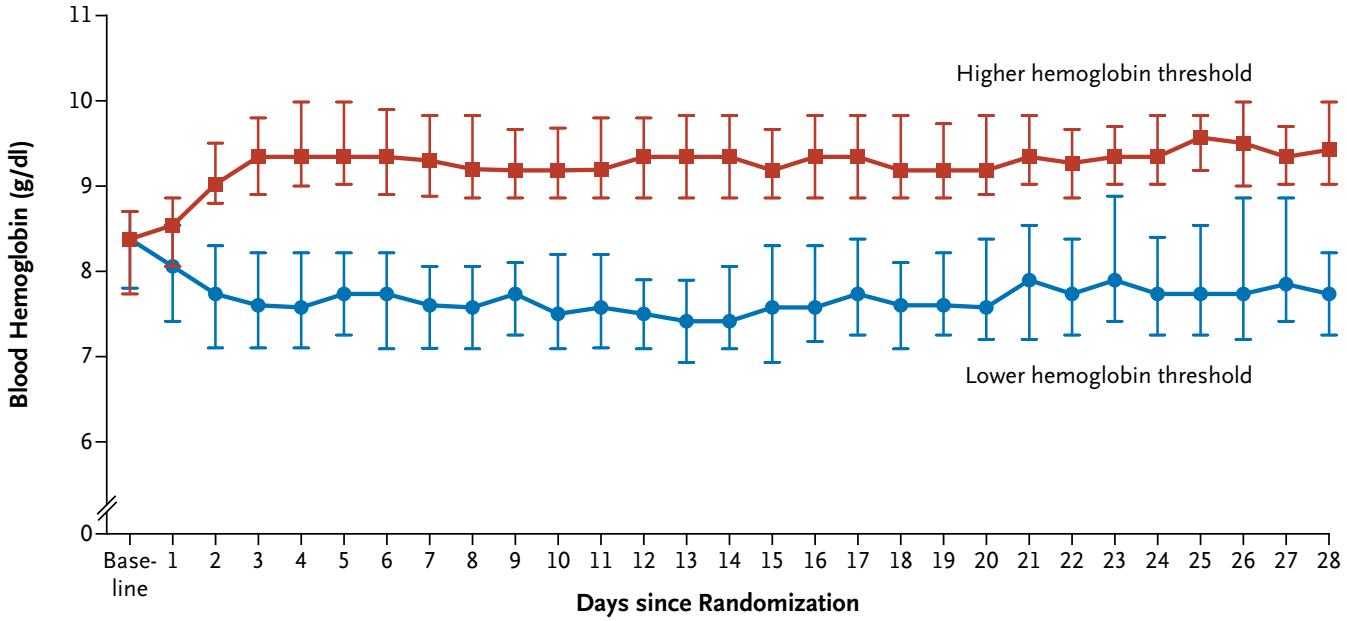

Figure 2. Blood Hemoglobin Levels in Patients in the ICU at Baseline and after Randomization.

The graphs show the median daily lowest levels of blood hemoglobin in the lower-threshold group and the higher-threshold group. Baseline values were the lowest blood hemoglobin level measured in the 24 hours before randomization. Day 1 was defined as the time of randomization to the end of that day and lasted a median of 15 hours in the lower-threshold group and 14 hours in the higher-threshold group. The I bars indicate the 25th and 75th percentiles.

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Table 2. Primary and Secondary Outcome Measures.*

Outcome	Lower Hemoglobin Threshold	Higher Hemoglobin Threshold	Relative Risk (95% CI)	P Value
Primary outcome: death by day 90 — no./total no. (%)	216/502 (43.0)	223/496 (45.0)	0.94 (0.78–1.09)	0.44†
Secondary outcomes‡				
Use of life support — no./total no. (%)§				
At day 5	278/432 (64.4)	267/429 (62.2)	1.04 (0.93–1.14)	0.47†
At day 14	140/380 (36.8)	135/367 (36.8)	0.99 (0.81–1.19)	0.95†
At day 28	53/330 (16.1)	64/322 (19.9)	0.77 (0.54–1.09)	0.14†
Ischemic event in the ICU — no./total no. (%)¶	35/488 (7.2)	39/489 (8.0)	0.90 (0.58–1.39)	0.64‖
Severe adverse reaction — no./total no. (%)**	0/488	1/489 (0.2)	—	1.00
Alive without vasopressor or inotropic therapy — mean % of days††	73	75	—	0.93
Alive without mechanical ventilation — mean % of days††	65	67	—	0.49
Alive without renal-replacement therapy — mean % of days††	85	83	—	0.54
Alive and out of the hospital — mean % of days††	30	31	—	0.89

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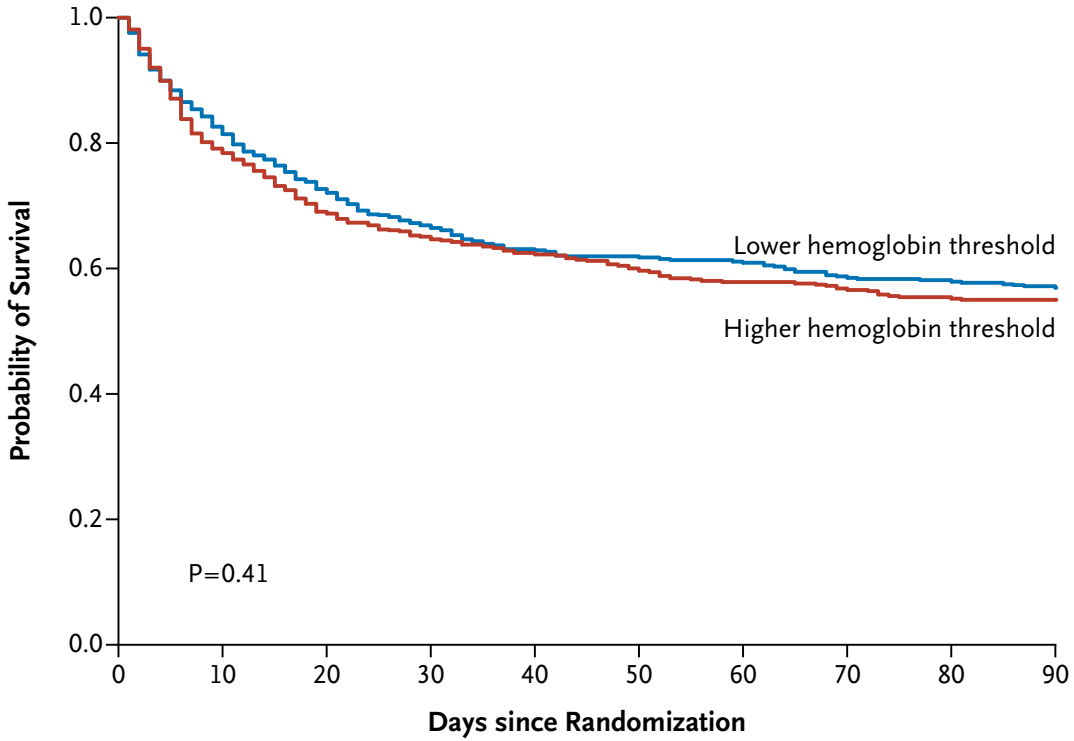
A **Time to Death**



No. at Risk

Lower hemoglobin threshold	502	334	306	286
Higher hemoglobin threshold	496	321	287	273

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B **Relative Risk of the Primary Outcome**

Subgroup	Lower Hemoglobin Threshold	Higher Hemoglobin Threshold	Relative Risk (95% CI)	P Value for Heterogeneity
	no. of events/no. of patients in subgroup			
Age				0.85
>70 yr	93/173	98/185	0.98 (0.79–1.18)	
≤70 yr	123/329	125/311	0.94 (0.75–1.14)	
Chronic cardiovascular disease				0.25
Yes	42/75	33/66	1.08 (0.75–1.40)	
No	174/427	190/430	0.90 (0.75–1.06)	
SAPS II at baseline				0.06
>53	112/207	139/226	0.83 (0.64–1.04)	
≤53	104/295	84/270	1.10 (0.91–1.30)	
All patients	216/502	223/496	0.94 (0.78–1.09)	

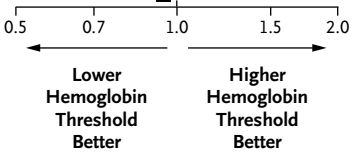

Figure 3. Time to Death and Relative Risk of Death at 90 Days.

Panel A shows the survival curves, with data censored at 90 days, in the two intervention groups in the intention-to-treat population. Kaplan–Meier analysis showed that the survival time did not differ significantly between the two groups (P=0.41 by Cox regression analysis, with adjustment for the stratification variables). Panel B shows the relative risks (black boxes) with 95% confidence intervals (horizontal lines) for the primary outcome measure of death by day 90 in the lower-threshold group, as compared with the higher-threshold group, among all the patients and in the three prespecified subgroups, as assessed by means of logistic-regression analysis, with adjustment for the stratification variables. The size of each black box is proportional to the size of the corresponding subgroup. Chronic cardiovascular disease was defined as any history of myocardial infarction, any history of stable or unstable angina pectoris, previous treatment with nitrates, percutaneous coronary intervention, coronary-artery bypass grafting or noncoronary vascular interventions, any history of chronic heart failure (defined as New York Heart Association class III or IV), or any history of cerebral infarction or transitory cerebral ischemia. The Simplified Acute Physiology Score (SAPS) II[25] is calculated from 17 baseline variables; scores range from 0 to 163, with higher scores indicating higher severity of disease. A total of 1 or 2 of the 17 variables were missing for 77 patients in the higher-threshold group and for 99 in the lower-threshold group. In this analysis, these missing variables were considered to be within the normal range, thereby not contributing to the composite SAPS II of these patients.

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Seuils transfusionnels

Chirurgie cardiaque adulte

Patients ayant une cardiopathie

The NEW ENGLAND JOURNAL of MEDICINE

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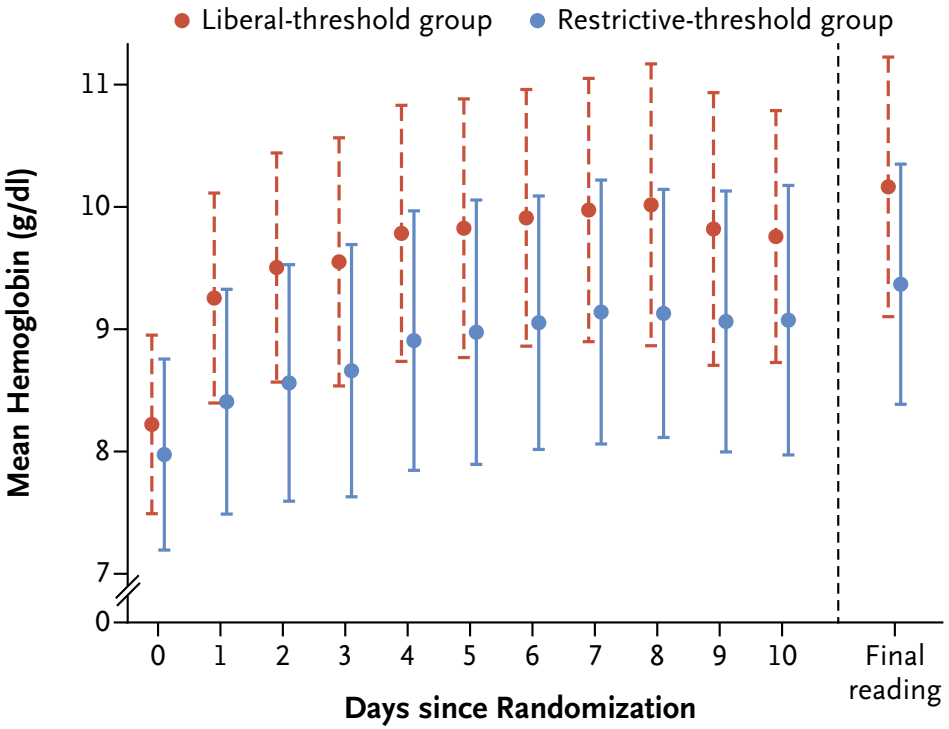
Liberal or Restrictive Transfusion after Cardiac Surgery

Gavin J. Murphy, F.R.C.S., Katie Pike, M.Sc., Chris A. Rogers, Ph.D., Sarah Wordsworth, Ph.D., Elizabeth A. Stokes, M.Sc., Gianni D. Angelini, F.R.C.S., and Barnaby C. Reeves, D.Phil., for the TITRe2 Investigators*

N Engl J Med 2015;372:997-1008.



No. at Risk

Liberal-threshold group	994	967	894	773	732	501	405	338	245	204	170	998
Restrictive-threshold group	998	971	894	758	713	502	401	303	226	175	147	1003

Figure 1. Mean Daily Nadir in Hemoglobin Level.

I bars indicate standard deviations, which were calculated independently at each time point.

N Engl J Med 2015;372:997-1008.

N Engl J Med 2015;372:997-1008.

Table 3. Outcomes.

Outcome	Restrictive Transfusion Threshold (N=1000)	Liberal Transfusion Threshold (N=1003)	Estimated Treatment Effect	
			Odds Ratio or Hazard Ratio (95% CI)	P Value
Serious infection or ischemic event: primary outcome				
Overall	331/944 (35.1)	317/962 (33.0)	1.11 (0.91–1.34)*	0.30
Infectious event†	238/936 (25.4)	240/954 (25.2)	1.02 (0.83–1.26)*	0.83
Sepsis	210/982 (21.4)	214/983 (21.8)		
Wound infection	55/921 (6.0)	46/936 (4.9)		
Ischemic event	156/991 (15.7)	139/99 (114.0)	1.16 (0.90–1.49)*	0.26
Permanent stroke	15/989 (1.5)	17/985 (1.7)		
Myocardial infarction	3/987 (0.3)	4/981 (0.4)		
Gut infarction	6/987 (0.6)	1/982 (0.1)		
Acute kidney injury	140/989 (14.2)	122/989 (12.3)		
Stage 1	49/989 (5.0)	40/989 (4.0)		
Stage 2	39/989 (3.9)	35/989 (3.5)		
Stage 3	50/989 (5.1)	46/989 (4.7)		
Secondary outcomes				
No. of hours in ICU or high-dependency unit‡				
Median	49.5	45.9	0.97 (0.89–1.06)§	0.53
Interquartile range	21.9–99.7	20.1–94.8		
No. of days in hospital¶				
Median	7.0	7.0	1.00 (0.92–1.10)§	0.94
Interquartile range	5.0–10.0	5.0–10.0		
All-cause mortality at 90 days	42/1000 (4.2)	26/1003 (2.6)	1.64 (1.00–2.67)§	0.045
Clinically significant pulmonary complications	127/979 (13.0)	116/982 (11.8)	1.11 (0.85–1.45)*	0.45
All-cause mortality at 30 days	26/1000 (2.6)	19/1003 (1.9)		

* This value is an odds ratio.
† Since the amount of missing data was greater than 5% (owing primarily to missing data on posthospital discharge), a separate treatment estimate was estimated for infections that occurred before hospital discharge (according to the rules regarding missing data outlined in the statistical analysis plan in the study protocol). For this treatment effect, we estimated an odds ratio of 1.07 (95% CI, 0.85 to 1.36; P=0.55).
‡ The duration of stay in the intensive care unit (ICU) or high-dependency unit after randomization was 0 days for 63 patients in the restrictive-threshold group and 61 patients in the liberal-threshold group; data were censored for 23 patients in the restrictive-threshold group and 15 patients in the liberal-threshold group. In addition, 37 patients in the restrictive-threshold group and 32 patients in the liberal-threshold group had more than one admission to the ICU or high-dependency unit.
§ This value is a hazard ratio.
¶ The duration of hospital stay after randomization was 0 days for 4 patients in the restrictive-threshold group and 2 patients in the liberal-threshold group; data were censored for 25 patients in the restrictive-threshold group and 17 patients in the liberal-threshold group.

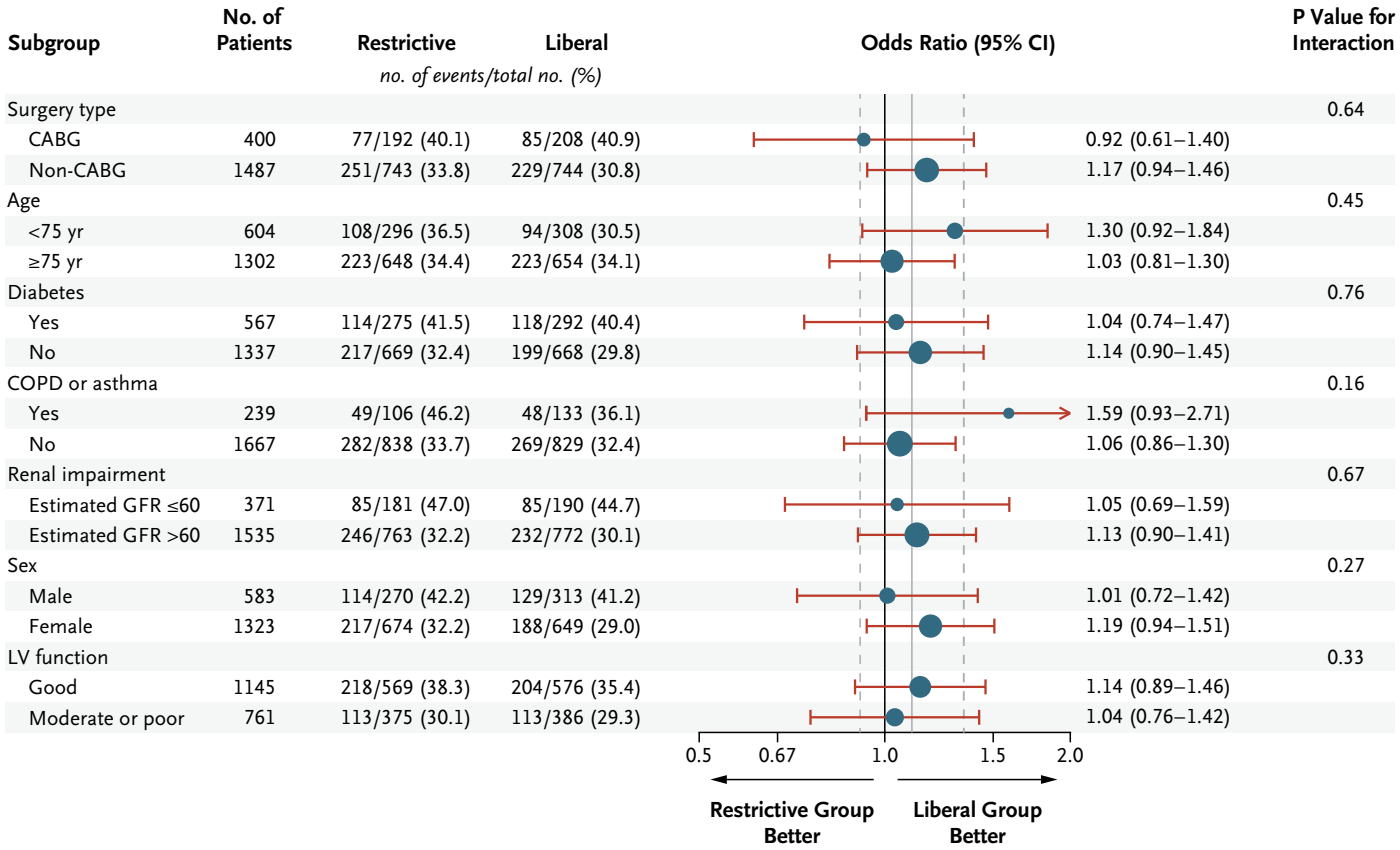


Figure 2. Subgroup Analyses.

The gray vertical lines represent the overall treatment estimate (solid line) and the 95% confidence interval (dashed lines) for the primary outcome as calculated for the entire analysis cohort. The sizes of the circles designating the point estimates reflect the sizes of the subgroups. The restrictive transfusion threshold for hemoglobin was less than 7.5 g per deciliter, and the liberal transfusion threshold was less than 9 g per deciliter. CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, GFR glomerular filtration rate, and LV left ventricular.

N Engl J Med 2015;372:997-1008.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery

C.D. Mazer, R.P. Whitlock, D.A. Fergusson, J. Hall, E. Belley-Cote, K. Connolly, B. Khanykin, A.J. Gregory, É. de Médicis, S. McGuinness, A. Royse, F.M. Carrier, P.J. Young, J.C. Villar, H.P. Grocott, M.D. Seeberger, S. Fremes, F. Lellouche, S. Syed, K. Byrne, S.M. Bagshaw, N.C. Hwang, C. Mehta, T.W. Painter, C. Royse, S. Verma, G.M.T. Hare, A. Cohen, K.E. Thorpe, P. Jüni, and N. Shehata, for the TRICS Investigators and Perioperative Anesthesia Clinical Trials Group*

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Table 1. Baseline and Operative Characteristics.*

Characteristic	Restrictive Threshold (N = 2430)	Liberal Threshold (N = 2430)
Preoperative characteristics		
Age — yr	72±10	72±10
Male sex — no. (%)	1553 (63.9)	1586 (65.3)
Body-mass index†	28.1±6.0	28.0±5.2
EuroSCORE I‡	7.9±1.8	7.8±1.9
Previous cardiac surgery — no. (%)	307 (12.6)	280 (11.5)
Myocardial infarction in previous 90 days — no. (%)	562 (23.1)	601 (24.7)
Left ventricular function — no./total no. (%)§		
Good	1485/2430 (61.1)	1523/2427 (62.8)
Moderately reduced	733/2430 (30.2)	710/2427 (29.3)
Poor	166/2430 (6.8)	156/2427 (6.4)
Very poor	46/2430 (1.9)	38/2427 (1.6)
Diabetes mellitus — no. (%)	646 (26.6)	686 (28.2)
Treated hypertension — no. (%)	1797 (74.0)	1803 (74.2)
Emergency surgery — no. (%)	37 (1.5)	34 (1.4)
Renal function — no./total no. (%)¶		
Normal	1090/2332 (46.7)	1071/2348 (45.6)
Moderately impaired	857/2332 (36.7)	866/2348 (36.9)
Severely impaired	355/2332 (15.2)	385/2348 (16.4)
Use of dialysis	30/2332 (1.3)	26/2348 (1.1)
Use of aspirin — no./total no. (%)	1274/2428 (52.5)	1293/2423 (53.4)
Hemoglobin — g/dl	13.1±1.8	13.1±1.7
Operative characteristics		
Type of surgery — no./total no. (%)		
CABG only	622/2429 (25.6)	645/2430 (26.5)
CABG and valve surgery	464/2429 (19.1)	472/2430 (19.4)
CABG and other, nonvalve surgery	205/2429 (8.4)	203/2430 (8.4)
Valve surgery only	703/2429 (28.9)	716/2430 (29.5)
Other, non-CABG surgery	433/2429 (17.8)	394/2430 (16.2)
Duration of cardiopulmonary bypass — min	120±59	121±57
Intraoperative tranexamic acid — no./total no. (%)	2219/2428 (91.4)	2235/2428 (92.1)

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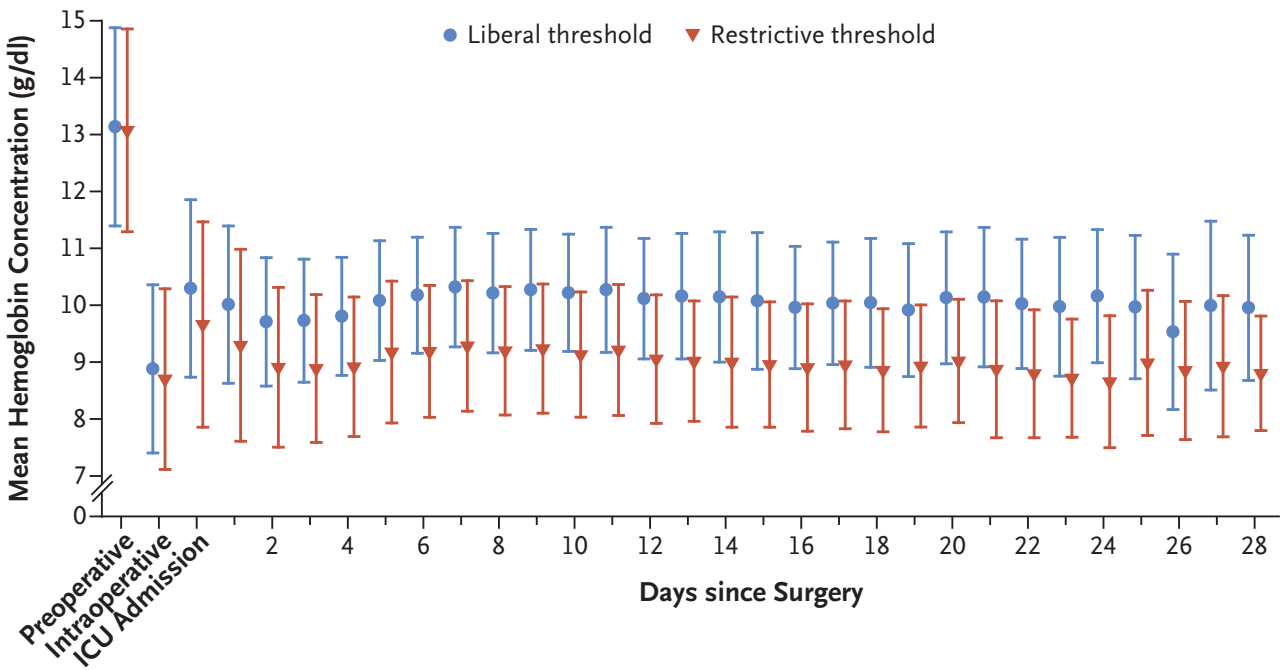

No. at Risk

Liberal threshold	2428	2435	2015	1354	731	443	327	233	153	122	112	76	69	57	51
Restrictive threshold	2429	2454	2007	1431	841	527	376	305	215	165	131	117	91	77	76

Figure 1. Hemoglobin Concentration during the Trial Period.

The restrictive transfusion threshold was less than 7.5 g per deciliter intraoperatively and postoperatively, and the liberal transfusion threshold was less than 9.5 g per deciliter intraoperatively or postoperatively in the intensive care unit (ICU) or less than 8.5 g per deciliter on the non-ICU ward. I bars indicate the standard deviation.

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Table 2. Transfusion Outcomes in the Per-Protocol Population.

Characteristic	Restrictive Threshold (N = 2430)	Liberal Threshold (N = 2430)	Odds Ratio or Rate Ratio (95% CI)
Red-cell transfusions after randomization			
≥1 Unit of red cells — no. (%)	1271 (52.3)	1765 (72.6)	0.41 (0.37–0.47)
No. of units of red cells transfused			
Median	2	3	0.85 (0.82–0.88)*
Interquartile range	1–4	2–5	
Distribution — no. (%)			
0	1159 (47.7)	665 (27.4)	
1	383 (15.8)	366 (15.1)	
2	283 (11.6)	367 (15.1)	
3	174 (7.2)	267 (11.0)	
4	140 (5.8)	225 (9.3)	
≥5	291 (12.0)	540 (22.2)	
Intraoperative red-cell transfusion			
No. of patients with transfusion (%)	674 (27.7)	1259 (51.8)	0.36 (0.32–0.40)
Median no. of units transfused	2	2	0.88 (0.82–0.95)*
Interquartile range	1–3	1–3	
Postoperative red-cell transfusion in ICU			
No. of patients with transfusion (%)	867 (35.7)	1253 (51.6)	0.52 (0.46–0.58)
Median no. of units transfused	2	2	0.98 (0.93–1.04)*
Interquartile range	1–3	1–3	
Postoperative red-cell transfusion not in ICU			
No. of patients with transfusion (%)	278 (11.4)	229 (9.4)	1.24 (1.03–1.49)
Median no. of units transfused	1	1	0.78 (0.60–1.03)*
Interquartile range	1–1	1–2	
Protocol suspension at any time — no. (%)	348 (14.3)	270 (11.1)	1.34 (1.13–1.58)
Other transfusions			
Plasma — no. (%)	571 (23.5)	658 (27.1)	0.83 (0.73–0.94)
Platelets — no. (%)	700 (28.8)	716 (29.5)	0.97 (0.86–1.10)
Cryoprecipitate — no./total no. (%)	275/2334 (11.8)	275/2349 (11.7)	1.01 (0.84–1.20)
Prothrombin complex concentrate — no./total no. (%)	73/2334 (3.1)	61/2349 (2.6)	1.21 (0.86–1.71)

* This value is a rate ratio. For all ratios, the restrictive-threshold group is in the numerator and the liberal-threshold group in the denominator.

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Table 3. Primary and Secondary Outcomes in the Per-Protocol Population.

Characteristic	Restrictive Threshold (N = 2430)	Liberal Threshold (N = 2430)	Odds Ratio or Hazard Ratio (95% CI)
Primary outcome			
Composite-outcome event — no./total no. (%)	276/2428 (11.4)	303/2429 (12.5)	0.90 (0.76–1.07)
Death — no./total no. (%)	74/2427 (3.0)	87/2429 (3.6)	0.85 (0.62–1.16)
Stroke — no./total no. (%)	45/2428 (1.9)	49/2429 (2.0)	0.92 (0.61–1.38)
Myocardial infarction — no./total no. (%)	144/2428 (5.9)	144/2429 (5.9)	1.00 (0.79–1.27)
New-onset renal failure with dialysis — no./total no. (%)	61/2428 (2.5)	72/2429 (3.0)	0.84 (0.60–1.19)
Secondary outcomes			
Length of stay in ICU			
No. of patients with data	2422	2418	
Median — days	2.1	1.9	0.89 (0.84–0.94)*
Interquartile range — days	1.0–4.0	1.0–3.9	
Length of stay in hospital			
No. of patients with data	2419	2419	
Median — days	8.0	8.0	0.93 (0.88–0.99)*
Interquartile range — days	7.0–13.0	7.0–12.0	
Duration of mechanical ventilation			
No. of patients with data	2416	2421	
Median — days	0.38	0.36	0.94 (0.89–1.00)*
Interquartile range — days	0.22–0.75	0.22–0.71	
Prolonged low-output state — no./total no. (%)†	994/2429 (40.9)	987/2430 (40.6)	1.01 (0.90–1.14)
Infection — no./total no. (%)	121/2428 (5.0)	101/2429 (4.2)	1.21 (0.92–1.58)
Bowel infarction — no./total no. (%)	6/2428 (0.2)	5/2429 (0.2)	1.20 (0.37–3.94)
Acute kidney injury — no./total no. (%)	792/2332 (34.0)	797/2348 (33.9)	1.00 (0.89–1.13)
Seizure — no./total no. (%)	50/2428 (2.1)	42/2429 (1.7)	1.20 (0.79–1.81)
Delirium — no./total no. (%)	306/2428 (12.6)	264/2429 (10.9)	1.18 (0.99–1.41)
Encephalopathy — no./total no. (%)	26/2428 (1.1)	22/2429 (0.9)	1.18 (0.67–2.10)

* This value is a hazard ratio. For all ratios, the restrictive-threshold group is in the numerator and the liberal-threshold group in the denominator.

† A prolonged low-output state was defined as the infusion of two or more inotropes for 24 hours or more, the use of an intraaortic balloon pump postoperatively, or the use of a ventricular assist device postoperatively, as described in the Supplementary Appendix.

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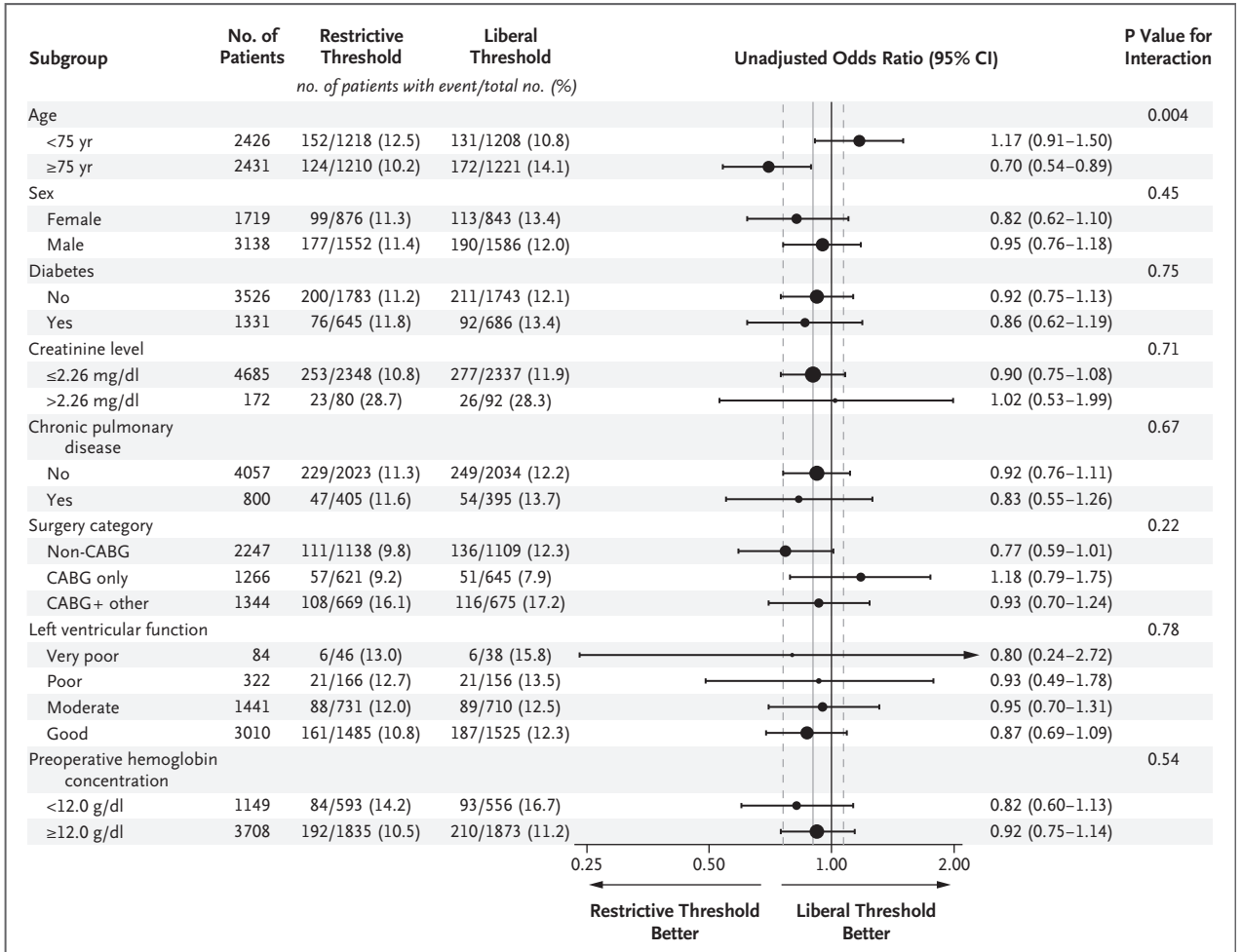

Figure 2. Subgroup Analyses.

The solid gray vertical line indicates the overall treatment estimate for the primary outcome in the primary analysis cohort (per-protocol population), and the dashed lines the 95% confidence interval. The size of the circles is proportional to the statistical precision of the estimates. An arrow indicates that the 95% confidence interval is outside the range shown. Data were missing for two patients in the restrictive-threshold group and for one in the liberal-threshold group. To convert the values for creatinine to micromoles per liter, multiply by 88.4. Chronic pulmonary disease was defined as the long-term use of bronchodilators or glucocorticoids for lung disease. Left ventricular function was defined according to the following categories: good (left ventricular ejection fraction, ≥51%), moderately reduced (31 to 50%), poor (21 to 30%), and very poor (≤20%). CABG denotes coronary-artery bypass grafting.

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Seuils transfusionnels chez les patients ayant une cardiopathie/coronaropathie instable

SCA et IDM

Docherty and Walsh *Critical Care* (2017) 21:61
DOI 10.1186/s13054-017-1638-9

Critical Care

REVIEW Open Access

Anemia and blood transfusion in the critically ill patient with cardiovascular disease

Annemarie B. Docherty[1,2*] and Timothy S. Walsh[1,2]

Docherty and Walsh Critical Care (2017) 21:61

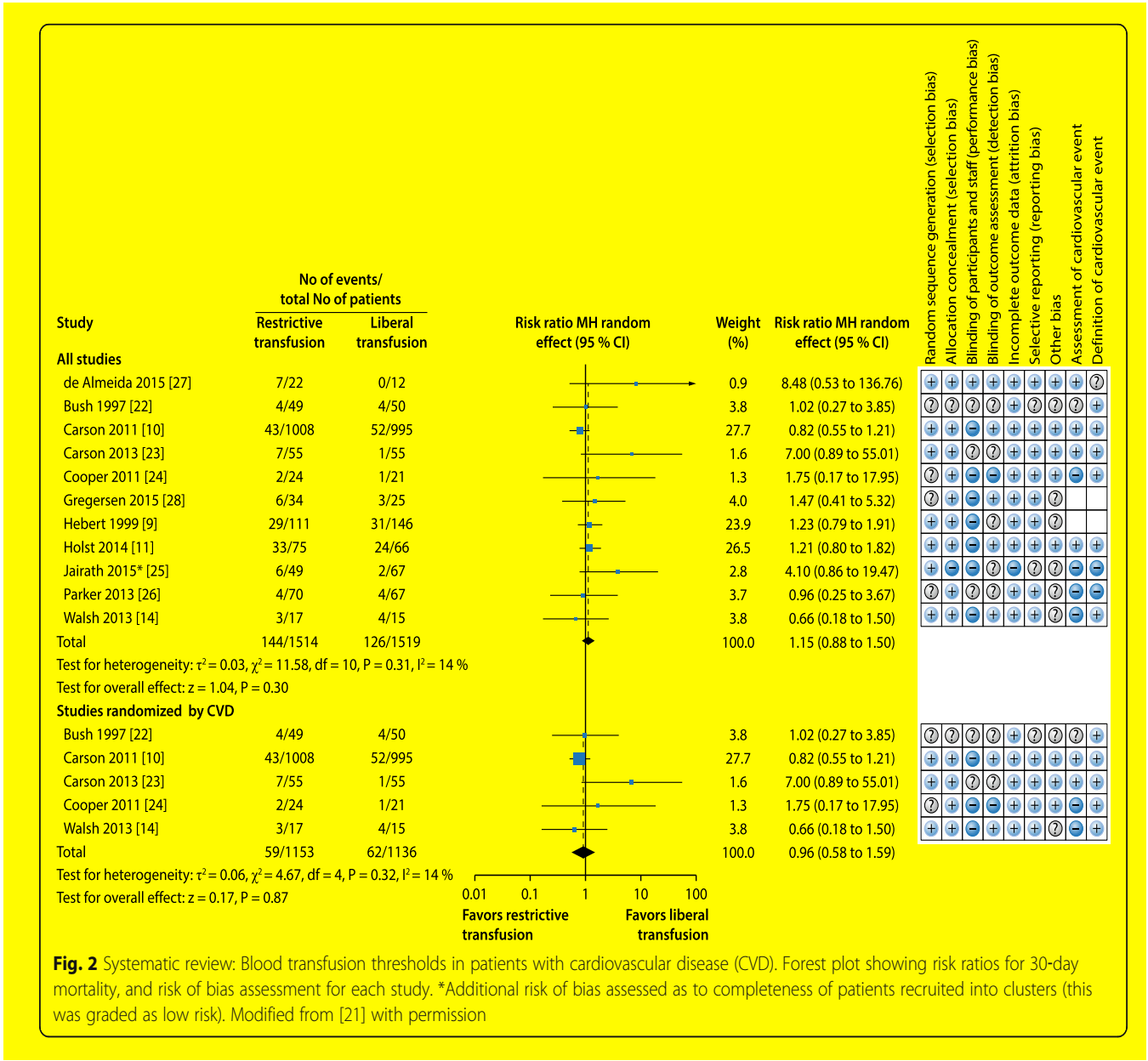

Fig. 2 Systematic review: Blood transfusion thresholds in patients with cardiovascular disease (CVD). Forest plot showing risk ratios for 30-day mortality, and risk of bias assessment for each study. *Additional risk of bias assessed as to completeness of patients recruited into clusters (this was graded as low risk). Modified from [21] with permission

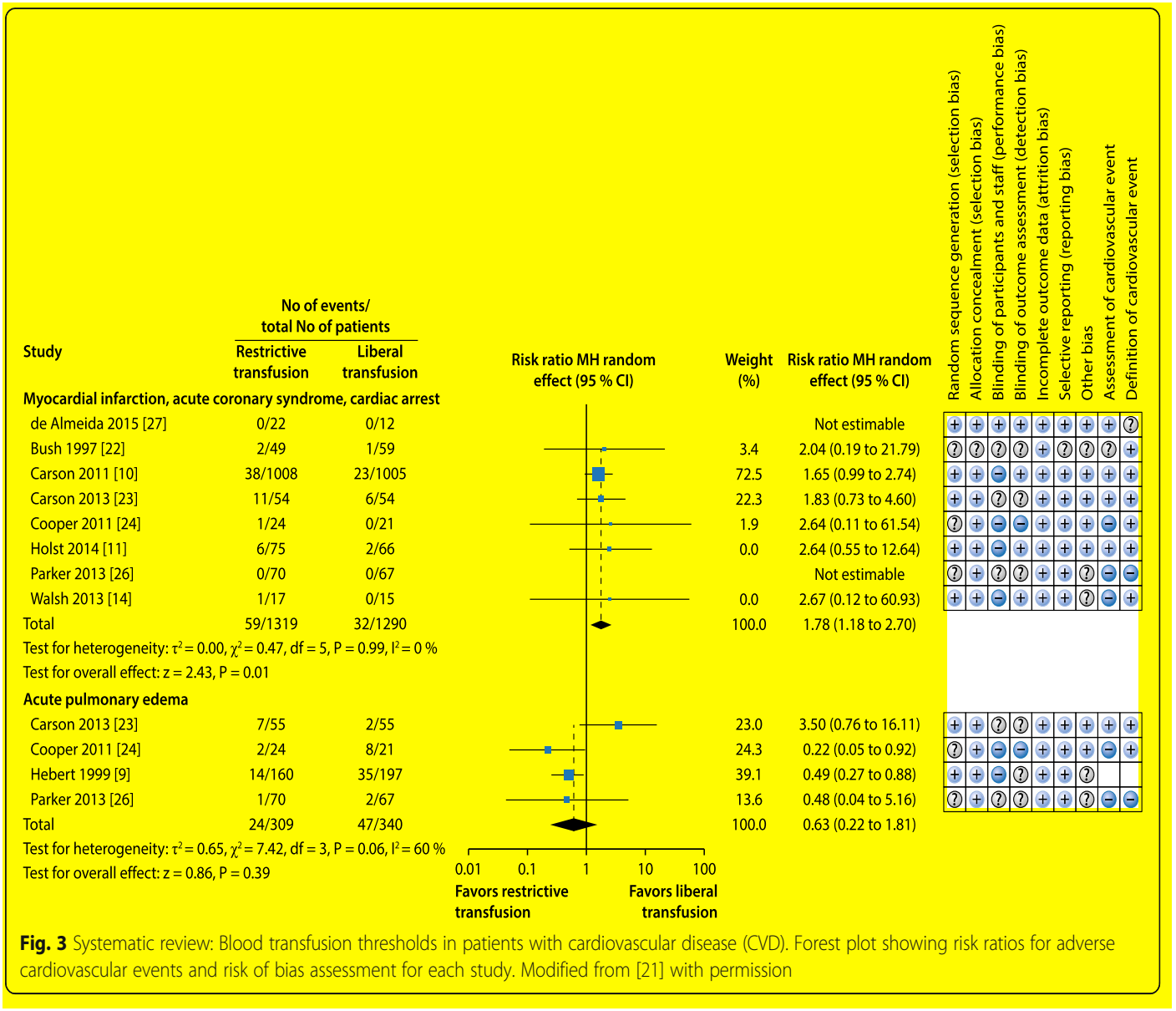

Fig. 3 Systematic review: Blood transfusion thresholds in patients with cardiovascular disease (CVD). Forest plot showing risk ratios for adverse cardiovascular events and risk of bias assessment for each study. Modified from [21] with permission

Docherty and Walsh Critical Care (2017) 21:61

Table 1 Table of guidelines for red blood cell transfusion in patients with cardiovascular disease

Organization	Year	Recommendation for general	Recommendation for CVD
British Committee for Standards in Haematology [38]	2013	7.0 g/dl, target 7.0–9.0 g/dl	Stable angina should have a Hb maintained > 7.0 g/dl
NICE: National Institute for Health and Clinical Excellence [51]	2015	7.0 g/dl, target 7.0–9.0 g/dl	ACS: transfusion threshold of 8.0 g/dl, target of 8.0–10.0 g/dl Chronic: further research
Association of Anaesthetists of Great Britain and Ireland [52]	2016	7.0 g/dl	Uncertainty remains for patients with ischemic heart disease, higher thresholds (8.0 g/dl) may be appropriate
American Association of Blood Banks (AABB) [53]	2016	7.0 g/dl	Patients with symptoms or a Hb level of 8.0 g/dl or less

ACS acute coronary syndrome, *CVD* cardiovascular disease, *Hb* hemoglobin

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Blood Transfusion During Acute Myocardial Infarction

Association With Mortality and Variability Across Hospitals

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J Am Coll Cardiol 2014;64:811–9

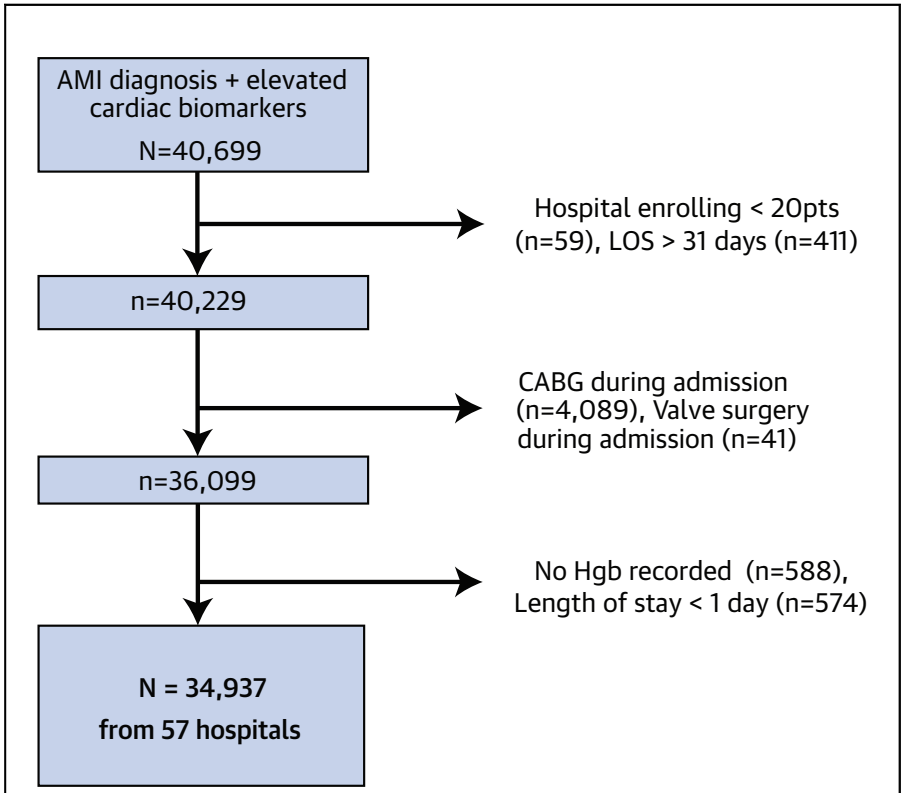


FIGURE 1 Patient Population

Inclusions and exclusions. AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; Hgb = hemoglobin; LOS = length of stay.

J Am Coll Cardiol 2014;64:811–9

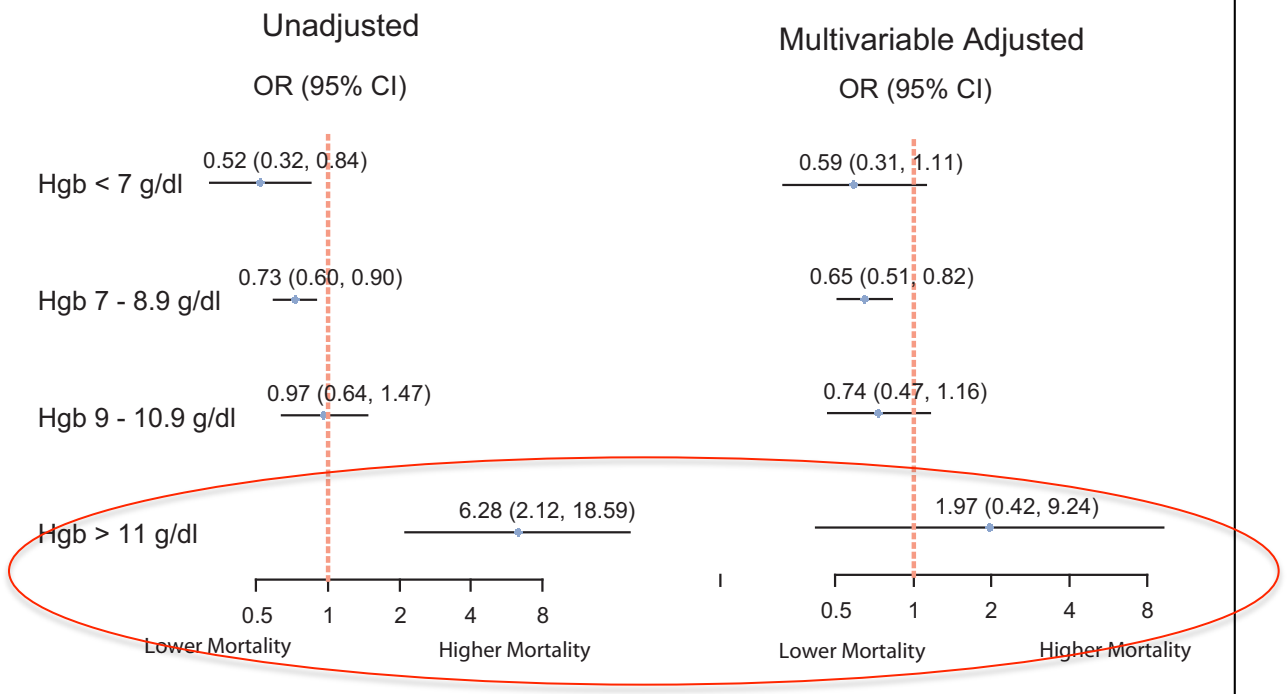


FIGURE 3 Transfusion and Mortality Stratified According to Nadir Hgb

Association of transfusion with mortality stratified according to lowest in-hospital Hgb value. A total of 227 (42.3%) of 537 patients with nadir Hgb <7 g/dl, 1,210 (29.5%) of 4,098 with nadir 7 to 8.9 g/dl, 319 (3.9%) of 8,083 with nadir 9 to 10.9 g/dl, and 22 (0.1%) of 22,219 with nadir ≥11 g/dl were transfused. CI = confidence interval; OR = odds ratio; other abbreviation as in Figure 1.

J Am Coll Cardiol 2014;64:811–9

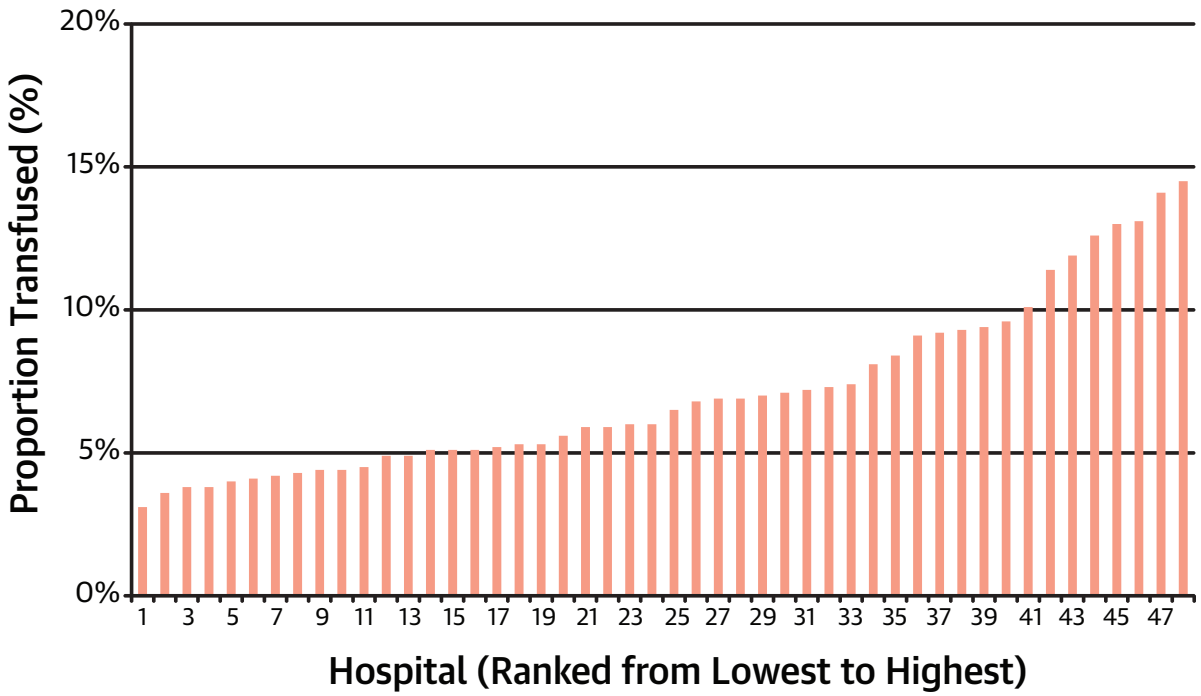


FIGURE 4 **Variation in Blood Transfusion Rates Across Health Facts Hospitals**

Shrinkage-adjusted rates of blood transfusion at the time of acute myocardial infarction across participating hospitals in Health Facts, ranked from lowest to highest transfusion incidence.

J Am Coll Cardiol 2014;64:811–9

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Severe anemia is common in patients hospitalized with AMI, but blood transfusion is controversial, given the lack of evidence of a favorable impact on patient outcomes.

COMPETENCY IN PATIENT CARE 1: In a large cohort of consecutive propensity-matched patients with AMI, blood transfusions were not associated with a greater risk of adverse outcomes.

COMPETENCY IN PATIENT CARE 2: In the absence of definitive data from randomized trials, clinicians should determine whether to transfuse blood to individual patients with AMI based on careful consideration of benefits and risks.

TRANSLATIONAL OUTLOOK: Randomized trials are necessary to overcome selection bias and to further investigate the relationship between blood transfusion and clinical outcomes in patients with AMI.

L'anémie est fréquente chez les patients ayant un IDM aigu

Dans une grande cohorte de patients ayant un IDM aigu: pas d'effet délétère lié à la transfusion de CGR

Analyse du rapport bénéfice/risque individuel (tolérance de l'anémie)

Recherche prospective !

J Am Coll Cardiol 2014;64:811–9

Le problème des seuils transfusionnels

- Littérature (statistique)
  - Seuils de transfusion de CGR bas (7 g/dL) y compris chez les patients en état de choc ou ayant une cardiopathie (dont chirurgie cardiaque)
  - Seuils transfusionnels chez les patients ayant une cardiopathie/chirurgie cardiaque
    - Sévère
    - Coronaropathie
    - SCA/IDM

Conclusions sur les seuils transfusionnels

- Pas de preuves que les seuils “libéraux” améliorent la survie
  - Seuil libéral: > 8 mais < 9 g/dL
- Il est probable que les patients ayant un SCA peuvent bénéficier d’un seuil > 8 mais < 10 g/dL
  - Aucun bénéfice pour Hb > 10 g/dL

Conclusions sur les seuils transfusionnels

- Les seuils bas sont associés statistiquement:
  - Soit à un meilleur “outcome”
  - Soit au même “outcome”
- Transfuser de manière libérale est
  - Dangereux
  - Inutile
  - (presque) JAMAIS bénéfique en normovolémie

Le problème des seuils transfusionnels

- Littérature (statistique)
  - Seuils de transfusion de CGR bas (7 g/dL) y compris chez les patients en état de choc ou ayant une cardiopathie
- Pour un patient donné (raisonnement clinique)
  - Mesure de l'hémoglobine: BRUIT (biologique/ mesure)
  - Tolérance de l'anémie
  - Correction de l'anémie par autre chose que la transfusion de CGR

The Association of Anaesthetists of Great Britain and Ireland made the following recommendations regarding transfusion of red cells (Thomas *et al.*, 2001):

1 Patients should not be transfused if Hb is >10 g dL^{-1}

2 A strong indication for transfusion is Hb <7 g dL^{-1}

3 Transfusion will become essential when Hb is <5 g dL^{-1}

4 Hb concentration between 8 and 10 g dL^{-1} is a safe level even for those with significant cardiorespiratory disease.

5 Symptomatic patients should be transfused.

L’anémie d’hémodilution

- Est définie par une diminution de la valeur de l’Hb (donc anémie)
- Avec une diminution de la masse globulaire rouge soit nulle soit moins importante que l’augmentation du volume plasmatique
- Les calculs du CaO2 et du TaO2 peuvent être faux
- Quand la valeur d’Hb (anémie d’hémodilution) est proche du seuil transfusionnel, indication théorique de transfusion de CGR

Calculs du CaO2 et du TaO2

- TaO2 = (VES= 45 ml) x (FC = 100 bpm) x 0,00134 x (Hb = 10.5 g/dL x Saturation = 1) x 10
  = 633 ml/min (9 ml/kg/min; 70 kg)

- Après optimisation hémodynamique :
  TaO2 = (VES= 55 ml) x (FC = 90 bm) x 0,00134 x (Hb = 9.5 g/dL x x Saturation= 1) x 10 = 630 ml/min (9 ml/kg/min)

- Après optimisation hémodynamique avec valeur Hb inchagée (la masse globulaire rouge n'a pas changé) :
  TaO2 = (VES= 55 ml) x (FC= 90bpm) x 1,34 (Hb = 10,5 g/dL x x Saturation= 1) x 10 = 696 ml/min (10 ml/kg/min)

Scénario clinique

- Patiente hypotendue, remplie avec 500 ml de NaCl 0,9 % en 10 minutes
  - TaO2 avant remplissage = DC (3l/min) x Hb (10 g/dL) x SaO2 (100 %) x 10 = 300 ml/min
  - TaO2 après remplissage: DC (4 l/min) x Hb (8g/dL) x SaO2 (100 %) x 10 = 320 ml/min (soit 7 % d'augm.)
  - Qui est d'accord avec ce calcul ?

Scénario clinique

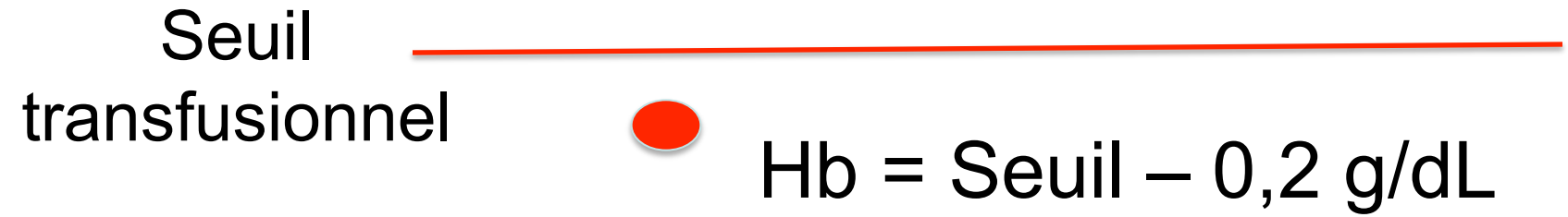
- Patiente hypotendue, remplie avec 500 ml de NaCl 0,9 % en 10 minutes
  - TaO2 avant remplissage = DC (3l/min) x Hb (10 g/dL) x SaO2 (100 %) x 10 = 300 ml/min
  - TaO2 après remplissage: DC (4 l/min) x Hb (8g/dL) x SaO2 (100 %) x 10 = 320 ml/min (soit 7 % d'augm)

  - Qui est d'accord avec ce calcul ?
  - TaO2 après remplissage: DC (4 l/min) x Hb (10g/dL) x SaO2 (100 %) x 10 = 400 ml/min (soit 30 % d'augm)

Scénario clinique

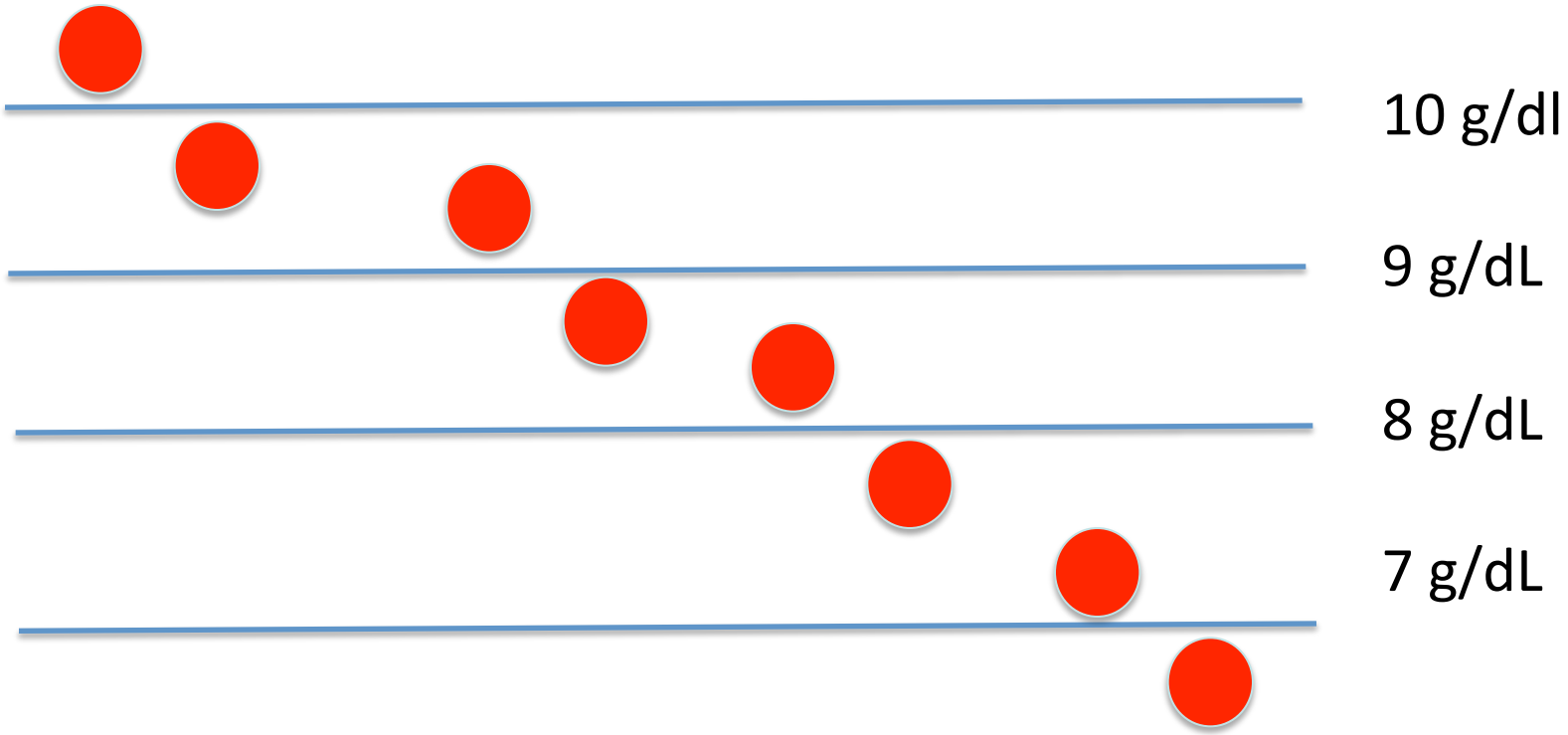
- Patiente hypotendue, remplie avec 500 ml de NaCl 0,9 % en 10 minutes
  - TaO2 avant remplissage = DC (3l/min) x Hb (8 g/dL) x SaO2 (100 %) x 10 = 240 ml/min
  - TaO2 après remplissage: DC (4 l/min) x Hb (6g/dL) x SaO2 (100 %) x 10 = 240 ml/min
    - On passe en dessous du seuil transfusionnel (7 g/dL) et on transfuse des CGR
  - Qui est d'accord avec cette décision ?

Les questions qu'il faut poser avant de prescrire une transfusion de CGR



Pour cette patiente: Hb = 6,8 g/dL

Le problème des seuils transfusionnels pour un patient donné. Raisonnement clinique



Les questions qu'il faut poser avant de prescrire une transfusion de CGR

Pertes sanguines
Par rapport aux pertes
Acceptables calculées

Historique/tendances de la valeur d'Hb

Hémodilution

Expansion volémique

Seuil transfusionnel

Hb = Seuil – 0,2 g/dL

Tolérance de l'anémie

Anticipation (temps, pertes sanguines)

Alternatives
Transfusion CGR

QCM 6

- Concernant le bruit de mesure de l'hémoglobine (plusieurs réponses correctes possibles)
  - 1. Il ne dépend que de la technique de mesure (bruit analytique)
  - 2. Il peut être en relation avec des variations physiologiques circadiennes de l'hémoglobine
  - 3. Il est inférieur à 0,1 g/dL quelle que soit la technique de mesure
  - 4. Il est > 1 g/dL quelle que soit la technique de mesure
  - 5. Je ne sais pas vraiment

Les questions qu'il faut poser avant de prescrire un transfusion de CGR

Bruit de mesure Hb ?

Pertes sanguines
Par rapport aux pertes
Acceptables calculées

Historique de
la valeur d'Hb

Hémodilution

Expansion
volémique

Seuil
transfusionnel

Hb = Seuil – 0,2 g/dL

Tolérance de
l'anémie

Anticipation (temps,
Pertes sanguines)

Alternatives
Transfusion CGR

Bruit de la mesure de l’Hb

Quel est le bruit de la mesure de l'Hb ?
Quelles sont les sources du bruit de la mesure ?
Comment faut-il gérer le bruit de la mesure ?

Site de prélèvement

Erreurs pré-analytiques

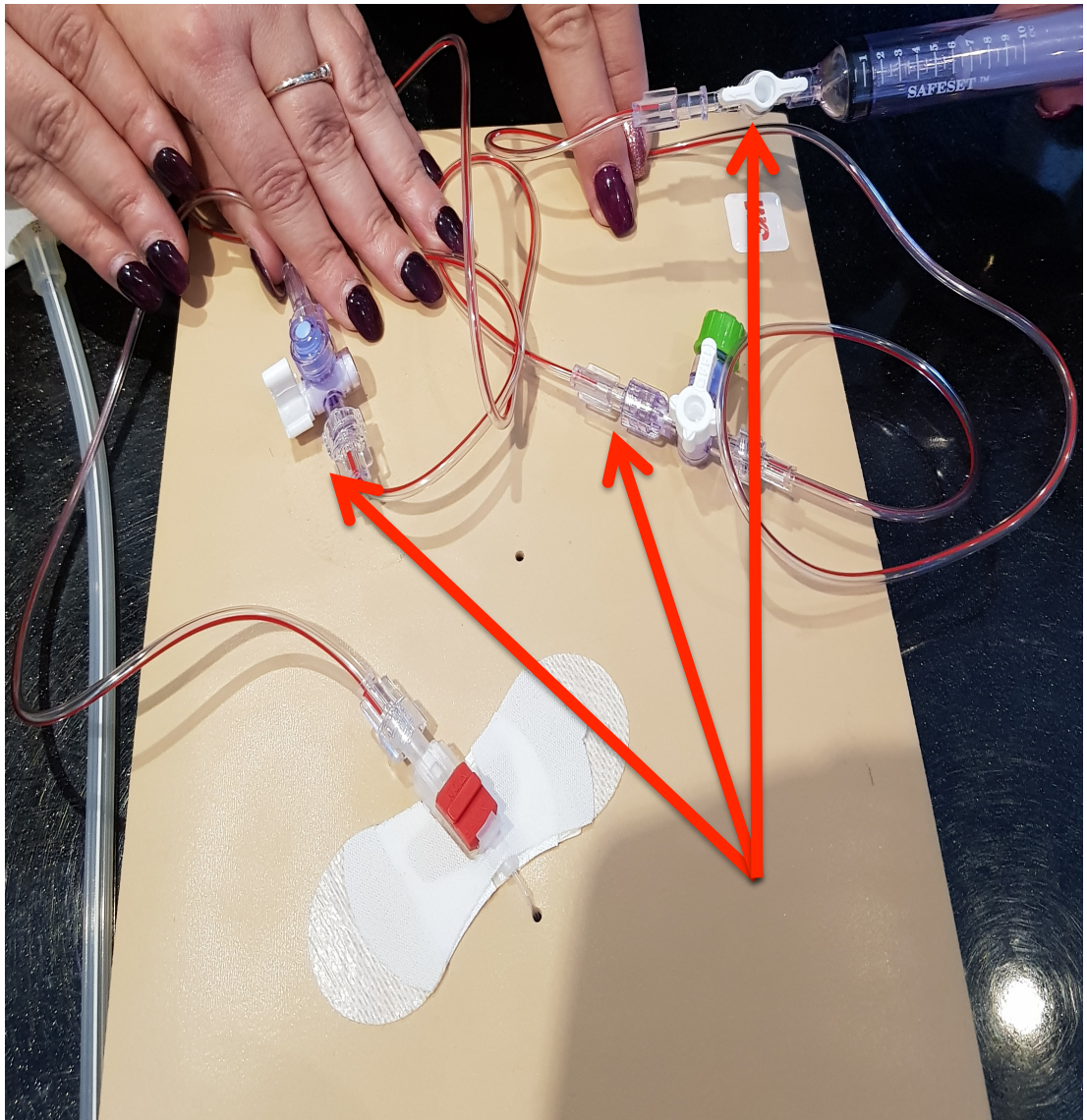
Hb (g/dL)

Hémodilution

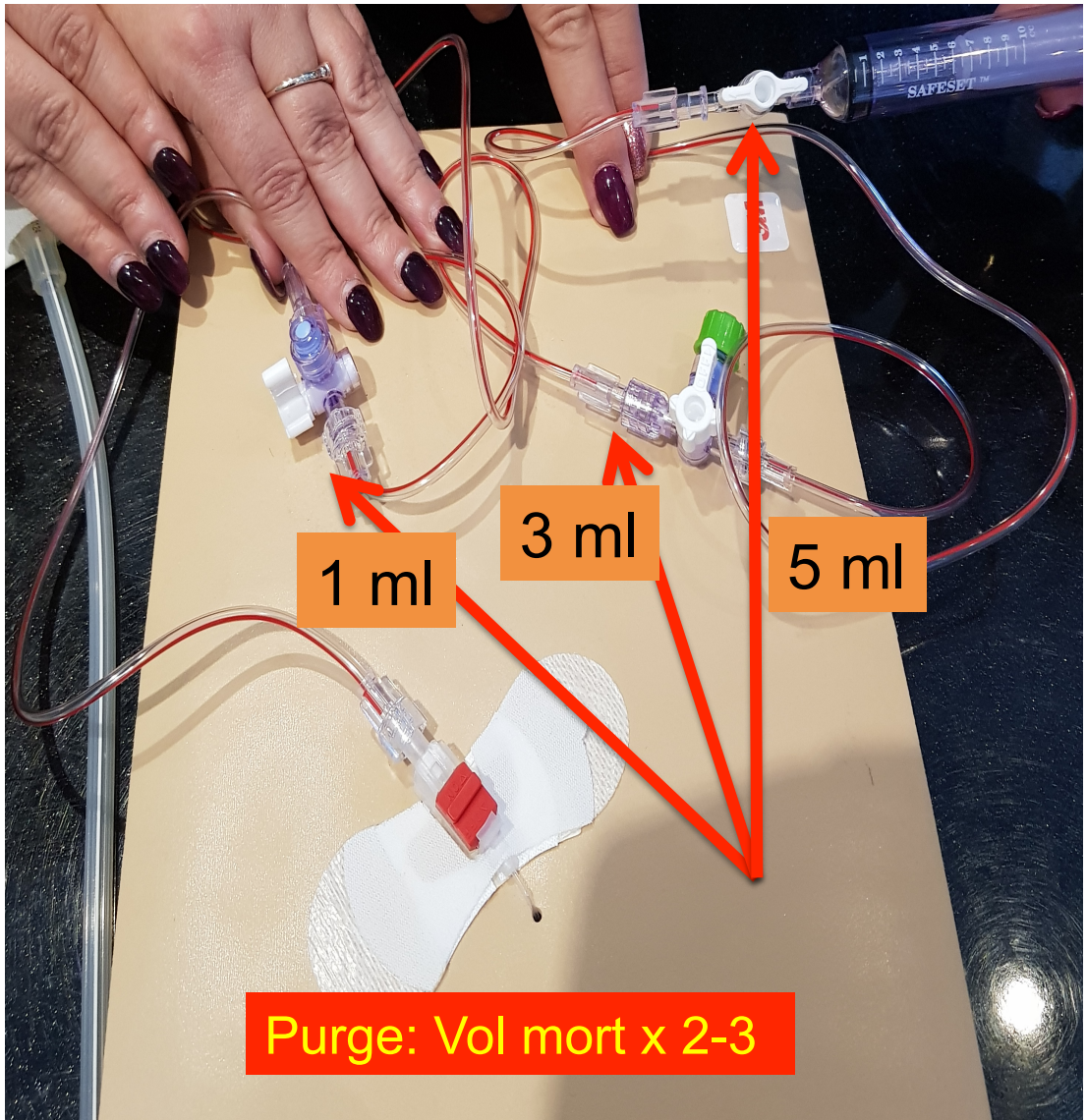
Techniques de mesure

Exemple d’erreur pré-analytique dans la mesure de l’Hb

Montage: Quel est le volume mort ?



Montage: Quel est le volume mort ?



Le bruit analytique (mesure sur le même échantillon)

Avec la même technique

Avec des techniques différentes

Qui peut énumérer les conditions de qualité de mesure avec l'Hemocue ?

TRANSFUSION 2016;00;00–00

Les conditions de qualité de mesure avec l'Hemocue ?

- Ponction sur la face latérale du médian, sans pression
- Bras non-dominant
- Troisième goutte
- Position assise ?

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Sources de variabilité (bruit) de la mesure

- La peau plus foncée diminue la variabilité (méthodes non-invasives et invasives)
- Le fait de fumer diminue la différence entre non-invasif et laboratoire.
  - Carboxyhémoglobine diminue la sensibilité en non-invasif
  - La saturation en O2 mieux mesurée ?
- Anomalies des doigts (callosités)

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BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

Meta-analytic estimation of measurement variability and assessment of its impact on decision-making: the case of perioperative haemoglobin concentration monitoring

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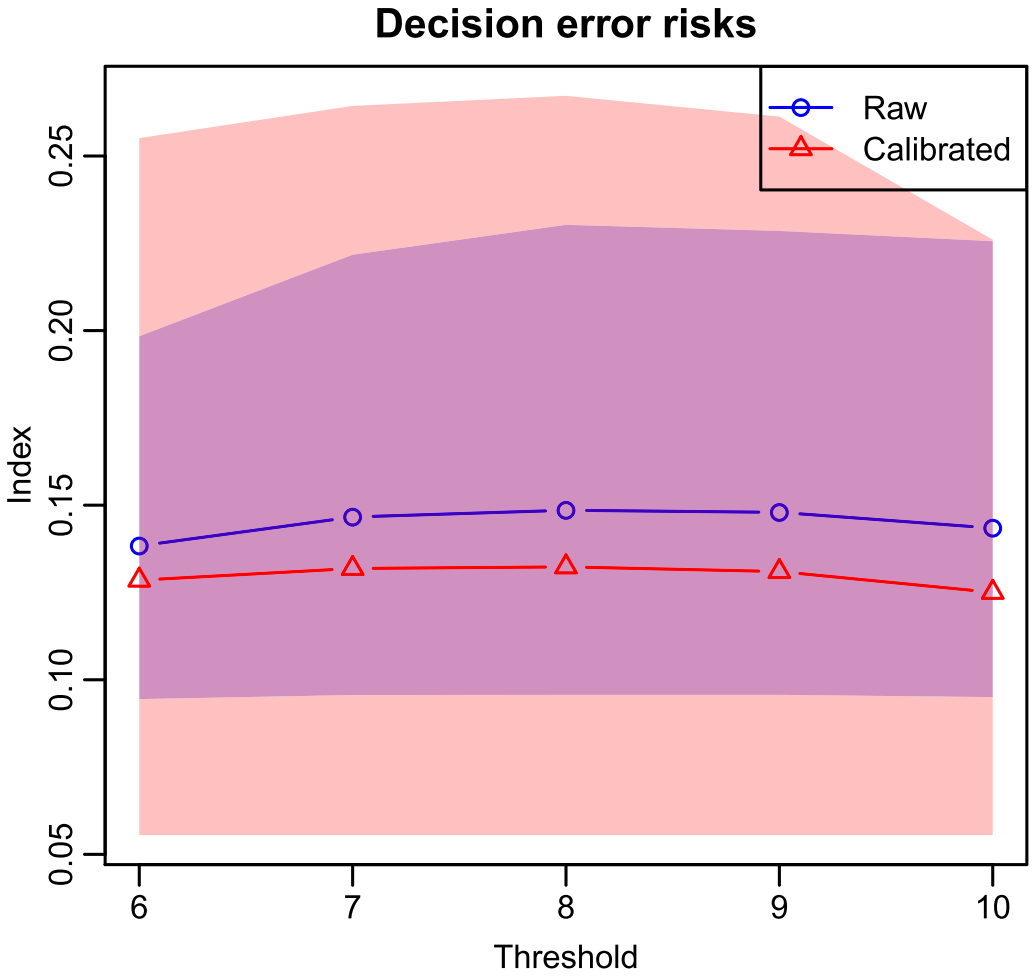

Fig. 5 Decision error risks. Mean values and 95 % credible intervals

Conclusions des auteurs

- A cause du bruit de la mesure de l'Hb (en situation stable) lorsque l'on prend des décisions de type dichotomique on se trompe une fois sur 7
  - Bruit de la mesure beaucoup plus grand en situation instable (bloc opératoire, saignement..)
- Le bruit de la mesure de l'Hb, quelle que soit la méthode, est d'au moins 1 g/dL

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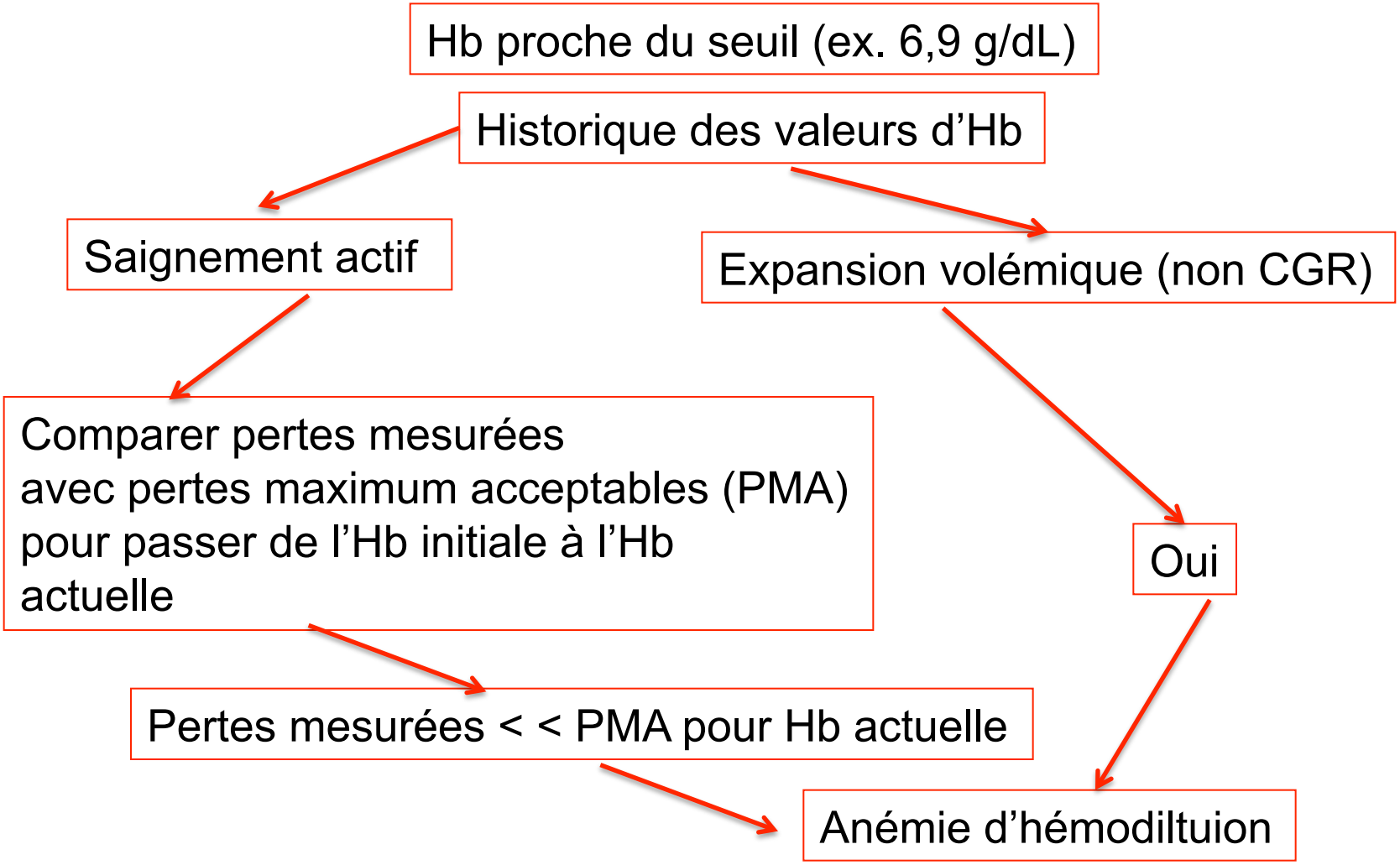
Messages

- Le bruit de la mesure de l'Hb est souvent > 1 g/dL
- Les conséquences de ce bruit de mesure (biologique, pré-analytique et analytique) sont:
  - Une valeur d'Hb autour du seuil est "incertaine" par définition
  - Il faut prendre en considération l'incertitude de la valeur dans la décision de transfuser
  - Evaleur la tolérance de l'anémie

Exemple d'algorithme décisionnel pour une Hb proche du seuil transfusionnel en normovolémie



Messages de fin (1)

- Dans beaucoup d'études observationnelles et dans les études prospectives, randomisées
  - La transfusion de CGR n'apporte pas de bénéfice en termes de survie/ diminution de la morbidité
- Dans quelques études observationnelles, la transfusion de CGR, même en faible quantité est associée à une augmentation du risque de mortalité
  - Hétérogénéité des pratiques transfusionnelles

Messages de fin (2)

- Pour relier ces données statistiques (slogans) à la prise de décision pour un patient donné (raisonnement clinique)
  - « Masse GR » n'est pas superposable à « concentration d'Hb »
    - Anémie d'hémodilution
    - Bruit de la mesure de l'Hb
  - En normovolémie et en situation hémodynamique « stable », une Hb entre 5-7 g/dL N'EST PAS une urgence transfusionnelle (on peut réfléchir à l'indication de la CGR)