

Transfuzní trigger

- *aneb kolik hemoglobinu
potřebuje člověk?*

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no conflict of interest

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přehled

1. anémie
2. transfúzní trigger
3. doporučení
4. *elderly patients?*
5. kolik Hb potřebuje člověk?





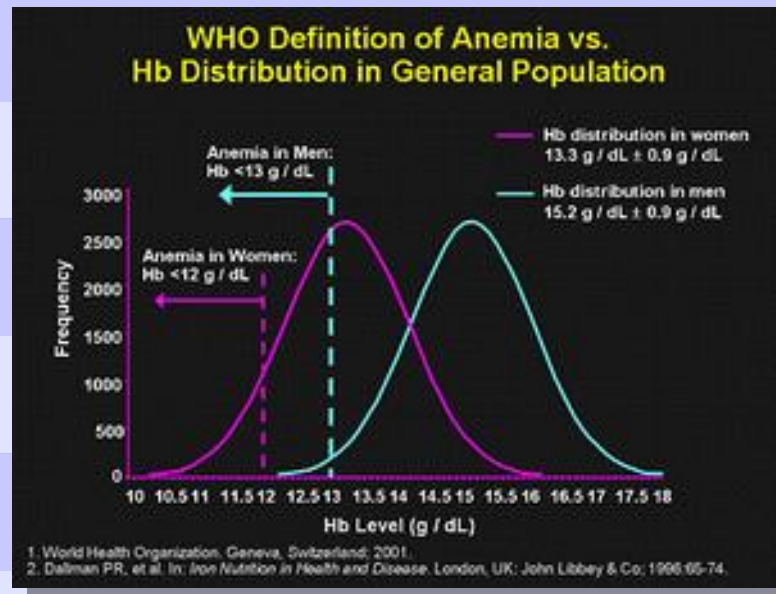
anémie



Anemia (WHO)

Hb level <13,0 g/dL in men

Hb level <12,0 g/dL in women



derived in the 1960s from

very small and low-quality studies

*WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES*

No. 405

NUTRITIONAL ANAEMIAS

**Report of a
WHO Scientific Group**

GENEVA

1968

3. CRITERIA FOR THE DIAGNOSIS OF ANAEMIA

In detecting and evaluating an anaemia problem in a community, reference standards are necessary, even though they may be somewhat arbitrary. The report² of the 1958 WHO Study Group recommended haemoglobin values below which anaemia could be considered to exist. These figures were chosen arbitrarily and it is still not possible to define normality precisely.³ However, more recent data⁴ indicate that the values given previously should be modified. It is recommended that, in future studies, anaemia should be considered to exist in those whose haemoglobin levels are lower than the figures given below (the values given are in g/100 ml of venous blood of persons residing at sea level):

children aged 6 months to 6 years :	11
children aged 6-14 years :	12
adult males :	13
adult females, nonpregnant :	12
adult females, pregnant :	11

⊕ Anemia Frequency

>60% of ICU patients upon admission
90% of ICU patients by day 3 in ICU
97% of ICU patients by day 8

Thomas J, Jensen L, Nahirniak S, Gibney RT. Anemia and blood transfusion practices in the critically ill: a prospective cohort review. *Heart Lung*. 2010;39(3):217-225.

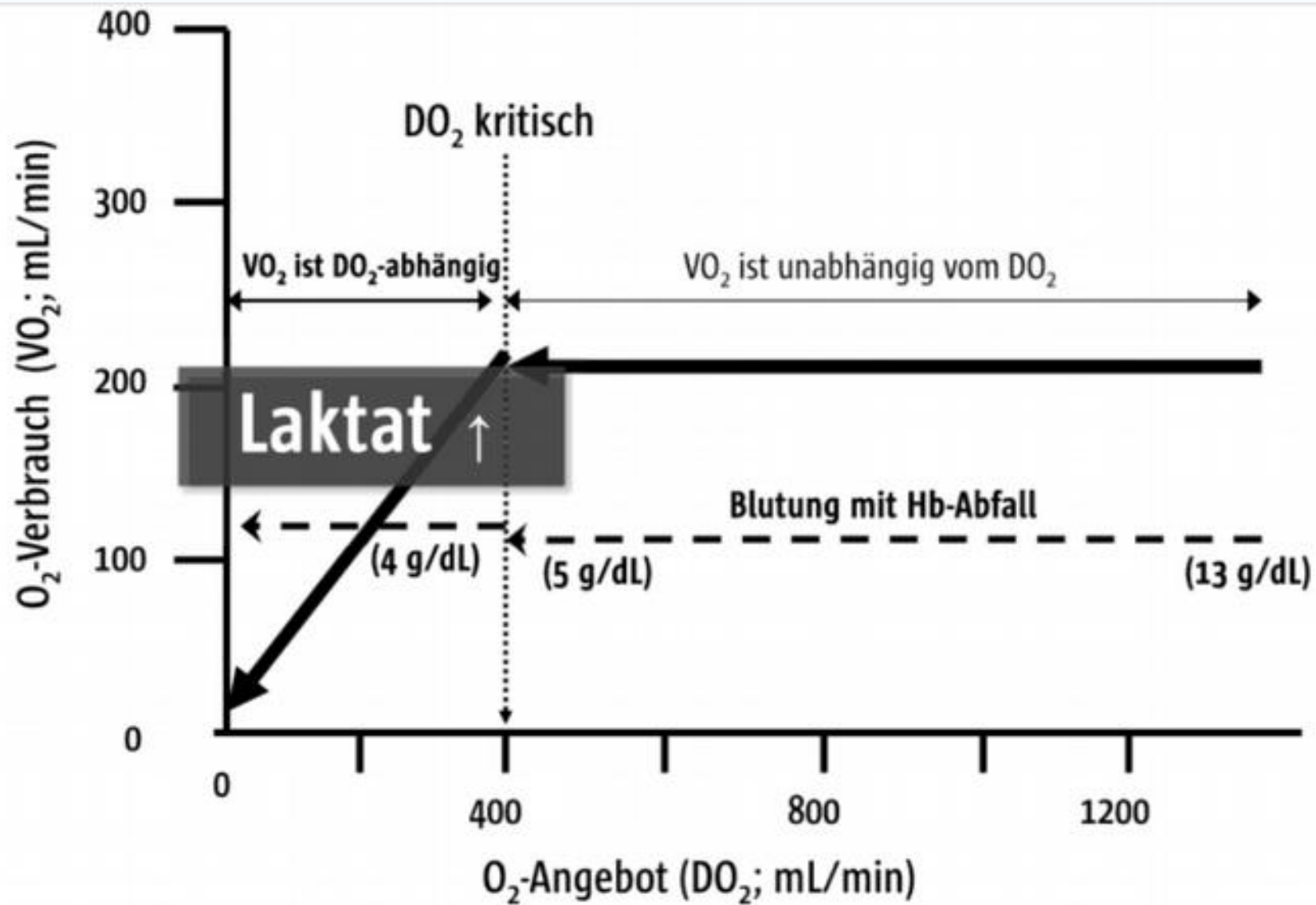
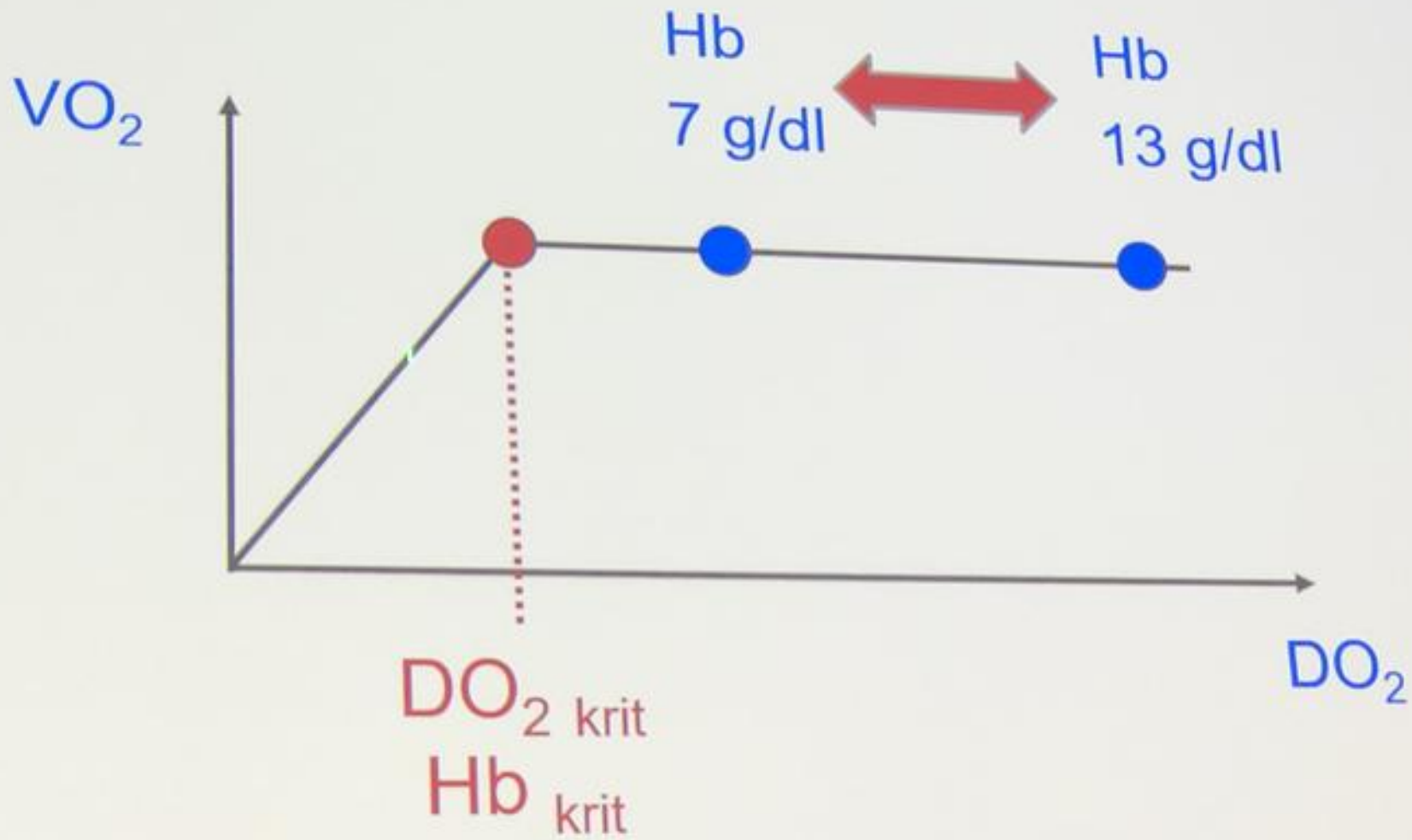


Abb. 1 Mismatch zwischen Sauerstoffangebot- und verbrauch



***transfúzní
trigger***

Transfúzní trigger

✓ ***Adams, Lundy*** **1942**

✓ ***Allen*** **1982**

✓ ***Hébert*** **1999**

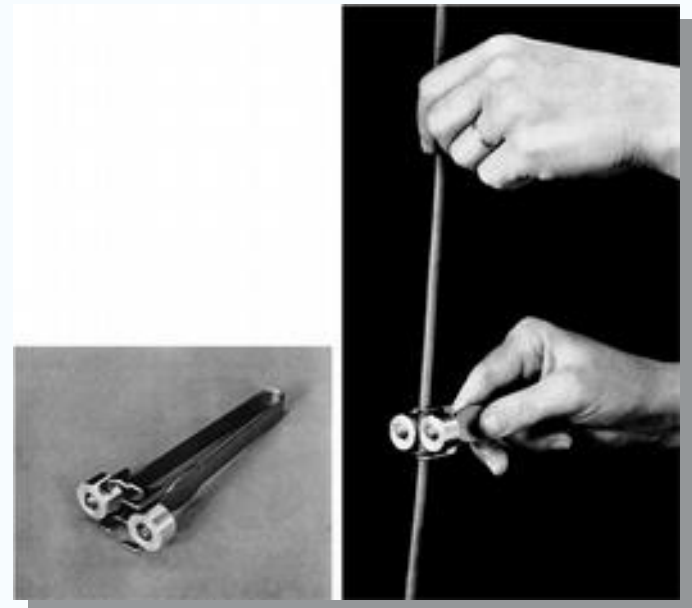
Adams RC, Lundy JS

Adams RC, Lundy JS: Anesthesia in cases of poor surgical risk. Some suggestions for decreasing the risk.

Surg Gynecol Obstet **1942**;64:1011-1019



Dr. John Silas Lundy, 1934



Lundy's rapid-infusing hand roller

Allenové pravidlo

Allen JB, Allen FB. The minimum acceptable level of hemoglobin.

Int Anesthesiol Clin **1982**; 20: 1-22



.... recommended that patients should be transfused when hemoglobin levels decreased below 10 g/dl or hematocrit values decreased below 30% (10/30 rule).



These recommendations were not based on randomized controlled trials, but rather on tradition....

Thus, this 10/30 rule, first proposed in the early 1940s and made even more popular in 1982 as a transfusion trigger, is not supported by good clinical evidence in the critically ill patient.

"It is unlikely that any level of hemoglobin can be used as an universal treshold for transfusion"

Goodnough LT et al, NEJM 340:438-444, 1999

" The decision to transfuse is too complex and important to be guided by a single number."

Vincent JL et al, Ann Intern Med. 157(1):49-58 , 2012

fyziologický transfúzní trigger

- známky globální tkáňové hypoxie z anémie
- známky regionální tkáňové hypoxie z anémie
- hemodynamická instabilita
- oxygen extraction (O_2ER) > 50%
- $S_{VC}O_2 < 50 \%$
- známky myokardiální ischemie
- vzestup laktátu, prohloubení BE
-

Benefits vs harms

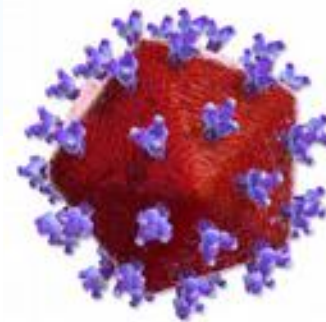


Risks of anemia

Low DO₂
Ischemia
Organ dysfunction
Multiple organ dysfunction

Risks of transfusion

Infectious
Non-infectious
Storage-lesion
Immuno-modulation



1st Pillar

Optimise
patient's own
red cell mass

2nd Pillar

Minimise
blood loss

3rd Pillar

Harness &
optimise
physiologic
reserve of
anemia

Multidisciplinary team approach

Three Pillars of Patient Blood Management

doporučení

JAMA | Special Communication

Patient Blood Management Recommendations From the 2018 Frankfurt Consensus Conference

Markus M. Mueller, MD; Hans Van Remoortel, PhD; Patrick Meybohm, MD, PhD; Kari Aranko, MD, PhD; Cécile Aubron, MD, PhD; Reinhard Burger, PhD; Jeffrey L. Carson, MD, PhD; Klaus Cichutek, PhD; Emmy De Buck, PhD; Dana Devine, PhD; Dean Fergusson, PhD; Gilles Folléa, MD, PhD; Craig French, MB, BS; Kathrine P. Frey, MD; Richard Gammon, MD; Jerrold H. Levy, MD; Michael F. Murphy, MD, MBBS; Yves Ozier, MD; Katerina Pavenski, MD; Cynthia So-Osman, MD, PhD; Pierre Tiberghien, MD, PhD; Jimmy Volmink, DPhil; Jonathan H. Waters, MD; Erica M. Wood, MB, BS; Erhard Seifried, MD, PhD; for the ICC PBM Frankfurt 2018 Group

Conclusions

The 2018 PBM international consensus defined the current status of the PBM evidence base for clinical practice and research purposes and established 10 clinical recommendations and 12 research recommendations for preoperative anemia, RBC transfusion thresholds for adults, and implementation of PBM programs. The relative paucity of strong evidence to answer many of the PICO questions supports the need for additional research and an international consensus for accepted definitions and hemoglobin thresholds, as well as clinically meaningful end points for multicenter trials.

RBC TRANSFUSION THRESHOLDS

Critically ill, clinically stable ICU patients (with septic shock):
Hb <7 g/dL

Cardiac surgery:
Hb <7.5 g/dL

Hip fracture with CV disease or risk factors:
Hb <8 g/dL

Acute GI bleeding (hemodynamically stable): Hb 7-8 g/dL and further research needed

Acute bleeding:
No further research on Hb thresholds*

Hematology - oncology:
Further research needed**

Coronary artery disease:
Further research needed

Non-cardiac/orthopedic surgery:
Further research needed

Brain injury:
Further research needed***

- Strong recommendation, moderate-quality evidence
- Conditional recommendation, moderate-quality evidence
- Conditional + research recommendation, low-quality evidence
- Research recommendation, low-quality evidence
- Research recommendation, very-low quality evidence
- No evidence found

✓ Laborübersicht

08.01.2020 11:53 - 15.01.2020 11:53

Variablen	Zeit	09.01.20	10.01.20	11.01.20	12.01.20	13.01.20	14.01.20	15.01.20
		05:53	05:42	05:43	05:51	05:38	05:36	05:45
Blutbild visite								
Leukozyten 3.6-10.2[G/l]		28.1	19.1	13.0	11.7	10.5	9.7	9.4
Erythrozyten 4.3-5.15[T/l]		3.31	3.13	3.24	3.32	3.21	3.22	3.26
Hämoglobin 13.5-15.4[g/dl]		8.9	8.3	8.7	8.9	8.5	8.5	8.7
Hämatokrit 39.5-45.5[%]		27.7	26.8	28.0	28.8	27.7	27.0	27.7
Thrombozyten 160-370[G/l]		191	182	168	178	171	178	214
Elektrolyte								
Serumnatrium 136-145[mmol/l]		144	151	153	147	142	143	140
Serumkalium 3.5-5.3[mmol/l]		4.4	4.1	5.2	4.3	4.0	4.5	4.3
Chlorid 98-107[mmol/l]		96	103	109	108	105	104	102
Serum Kalzium 2.2-2.7[mmol/l]		2.16	2.10	2.35	2.33	2.21	2.21	2.28
Magnesium 0.66-0.99[mmol/l]		0.93	0.93	0.91	0.80	0.79	0.82	0.87
Phosphor 0.81-1.45[mmol/l]		1.93	1.23	1.04	0.92	1.43	1.30	1.38

✓ Blutbild Verlauf

08.01.2020 12:00 - 15.01.2020 12:00

*

For patients with critical bleeding (major blood loss), Hb level is not the most important, or deciding, factor in transfusion management. It is difficult to perform studies in exsanguinating patients, and they have been excluded from most trials. Stopping the bleeding is the priority – refer to published national/international guidelines on management of massive hemorrhage requiring transfusion support.



RBC TRANSFUSION THRESHOLDS

Brain injury:
Further research
needed***

Critically ill, clinically
stable ICU patients
(with septic shock):
Hb <7 g/dL

Cardiac surgery:
Hb <7.5 g/dL

Non-cardiac/
orthopedic surgery:
Further research
needed

Hip fracture with CV
disease or risk factors:
Hb <8 g/dL

Coronary artery
disease:
Further research
needed

Acute GI bleeding
(hemodynamically
stable): Hb 7-8 g/dL
and further research
needed

Hematology -
oncology:

Acute bleeding:

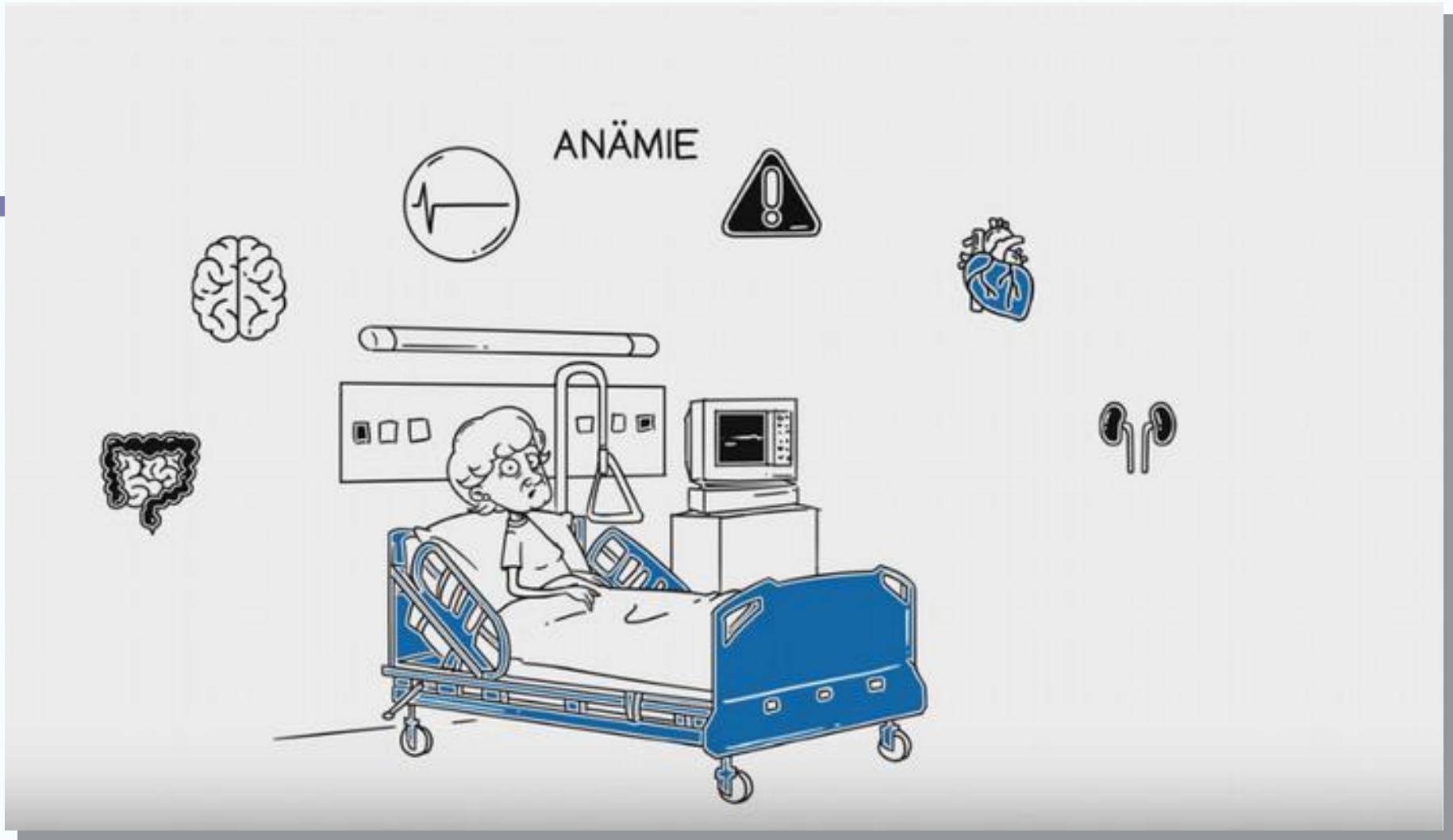
Patients with cerebral perfusion disorders or acute central nervous system injury (excluded: sickle cell disease)

***elderly
patients?***

LIBERAL-Studie

Liberal transfusion strategy to prevent mortality and anaemia-associated, ischemic events in elderly non-cardiac surgical patients (LIBERAL)

Die Studie wird durch die Deutsche Forschungsgemeinschaft gefördert.
Förderungskennzeichen ME 3559/3-1




LIBERAL trial

STUDY PROTOCOL

Open Access



Liberal transfusion strategy to prevent mortality and anaemia-associated, ischaemic events in elderly non-cardiac surgical patients – the study design of the LIBERAL-Trial

Patrick Meybohm^{1*} , Simone Lindau¹, Sascha Treskatsch², Roland Francis², Claudia Spies², Markus Velten³, Maria Wittmann³, Erdem Guerresir⁴, Christian Stoppe⁵, Ana Kowark⁶, Mark Coburn⁶, Sixten Selleng⁷, Marcel Baschin⁷, Gregor Jenichen⁷, Melanie Meersch⁸, Thomas Ermert⁸, Alexander Zarbock⁸, Peter Kranke⁹, Markus Kredel⁹, Antonia Helf⁹, Rita Laufenberg-Feldmann¹⁰, Marion Ferner¹⁰, Eva Wittenmeier¹⁰, Karl-Heinz Gürtler¹¹, Peter Kienbaum¹², Marcel Gama de Abreu¹³, Michael Sander¹⁴, Michael Bauer¹⁵, Timo Seyfried¹⁶, Matthias Gruenewald¹⁷, Suma Choorapoikayil¹, Markus M. Mueller¹⁸, Erhard Seifried¹⁸, Oana Brosteanu¹⁹, Holger Bogatsch¹⁹, Dirk Hasenclever²⁰, Kai Zacharowski¹ and LIBERAL Collaboration Group

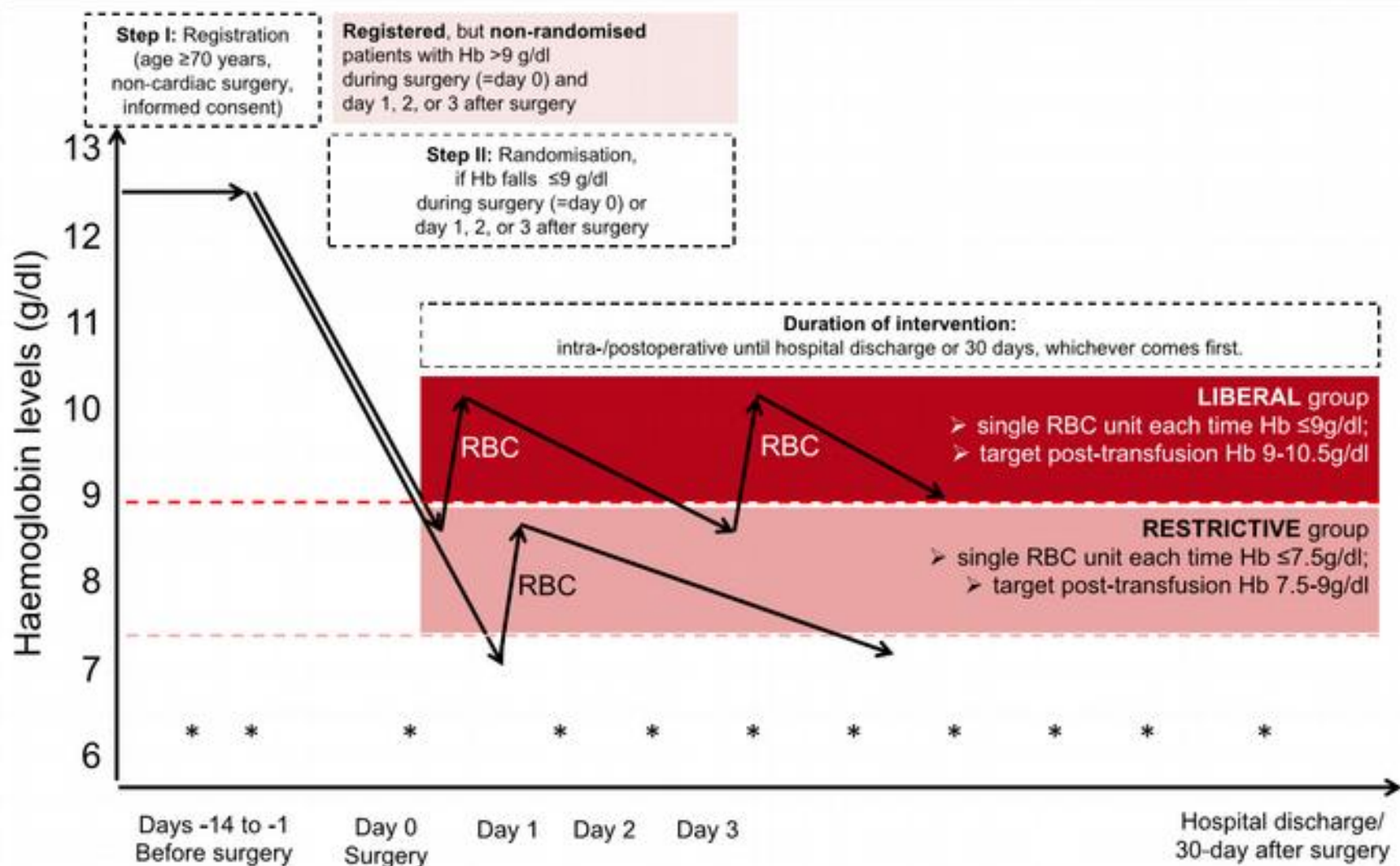


Fig. 2 Study intervention. Hb levels will be determined from blood samples (*) mainly as part of the patient's usual care at any time during or after surgery (up to 30 days after surgery; at least every 3 days), and after each transfused unit. Consenting patients will be registered (Step I) and will be randomised as soon as Hb falls ≤ 9 g/dl during surgery (=day 0) or day 1, 2, or 3 after surgery. Physicians will be instructed to transfuse RBC units each time Hb is lower the defined threshold and as soon as possible. The target post-transfusion Hb level needs to be reached within 24 h upon receipt of lab result at latest. The intervention per patient will be followed until hospital discharge or up to 30 days, whichever occurred first, comparable to recent large trials [5-7, 15]. In case of any massive or life-threatening bleeding, the single-unit policy should be paused

hemoglobin
< 5 g/dl?

Anaesthesist

<https://doi.org/10.1007/s00101-017-0402-5>

Eingegangen: 19. Juni 2017

Überarbeitet: 7. Dezember 2017

Angenommen: 10. Dezember 2017

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Perioperative Blutung bei einem Zeugen Jehovas

45 let, ♂, st.p. transplantace ledviny 2001

170 cm, 51 kg, AHT, KHK, anémie, anurie (IHD)

notářsky ověřené pacientovo přání:

- odmítání: EBR

- akceptace: TK, FFP, koagul. faktory

OP:

- rejekce transplantátu
- explantace



1.post OP:

- IHD, retroperitoneální hematom
- revize pro krvácení
- extubace, ad ICU

2.post OP:

- ad urologické oddělení, O₂ 2 l/min nosní brýle



Abb. 1 ▲ Hämoglobin- und Hämatokritwerte während des Krankenhausaufenthalts, Explantation am Tag 1, Revision am Tag 2



intraop:

FiO₂ 0,80

phenylephrin 0,5 µg/kg/min, noradrenalin 0,1 µg/kg/min

0,9% NaCl 850 ml

FFP 1200 ml

Fibrinogen 2 g, Prothrombin 600 IE, Tranexam 1g

(PT 68%, INR 1,26, fibrinogen 3,33 g/l)

postop:

Epoetin alfa[®] 10.000 IE s.c. 7 dní

Ferinject[®] 500 mg i.v. + Ferrograd Fol[®] 105mg p.o. 7 dní

TRANSFUSION

Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion

Jeffrey L. Carson, Helaine Noveck, Jesse A. Berlin, Steven A. Gould

First published: 24 July 2002 | <https://doi.org/10.1046/j.1537-2995.2002.00123.x> | Citations: 318

retrospective cohort study

patients who declined transfusions for religious reasons

300 pts with **Hb < 8 g/dL** postoperatively

primary outcome: in-hospital death within 30 days

secondary outcome: in-hospital 30-day morbidity

TRANSFUSION

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Hb 7,1-8,0 **0%** died

Hb 4,1-5,0 **34,4%** died

Hb 2,1-3,0 **91,0%** died

odds of **death** in patients with a postop. Hb of **≤ 8 g/dL** increased **2.5 times** for **each gram** decrease in Hb

hemoglobin
< 2 g/dl?

Anesthesiology

1997; 87:985-7

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Lippincott-Raven Publishers

Extreme Hemodilution Due to Massive Blood Loss in Tumor Surgery

Andreas Zollinger, M.D., Pablo Hager, M.D.,† Thomas Singer, M.D.,† Hans P. Friedl, M.D.,‡ Thomas Pasch, M.D.,§
Donat R. Spahn, M.D.||*

58 let, ♂, renal cell carcinoma, metastases L2-L4

nephrectomy 16 months ago

palliative stabilisation L2-L4 10 months ago

now: second palliative tumor debulking L2-L3

Anesthesiology

1997; 87:985-7

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Extreme Hemodilution Due to Massive Blood Loss in Tumor Surgery

Andreas Zollinger, M.D.,* Pablo Hager, M.D.,† Thomas Singer, M.D.,† Hans P. Friedl, M.D.,‡ Thomas Pasch, M.D.,§
Donat R. Spahn, M.D.||

ACCEPTING minimal intraoperative hemoglobin levels is an important concept to minimize allogeneic blood transfusions.¹⁻³ A fundamental question is the definition of the "critical hemoglobin value," which has not been defined at present time.^{3,4} We report a case of massive intraoperative blood loss, resulting in a nadir hemoglobin of 1.1 g/dl.

Case Report

The patient was a 58-yr-old man with renal cell carcinoma and

normal (table 1). The patient was turned into a prone position. Before incision, the patient received approximately 2 l of Ringer's lactate. Methylprednisolone was given as an initial bolus of 30 mg/kg followed by a continuous infusion of $5.4 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for 23 h.⁵ Mean arterial blood pressure during anesthesia initially was 70-80 mmHg with central venous pressures in the prone position of approximately 15 mmHg. Shortly after the start of the operation, massive bleeding from epidural blood vessels in close proximity to the tumor occurred, and 6 l of succinylated gelatin (Physiogel 4%, Braun Medical, Emmenbrücke, Switzerland), and 6 units of packed erythrocytes (PRBC) (1,800 ml) were transfused within 60 min. Dopamine ($2.3-5.7 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was also given. At this time, hemoglobin was 5.1 g/dl as determined by a CO-Oximeter (IL 482, Instrumentation Laboratory,



intraop:

massive bleeding

2 l Ringer, 6 l gelatine, 6 x EBR

dopamine 2-6 $\mu\text{g}/\text{kg}/\text{min}$

FiO₂ 1,0, 10 l gelatine

22 x EBR, 14 x FFP, 18 x TK

(PT 68%, INR 1,26, fibrinogen 3,33 g/l)

postop:

extubation 10 h postoperatively

transfer to a standard ward on postop day 2

CASE REPORTS

Table 1. Hemodynamics, Arterial Blood Gas Values, and Ventilatory Data Recorded in the Prone Position

Time	Temperature (°C)	MAP (mmHg)	CVP (mmHg)	pH	Pa _{CO₂} (mmHg)	Pa _{O₂} (mmHg)	HCO ₃ ⁻ (mmol/l)	BE (mmol/l)	Fi _{O₂}	Hb (g · dl ⁻¹)	%O _{2pl} (%)	Comment
09.25	36.5	65	15	7.42	36	151	23.3	-0.2	0.4	14.1	2.4	Mechanical ventilation
12.15	35.9	68	15	7.30	37	221	18.2	-6.7	0.5	5.1	8.8	—
12.45	34.0	60	15	7.20	35	431	13.8	-11.9	1.0	1.1	46.6	—
13.05	33.9	87	31	7.04	50	400	13.6	-15.3	1.0	7.7	10.4	After PRC transfusion only
13.12	33.9	82	32	7.07	50	407	14.5	-14.5	1.0	11.1	7.6	After PCR transfusion only
13.50	34.2	80	28	7.37	38	416	21.5	-2.8	1.0	10.1	8.4	After 200 mmol NaHCO ₃
15.30	35.0	61	ND	7.38	39	133	23.5	-0.8	0.5	10.1	2.9	After 100 mmol NaHCO ₃

MAP = mean arterial pressure; CVP = central venous pressure; Pa_{CO₂} = arterial CO₂ partial pressure; Pa_{O₂} = arterial O₂ partial pressure; HCO₃⁻ = bicarbonate concentration; BE = base excess; Fi_{O₂} = fraction of inspiratory O₂; Hb = hemoglobin concentration; %O_{2pl} = % O₂ dissolved in plasma; ND = not documented.

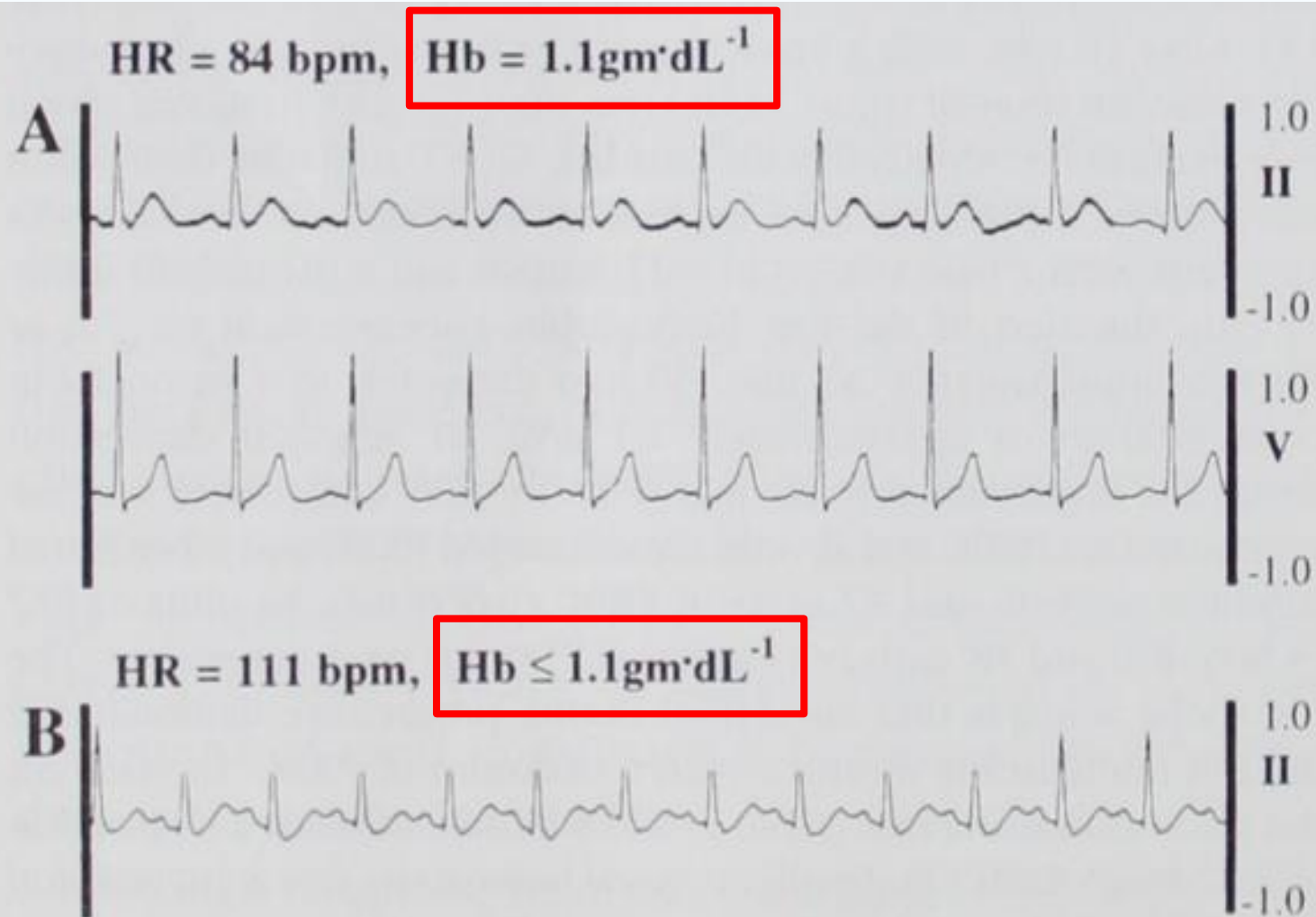


Fig. 1. (A) Electrocardiographic (ECG) recorded at a hemoglobin of 1.1 g/dl with a heart rate of 84 beats/min. Note there are no ST segment changes, neither in lead II nor in lead V5. **(B)** ECG (lead II) recorded at a hemoglobin of < 1.1 g/dl with a heart rate of 111 beats/min.

TABLE 22.1 RECOMMENDATIONS FOR RED BLOOD CELL TRANSFUSION
BASED ON HEMOGLOBIN [5–10]

Hgb < 7–8 g/dL—red blood cell transfusion is indicated

Hgb 8–10 g/dL—optimal transfusion threshold is unclear

Hgb > 10 g/dL—red blood cell transfusion is usually not necessary

Transfusion may be considered when the hemoglobin is between 8 and 10 g/dL, and there is ongoing or anticipated blood loss or there is clinical evidence of decreased tissue perfusion and oxygenation



...děkuji Vám za pozornost