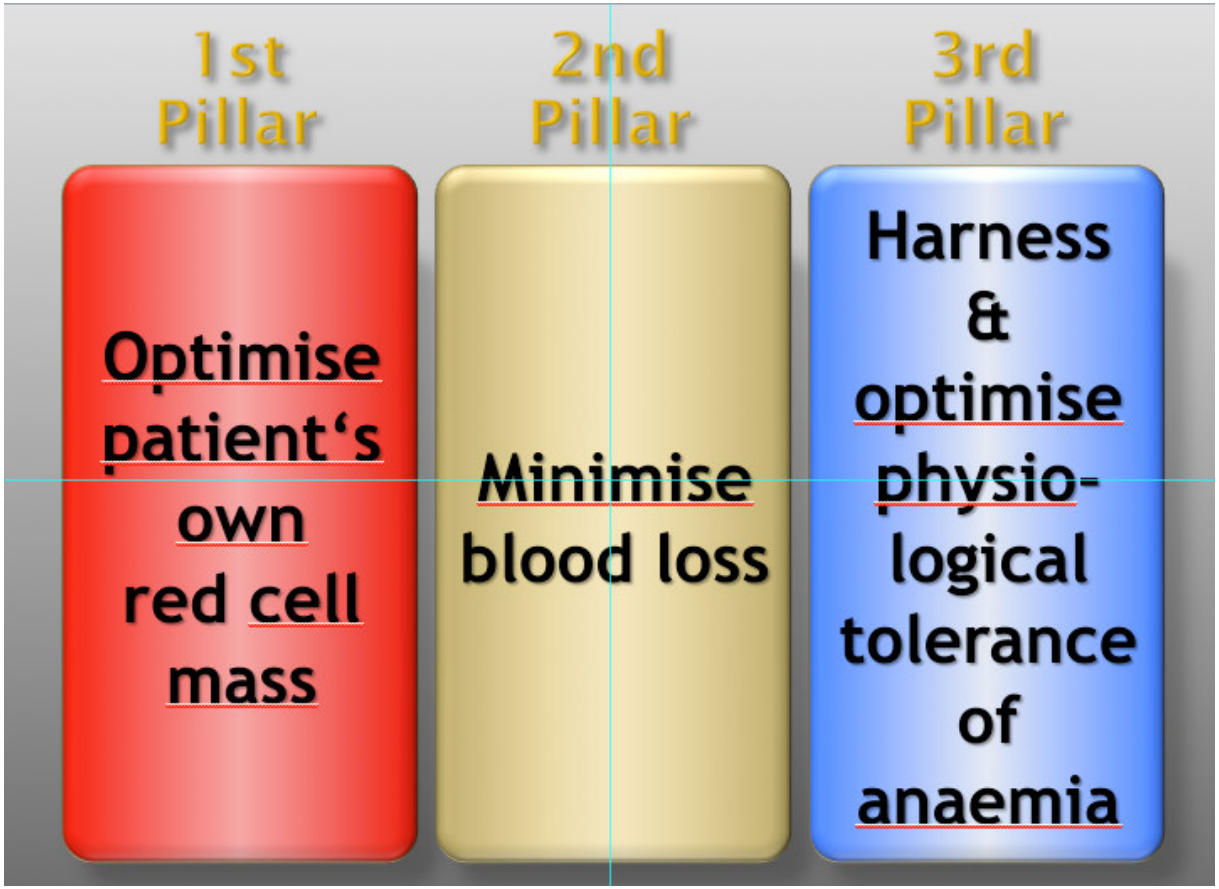
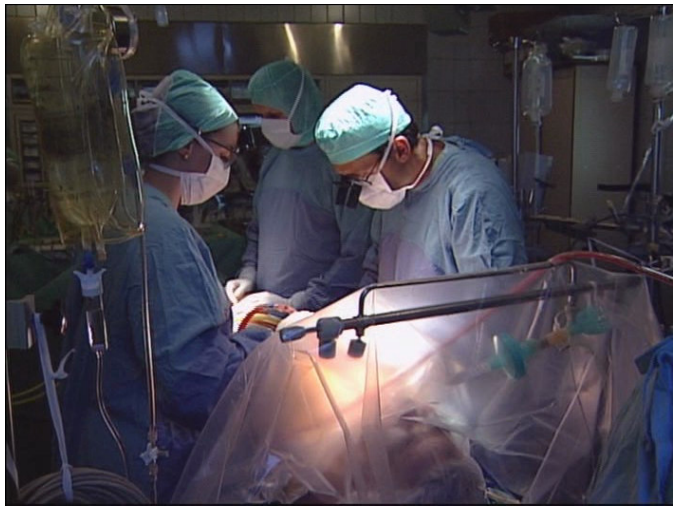




Performed by a multi-disciplinary clinical Team =

Patient Blood Management

Predictors of Transfusion

- Type of surgery/surgeon
- Baseline hemoglobin and RBC mass
- Actual blood loss
- Co-morbidities
- Tolerable blood loss ând transfusion trigger (individual)

Predictors of Transfusion

- Type of surgery/surgeon
- Baseline hemoglobin and RBC mass
- Actual blood loss
- Co-morbidities
- Tolerable blood loss ând transfusion trigger (individual)

"Yes - that's my surgeon - the one who cuts himself shaving ..."

Measures to optimize the use of blood components in selected surgical procedures in Austrian hospitals

Predictors of RBC transfusions

Procedure	THR	TKR	CABG
Independent Variable	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Hemoglobin preop.(%)*	0.65 (0.60;0.70)	0.68 (0.63;0.73)	0.69 (0.63;0.75)
Min. hemoglobin postop. (%)*	1.50 (1.38;1.64)	1.48 (1.35;1.63)	1.52 (1.36;1.70)
Lost RBC -volume (%) **	1.82 (1.64;2.01)	1.81 (1.62;2.02)	1.81 (1.58;2.07)
Center rank‡	**1.34 (1.24;1.46)**	**1.35 (1.25;1.46)**	-
Correctly classified (%)	97.4%	97.2%	97.0%

* Percentage of WHO cut-off values

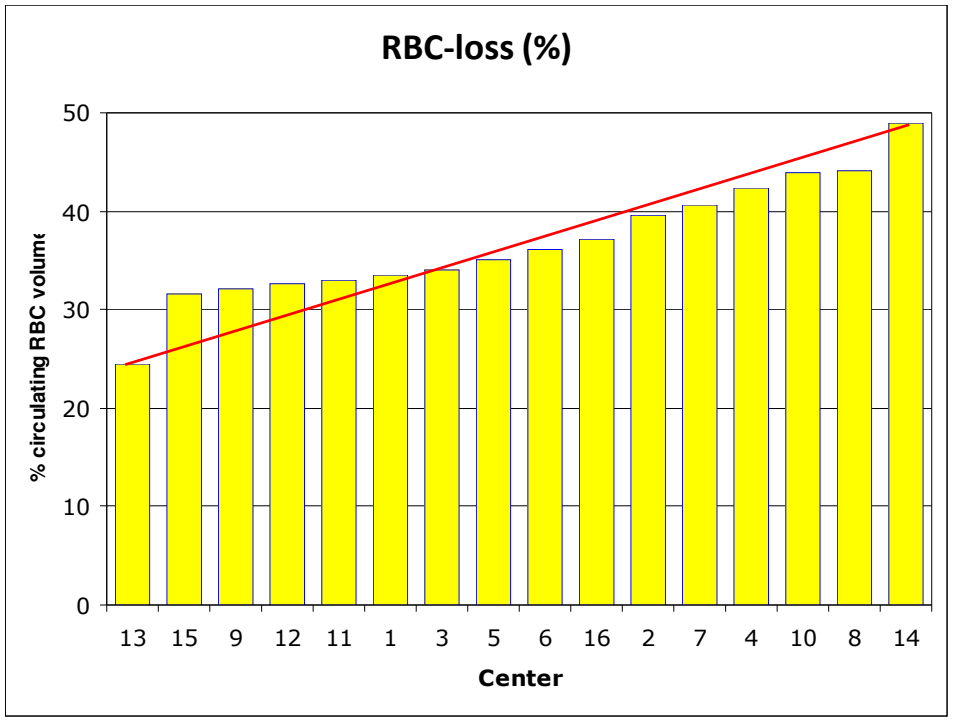
** Percentage of the preoperatively circulating RBC volume

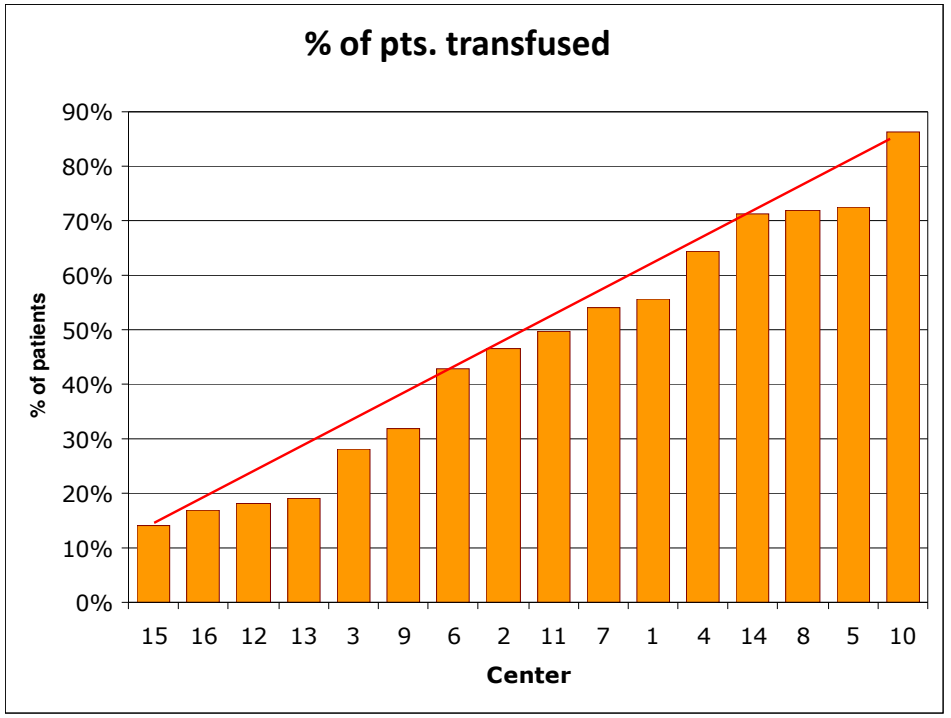
‡ Centers ranked according to the mean perioperative RBC loss

Gombotz et al: TRANSFUSION 2007;47:1468-1480.

Measures to optimize the use of blood components in selected surgical procedures in Austrian hospitals

RBC loss (%) and % patients transfused in THR and TKR





Gombotz et al: TRANSFUSION 2007;47:1468-1480.

Predictors of Transfusion

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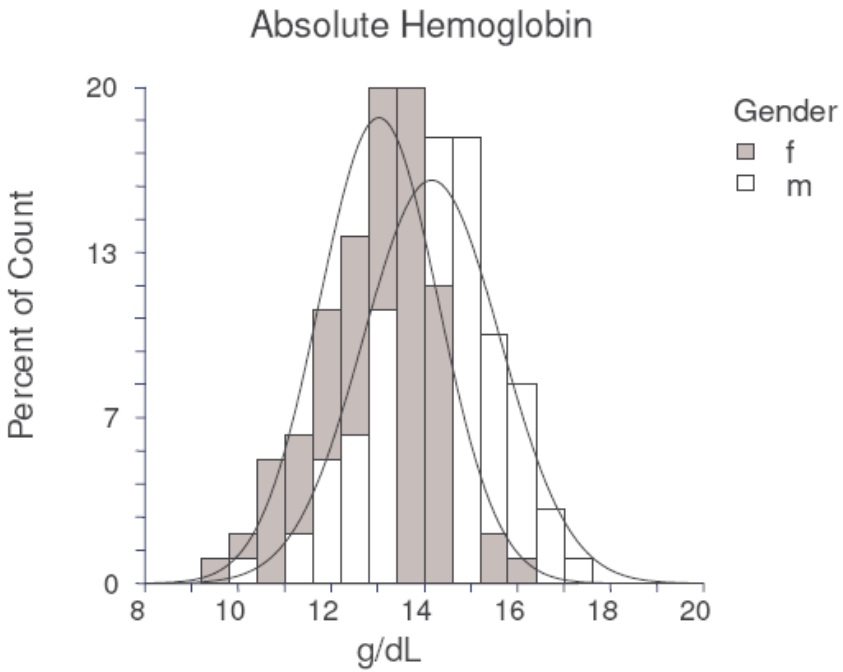
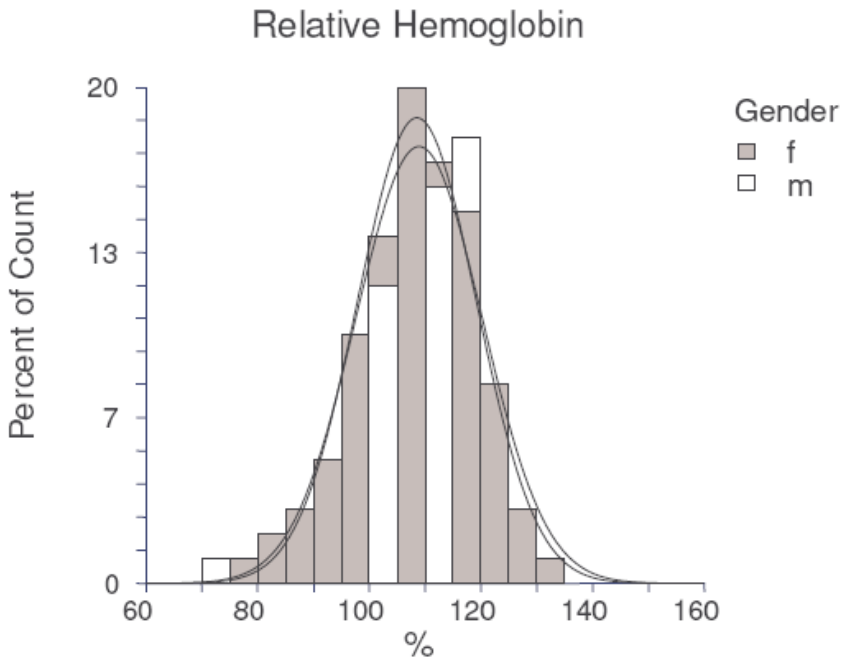
Statistical Analysis (II)





Distribution of hemoglobin by gender

Measures to optimize the use of blood components in selected surgical procedures in Austrian hospitals

Predictors of RBC transfusions

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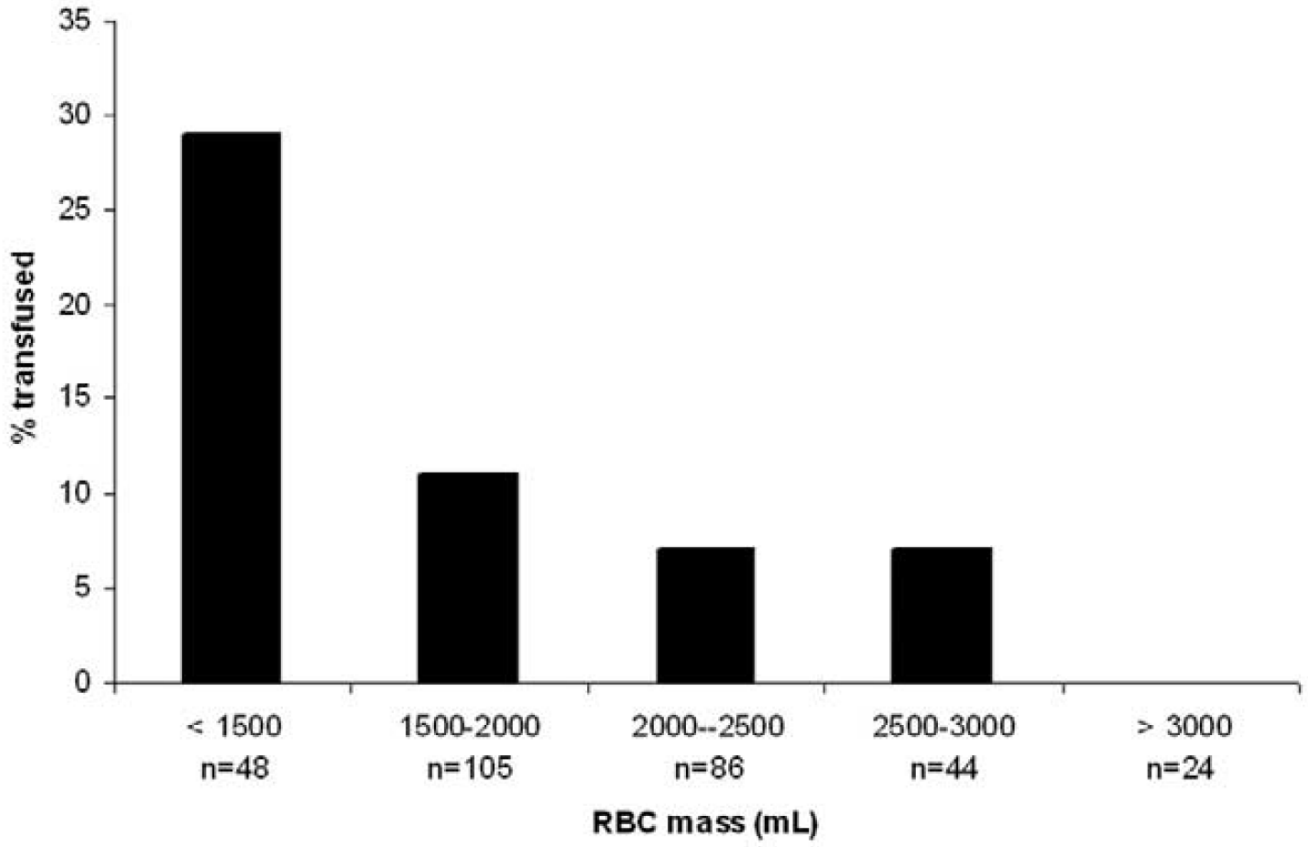
‡ Centers ranked according to the mean perioperative RBC loss

Gombotz et al: TRANSFUSION 2007;47:1468-1480.

Red blood cell (RBC) mass versus transfusion rate



Moskowitz et al: Ann Thorac Surg 2004;77:626 –34

Measures to optimize the use of blood components in selected surgical procedures in Austrian hospitals

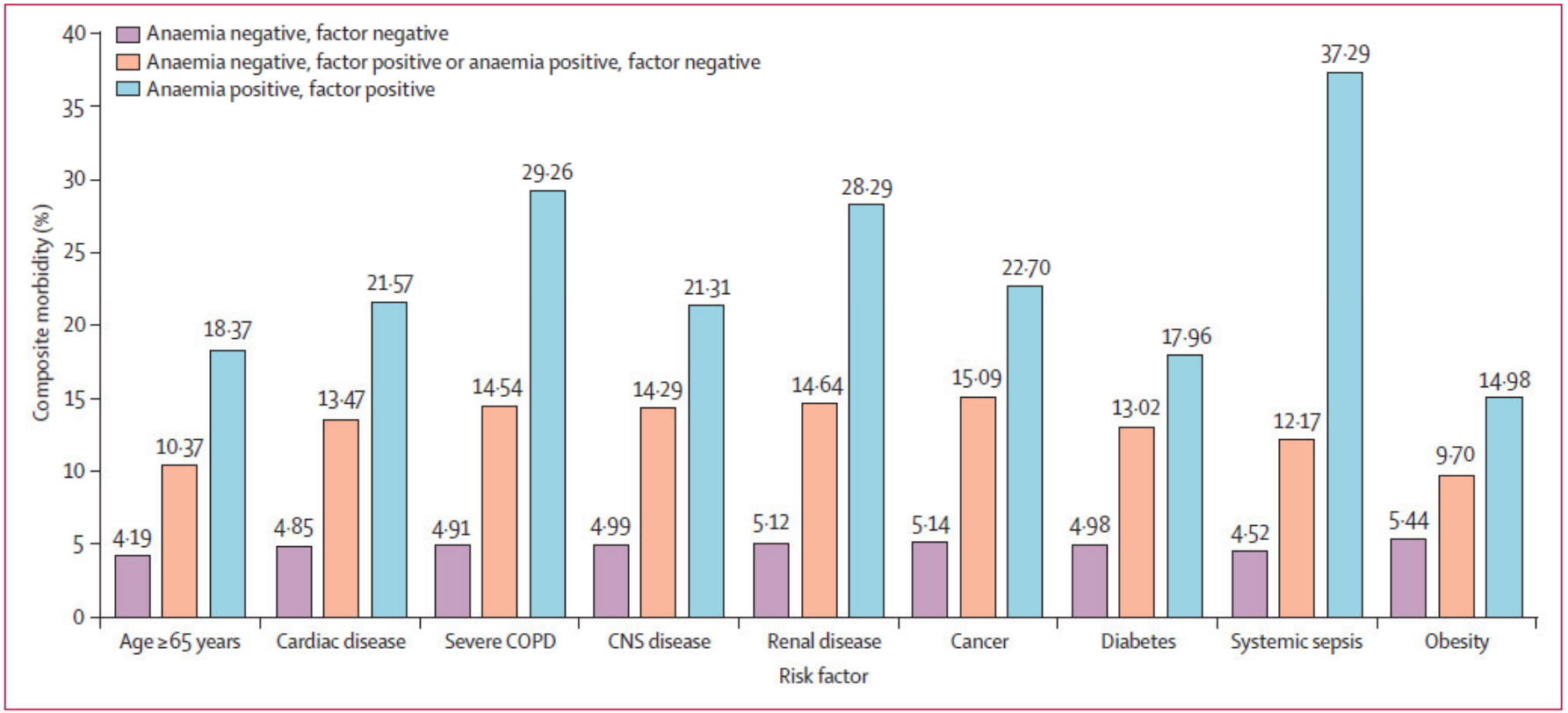
Consequences of Preoperative Anemia

	N pts.	Anemic pts.	I	II	p-value
CABG	777	24%	48%	76%	<0.001
HECO	148	30%	11%	58%	<0.001
THR	1401	16%	28%	54%	<0.001
TKR	1296	18%	28%	60%	<0.001
total	**3622**	**19%**	**32%**	**62%**	**<0.001**

I = % non-anemic pts. transfused with allogeneic RBCs,
II = % of anemic pts. transfused with allogeneic RBCs
Fisher's exact test

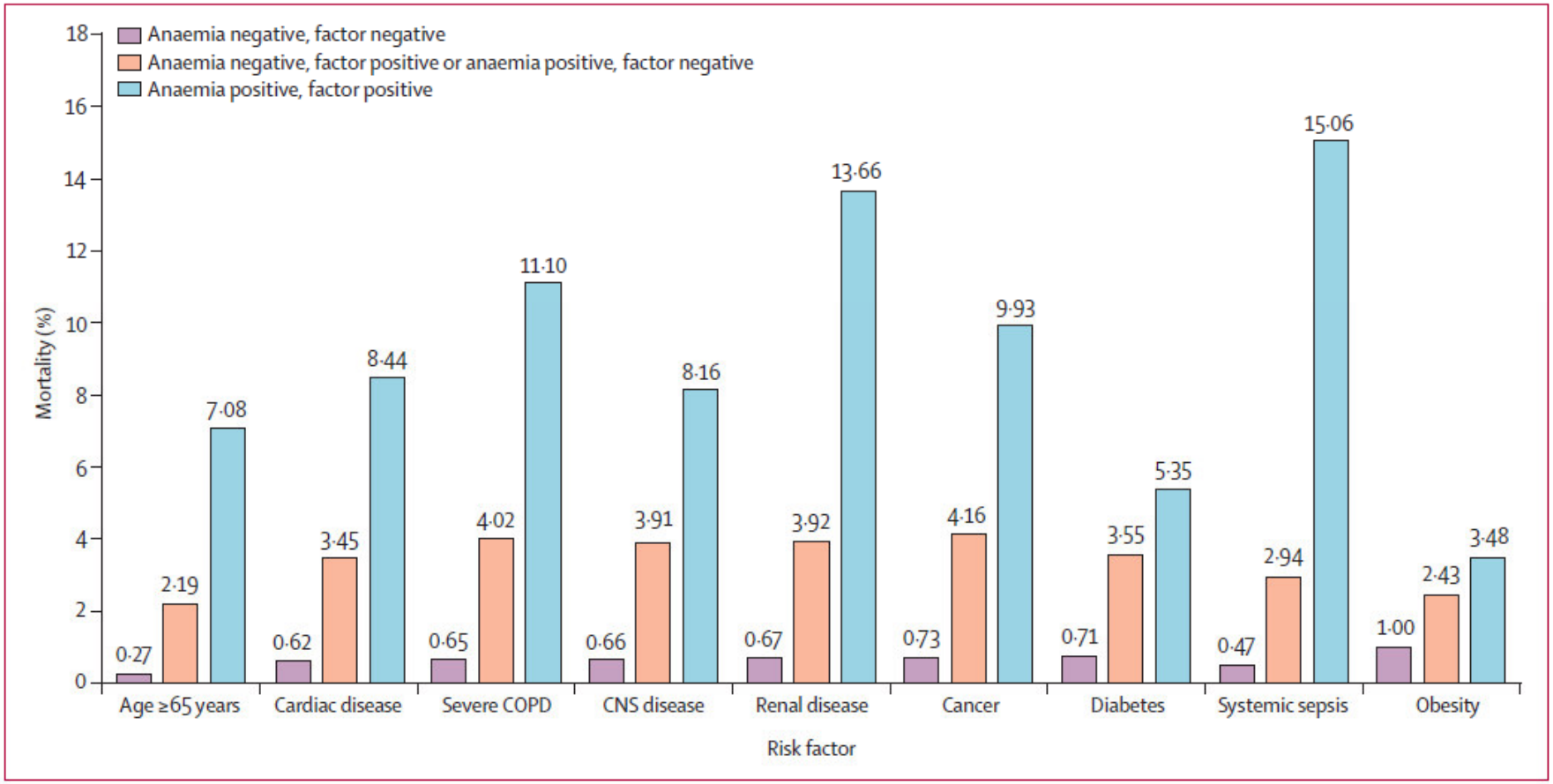
Gombotz et al: TRANSFUSION 2007;47:1468-1480.

30-day composite morbidity, by anaemia and risk factor status



Mussallam et al: www.thelancet.com Published online October 6, 2011 DOI:10.1016/S0140-6736(11)6138

30-day mortality, by anaemia and risk factor status



Mussallam et al: www.thelancet.com Published online October 6, 2011 DOI:10.1016/S0140-6736(11)6138

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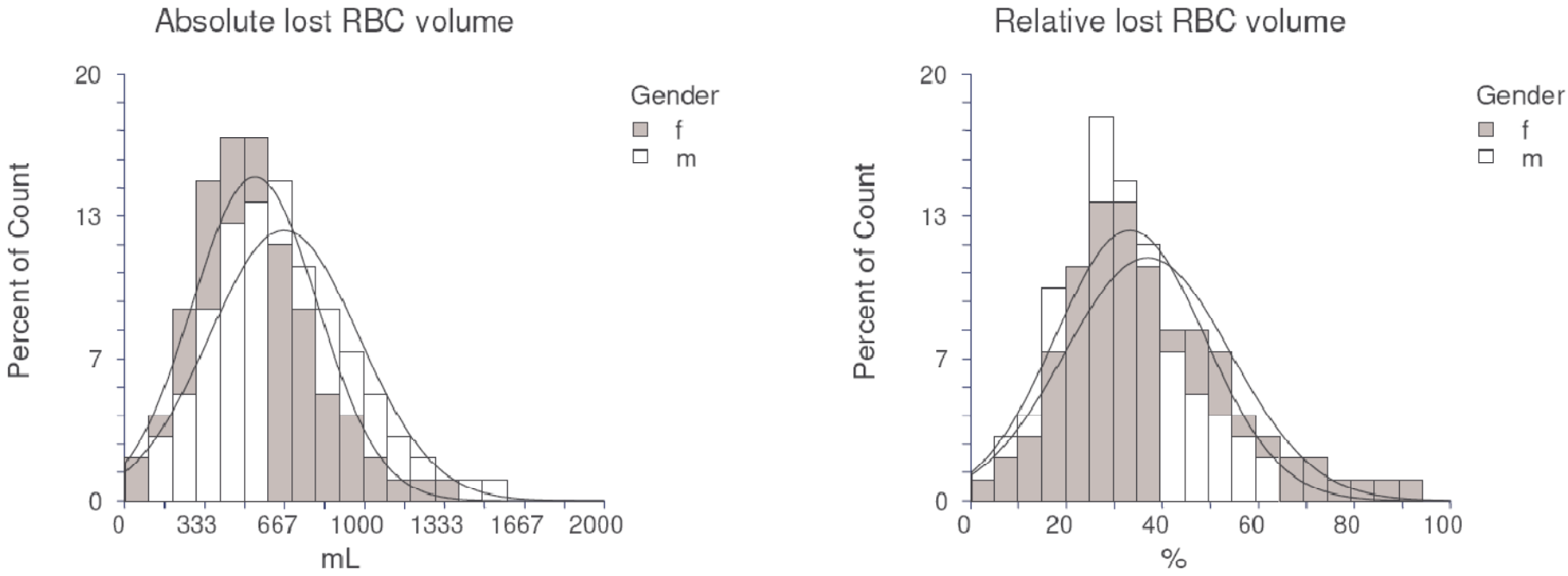
Gombotz et al: TRANSFUSION 2007;47:1468-1480.

Statistical Analysis (III)



Distribution of lost red cell volume by gender

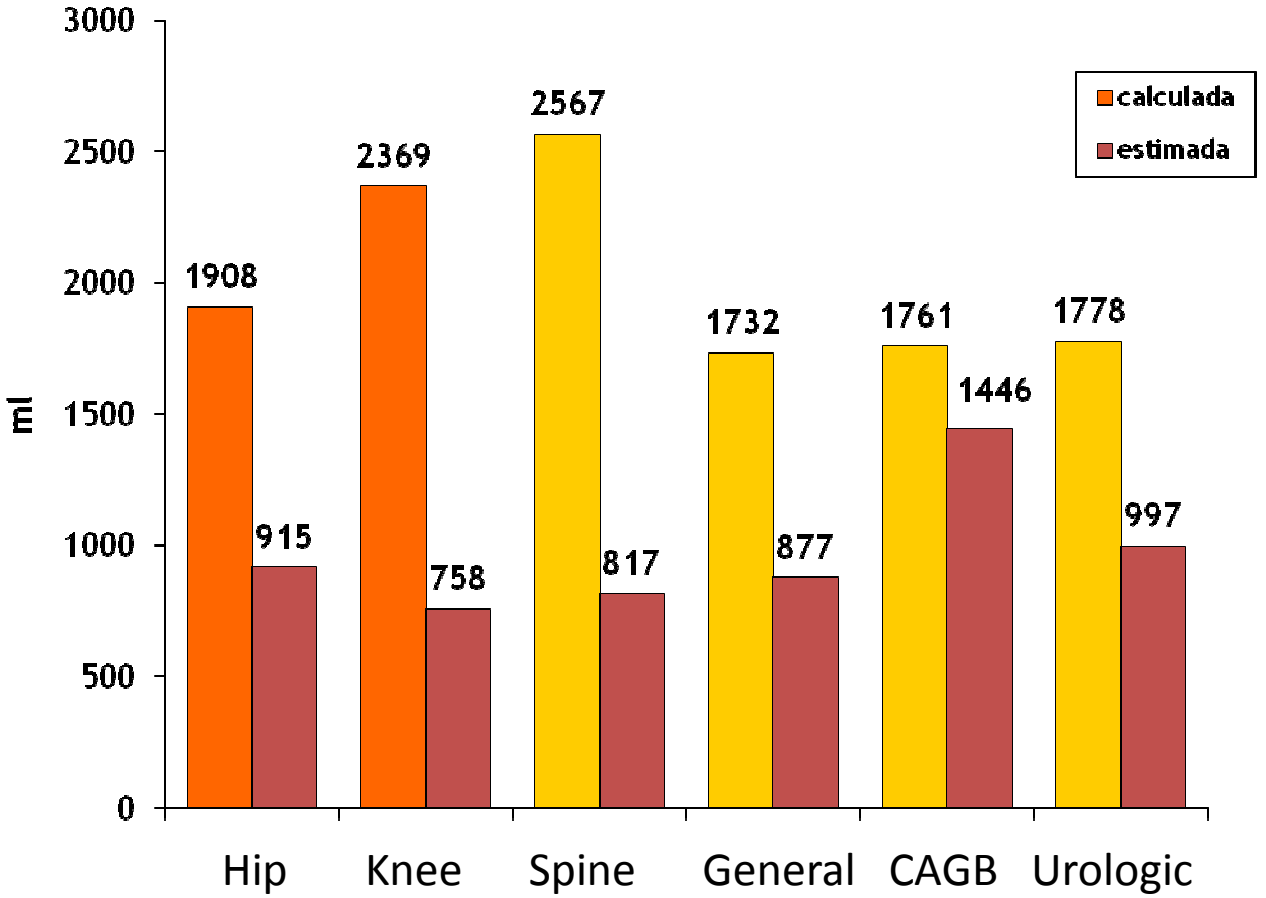
AKH LINZ

BUNDESMINISTERIUM FÜR GESUNDHEIT UND FRAUEN

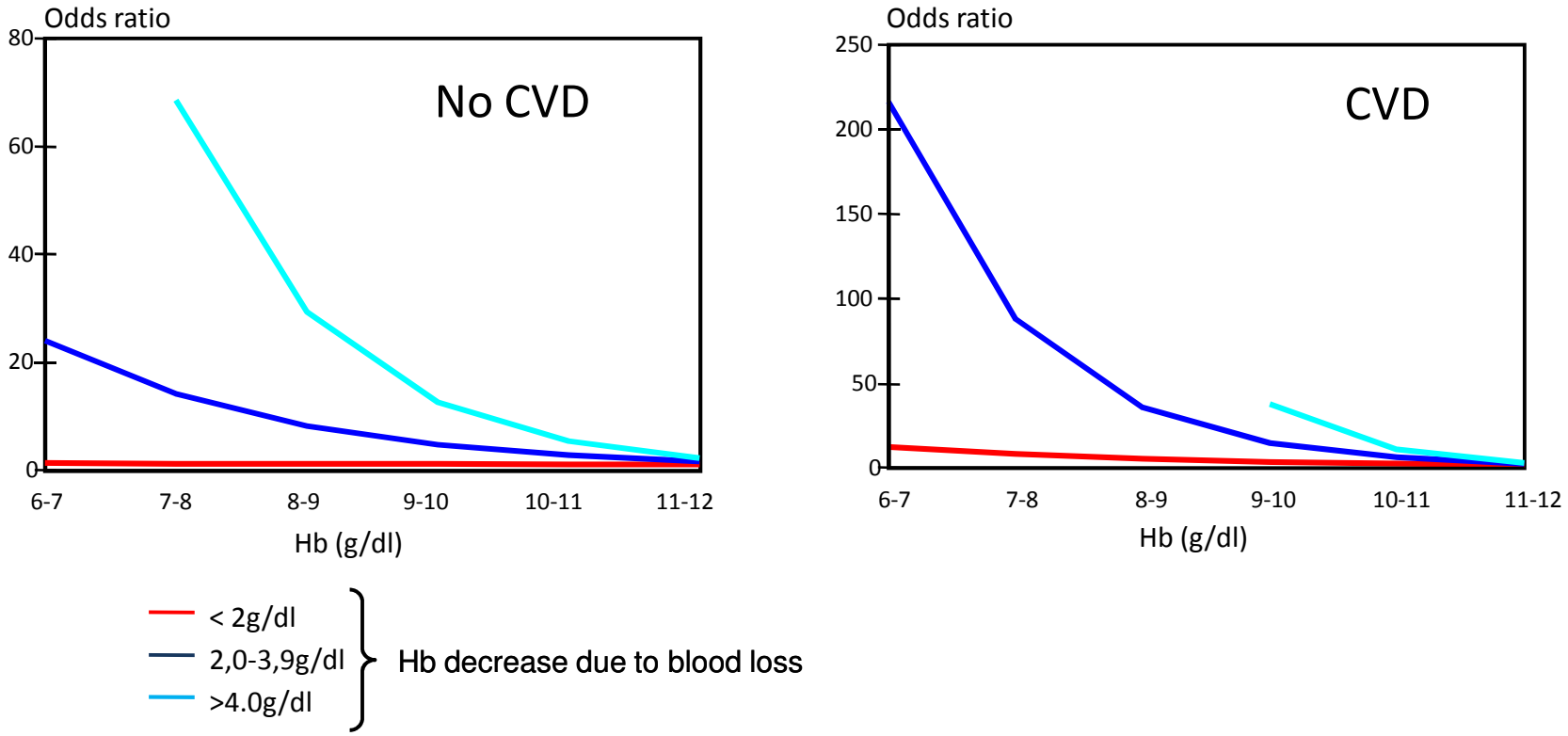
bmgf

ÖGARI

ESTIMATED AND CALCULATED BLOOD LOSS IN DIFFERENT TYPES OF SURGERY

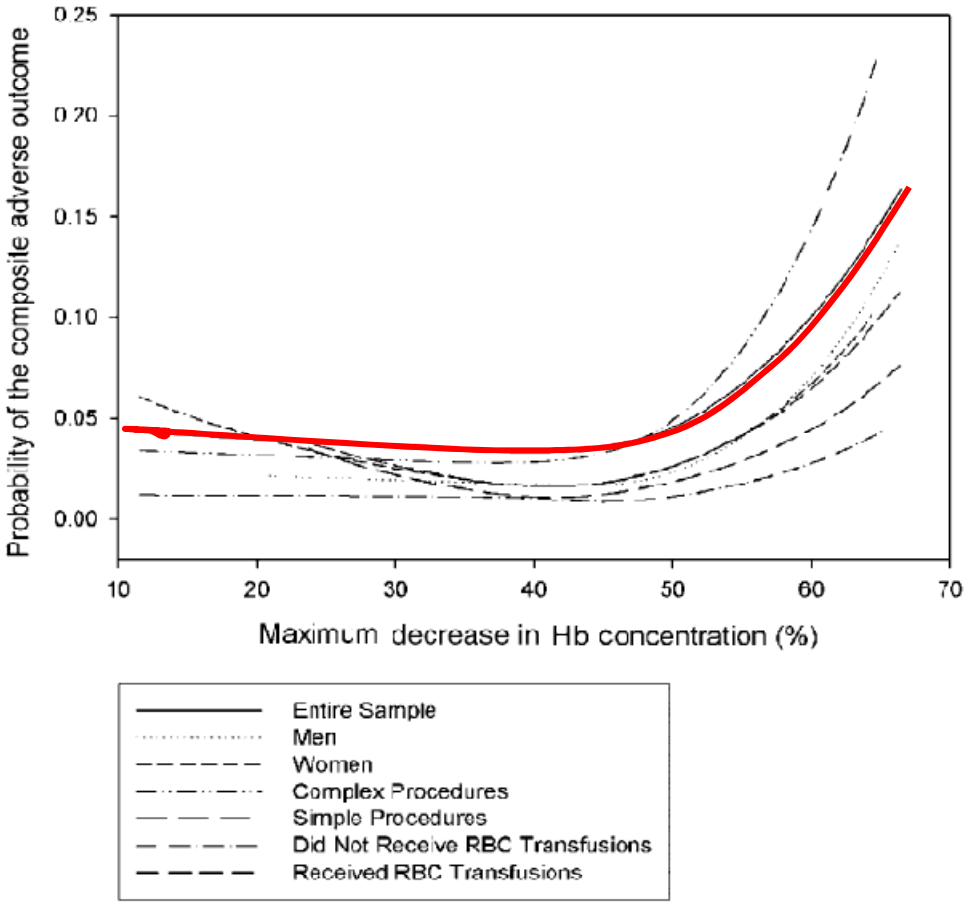


Adjusted Odds Ratio for Mortality and Preop. Hb. and Decline in Hb. Stratified by Cardiovascular Disease (n=1080)



Carson J. et al.: Lancet 348:1055-60, 1996

The influence of baseline hb concentration on tolerance of anemia in cardiac surgery



The relationship between maximum decrease in Hb concentration and adverse outcomes was independently associated with increased risk!!

Karkouti et al: TRANSFUSION 2008;48:666-672.

Predictors of Transfusion

- Type of surgery/surgeon
- Baseline hemoglobin and RBC mass
- Actual blood loss
- Co-morbidities
- Tolerable blood loss and transfusion trigger (individual)

Anesthesiology 2009; 110:574–81

Risk Associated with Preoperative Anemia in Noncardiac Surgery

A Single-center Cohort Study

W. Scott Beattie, M.D., Ph.D., F.R.C.P.C., Keyvan Karkouti, M.D., M.Sc., F.R.C.P.C.,† Duminda N. Wijeysundera, M.D., F.R.C.P.C.,‡ Gordon Tait, Ph.D.§*

Table 2. Regression Analysis of Anemia Model Predicting Mortality

Parameter	OR (95% CI)	*P* Value
Anemia (WHO gender defined)	2.43 (1.65–3.60)	< 0.0001
Comorbidities		
Age > 70 yr	2.31 (1.64–3.26)	< 0.0001
In-hospital status*	3.51 (2.26–5.44)	< 0.0001
History of CHF	7.99 (4.73–13.5)	< 0.0001
Preoperative renal dysfunction†	2.08 (1.22–3.53)	0.0067
Perioperative medications		
β-Blockers		
No β-blockers	Reference	
Metoprolol	1.67 (1.05–2.68)	0.020
Atenolol or bisoprolol	0.97 (0.63–1.52)	0.198
ACE inhibitors	0.56 (0.33–0.95)	0.033
CCBs	0.57 (0.34–0.96)	0.036
Any postoperative NSAID‡	0.58 (0.38–0.88)	0.011
Transfusion		
No blood products	Reference	
1–2 units	1.83 (1.20–2.80)	0.032
3–4 units	2.99 (1.77–5.07)	0.013
5–10 units	3.19 (1.62–6.32)	0.021
More than 10 units	3.43 (1.12–10.5)	0.040

Retrospective study 7759

Prevalence of anemia 39%

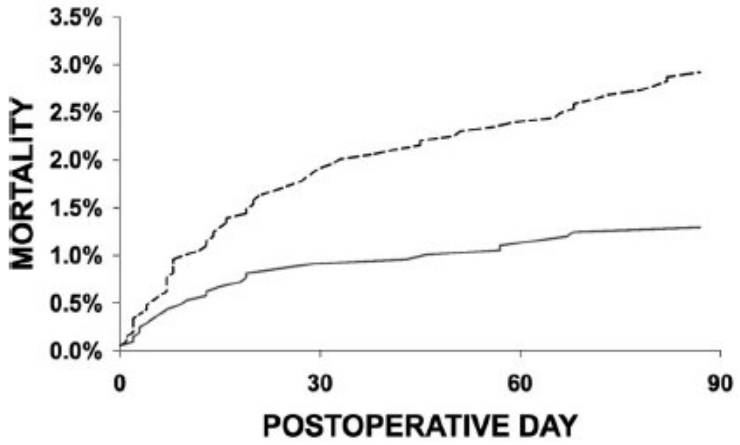


Fig. 2. The risk adjusted effect of anemia on postoperative mortality. This figure represents the time to event comparing anemic to nonanemic patients in the propensity-matched cohorts. *x axis* = postoperative day; *y axis* = percent mortality; *broken line* = patients with preoperative anemia; *solid line* = nonanemic patients.

TABLE 1. FACTORS THAT INCREASE THE RISK OF PERIOPERATIVE CARDIAC COMPLICATIONS IN PATIENTS UNDERGOING NONCARDIAC SURGERY AND INDICATIONS FOR THE USE OF PERIOPERATIVE BETA-BLOCKER THERAPY.

RISK FACTOR	ODDS RATIO (95% CI)*	PERIOPERATIVE BETA-BLOCKER INDICATED
Ischemic heart disease†	2.4 (1.3–4.2)	Yes
Congestive heart failure	1.9 (1.1–3.5)	Yes
High-risk surgery‡	2.8 (1.6–4.9)	Uncertain, but probably
Diabetes mellitus (especially insulin-requiring)	3.0 (1.3–7.1)	Yes
Renal insufficiency	3.0 (1.4–6.8)	Uncertain, but probably if renal insufficiency is due to diabetes or vascular disease
Poor functional status§	1.8 (0.9–3.5)	Yes, if poor status is thought to be due to coronary artery disease or heart failure

*Data are from Lee et al.[2] and Reilly et al.[3] CI denotes confidence interval.

†Ischemic heart disease includes angina and prior myocardial infarction.

‡High-risk surgery includes intraperitoneal, intrathoracic, and suprainguinal vascular procedures.

§Poor functional status is defined as the inability to walk four blocks or climb two flights of stairs.

Fleisher, L. A. et. al. N Engl J Med 2001;345:1677-1682

Major Cardiac Event Rates by the Revised Cardiac Risk Index

Class	Events/Patients, *n/n*	Event Rate (95% CI), %
I (0 risk factors)	2/488	0.4 (0.05–1.5)
II (1 risk factor)	5/567	0.9 (0.3–2.1)
III (2 risk factors)	17/258	6.6 (3.9–10.3)
IV (≥3 risk factors)	12/109	11.0 (5.8–18.4)
ROC curve area	0.806†	

* Adapted from Lee et al. (21). ROC = receiver-operating characteristic.
† $P = 0.034$ versus original cardiac risk index (ROC curve area, 0.701), modified cardiac risk index (ROC curve area, 0.582), and American Society of Anesthesia Classification (ROC curve area, 0.697). Major cardiac events include myocardial infarction, cardiac arrest, pulmonary edema, and complete heart block. Risk factors are high-risk surgical procedure (intraperitoneal, intrathoracic, or suprainguinal vascular reconstruction), history of ischemic heart disease (excluding previous revascularization), history of congestive heart failure, history of stroke or transient ischemic attack, preoperative insulin therapy, and preoperative serum creatinine levels > 152.5 μmol/L (> 2.0 mg/dL).

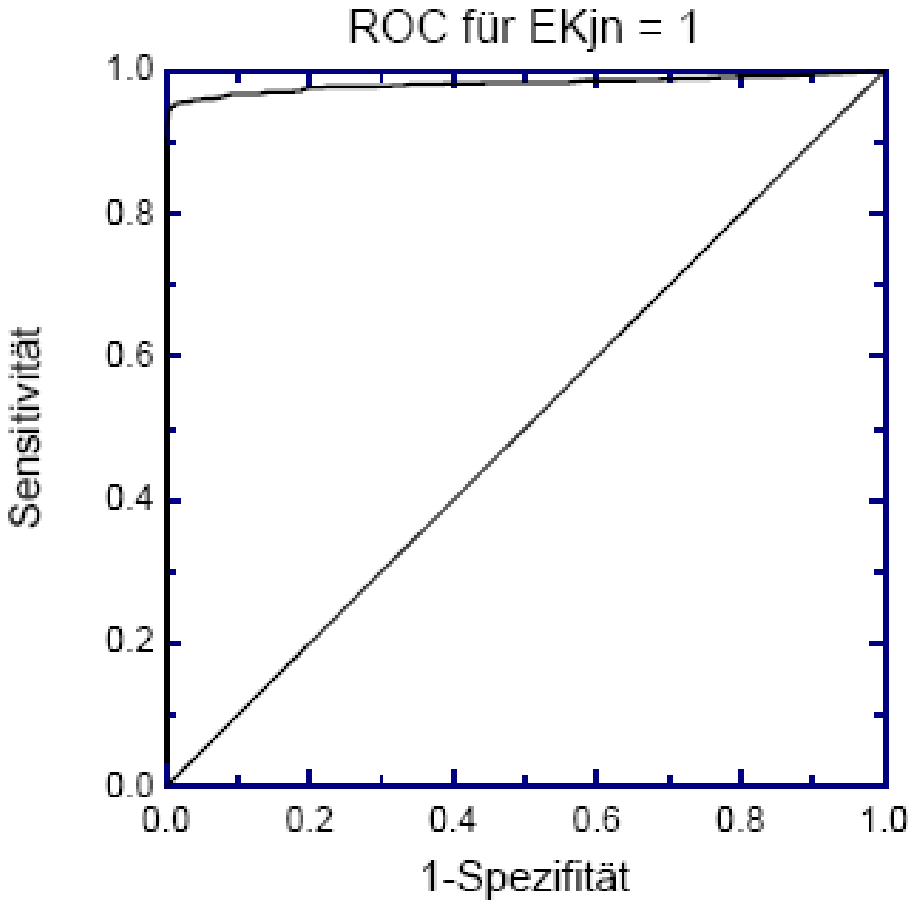
P. A. Grayburn, and L. D. Hillis, Ann Intern Med. 2003;138:506-511

BLOODless Surgery FREMDBLUTFREIE OPERATIONEN

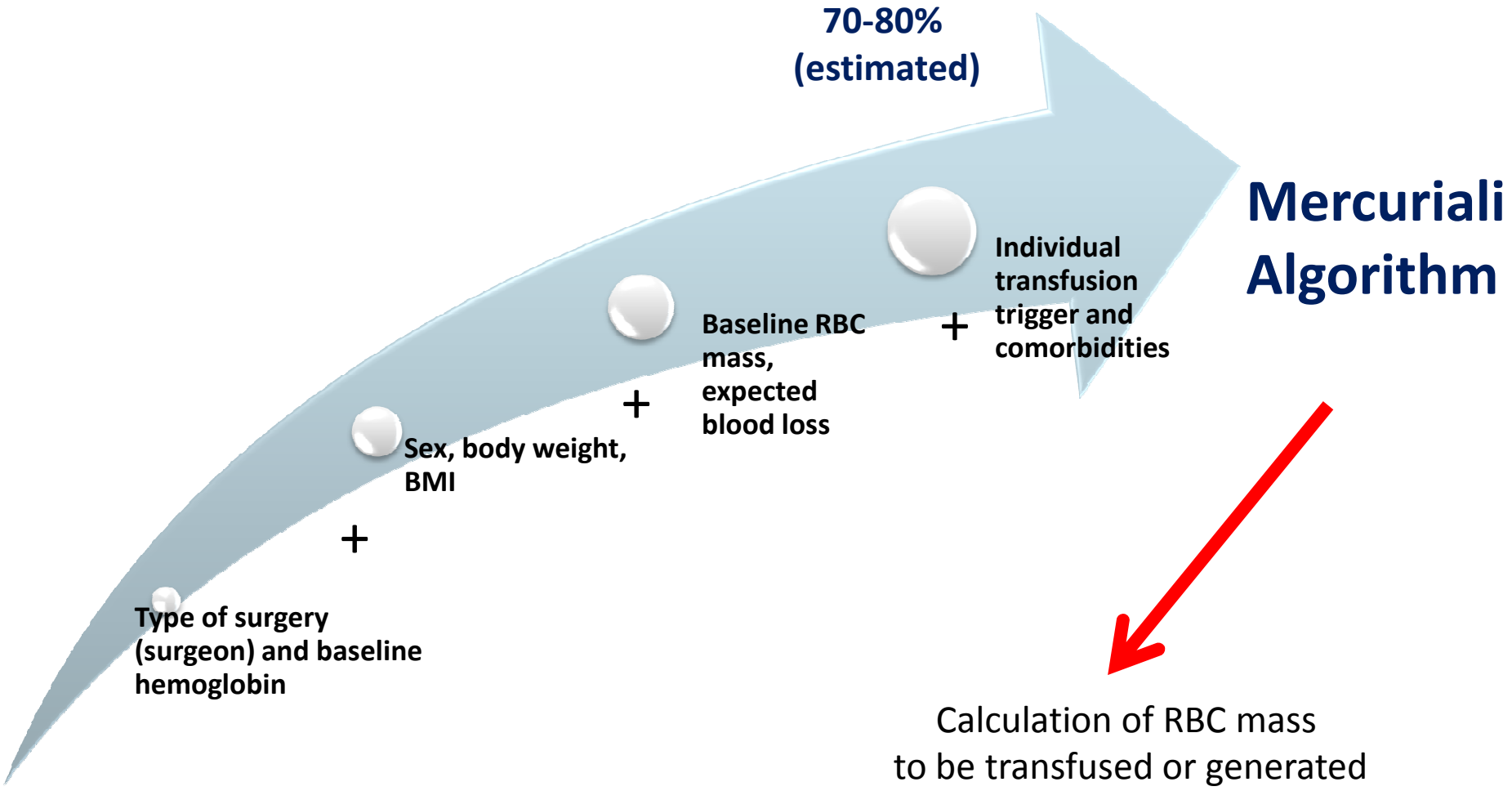
Predictors of Transfusion

- Type of surgery/surgeon
- Baseline hemoglobin and RBC mass
- Actual blood loss
- Co-morbidities
- Tolerable blood loss and transfusion trigger (individual)

ROC for Hb_{min}, Hb_{preop} and $blood\ loss_{rel}$



Probability of Transfusion



Transfusion Algorithm

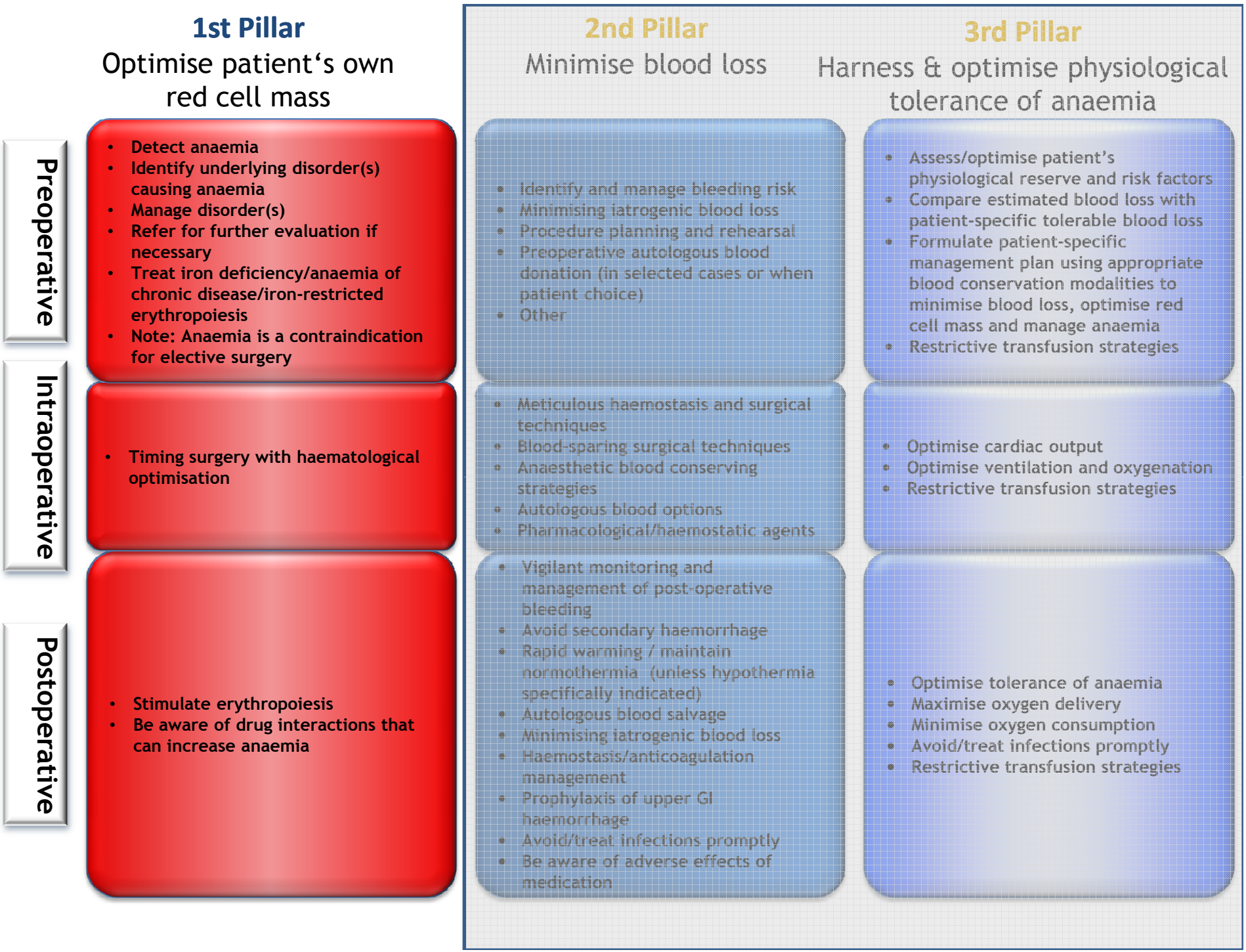
(Mercuriali F., Inghilleri G.: Curr. Med. Res. Opin. 13, 465-478, 1996)

Transfusion needs =

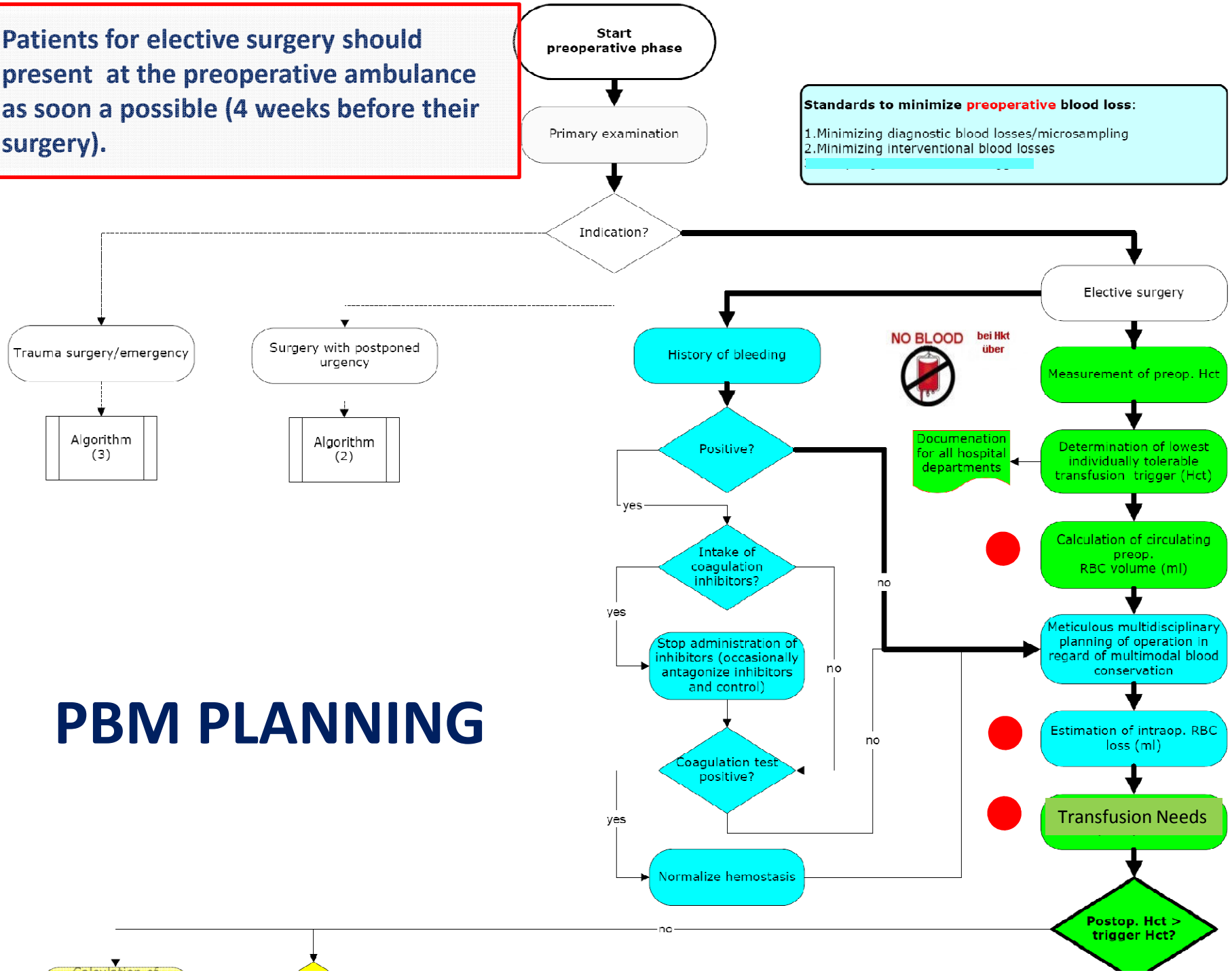
Predicted RBC loss - tolerable RBC loss

Predicted RBC loss = C-RBC-V_{preop} - C-RBC-V_{POD5} + RBC transfused

Tolerableblood loss = (PBVx $hct_{baseline}$) - (PBV x $hct_{min.\ acc}$)


1st Pillar
Optimise patient's own red cell mass
2nd Pillar
Minimise blood loss
3rd Pillar
Harness & optimise physiological tolerance of anaemia
Preoperative
Detect anaemia
Identify underlying disorder(s) causing anaemia
Manage disorder(s)
Refer for further evaluation if necessary
Treat iron deficiency/anaemia of chronic disease/iron-restricted erythropoiesis
Note: Anaemia is a contraindication for elective surgery
Identify and manage bleeding risk
Minimising iatrogenic blood loss
Procedure planning and rehearsal
Preoperative autologous blood donation (in selected cases or when patient choice)
Other
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
Restrictive transfusion strategies
Intraoperative
Timing surgery with haematological optimisation
Meticulous haemostasis and surgical techniques
Blood-sparing surgical techniques
Anaesthetic blood conserving strategies
Autologous blood options
Pharmacological/haemostatic agents
Optimise cardiac output
Optimise ventilation and oxygenation
Restrictive transfusion strategies
Postoperative
Stimulate 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
Minimising iatrogenic blood loss
Haemostasis/anticoagulation management
Prophylaxis of upper GI haemorrhage
Avoid/treat infections promptly
Be aware of adverse effects of medication
Optimise tolerance of anaemia
Maximise oxygen delivery
Minimise oxygen consumption
Avoid/treat infections promptly
Restrictive transfusion strategies

Patients for elective surgery should present at the preoperative ambulance as soon a possible (4 weeks before their surgery).



PBM PLANNING

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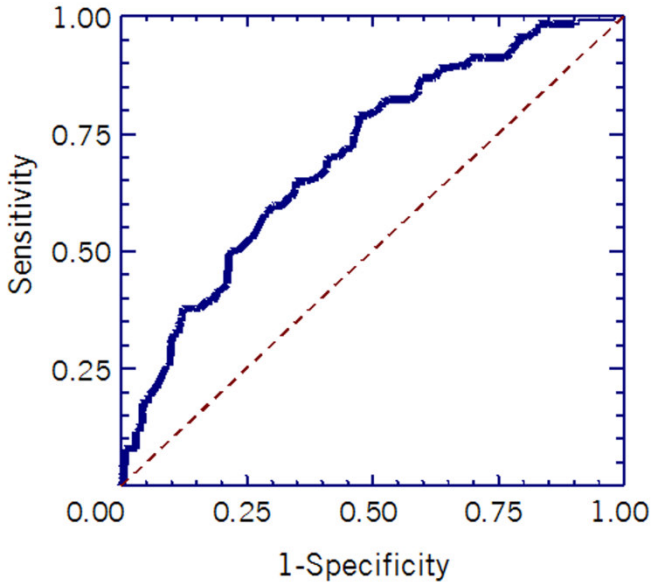
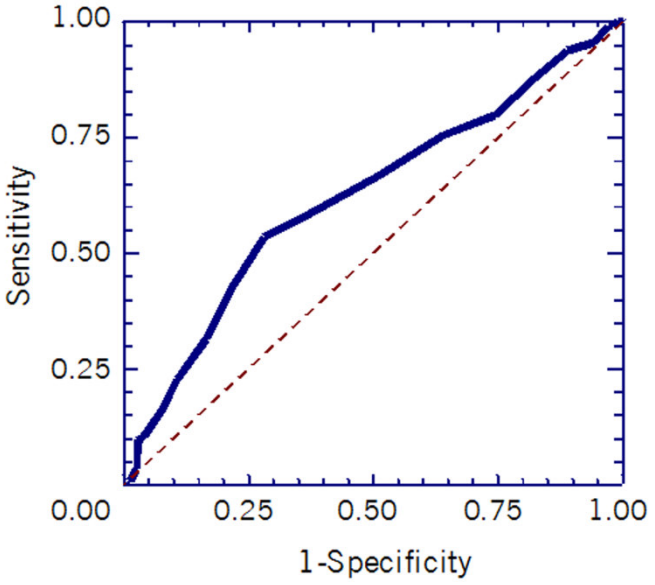
Predictability of Patient Specific Transfusion Requirements

ROC Curve of ATR



ROC Curve of baseline hct



ROC = Receiver Operating Characteristics

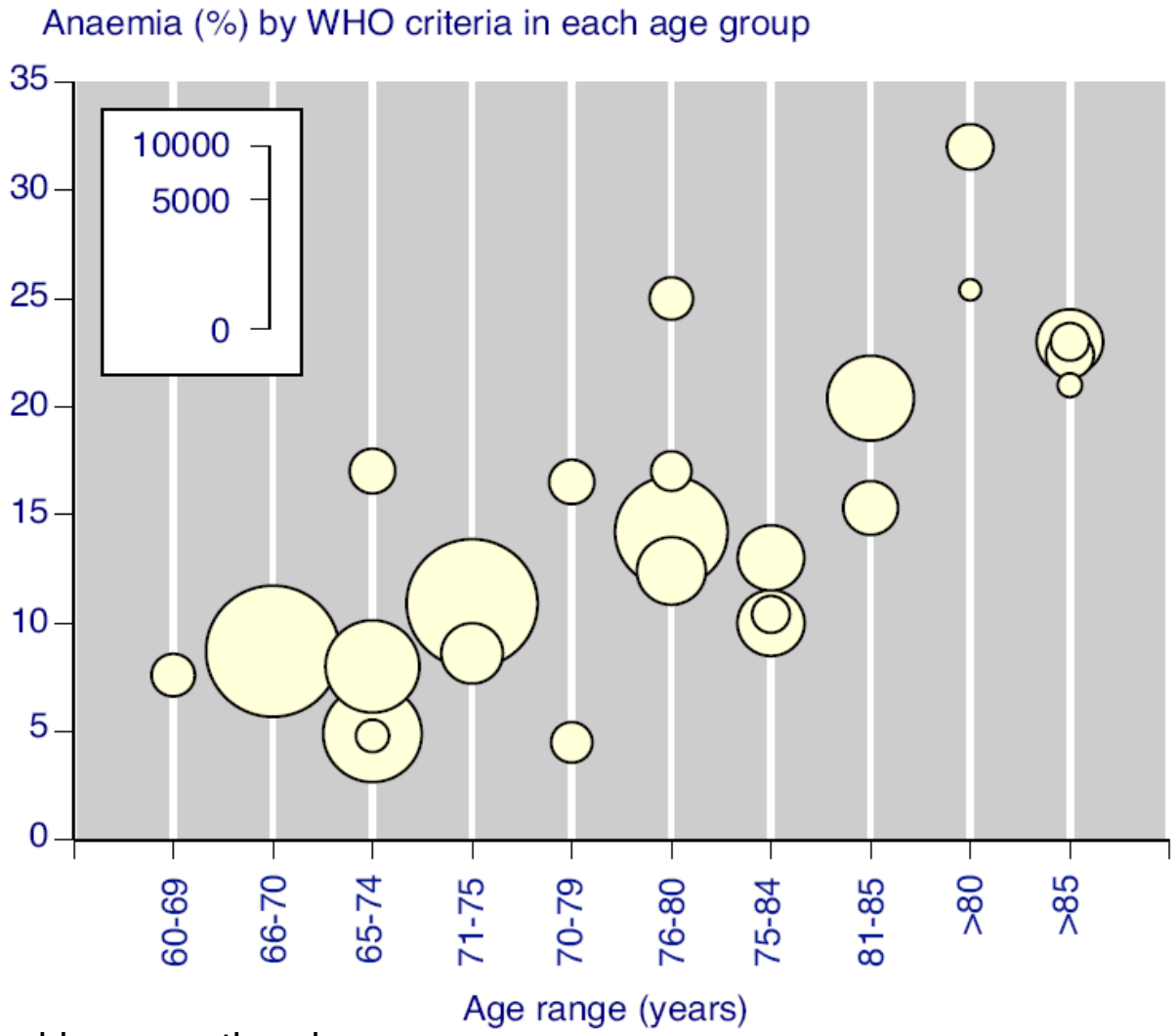
Hackl et al: EJA , 20, Suppl 30, A-303, 2003

Prävalenz der (präoperativen) Anämie

Nach Grunderkrankung	
Diabetes	14 - 15 %
Herzinsuffizienz	10 - 80 %
Akuter Myokardinfarkt	6 - 18 %
Infektionen	bis zu 95%
Tumorerkrankungen	bis zu 77%
Autoimmunerkrankung	bis zu 71%
Nierenerkrankungen	bis zu 50%
COPD	23%
Präoperativ	
ASA I und ASA II	1 %
Knie- und Hüftoperation	20 - 35 %
Allgemeinchirurgische Eingriffe	bis zu 40 %
Colonchirurgie	25 - 70 %
Herz- und Gefäßoperationen	16 - 40 %

Gombotz et al: AINS 2011 Jul;46(7-8):466-74

Anaemia prevalence by age range



Size of the symbol is proportional
to the size of the cohort (inset scale)

Gaskell et al. BMC Geriatrics 2008, 8:1

Distribution of types of anemia in persons 65 years and older

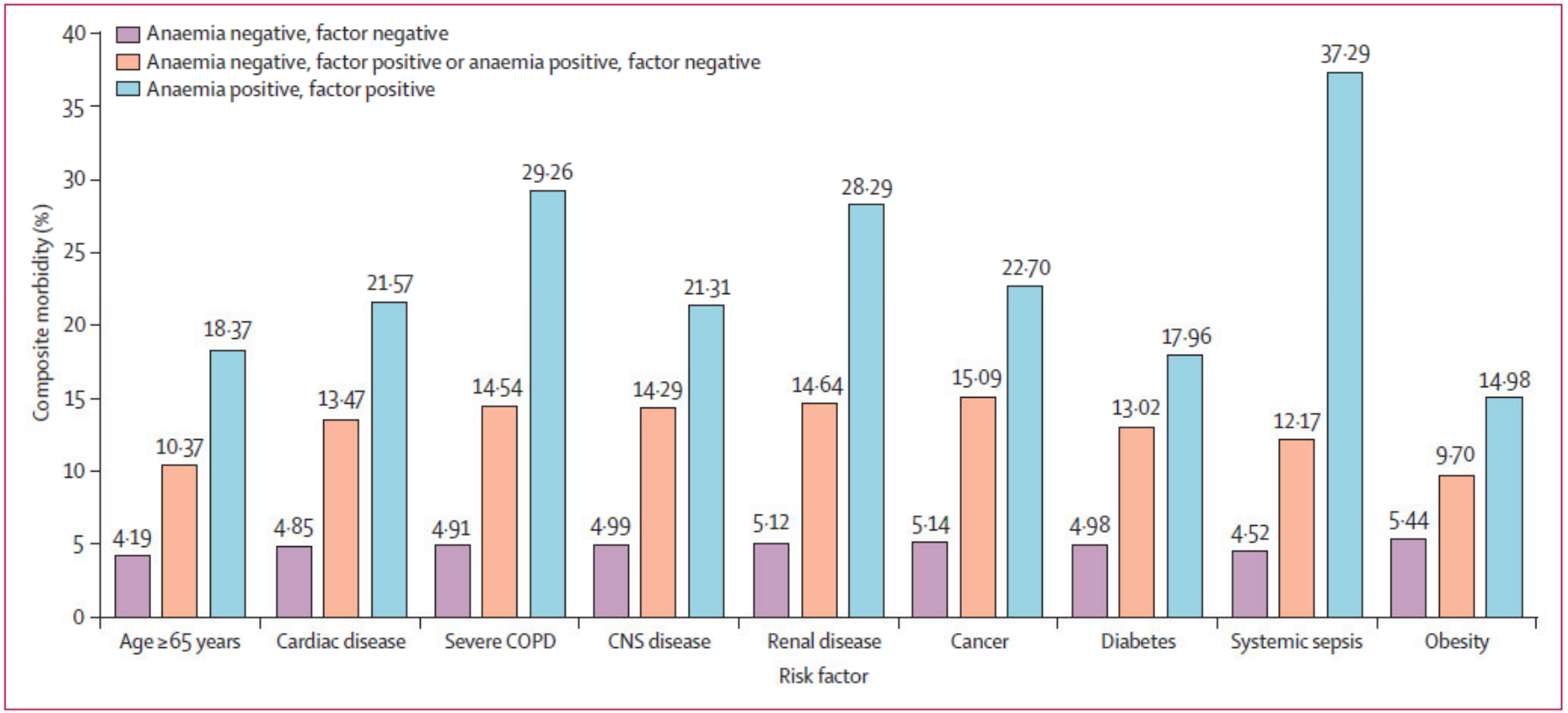
Anemia	No. in the United States	Type, %	All anemia, %
With nutrient deficiency			
Iron only	467 000	48.3	16.6
Folate only	181 000	18.8	6.4
B_{12} only	166 000	17.2	5.9
Folate and B_{12}	56 000	5.8	2.0
Iron with folate or B_{12} or both	95 000	9.9	3.4
Total	965 000	100.0	34.3
Without nutrient deficiencies			
Renal insufficiency only	230 000	12.4	8.2
ACI, no renal insufficiency	554 000	30.0	19.7
Renal insufficiency and ACI	120 000	6.5	4.3
UA	945 000	51.1	33.6
Total	1 849 000	100.0	65.7
Total, all anemia	2 814 000	NA	100.0

NA indicates not applicable.

30%

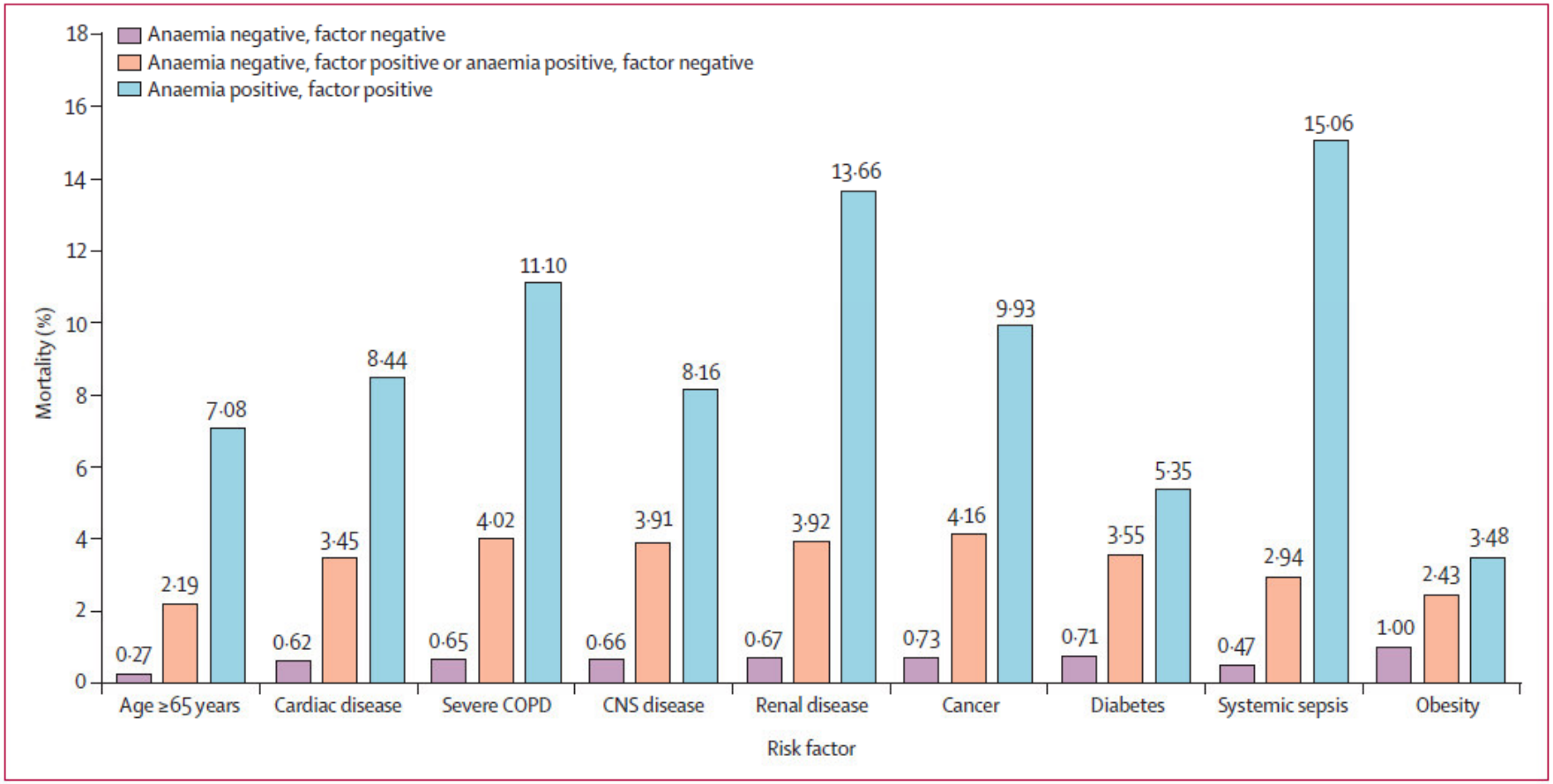
Guralnik et al: Blood. 2004;104:2263-2268

30-day composite morbidity, by anaemia and risk factor status



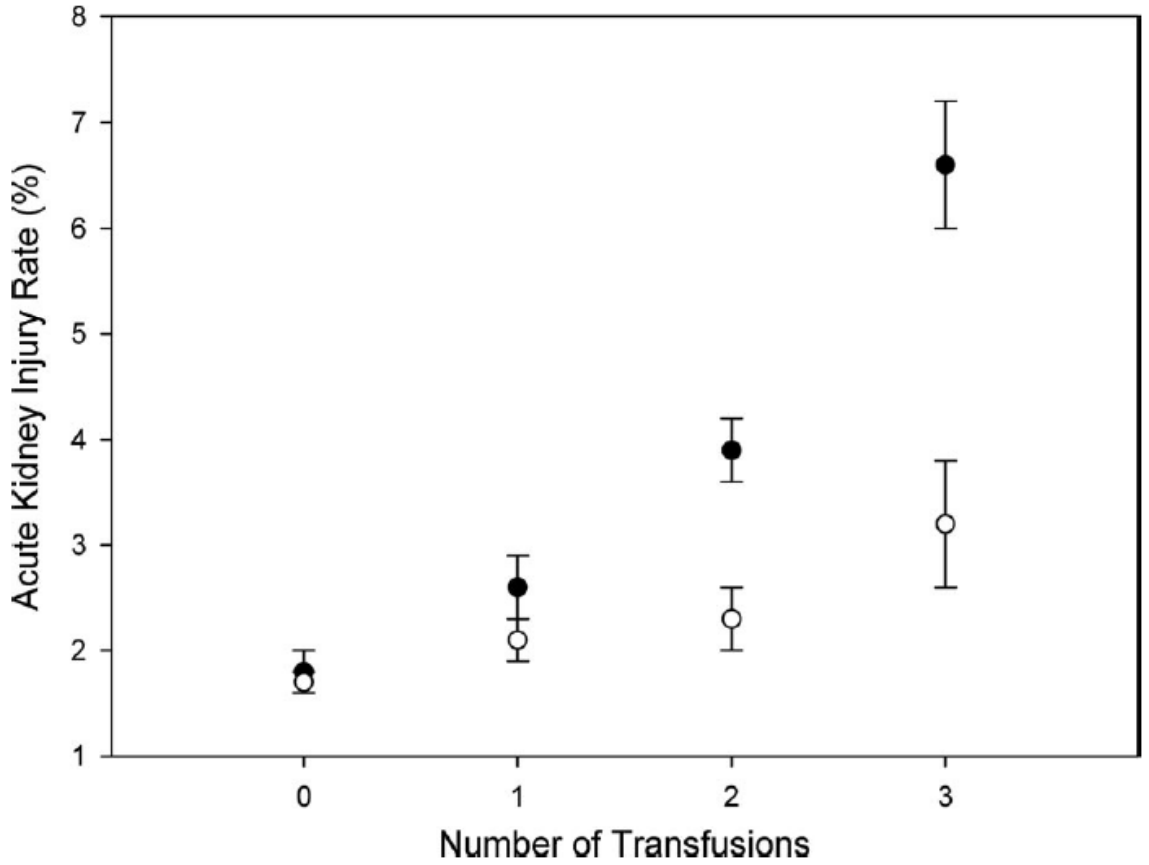
Mussallam et al: www.thelancet.com Published online October 6, 2011 DOI:10.1016/S0140-6736(11)6138

30-day mortality, by anaemia and risk factor status

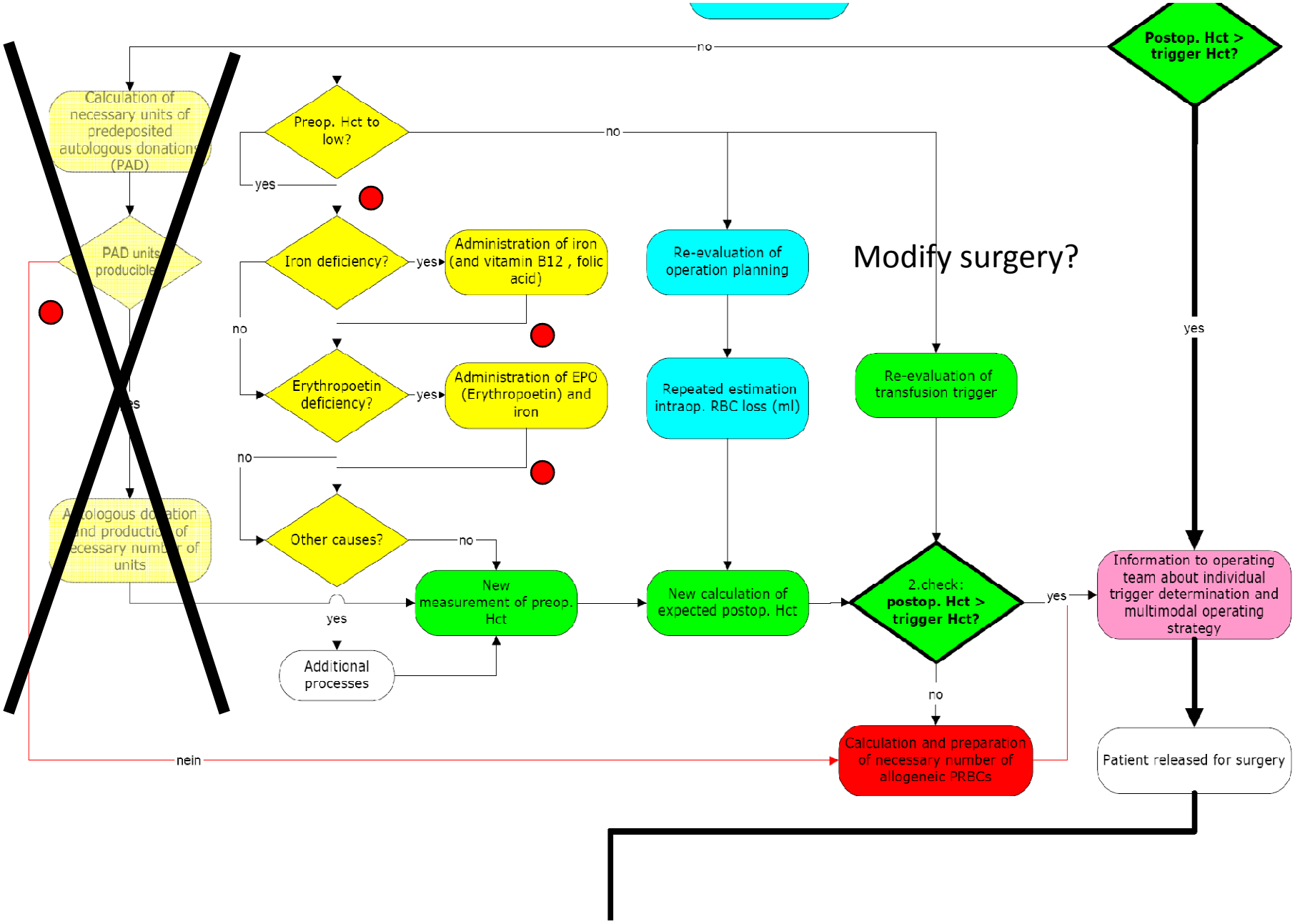


Mussallam et al: www.thelancet.com Published online October 6, 2011 DOI:10.1016/S0140-6736(11)6138

Influence of Erythrocyte Transfusion on the Risk of Acute Kidney Injury after Cardiac Surgery Differs in Anemic and Nonanemic Patients



Karkouti et al: Anesthesiology 2011; 115:523–30


Postop. Hct > trigger Hct?
no
yes
Calculation of necessary units of predeposited autologous donations (PAD)
Preop. Hct to low?
no
yes
PAD units producible
Iron deficiency?
yes
Administration of iron (and vitamin B12 , folic acid)
Re-evaluation of operation planning
Modify surgery?
no
Erythropoetin deficiency?
yes
Administration of EPO (Erythropoetin) and iron
Repeated estimation intraop. RBC loss (ml)
Re-evaluation of transfusion trigger
no
Other causes?
no
Autologous donation and production of necessary number of units
New measurement of preop. Hct
New calculation of expected postop. Hct
2.check: postop. Hct > trigger Hct?
yes
Information to operating team about individual trigger determination and multimodal operating strategy
yes
Additional processes
no
nein
Calculation and preparation of necessary number of allogeneic PRBCs
Patient released for surgery

Treatment of Iron Deficit (Ganzoni Formula)

Total iron deficit: (target Hg – actual Hb) x body weight x 2.4 + iron reserve

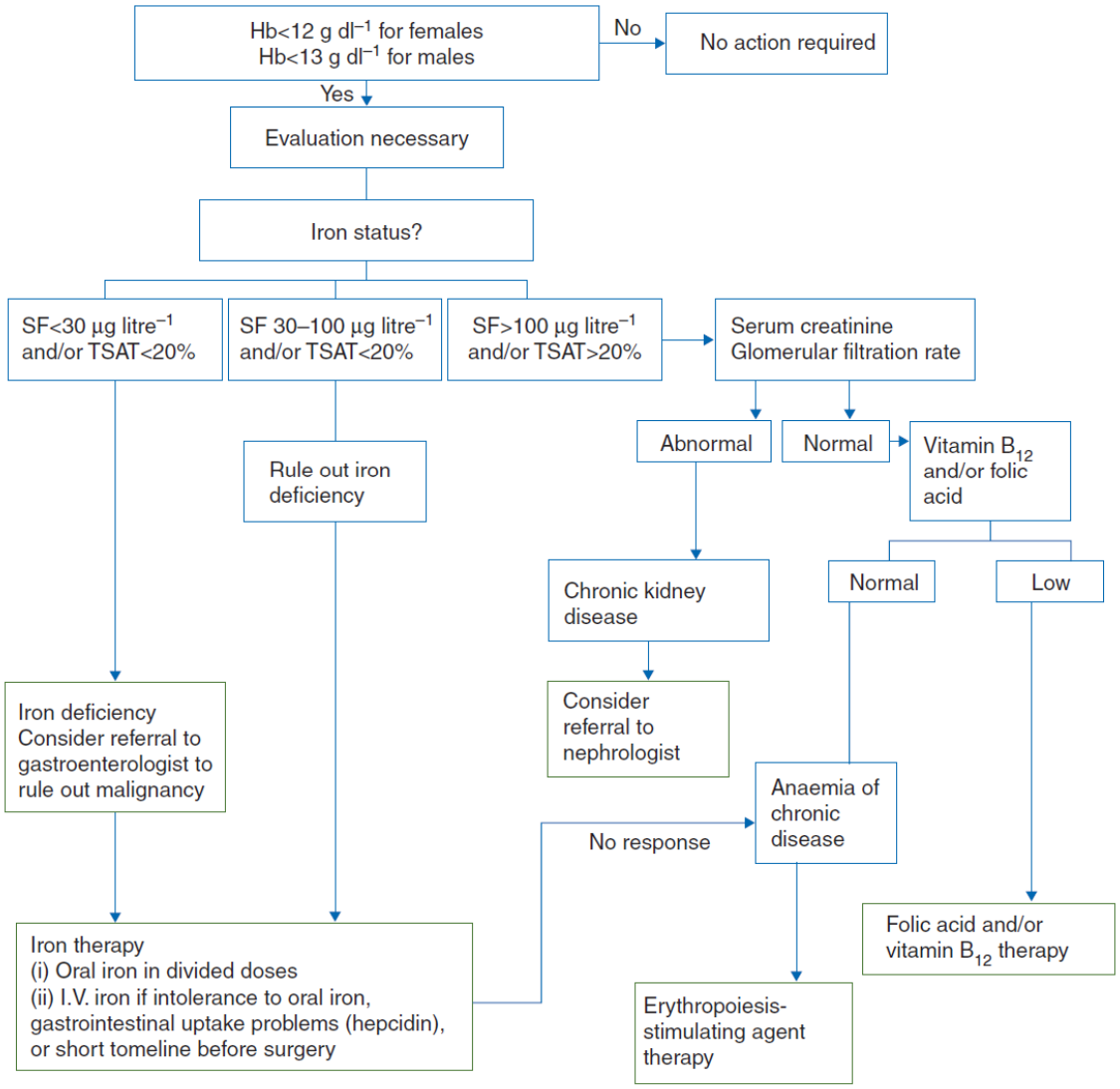
Iron reserve <35kg 15mg/kg, >35kg 500mg, only for nonanemic (pts.)

e.g.: 13 - 9.5 x 75 x 2.4 + 500 = 1.130mg iron

Ganzoni AM. Schweiz Med Wochenschr 1970;100(7):301-3.

- If > 2 months to surgery, a trial of oral iron, B12 and folate, followed by review of response
- If < 2 months to surgery, consideration should be given to IV iron and other appropriate therapy
- A number of options could be considered for IV iron infusions including the same day unit, private clinic or GP clinic infusion centres

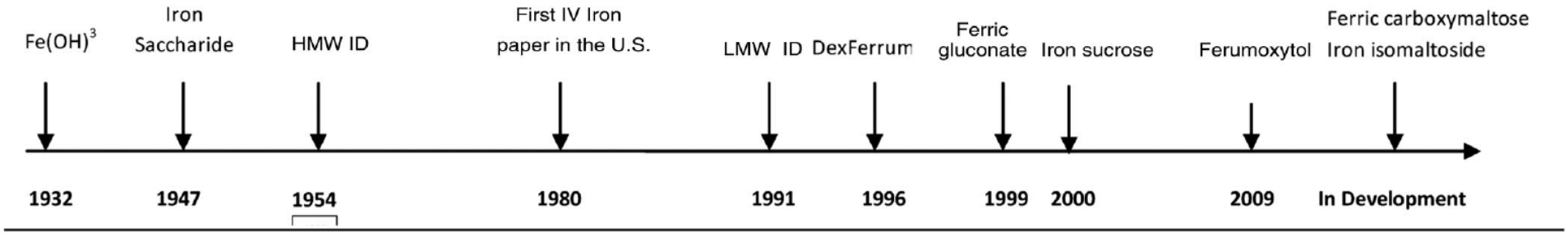
Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines.

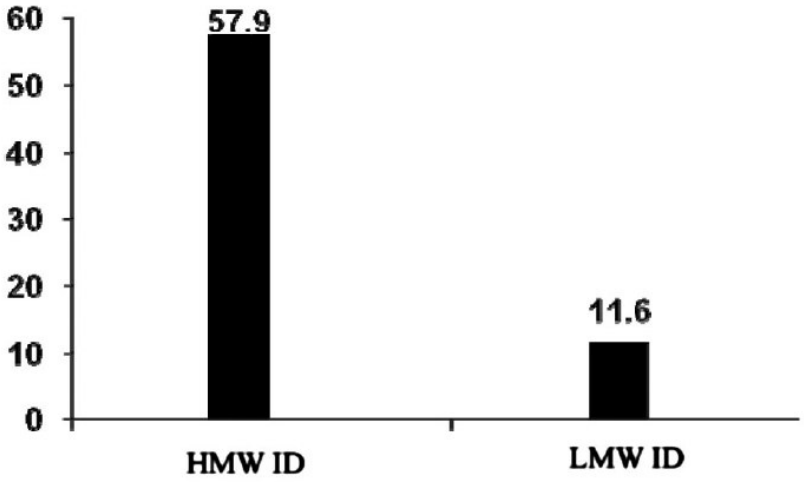


Goodnough et al: Br J Anaesth 2011; 106(1):13-22

Clinical Use of Intravenous Iron: Administration, Efficacy, and Safety

History of Intravenous Iron in the U.S.



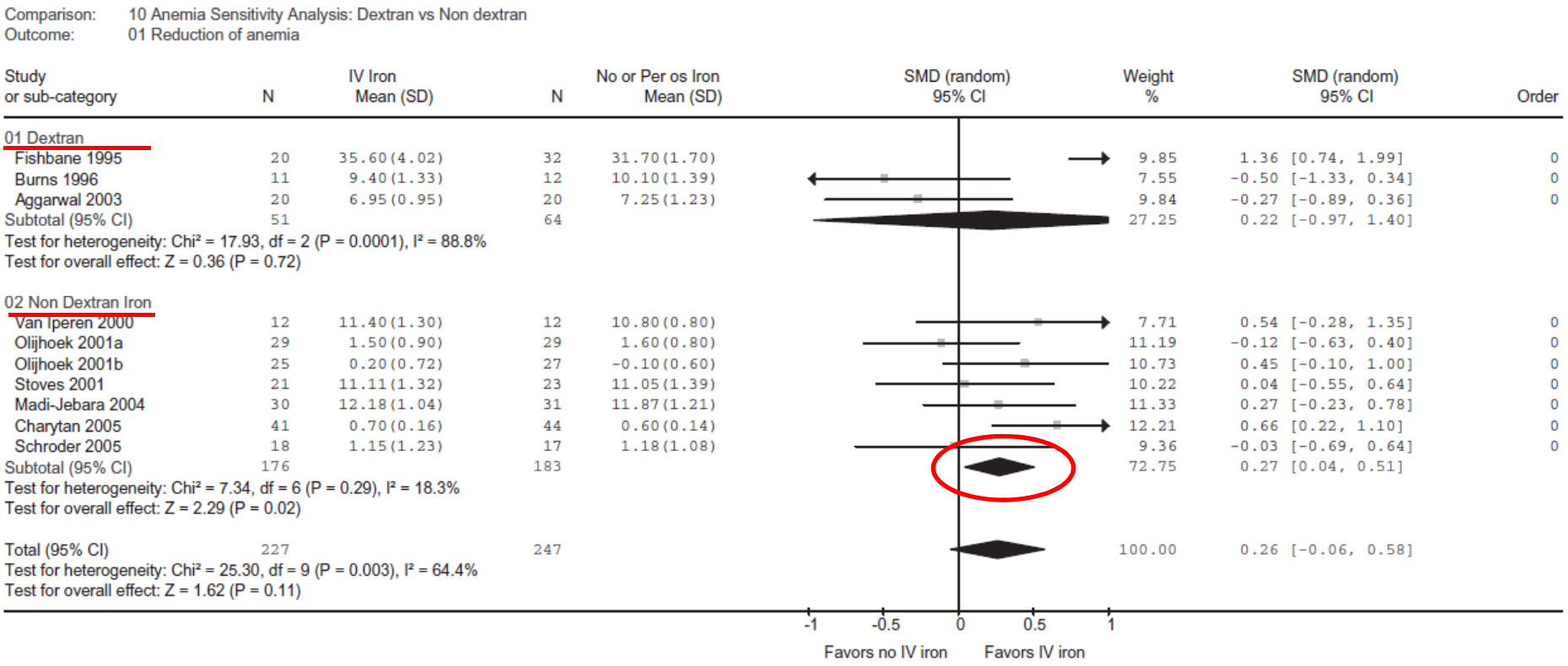


Modified from Chertow et al[19] (with permission).

Figure 2. Total reported serious ADEs per million doses of 100 mg of iron dextran.

Auerbach et al: Hematology 2010, 338-347

Short-term benefits and risks of intravenous iron: a systematic review and meta-analysis



No increase in transferrin saturation was observed.

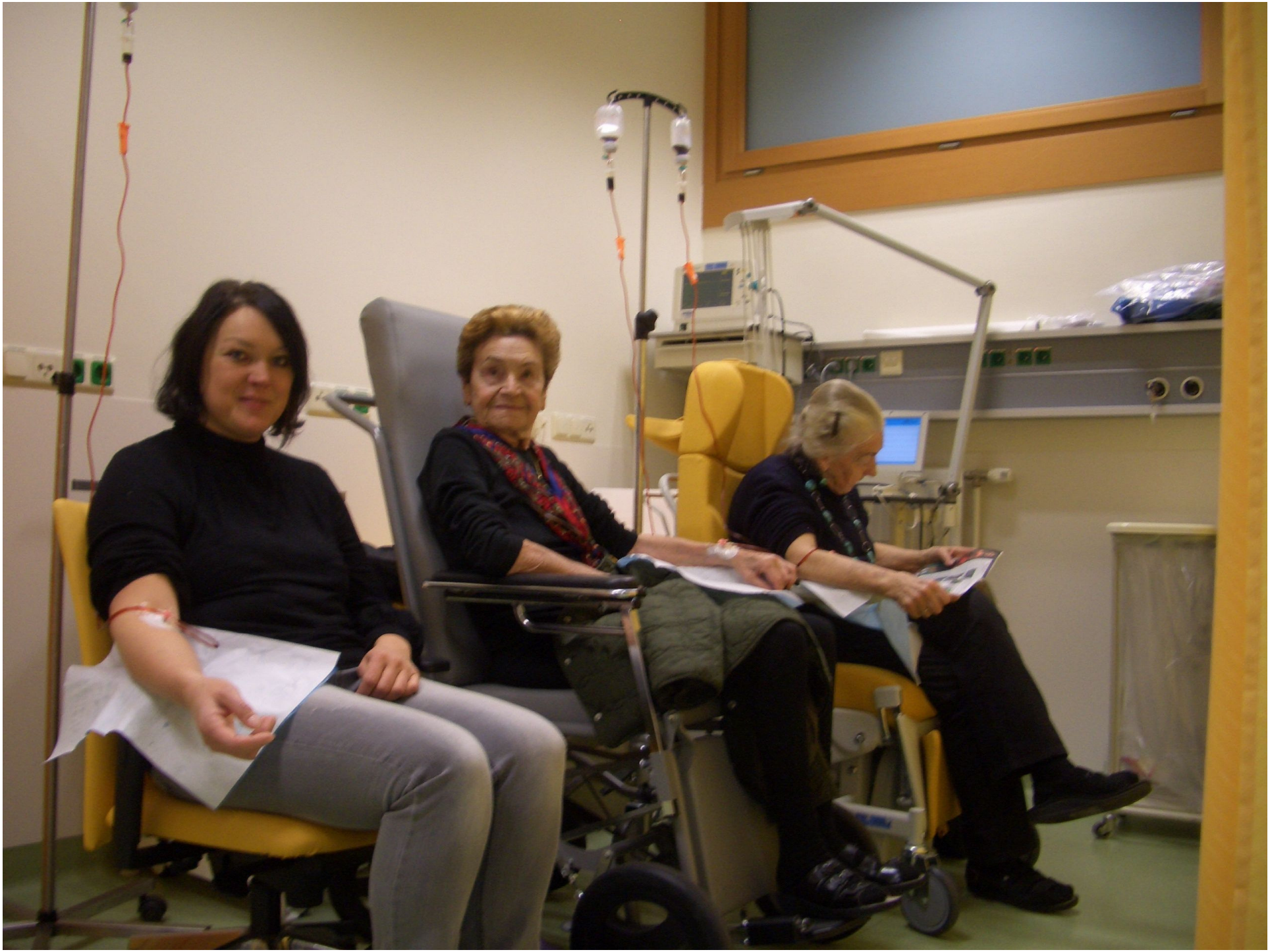
Meta-analysis of the allergic and hemodynamic reactions was not possible as most studies did not clearly describe these outcomes.

Reduction of anemia

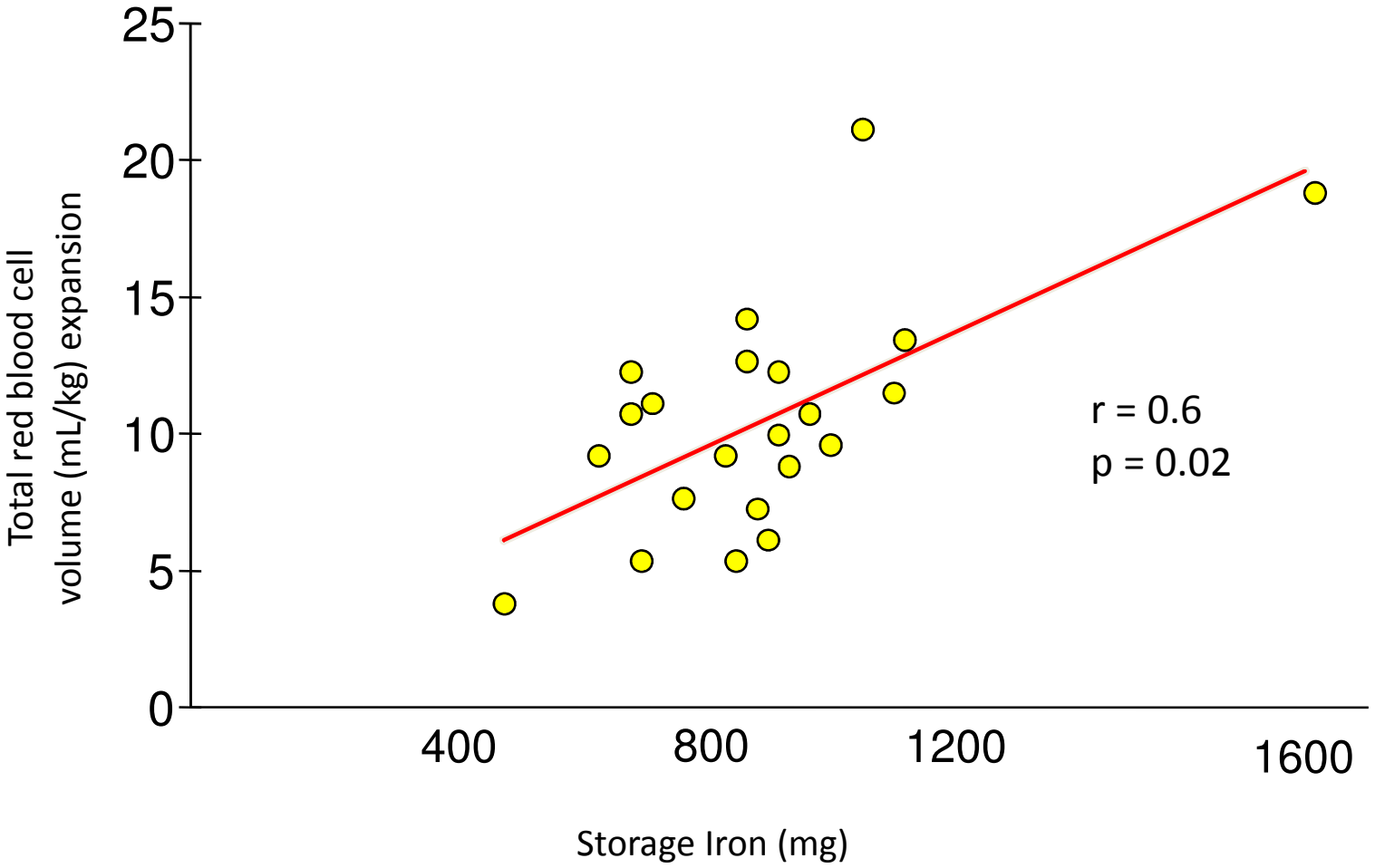
Notebaert et al: TRANSFUSION 2007;47:1905-191

Präop. Aufklärung AKH Linz

"Sollten Sie unter Anämie leiden, weisen wir Sie darauf hin, dass eine präoperative Anämiebehandlung diverse Risiken, die mit der Operation verbunden sind (z.B erhöhte Transfusionsrate, erhöhte Infektionsrate und Infarktrate und damit verbunden ein längerer Krankenhausaufenthalt), wesentlich reduzieren würden. Aus diesem Grund empfehlen wir bei allen elektiven, also nicht ganz dringlichen Eingriffen eine entsprechende Behandlung."



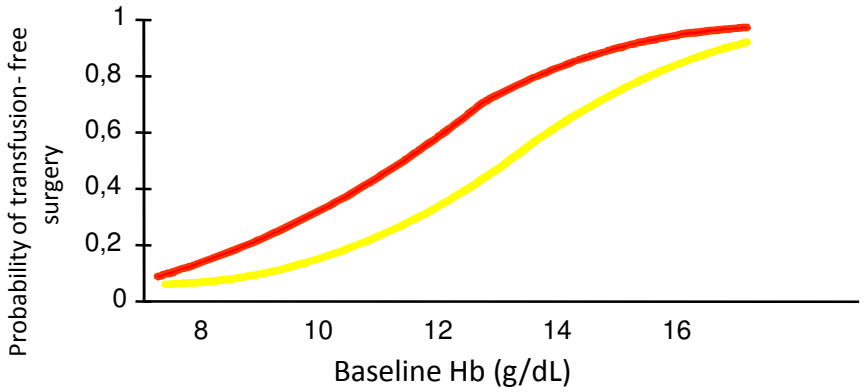
Storage iron and red cell volume expansion in patients undergoing EPO-therapy



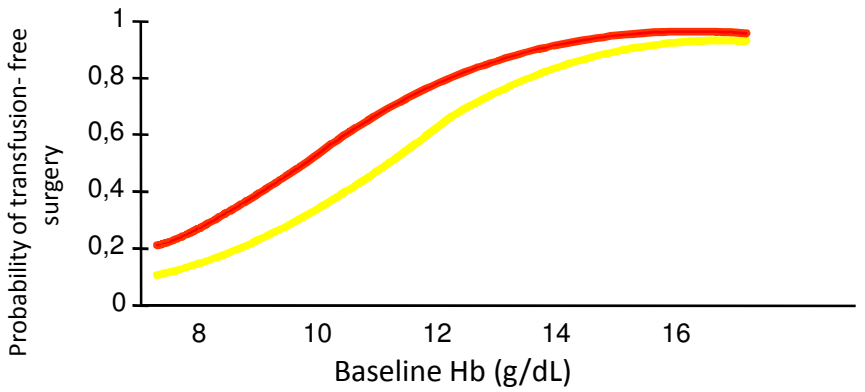
Goodnough et al. Vox Sang 75, 128, 1998

Baseline hemoglobin and transfusion-free surgery in orthopedic patients

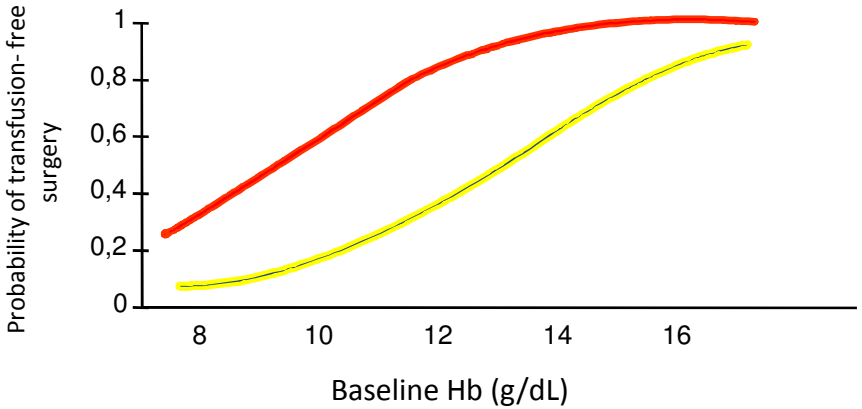
Canadian Study



De Andrade Study



Faris Study



Logistic regression curves

300 U/kg EPO

Placebo

Editorial

Anemia and Chronic Heart Failure

Are We Asking the Right Questions?

Andrew L. Clark, MD; John G.F. Cleland, MD

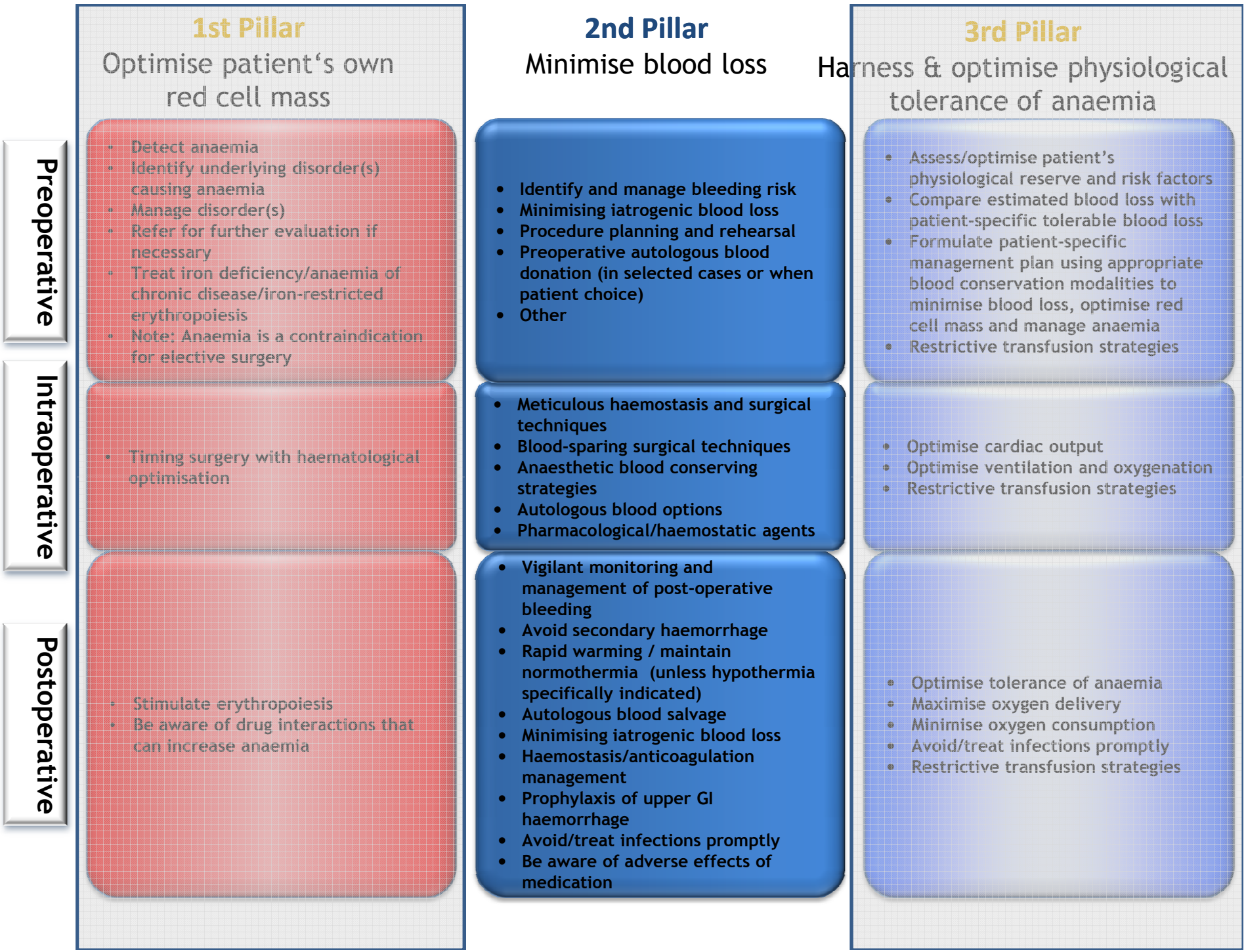
Circulation 2005;112;1681-1683

CMAJ ANALYSIS

Clinical paradigms

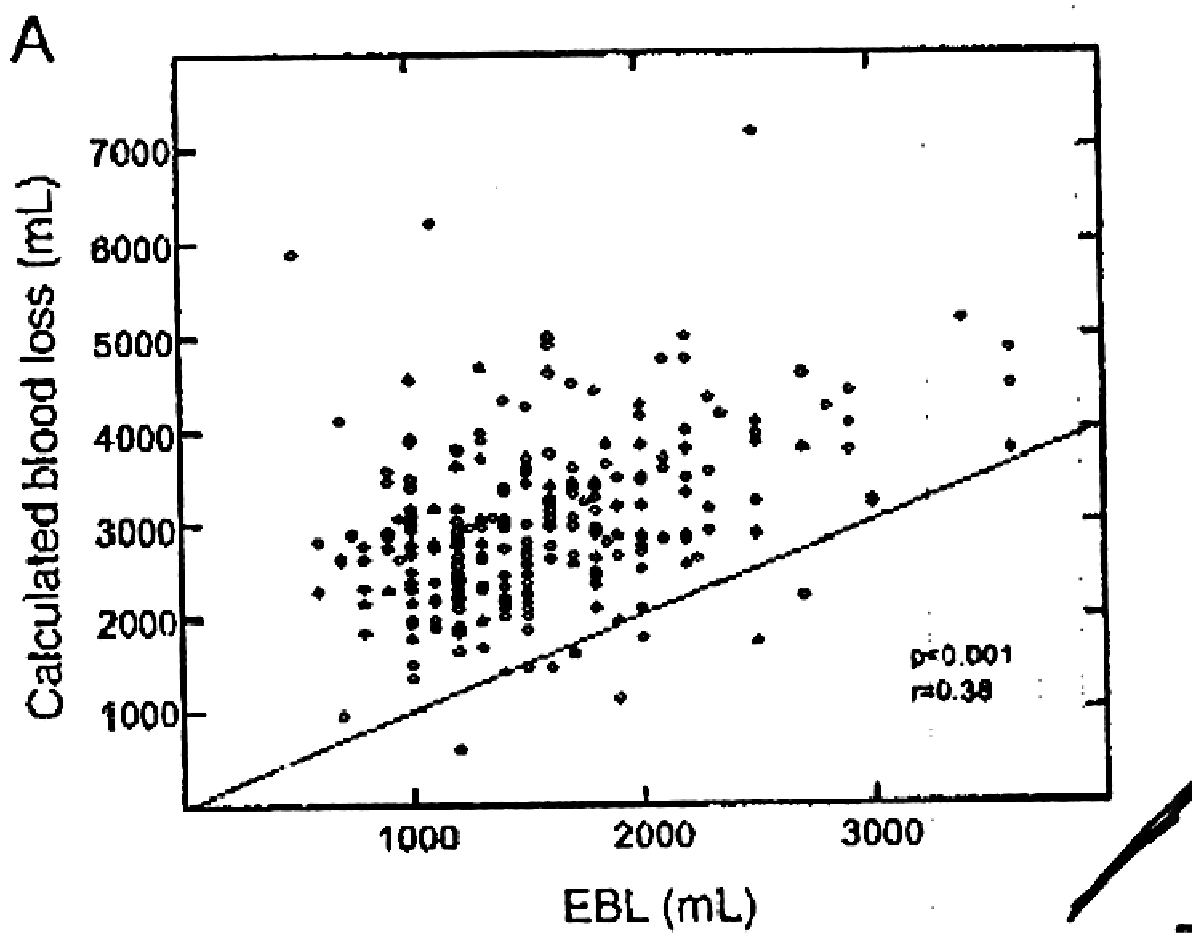
Anemia of chronic disease: A harmful disorder or an adaptive, beneficial response?

Ryan Zarychanski MD, Donald S. Houston MD PhD


1st Pillar
Optimise patient's own red cell mass
2nd Pillar
Minimise blood loss
3rd Pillar
Harness & optimise physiological tolerance of anaemia
Preoperative
Intraoperative
Postoperative
Detect anaemia
Identify underlying disorder(s) causing anaemia
Manage disorder(s)
Refer for further evaluation if necessary
Treat iron deficiency/anaemia of chronic disease/iron-restricted erythropoiesis
Note: Anaemia is a contraindication for elective surgery
Identify and manage bleeding risk
Minimising iatrogenic blood loss
Procedure planning and rehearsal
Preoperative autologous blood donation (in selected cases or when patient choice)
Other
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
Restrictive transfusion strategies
Timing surgery with haematological optimisation
Meticulous haemostasis and surgical techniques
Blood-sparing surgical techniques
Anaesthetic blood conserving strategies
Autologous blood options
Pharmacological/haemostatic agents
Optimise cardiac output
Optimise ventilation and oxygenation
Restrictive transfusion strategies
Stimulate 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
Minimising iatrogenic blood loss
Haemostasis/anticoagulation management
Prophylaxis of upper GI haemorrhage
Avoid/treat infections promptly
Be aware of adverse effects of medication
Optimise tolerance of anaemia
Maximise oxygen delivery
Minimise oxygen consumption
Avoid/treat infections promptly
Restrictive transfusion strategies

Blood loss – What‘s your estimate?

A standardized method for calculating blood loss



Brecher et al: Transfusion 37, 1070, 1997

Calculating Blood loss (I)

Blood volume (BV) **(Nadler et al.: Surgery 1962;51:224-32)**

Male

BVm[ml] = [(0.3669 * height[m]3 + (0.03219 * weight[kg] + 0.6041] x 1000

Female

BVf[ml] = [(0.3561 * height[m]3 + (0.03308 * weight[kg] + 0.1833] x 1000

Circulating red cell volume (preop)

RBCpre[ml] = BV[ml] * HCTpre[l/l] * 0.911

Circulating red cell volume (POD5)

RBC(POD5)[ml] = BV[ml] * HCT(POD5)[l/l] * 0.911

Calculating Blood Loss (II)

Red cell volume (ml)

RBC(loss)[ml] = RBCpre[ml] – RBC(POD5)[ml] + RBC(transfused)[ml]

Red cell volume (% of RBCpre[ml])

RBC(loss)[%] = RBC(loss)[ml] * 100/RBCpre[ml]

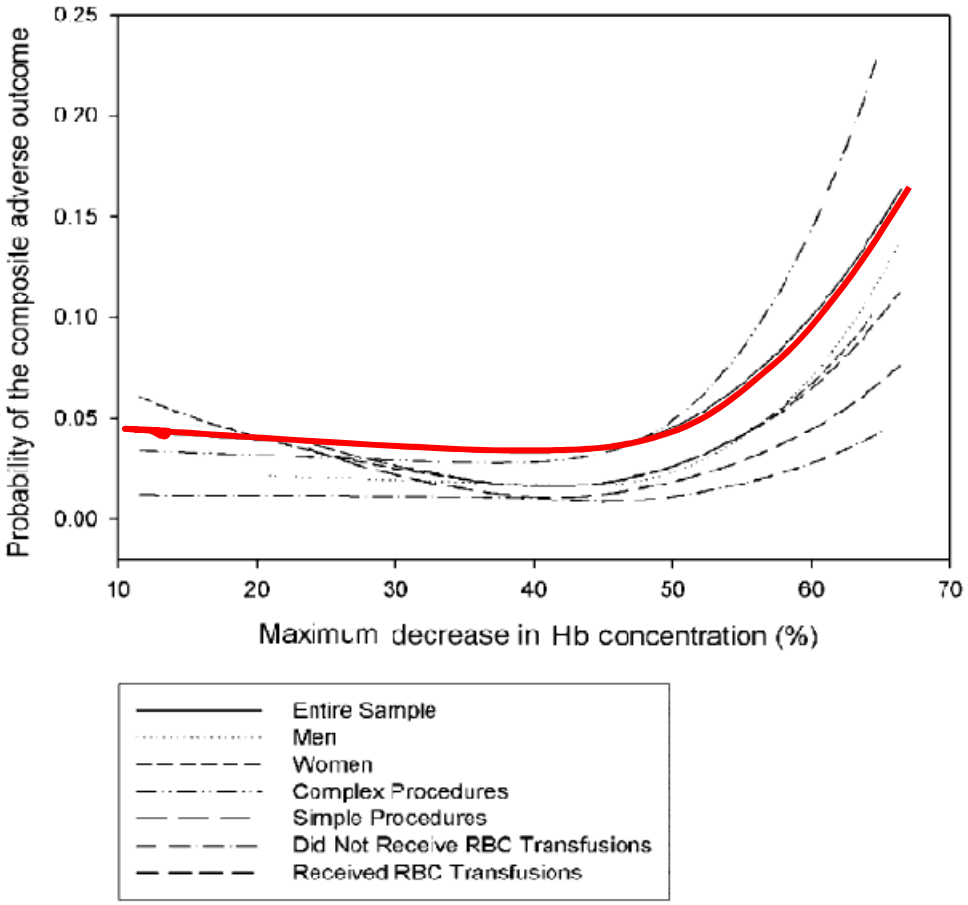
Relationships among haemoglobin level, packed red cell transfusion and clinical outcomes in patients after cardiac surgery.

- Low haemoglobin concentrations and transfusions in patients undergoing cardiac surgery are associated with increased morbidity and mortality.
- Also, anemia and transfusions are associated with poor outcome.
- Therefore, intra- and postoperative bleeding seem to be a risk factor in patients undergoing cardiac surgery

1216 Consecutive patients

Oliver at al: Intensive Care Med. 2009 Sep;35(9):1548-55. Epub 2009 Jun 23

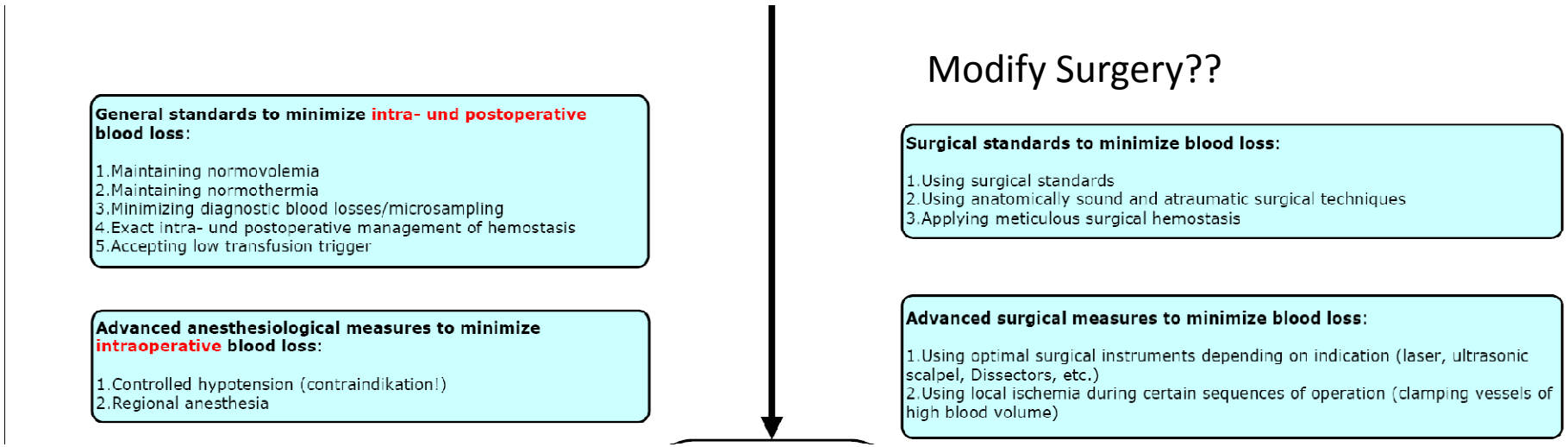
The influence of baseline hb concentration on tolerance of anemia in cardiac surgery

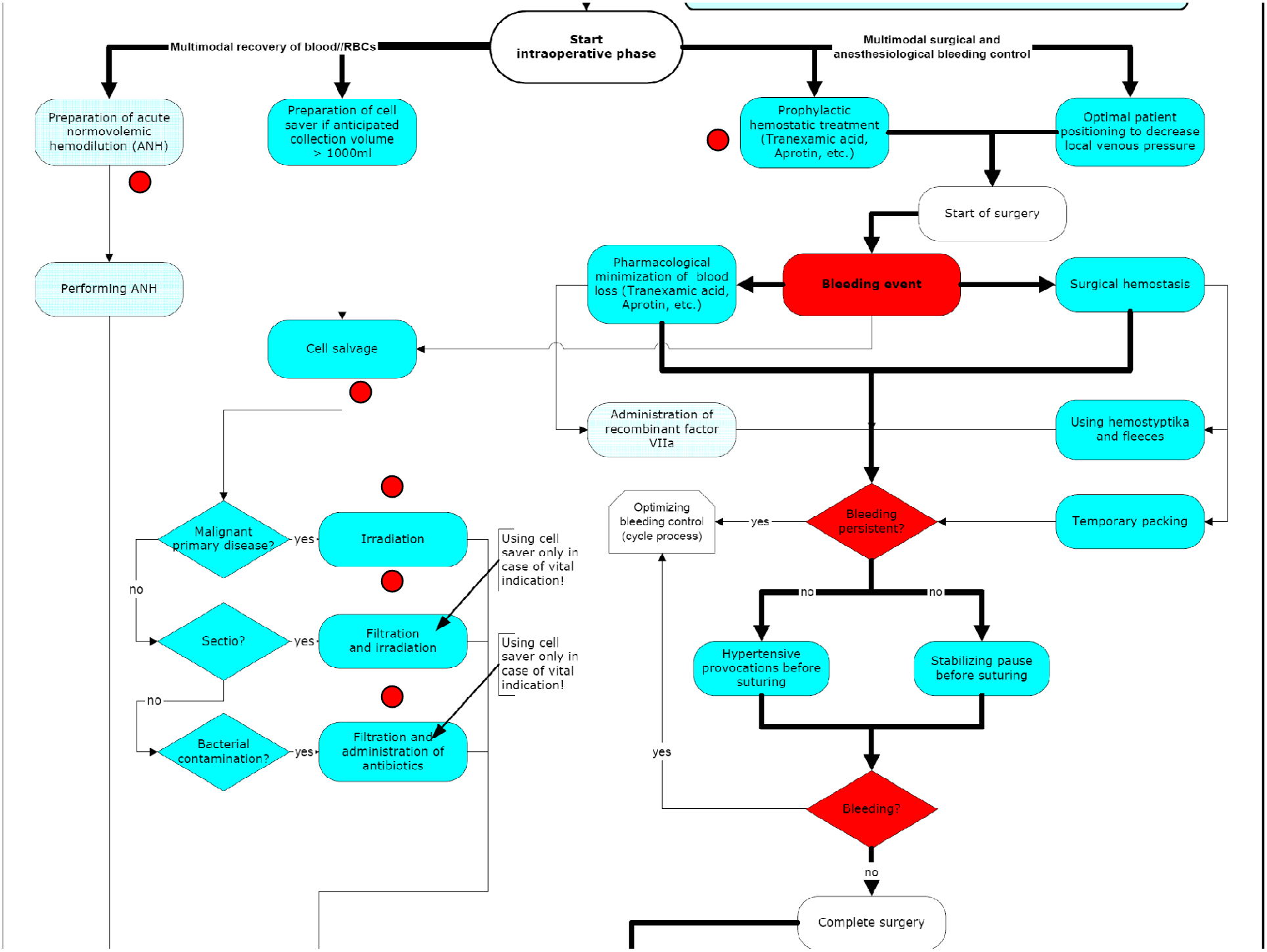


The relationship between maximum decrease in Hb concentration and adverse outcomes was independently associated with increased risk!!

Karkouti et al: TRANSFUSION 2008;48:666-672.

General standards and advanced measures



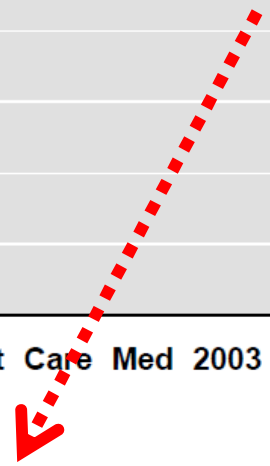

Start intraoperative phase
Multimodal recovery of blood//RBCs
Multimodal surgical and anesthesiological bleeding control
Preparation of acute normovolemic hemodilution (ANH)
Preparation of cell saver if anticipated collection volume > 1000ml
Prophylactic hemostatic treatment (Tranexamic acid, Aprotin, etc.)
Optimal patient positioning to decrease local venous pressure
Performing ANH
Start of surgery
Pharmacological minimization of blood loss (Tranexamic acid, Aprotin, etc.)
Bleeding event
Surgical hemostasis
Cell salvage
Administration of recombinant factor VIIa
Using hemostyptika and fleeces
Malignant primary disease?
yes
Irradiation
Optimizing bleeding control (cycle process)
Bleeding persistent?
Temporary packing
no
Using cell saver only in case of vital indication!
Sectio?
Filtration and irradiation
Hypertensive provocations before suturing
Stabilizing pause before suturing
Bacterial contamination?
Filtration and administration of antibiotics
Bleeding?
Complete surgery

Comparisons of different blood conservation methods

Author	PDAB	ANH	ANH+ EPO	EPO	N/pts.(m/f)	% pts.with allogenic blood	P-value
Monk 1999	I	I	I	---	79 (79/0)	15-19-4	NS
Chun 1997	I	---	---	I	120 (120/0)	9.6-9.7	NS
Gombotz 2000	I	---	I	I	60 (0/60)	40-30-20	NS
Stowell 1999	I	---	---	I	428 (47/381)	19.2-12.9	NS
Goodnough 2000	I	I	---	---	48 (22/26)	0 - 17	NS

Approximate contributions of selected PBM modalities in the surgical patient	Number of RBC units saved
Perioperative	
Harnessing patient's tolerance of anaemia (restrictive transfusion trigger)	1-2[146]
Restricted phlebotomy	1[128]
Pre-operative	
Optimisation of RBC mass (perioperative anaemia management)	2[184, 185]
Intra-operative	
Meticulous haemostasis & surgical technique	1 or more[186]
Acute normovolaemic haemodilution (ANH)	1 or more[89, 187]
Autologous cell salvage	1or more[188]
Post-operative	
Autologous blood salvage	1[189]

Adapted with author consent from Shander A. Surgery without blood. Crit Care Med 2003 Dec;31(12 Suppl):S708-S714.



Up to 50% reduction of blood loss!!!

The safety of aprotinin and lysine-derived antifibrinolytic drugs in cardiac surgery: a meta-analysis

- The addition of data from the BART study increased the relative risk of death with the use of aprotinin compared with the use of either tranexamic acid or epsilon aminocaproic acid.
- The balance of evidence now favours the use of lysine analogues over aprotinin. This represents a shift in the conclusions of the Cochrane review, which was last updated in 2007.
- Compared with aprotinin, lysine analogues are almost as effective, are cheaper and do not appear to increase mortality.

Henry D. et al: CMAJ 2009;180(2)183-93

Cardiovascular Anesthesiology
Section Editor: **Charles W. Hogue, Jr.**

Perioperative Echocardiography and Cardiovascular Education
Section Editor: **Martin J. London**

Hemostasis and Transfusion Medicine
Section Editor: **Jerrold H. Levy**

The Risk-Benefit Profile of Aprotinin Versus Tranexamic Acid in Cardiac Surgery

Keyvan Karkouti, MD*†

Duminda N. Wijeysundera, MD*†

Terrence M. Yau, MD‡

Stuart A. McCluskey, MD*

Gordon Tait, PhD*

W. Scott Beattie, MD*

BACKGROUND: Aprotinin is superior to other antifibrinolytic drugs for preventing major blood loss after cardiac surgery but may also increase perioperative mortality. It remains unclear whether its risk-benefit profile differs among low-, moderate-, and high-risk cardiac surgical patients.

METHODS: In this retrospective single-center cohort study, we included 15,365 patients who underwent cardiac surgery with cardiopulmonary bypass from 2000 to 2008. Of these, 1017 received aprotinin (6×10^6 U) and 14,358 received tranexamic acid (50–100 mg/kg). Propensity score methods were used to create a matched-pairs cohort ($n = 1544$) that adjusted for important between-group differences. The influence of patients' risk status on aprotinin's association with in-hospital mortality, morbidity, and blood loss was measured.

RESULTS: In the matched set, aprotinin was only associated with increased acute kidney injury (>50% decrease in estimated glomerular filtration or dialysis; odds ratio 1.5; 95% confidence interval [CI] 1.1–2.1). Patients' risk status significantly influenced the associations of aprotinin with mortality, acute kidney injury, and massive blood loss (transfusion of ≥10 U of red blood cells or need for surgical reexploration). Among high-risk patients, the respective odds ratios were 0.6 (CI 0.3–1.0), 1.1 (CI 0.7–1.7), and 0.7 (CI 0.4–1.04), and among low- to moderate-risk patients, they were 1.5 (CI 0.9–2.7), 2.2 (CI 1.4–3.5), and 1.2 (CI 0.9–1.07) (Breslow-Day test for homogeneity of odds ratios between high-risk versus low- to moderate-risk patients: $P < 0.05$ for all 3 outcomes).

CONCLUSIONS: Aprotinin tends to have a better risk-benefit profile than tranexamic acid in high-risk, but not low- to moderate-risk, patients. Its use in high-risk cases may therefore be warranted.

(Anesth Analg 2010;110:21–9)

Tranexamic acid reduces blood transfusion in total knee arthroplasty even when a blood conservation program is applied

Juan C. Álvarez, Francisco X. Santiveri, Isabel Ramos, Enrique Vela, Lluis Puig, and Fernando Escolano

TABLE 2. Postoperative data in the study groups*

Data	Tranexamic acid (n = 46)	Controls (n = 49)	p Value
Crystalloids volume, mL, mean (SD)	902 (337)	931 (411)	0.71
Colloids volume, mL, mean (SD)	77 (183)	364 (483)	<0.0001
Drained blood, mL, mean (SD)			
0–6 hr	159 (110)	534 (351)	<0.0001
>6 hr to fourth day	132 (151)	132 (150)	0.98
Total	170 (109)	551 (352)	<0.001
Transfusion			
From cell saver, number (%)	2 (4)	36 (73)	<0.00001
Autologous blood, units	0	3	
Allogenic blood, units	1	8	

* Data are reported as mean and SD for continuous variable and number (%) or units for transfusion data.

High-Dose Tranexamic Acid Is Associated with Nonischemic Clinical Seizures in Cardiac Surgical Patients

John M. Murkin, MD, FRCPC*

Florian Falter, MD, FRCA†

Jeff Granton, MD, FRCPC*

Bryan Young, MD, FRCPC‡

Christiana Burt, MA, FRCA†

Michael Chu, MD, FRCSC§

BACKGROUND: In 2 separate centers, we observed a notable increase in the incidence of postoperative convulsive seizures from 1.3% to 3.8% in patients having undergone major cardiac surgical procedures. These events were temporally coincident with the initial use of high-dose tranexamic acid (TXA) therapy after withdrawal of aprotinin from general clinical usage. The purpose of this review was to perform a retrospective analysis to examine whether there was a relation between TXA usage and seizures after cardiac surgery.

METHODS: An in-depth chart review was undertaken in all 24 patients who developed perioperative seizures. Electroencephalographic activity was recorded in 11 of these patients, and all patients had a formal neurological evaluation and brain imaging studies.

RESULTS: Twenty-one of the 24 patients did not have evidence of new cerebral ischemic injury, but seizures were likely due to ischemic brain injury in 3 patients. All patients with seizures did not have permanent neurological abnormalities. All 24 patients with seizures received high doses of TXA intraoperatively ranging from 61 to 259 mg/kg, had a mean age of 69.9 years, and 21 of 24 had undergone open chamber rather than coronary bypass procedures. All but one patient were managed using cardiopulmonary bypass. No evidence of brain ischemic, metabolic, or hyperthermia-induced causes for their seizures was apparent.

CONCLUSION: Our results suggest that use of high-dose TXA in older patients in conjunction with cardiopulmonary bypass and open-chamber cardiac surgery is associated with clinical seizures in susceptible patients.

(Anesth Analg 2010;110:350–3)

Components of PBM

- ✓ Evaluation of the actual blood usage (data management)
- ✓ Optimising blood ordering schedules
- ✓ Increasing tolerance of anemia
- 3 pillar strategy
  - Optimising preoperative red cell mass
  - Minimising perioperative blood loss
  - Reducing transfusion trigger

CLINICAL PRACTICE GUIDELINES

Appropriate Use of Blood Components

- Use of blood components for clinical or laboratory indications not listed here is likely to be inappropriate. Consult the NHMRC/ASBT guidelines (www.nhmrc.gov.au) for further details.
- Clinical and laboratory indications for use should be documented.

Red blood cells

Hb*	Considerations
<70g/L	Lower thresholds may be acceptable in patients without symptoms and/or where specific therapy is available.
70-100g/L	Likely to be appropriate during surgery associated with major blood loss or if there are signs or symptoms of impaired oxygen transport.
>80g/L	May be appropriate to control anaemia-related symptoms in a patient on a chronic transfusion regimen or during marrow suppresive therapy.
>100g/L	Not likely to be appropriate unless there are specific indications.

* Hb should not be the sole deciding factor. Consider also patient factors, signs and symptoms of hypoxia, ongoing blood loss and the risk to the patient of anaemia.

Platelets

Use of platelets is likely to be **appropriate as prophylaxis:**

Indication	Considerations
Bone marrow failure	At a platelet count of $<10x10^9$/L in the absence of risk factors and $<20x10^9$/L in the presence of risk factors (eg fever, antibiotics, evidence of systemic haemostatic failure).
Surgery/ invasive procedure	To maintain platelet count at $>50x10^9$/L. For surgical procedure with high risk of bleeding (eg ocular or neurosurgery) it may be appropriate to maintain at $100x10^9$/L.
Platelet function disorders	May be appropriate in inherited or acquired disorders, depending on clinical features and setting. In this situation, platelet count is not a reliable indicator.

Platelets

Use of platelets is likely to be **appropriate as therapy:**

Indication	Considerations
Bleeding	May be appropriate in any patient in whom thrombocytopenia is considered a major contributory factor.
Massive haemorrhage/ transfusion	Use should be confined to patients with thrombocytopenia and/or functional abnormalities who have significant bleeding from this cause. May be appropriate when the platelet count is $<50x10^9$/L ($<100x10^9$/L in the presence of diffuse microvascular bleeding).

Fresh frozen plasma

Use of fresh frozen plasma is likely to be **appropriate:**

Indication	Considerations
Single factor deficiencies	Use specific factors if available.
Warfin effect	In the presence of life-threatening bleeding. Use in addition to vitamin-K-dependent concentrates.
Acute DIC	Indicated where there is bleeding and abnormal coagulation. Not indicated for chronic DIC.
TTP	Accepted treatment.
Coagulation inhibitor deficiencies	May be appropriate in patients undergoing high-risk procedures. Use specific factors if available.
Following massive transfusion or cardiac bypass	May be appropriate in the presence of bleeding and abnormal coagulation.
Liver disease	May be appropriate in the presence of bleeding and abnormal coagulation.

Cryoprecipitate

Use of cryoprecipitate is likely to be **appropriate:**

Indication	Considerations
Fibrinogen deficiency	May be appropriate where there is clinical bleeding, an invasive procedure, trauma or DIC.

Abbreviations: Hb = haemoglobin; DIC = disseminated intravascular coagulation; TTP = thrombotic thrombocytopenic purpura.

ISBN 1864960590 October 2001

Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion

- Restrictive transfusion strategies reduced the risk of receiving a red blood cell (RBC) transfusion by a relative 42%. This equates to an average absolute risk reduction (ARR) of 40%.
- The volume of RBCs transfused was reduced on average by 0.93 units.
- However, heterogeneity between these trials was statistically significant ($p<0.00001$) for these outcomes.
- Mortality, rates of cardiac events, morbidity, and length of hospital stay were unaffected. Trials were of poor methodological quality.

Hill SR, et al: The Cochrane Library, Issue 4, 2003.

The NEW ENGLAND JOURNAL of MEDICINE

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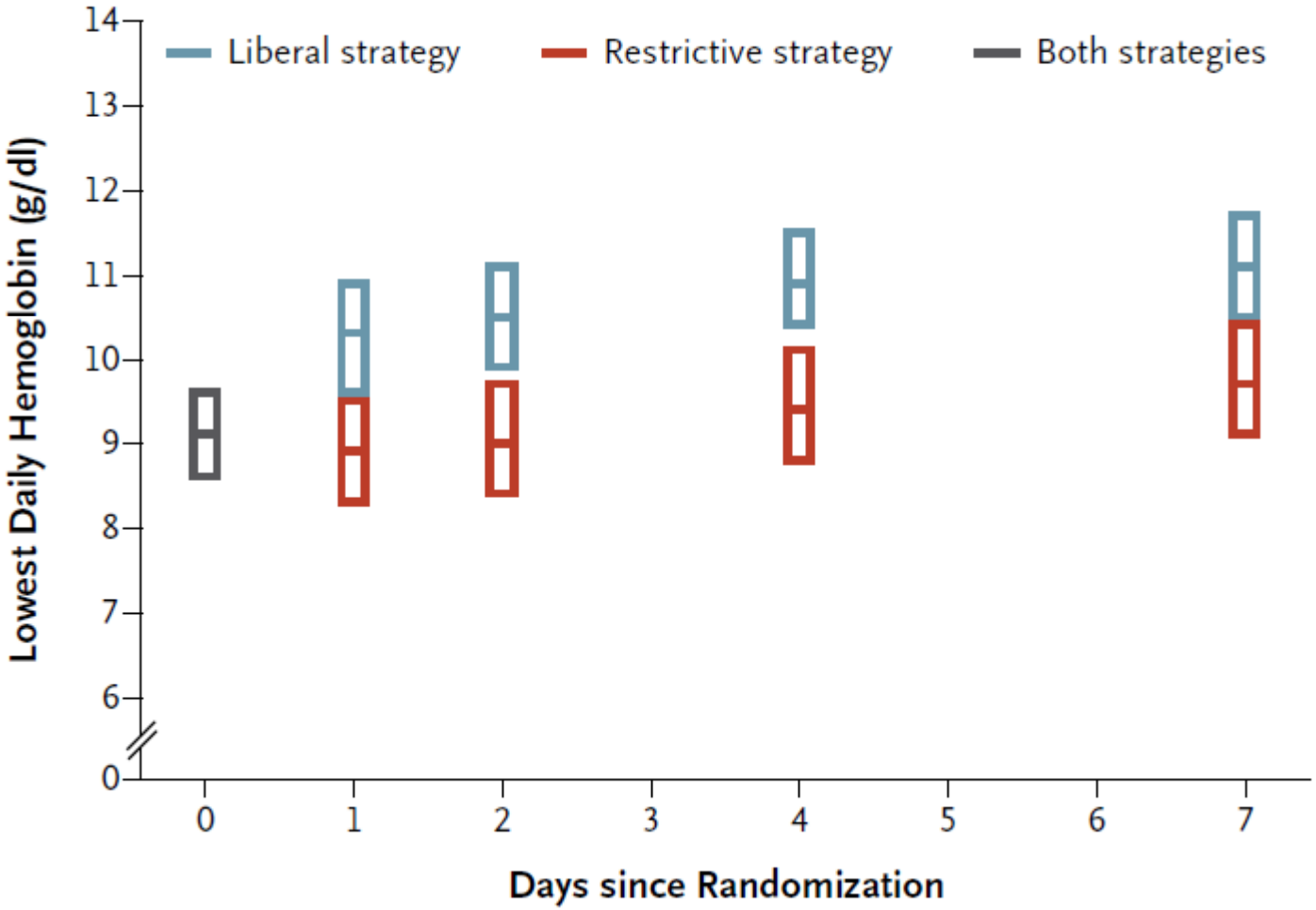
Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

Jeffrey L. Carson, M.D., Michael L. Terrin, M.D., M.P.H., Helaine Noveck, M.P.H., David W. Sanders, M.D., Bernard R. Chaitman, M.D., George G. Rhoads, M.D., M.P.H., George Nemo, Ph.D., Karen Dragert, R.N., Lauren Beaupre, P.T., Ph.D., Kevin Hildebrand, M.D., William Macaulay, M.D., Courtland Lewis, M.D., Donald Richard Cook, B.M.Sc., M.D., Gwendolyn Dobbin, C.C.R.P., Khwaja J. Zakriya, M.D., Fred S. Apple, Ph.D., Rebecca A. Horney, B.A., and Jay Magaziner, Ph.D., M.S.Hyg., for the FOCUS Investigators*

Methods

- Patients in the **liberal-strategy group** received 1 unit of packed red cells and additional blood as needed to maintain a hemoglobin level of 10 g or more per deciliter. An assessment of the hemoglobin level after transfusion was required, and an additional unit of blood was transfused if the patient's hemoglobin level was below 10 g per deciliter.
- Patients in the **restrictive-strategy group** were permitted to receive transfusions if symptoms or signs of anemia developed or at the discretion of their physicians if the hemoglobin level fell below 8 g per deciliter.

Lowest Daily Hemoglobin Levels



Hospital Outcomes

Variable	Liberal Strategy (N=1007)	Restrictive Strategy (N=1009)	Odds Ratio (99% CI)	Absolute Risk Difference (99% CI)
	number/total number (percent)			*percentage points*
Myocardial infarction, unstable angina, or in-hospital death†	43/1005 (4.3)	52/1008 (5.2)	0.82 (0.48 to 1.42)	–0.9 (–3.3 to 1.6)
Myocardial infarction†	23/1005 (2.3)	38/1008 (3.8)	0.60 (0.30 to 1.19)	–1.5 (–3.5 to 0.5)
Unstable angina†	2/1005 (0.2)	3/1008 (0.3)	0.67 (0.06 to 7.03)	–0.1 (–0.7 to 0.5)
In-hospital death	20/1005 (2.0)	14/1008 (1.4)	1.44 (0.58 to 3.56)	0.6 (–0.9 to 2.1)
Isolated troponin elevation‡	62/1005 (6.2)	59/1008 (5.9)	1.06 (0.65 to 1.71)	0.3 (–2.4 to 3.1)
Physician diagnosis of congestive heart failure	27/1005 (2.7)	35/1007 (3.5)	0.77 (0.39 to 1.50)	–0.8 (–2.8 to 1.2)
Stroke or transient ischemic attack				
On CT or MRI	5/1005 (0.5)	1/1007 (0.1)	5.03 (0.30 to 84.73)	0.4 (–0.2 to 1.0)
On physician diagnosis or CT or MRI	8/1005 (0.8)	3/1007 (0.3)	2.69 (0.47 to 15.42)	0.5 (–0.3 to 1.3)
Chest radiograph with new or progressive infiltrate	60/1005 (6.0)	48/1007 (4.8)	1.27 (0.76 to 2.12)	1.2 (–1.4 to 3.8)
New-onset purulent sputum	9/1005 (0.9)	3/1007 (0.3)	3.02 (0.54 to 16.91)	0.6 (–0.3 to 1.5)
Wound infection	14/1005 (1.4)	8/1007 (0.8)	1.76 (0.56 to 5.56)	0.6 (–0.6 to 1.8)
Deep-vein thrombosis or pulmonary embolism	12/1005 (1.2)	8/1007 (0.8)	1.51 (0.46 to 4.92)	0.4 (–0.7 to 1.5)
Death, myocardial infarction, pneumonia	89/1005 (8.9)	90/1007 (8.9)	0.99 (0.66, 1.48)	–0.1 (–3.4 to 3.2)
Death, myocardial infarction, pneumonia, thrombo-embolism, or stroke	103/1005 (10.2)	94/1007 (9.3)	1.11 (0.75 to 1.63)	0.9 (–2.5 to 4.3)
Returned to operating room	15/1005 (1.5)	18/1007 (1.8)	0.83 (0.34 to 2.06)	–0.3 (–1.8 to 1.2)
Transfer to intensive care unit	30/1005 (3.0)	29/1007 (2.9)	1.04 (0.53 to 2.05)	0.1 (–1.8 to 2.0)
	days		P Value	
Time from randomization to discharge§				
United States	3.67±3.38	3.97±3.89	0.15	
Canada	12.03±9.31	12.70±9.48	0.32	

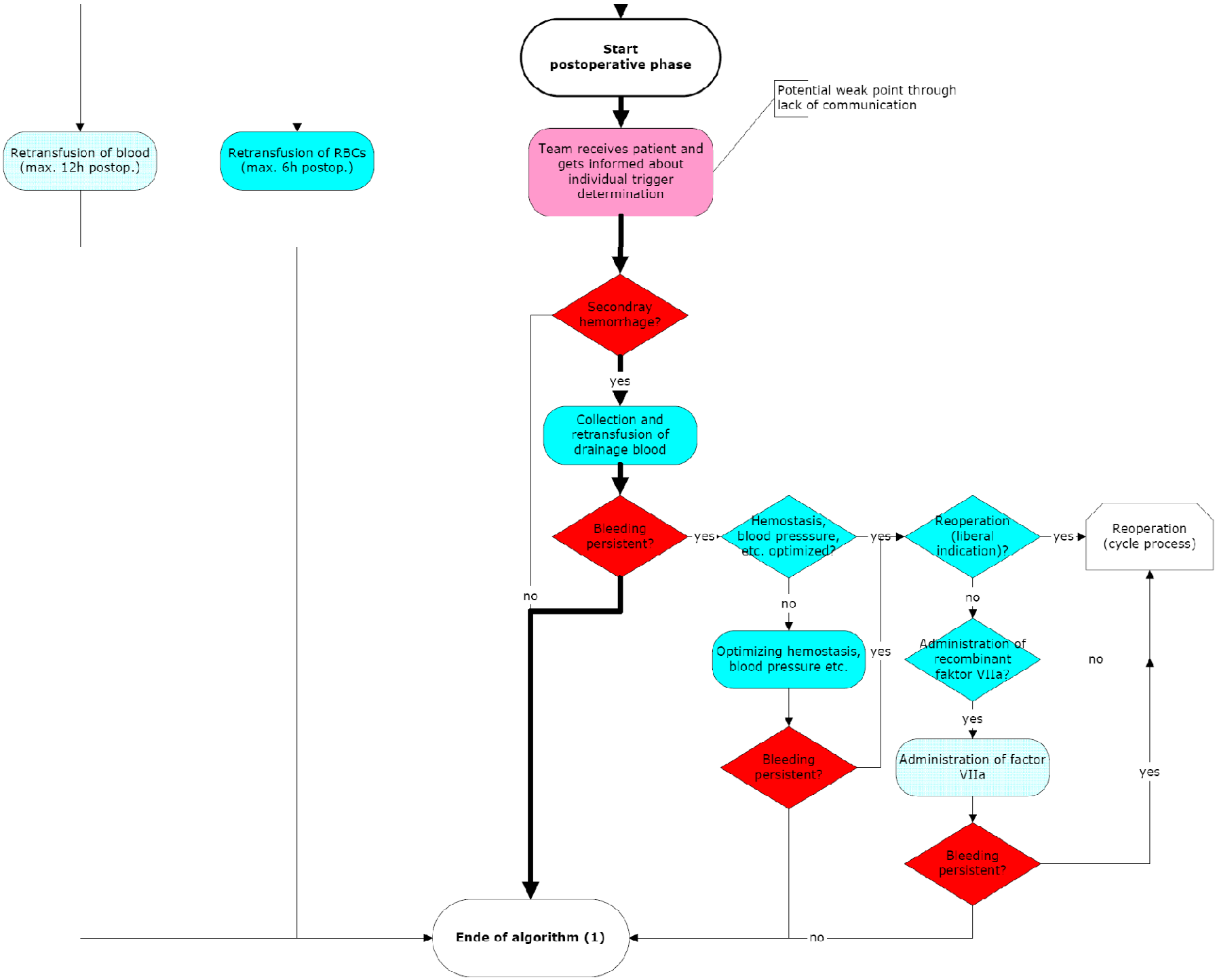
Outcomes at 30 Days and 60 Days

Variable	30-Day Period				60-Day Period			
	Liberal Strategy (N=1007)	Restrictive Strategy (N=1009)	Odds Ratio (99% CI)	Absolute Risk Difference (99% CI)	Liberal Strategy (N=1007)	Restrictive Strategy (N=1009)	Odds Ratio (95% CI)	Absolute Risk Difference (95% CI)
	no./total no.(%)			*percentage points*	*no./total no. (%)*			*percentage points*
Death or inability to walk independently	459/995 (46.1)	481/1000 (48.1)	0.92 (0.73 to 1.16)	−2.0 (−7.7 to 3.8)	351/998 (35.2)	347/1001 (34.7)	1.01 (0.84 to 1.22)	0.5 (−3.7 to 4.7)
Inability to walk independently	407/995 (40.9)	438/1000 (43.8)			275/998 (27.6)	281/1001 (28.1)		
Death	52/995 (5.2)	43/1000 (4.3)	1.23 (0.71 to 2.12)	0.9 (−1.5 to 3.4)	76/998 (7.6)	66/1001 (6.6)	1.17 (0.75 to 1.83)†	1.0 (−1.9 to 4.0)†
			P Value				P Value	
Residence			0.17				0.34	
Home or retirement home	457/994 (46.0)	425/999 (42.5)			617/996 (61.9)	603/1001 (60.2)		
Nursing home	135/994 (13.6)	161/999 (16.1)			137/996 (13.8)	161/1001 (16.1)		
Other	402/994 (40.4)	413/999 (41.3)			242/996 (24.3)	237/1001 (23.7)		
	score				*score*			
Function and symptom scales								
Lower-extremity physical ADL‡	7.3±4.0	7.4±3.9	0.72		5.1±4.2	5.1±4.3	0.85	
Instrumental ADL§	3.9±0.5	3.9±0.4	0.10		3.7±0.8	3.7±0.9	0.94	
FACIT-Fatigue scale¶	38.7±7.7	38.6±7.6	0.84		41.8±7.3	42.3±7.4	0.26	

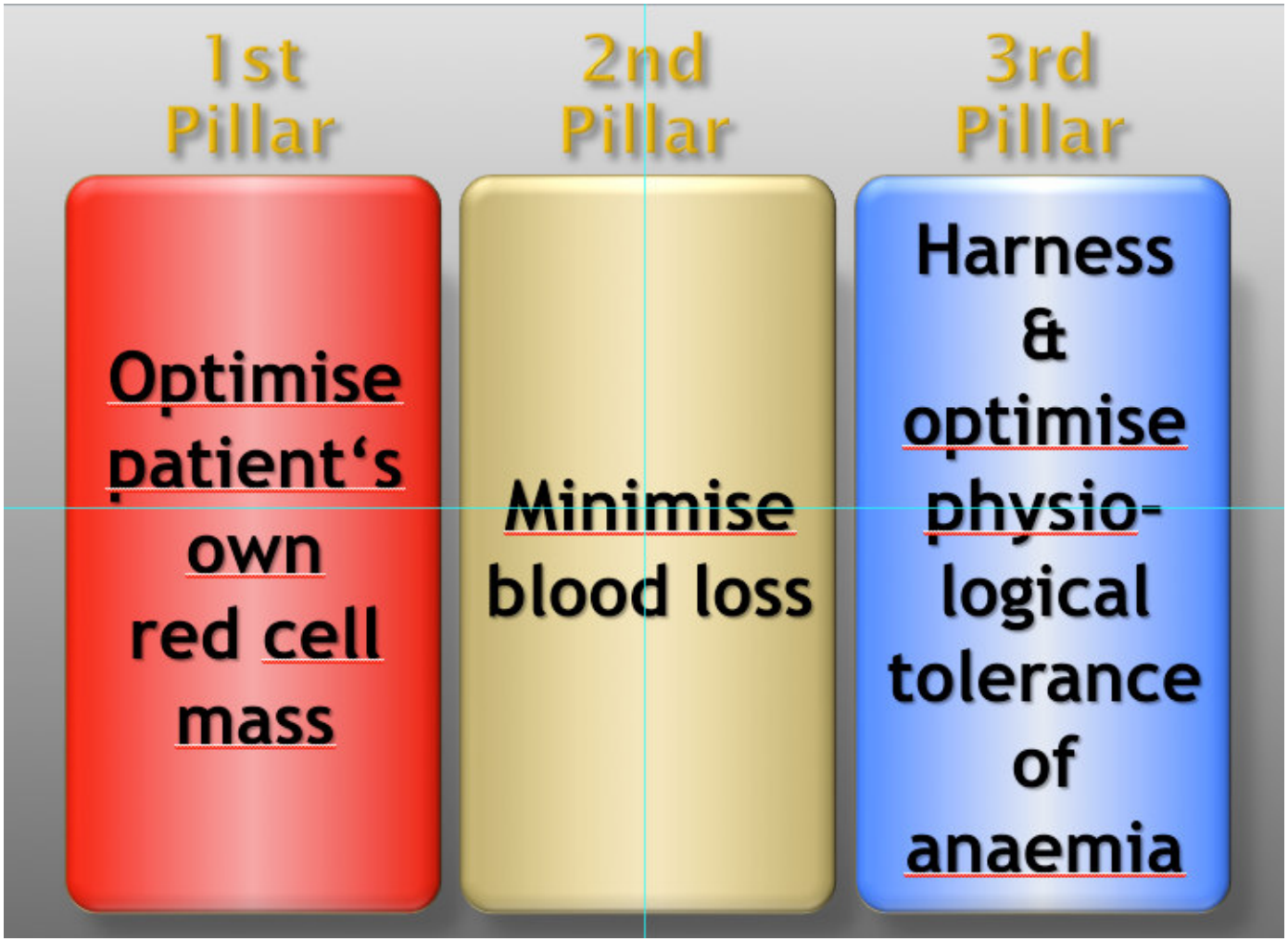
Effects of red blood cell transfusions on exercise tolerance and rehabilitation time after cardiac surgery.

- Two-hundred-seventeen patients who underwent cardiac surgery operations requiring packed red cells transfusions were studied during the rehabilitation stay.
- The exercise tolerance (6-min walk test) was not dependent on the number of packed red cells units transfused.
- Conversely, the length of stay in the rehabilitation hospital was independently associated (P=0.004) with the number of packed red cells transfused, with an increase of 0.6 days per each unit transfused.

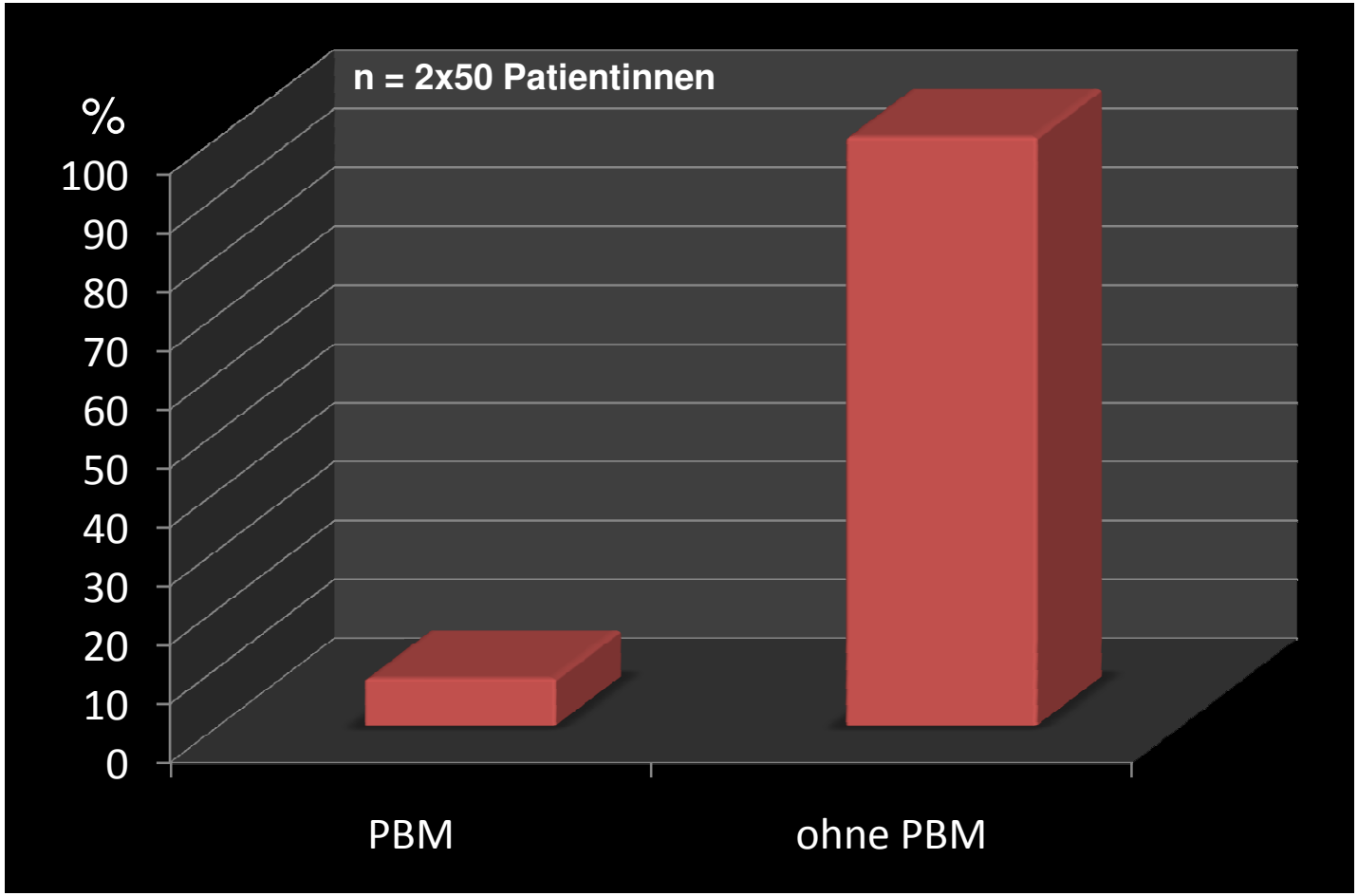
Ranucci et al: Transfus Apher Sci. 2011 Dec;45(3):299-303. Epub 2011 Oct 29


Retransfusion of blood (max. 12h postop.)
Retransfusion of RBCs (max. 6h postop.)
Start postoperative phase
Potential weak point through lack of communication
Team receives patient and gets informed about individual trigger determination
Secondray hemorrhage?
yes
Collection and retransfusion of drainage blood
Bleeding persistent?
yes
Hemostasis, blood presssure, etc. optimized?
yes
Reoperation (liberal indication)?
yes
Reoperation (cycle process)
no
no
Optimizing hemostasis, blood pressure etc.
yes
Administration of recombinant faktor VIIa?
no
yes
Bleeding persistent?
Administration of factor VIIa
yes
Bleeding persistent?
no
no
Ende of algorithm (1)

First Results



Retrospektiver Vergleich bei anämischen PatientInnen mit einseitigem Hüftgelenksersatz



Heschl et al: AIC 2011

Anemia and Patient Blood Management in Hip and Knee Surgery
A Systematic Review of the Literature

	Infection Rate (%)			Mean Length of Stay (days)			30-day Mortality (%)		
Reference	Active	Control	*P* Value	Active	Control	*P* Value	Active	Control	*P* Value
Moonen *et al.*[37]	2%	2%	NS						
Keating *et al.*[38]	7%	7%	NS						
Weber *et al.*[41]	9.4%	10.6%	NS		10.8	NS			
Canadian Study group[44]					11.7	NS			
Garcia *et al.*[39]				7.5	7.7	NS			
Garcia *et al.*[40]	12.5%	31.4%	0.016	15.3	15.0	NS	7.3%	15.0%	NS
Couvret *et al.*[42]				10.4	10.3	NS			
Cuenca *et al.*[34]				11	12	NS			
Cuenca *et al.*[35]	16.4%	33.3%	< 0.001	12.6	14.3	NS	5%	17%	NS

ASA = American Society of Anesthesiologists; Hb = hemoglobin; IU = International Units; LOS = length of stay; NA = not available; NS = nonsignificant; PAD = preoperative autologous donation; RCT = randomized controlled trial; rHuEPO = recombinant human erythropoietin; THA = total hip arthroplasty; TKA = total knee arthroplasty.

Spahn D.: Anesthesiology 2010; 113:482–95

ENGLEWOOD HOSPITAL AND MEDICAL CENTER

Study evaluating PBM Outcomes

The Impact of Blood Conservation on Outcomes in Cardiac Surgery: Is It Safe and Effective?

David M. Moskowitz, MD, Jock N. McCullough, MD, Aryeh Shander, MD, James J. Klein, MD, Carol A. Bodian, DrPH, Richard S. Goldweit, MD, and M. Arisan Ergin, MD

Department of Anesthesiology, Critical Care Medicine, Hyperbaric Medicine and Pain Management, Department of Cardiothoracic Surgery, and Division of Cardiology, Department of Internal Medicine, Englewood Hospital and Medical Center, Englewood, New Jersey; and Department of Anesthesiology, Division of Biostatistics, The Mount Sinai Hospital and Medical Center, New York, New York

Ann Thorac Surg 2010;90:451–9

propensity-score matched cohort of 586 pts from institutions without a PBMP

Isolated CABG includes elective & urgent and primary & redo procedures

The Impact of Blood Conservation on Outcomes in Cardiac Surgery: Is It Safe and Effective?

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Department of Anesthesiology, Critical Care Medicine, Hyperbaric Medicine and Pain Management, Department of Cardiothoracic Surgery, and Division of Cardiology, Department of Internal Medicine, Englewood Hospital and Medical Center, Englewood, New Jersey; and Department of Anesthesiology, Division of Biostatistics, The Mount Sinai Hospital and Medical Center, New York, New York

Ann Thorac Surg 2010;90:451–9

PBM strategies used:

1. Preop haemoglobin optimisation
2. Intraop ANH and Intra & Postop cell salvage
3. Meticulous surgical technique
4. Endovascular vein harvesting
5. Point-of-care coagulation testing
6. Targeted haemostatic therapy
7. Tolerance of perioperative anaemia (60 – 70 g/L depending on patient-specific physiology)

CABG Outcomes PBMP vs Non-PBMP

Outcome	PBMP cohort (n=586)	Non-PBMP cohort (n=586)	P-value
% Transfused	10.6%	42.5%	<0.0001
Mortality	0.8%	2.5%	0.02
Serious complication	11.1%	18.7%	0.0002

Moskowitz et al. The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective?
Ann Thorac Surg 2010;90:451-9

The Good News

More and more hospitals worldwide
start
to implement PBM
or comparable strategies