

CHIRURGIA AD ELEVATO IMPATTO EMORRAGICO

Moderatori: Tiziano Crespi, Andrea De Gasperi

14.30 - 14.50	Il paziente a rischio emorragico: identificazione e gestione.
	Claudio Roscitano

- 14.50 15.10 Monitoraggio intraoperatorio in chirurgia ortopedica ad alto rischio emorragico: variazioni emodinamiche, perfusione d'organo e ripercussioni sul microcircolo. *Tiziano Crespi*
- 15.10 15.30 Il rimpiazzo di fluidi e terapia trasfusionale per la corretta perfusione d'organo. *Andrea De Gasperi*

· Conflitti di interesse: nessuno

• Lettura e spese viaggio per BBRAUN (disinfettanti) (2022)

Optimising organ perfusion in the high-risk surgical and critical care patient: a narrative review British Journ

British Journal of Anaesthesia, 123 (2): 170-176 (2019)

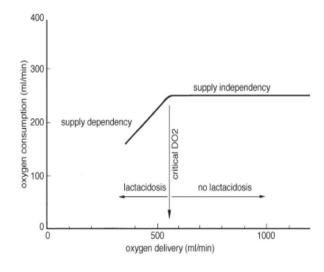
Thomas Parker, David Brealey, Alex Dyson and Mervyn Singer*

Tissue hypoxia is a major pathophysiological determinant of outcome in both high-risk surgical and sick ICU patients. An initial increase in oxygen consumption is characteristic of the stress response after a surgical insult. Failure to meet this increased demand, with consequent development of a conceptual tissue oxygen debt, is detrimental; an increased incidence of complications, organ failure, and death correlate with an increasing severity and duration of tissue hypoxia.²⁰

Perfusion indices revisited

Ahmed Hasanin^{1,2*}, Ahmed Mukhtar¹ and Heba Nassar¹

The balance between oxygen delivery (DO₂) and oxygen consumption (VO₂) considered the mainstay of understanding the concept of tissue perfusion and the development of organ dysfunction. In a steady state, the VO₂ constitutes only 25% of DO₂. In a shock state, the VO₂ increased out of proportion of DO₂ to the point that DO₂ falls below a critical threshold where the VO₂ is dependent on DO₂. Below that point, organ perfusion will be critically impaired and transition to anerobic metabolism will occur [2].



J. K. Wang & H. G. Klein

The balance between oxygen-delivery (DO2) and oxygen consumption (VQ) considered the mainstay of understanding the concept of tissue perfusion and the development of organ dysfunction. In a steady state, the VO2 constitutes only 25% of DO2. In a shock state, the VO2 increased out of proportion of DO2 to the point that DO2 falls below a critical threshold where the VO2 is dependent on DO2. Below that point, organ perfusion will be critically impaired and transition to anerobic metabolism will

Equations for oxygen transport and utilization



Oxygen delivery

Red blood cell transfusion in the treatment and management

of anaemia: the search for the elusive transfusion trigger

$$DO_2 = CO \times CaO_2$$

CO, cardiac output; Hb, haemoglobin; PaO₂, arterial oxygen pressure; PvO₂, venous oxygen pressure; SaO₂, arterial oxygen saturation; SvO₂, venous oxygen saturation.

No claim to original US government works © 2009 International Society of Blood Transfusion DOI: 10.1111/j.1423-0410.2009.01223.x

Red blood cell transfusion in the treatment and management of anaemia: the search for the elusive transfusion trigger

J. K. Wang & H. G. Klein

Table 1 Equations for oxygen transport and utilization

Arterial oxygen content $CaO_2 = (Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.003)$ Oxygen delivery $DO_2 = CO \times CaO_2$

CO, cardiac output; Hb, haemoglobin; PaO₂, arterial oxygen pressure; PvO₂, venous oxygen pressure; SaO₂, arterial oxygen saturation; SvO₂, venous oxygen saturation.

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Red blood cell transfusion in the treatment and management of anaemia: the search for the elusive transfusion trigger

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Table 1 Equations for oxygen transport and utilization

Arterial oxygen content

Oxygen delivery

Oxygen consumption

$$CaO_2 = (Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.003)$$

$$DO_2 = CO \times CaO_2$$

$$VO_2 = CO \times (CaO_2 - CvO_2)$$

$$VO_2 = CO \times ([Hb \times 1.34 \times (SaO_2 - SvO_2)]$$

+
$$[(PaO_2 - PvO_2) \times 0.003])$$

CO, cardiac output; Hb, haemoglobin; PaO₂, arterial oxygen pressure; PvO₂, venous oxygen pressure; SaO₂, arterial oxygen saturation; SvO₂, venous oxygen saturation.

Red blood cell transfusion in clinical practice

Harvey G Klein, Donat R Spahn, Jeffrey L Carson

A decrease in the haemoglobin concentration does not necessarily result in reduced DO₂ because cardiac output usually increases.

Arterial oxygen content $\begin{aligned} \text{CaO}_2 &= (\text{Hb} \times 1 \cdot 34 \times \text{SaO}_2) + (\text{PaO}_2 \times 0 \cdot 003) \\ \text{Oxygen delivery} & \text{DO}_2 &= \text{CO} \times \text{CaO}_2 \\ \text{Oxygen consumption} & \text{VO}_2 &= \text{CO} \times (\text{CaO}_2 - \text{CvO}_2) \\ \text{VO}_2 &= \text{CO} \times ([\text{Hb} \times 1 \cdot 34 \times (\text{SaO}_2 - \text{SvO}_2)] \\ &+ [(\text{PaO}_2 - \text{PvO}_2) \times 0 \cdot 003]) \end{aligned}$

Blood loss and concomitant crystalloid or colloid infusion results in normovolemic hemodilution, i.e. normovolemia with a decreased Hb concentration. Physiologically, cardiac output increases to compensate the lower CaO₂ at low Hb concentrations in order to maintain oxygen delivery. The increase in cardiac output is primarily due to an increase in stroke volume and inotropy and only secondarily due an increase in heart rate. O₂ extraction increases simultaneously favoring O₂ off-loading to the tissue.

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Red blood cell transfusion in the treatment and management of anaemia: the search for the elusive transfusion trigger

J. K. Wang & H. G. Klein

Table 1 Equations for oxygen transport and utilization

Arterial oxygen content	$CaO_2 = (Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.003)$
Oxygen delivery	$DO_2 = CO \times CaO_2$
Overgen consumption	$VO = CO \times (C_2O = C_2O)$

Oxygen consumption $VO_2 = CO \times (CaO_2 - CvO_2)$

$$VO_2 = CO \times ([Hb \times 1.34 \times (SaO_2 - SvO_2)]$$

$$+ [(PaO_2 - PvO_2) \times 0.003])$$

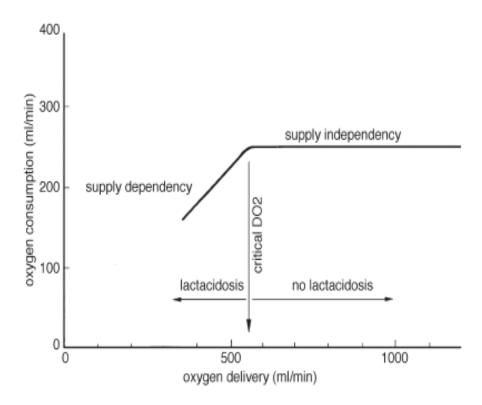
Oxygen extraction
$$EO_2 = VO_2/DO_2$$

CO, cardiac output; Hb, haemoglobin; PaO₂, arterial oxygen pressure; PvO₂, venous oxygen pressure; SaO₂, arterial oxygen saturation; SvO₂, venous oxygen saturation.

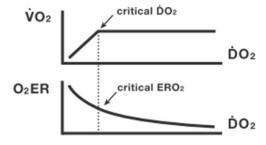
Transfus Med Hemother 2015;42:110–114 DOI: 10.1159/000381509 Received: December 17, 2014 Accepted: March 9, 2015 Published online: March 25, 2015

Evidence Base for Restrictive Transfusion Triggers in High-Risk Patients

Donat R. Spahn Gabriela H. Spahn Philipp Stein



Global oxygen consumption (VO₂) which describes the amount of oxygen consumed by the whole body per minute ranges under physiological conditions in a normal adult from 200 to 300 ml/min whereas DO₂ ranges from 800 to 1200 ml/min. The relationship VO₂/DO₂ defines the oxygen extraction ratio (O₂ER) which is thus in the range of 20 to 30%. A normal VO₂/DO₂-relationship is illustrated in Figure 1. It



Therefore, oxygen delivery depends critically on cardiac output, Hb concentration, and SaO₂. Hence tissue hypoxia (insufficient oxygen delivery) can be due to ischemia (reduction in cardiac output or blood supply), hypoxia (decrease of SaO₂), toxins (blocking Hb oxygen binding), and anemia.

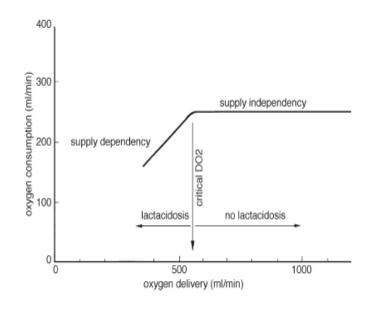
Venous Oxygen Saturation as a Physiologic Transfusion Trigger

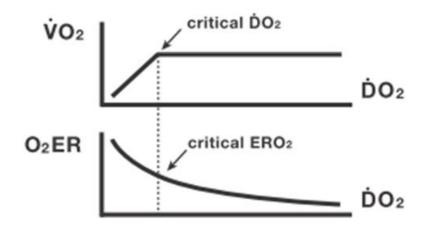
B. VALLET, E. ROBIN, and G. LEBUFFE

When DO₂ decreases, VO₂ is maintained (at least initially) by an increase in oxygen extraction (O₂ER) since O₂ER = VO₂/DO₂. As VO₂ \approx (SaO₂ – SvO₂) × (Hb × 1.34 × CO) and DO₂ \approx SaO₂ × Hb × 1.34 × CO, O₂ER and SvO₂ are thus linked by a simple equation: O₂ER \approx (SaO₂ – SvO₂)/SaO₂ or even simpler: O₂ER \approx 1 – SvO₂. Assuming SaO₂ = 1 [3], if SvO₂ is 40 %, then O₂ER is 60 %.

Because it integrates Hb, cardiac output, VO_2 and SaO_2 , the venous oxygen saturation therefore helps to assess the VO_2 -DO₂ relationship and tolerance to anemia during blood loss.

high or rising lactate concentration and a low or falling central venous haemoglobin oxygen saturation (measured from a central venous catheter) are clinically useful triggers that signal the need to increase oxygen delivery. When





Weiskopf

Human Cardiovascular and Metabolic Response to Acute, Severe Isovolemic Anemia

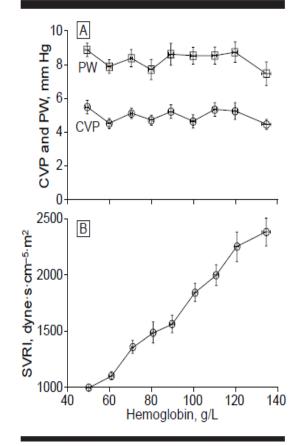
JAMA. 1998;279:217-221

Richard B. Weiskopf, MD; Maurene K. Viele, MD; John Feiner, MD; Scott Kelley, MD; Jeremy Lieberman, MD; Mariam Noorani; Jacqueline M. Leung, MD; Dennis M. Fisher, MD; William R. Murray, MD; Pearl Toy, MD; Mark A. Moore, MD

Table 2.—Response to Acute Isovolemic Anemia*

	Hemoglobin Range					
Variable	125-134 g/L (n=23)	45-54 g/L (n=28)				
SVRI, dyne·s·cm ⁻⁵ ·m ²	2372 (541)	1001 (176)				
HR, beats per minute	58 (11)	92 (12)				
SVI, mL/m ²	52 (9)	62 (8)				
CI, L/m ²	3.05 (0.69)	5.71 (0.87)				
TO ₂ , mL O ₂ ·kg ⁻¹ ·min ⁻¹	13.5 (2.7)	10.7 (2.0)				
S _v O ₂ , %	77.1 (3.3)	69.6 (5.6)				
VO ₂ , mL O ₂ ·kg ⁻¹ ·min ⁻¹	3.01 (0.42)	3.42 (0.54)				
Plasma lactate, mmol/L	0.77 (0.40)	0.62 (0.19)				
Arterial blood pH	7.395 (0.016)	7.445 (0.025)				
Base-excess, mEq/L	1.3 (1.5)	4.2 (2.2)				
Vo ₂ /To ₂	0.23 (0.03)	0.32 (0.04)				

*Data are mean (SD). Group sizes are less than 32 because not all subjects had a hemoglobin concentration within the range described. The statistical results provided in the text refer to all data for all subjects: all variables shown in this table, except plasma lactate concentration, changed significantly with decreasing hemoglobin concentration. SVRI indicates systemic vascular resistance index; HR, heart rate; SVI, stroke volume index; CI, cardiac index; To₂, oxygen transport; $S_{\nu}O_{2}$, mixed venous oxyhemoglobin saturation; and Vo_{2} , oxygen consumption.



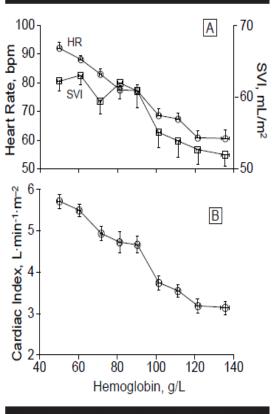


Figure 2.—Acute isovolemic reduction of hemoglo-

Weiskopf

Human Cardiovascular and Metabolic Response to Acute, Severe Isovolemic Anemia

JAMA. 1998;279:217-221

Richard B. Weiskopf, MD; Maurene K. Viele, MD; John Feiner, MD; Scott Kelley, MD; Jeremy Lieberman, MD; Mariam Noorani; Jacqueline M. Leung, MD; Dennis M. Fisher, MD; William R. Murray, MD; Pearl Toy, MD; Mark A. Moore, MD

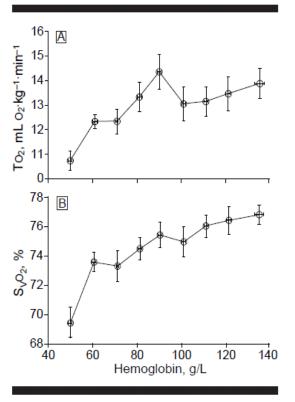


Figure 4.—Acute isovolemic reduction of hemoglobin concentration to 50 g/L decreased oxygen transport rate (To₂) (A; P<.001) and mixed venous oxyhemoglobin saturation (S_Vo₂)(B; P<.001). Data are gathered into groups by hemoglobin increments of 10 g/L and represented as mean (SE) (N=32).

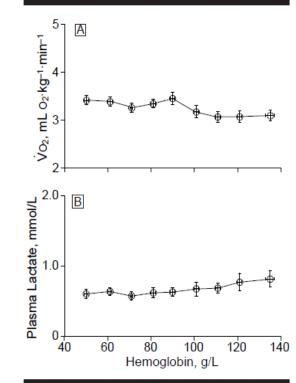


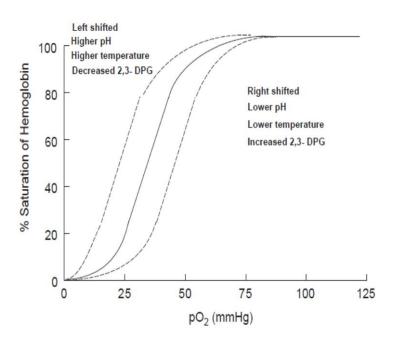
Figure 5.—Acute isovolemic reduction of hemoglobin concentration to 50 g/L increased oxygen consumption ($\dot{V}O_2$) (A; P<.001) but did not change plasma lactate concentration (B; P=.09). Data are gathered into groups by hemoglobin increments of 10 g/L and represented as mean (SE) (N=32).

Perfusion indices revisited

Ahmed Hasanin^{1,2*}, Ahmed Mukhtar¹ and Heba Nassar¹

CO₂ gap (P (v-a) CO₂) Background

The difference between PCO₂ in central venous blood and PCO₂ in arterial blood is known as central-venous-arterial CO₂ gap (P (v-a) CO₂). P (v-a) CO₂ has been considered as an indicator of the adequacy of venous blood flow to wash out CO₂ in peripheral tissues [23]. Elevated P (v-a) CO₂ (above 6 mmHg) occurs in cases of decreased systemic blood flow. Normalization of P (v-a) CO2 during resuscitation was associated with normalization of serum lactate [24].



Compensatory mechanisms in anemia

Oxygen delivery to tissue depends on the following factors: 1) level of hemoglobin (Hb) in the peripheral blood, 2) degree of saturation of Hb with oxygen, 3) Hb-oxygen dissociation curve, and 4) tension of oxygen in the tissue. When the Hb level decreases, certain compensatory mechanisms, such as changes in the Hb-oxygen dissociation curve and cardiac output, occur to maintain the oxygen delivery to the tissue (Fig. 1).

Emergency Transfusion for Acute Severe Anemia: A Calculated Risk

November 2010 • Volume 111 • Number 5

Richard B. Weiskopf, MD

n editorial about a case report is unusual, but no more so than the case reported by Dai et al. in this issue of the journal. They report survival, without

hemoglobin concentrations of approximately 8.5 and 10.5 g/dL.

Considering that the human mean fatal hemoglobin

hemoglobin concentration. Classic thought is that the amount of oxygen dissolved in plasma (the solubility of oxygen in plasma is 0.0031 mL/dL/mm Hg O₂) is too little to be of physiologic consequence. Whereas that may be so during ordinary circumstances with an F10₂ of 0.21, dissolved oxygen can be of substantial benefit during severe anemia, when the Fio₂ and Pao₂ are high. Hyperoxia reduces mortality of pigs subjected to acute severe anemia and maintained at their critical hemoglobin concentraWeiskopf and colleagues³⁹ made the interesting observation that the deterioration of neurocognitive function after isovolemic hemodilution from a hemoglobin of 12.7 \pm 1.0 to 5.7 \pm 0.3 was reversed by increasing PaO₂ from around 100 to 400 mm Hg. This value is equivalent to an increase in hemoglobin concentration of roughly 3 g/dL.²⁰ Similar results have been found in animal studies.³³

Weiskopf R, Viele M, Feiner J, et al. Human cardiovascular and metabolic response to acute, severe, isovolemic anemia. JAMA 1998;279:217–21.

Weiskopf R, Kramer J, Viele M, et al. Acute severe isovolemic anemia impairs cognitive function and memory in humans. Anesthesiology 2000;92(6): 1646–52.

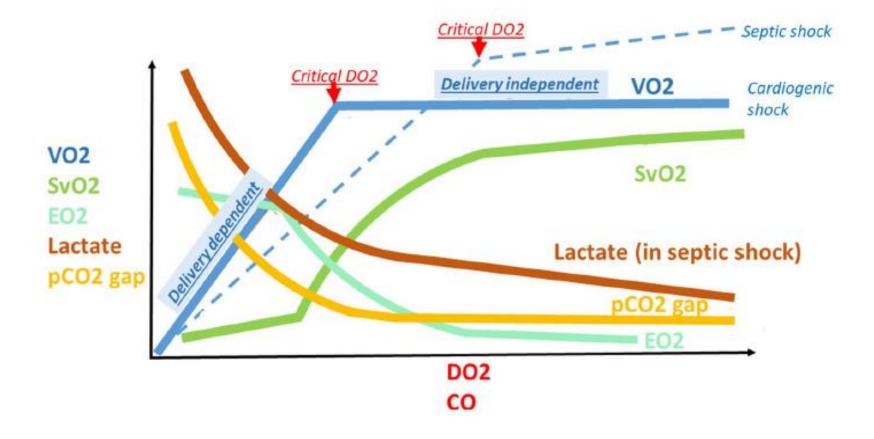
Weiskopf R, Feiner J, Hopf H, et al. Oxygen reverses deficits of cognitive function and memory and increased heart rate induced by acute severe isovolemic anemia. Anesthesiology 2002;96:871–7.

Vallet 2010

These observations and results clearly indicate that there is no 'universal' Hb threshold that could serve as a reliable transfusion trigger and that transfusion guidelines should take into account the patient's individual ability to tolerate and to compensate for the acute decrease in Hb concentration. Useful transfusion triggers should rather consider signs of inadequate tissue oxygenation that may occur at various hemoglobin concentrations depending on the patient's underlying disease(s) [18].

cardiac surgery [20]. The use of goal-directed erythrocyte transfusions should render the management of allogeneic red cell use more efficient and should help: 1) in saving blood and avoiding unwanted adverse effects; and 2) in promoting and optimizing the adequacy of this life-saving treatment [16]. These 'physiologic' transfusion triggers can be based on signs and symptoms of impaired global (lactate, SvO₂ or ScvO₂) or, even better, regional tissue (EKG ST-segment, DSST or P300 latency) oxygenation; they do, however, have to include two important simple hemodynamic targets: heart rate and MAP or systolic arterial pressure.

Fig. 2 Relationship between levels of the parameters of global oxygen (O₂) metabolism and O₂ delivery (DO₂) or cardiac output (CO). pCO₂ gap, central venous—arterial carbon dioxide difference; S_vO₂, mixed venous oxygen saturation; VO₂, oxygen consumption; EO₂, oxygen extraction



Clinical Practice Guidelines From the AABB Red Blood Cell Transfusion Thresholds and Storage

JAMA, 2016:316(19):2025-2035.

Jeffrey L. Carson, MD; Gordon Guyatt, MD; Nancy M. Heddle, MSc; Brenda J. Grossman, MD, MPH; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Terry Gernsheimer, MD; John B. Holcomb, MD; Lewis J. Kaplan, MD; Louis M. Katz, MD; Nikki Peterson, BA; Glenn Ramsey, MD; Sunil V. Rao, MD; John D. Roback, MD, PhD; Aryeh Shander, MD; Aaron A. R. Tobian, MD, PhD

Rationale for Recommendation

The AABB recommendation to use a hemoglobin transfusion threshold of 7 g/dL to 8 g/dL for most hospitalized adult patients who are hemodynamically stable rather than a hemoglobin transfusion threshold of 9 g/dL to 10 g/dL is based on consistent evidence from multiple large RCTs performed in various clinical settings in more than

As in the AABB's previous guideline, ²⁰ the committee chose not to recommend for or against a liberal or restrictive transfusion threshold in patients with acute coronary syndrome. There are 2 trials with a total of 154 patients that showed a trend toward a lower risk of death when the liberal transfusion threshold was used. ^{56,61} This finding is consistent with experimental studies in canines, ⁹⁰⁻⁹² in an observational study of patients undergoing surgery with underlying cardiovascular disease, ⁹³ and in the prespecified a priori hypothesis and direction in the 2 small trials. ^{56,61}

First Recommendation

Red blood cell transfusion is not indicated in hemodynamically stable adult hospitalized patients with a Hb level of 7 g/dL or more. This population includes critically ill patients.

Second Recommendation

Red blood cell transfusion is not indicated in patients undergoing orthopedic or cardiac surgery or in patients with underlying cardiovascular disease with a Hb level of 8 g/dL or more.

Thresholds for red blood cell transfusion in adults

Condition	Hemoglobin threshold for transfusion
Hospitalized patient	
Preexisting coronary artery disease	8 g/dL*
Acute coronary syndromes, including acute MI	8 to 10 g/dL ^{¶[2]}
ICU (hemodynamically stable)	7 g/dL*[3,4]
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL*[5,6]
Orthopedic surgery	8 g/dL*[1]
Cardiac surgery	7.5 g/dL* ^[7,8]
Ambulatory outpatient	
Oncology patient in treatment	7 to 8 g/dL [¶]
Palliative care setting	As needed for symptoms; hospice benefits may vary

These thresholds are not a substitute for direct assessment of the patient and clinical judgment. Refer to UpToDate topics on red blood cell transfusion and specific clinical settings for further details. Hospitalized patients with heart failure are an especially challenging case because there are no data from large randomized trials, and the improvement in oxygenation from transfusion must be balanced against the risks of worsening heart failure due to the volume of the transfused blood. The authors generally use a threshold of 7 to 8 g/dL in this population, erring on the side of a higher hemoglobin level in those who are expected to be able to better tolerate the volume load. In patients who do not fit into these clinical subgroups, we recommend that transfusion based on the location of care (ICU versus other) or the similarity of their underlying disease to those patient groups where data are available. In most cases, a 7 or 8 g/dL threshold is appropriate.

Indications and hemoglobin thresholds for red blood cell transfusion in the adult

Authors: Jeffrey L Carson, MD, Steven Kleinman, MD

Section Editor: Aaron Tobian, MD, PhD
Deputy Editor: Jennifer S Tirnauer, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Nov 2022. | This topic last updated: Aug 29, 2022.

MI: myocardial infarction; ICU: intensive care unit.

- * Based on results from clinical trial(s). Some experts may use different values. As an example, in individuals with gastrointestinal bleeding, it is often difficult, if not impossible, to estimate what the nadir hemoglobin will be, and some experts recommend a transfusion threshold of 8 g/dL^[6].
- \P There are no large clinical trials yet performed in this setting. These recommendations are based on the authors' opinions.

References:

- Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011; 365:2453.
- Ducrocq G, Gonzalez-Juanetey JR, Puymirat E, et al. Effect of a restrictive vs liberal blood transfusion strategy on major cardiovascular events among patients with acute myocardial infarction and anemia: The REALITY randomized clinical trial. JAMA 2021; 325:552.
- Hébert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 1999; 340:409.
- Lacroix J, Hebert PC, Hutchison JS, et al. Transfusion strategies for patients in pediatric intensive care units. N Engl J Med 2007; 356:1609.
- Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013; 368:11.
- Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: Guideline recommendations from the International Consensus Group. Ann Intern Med 2019; 171:805.
- Hajjar LA, Vincent JL, Galas FR, et al. Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. JAMA 2010; 304:1559.
- Mazer CD, Whitlock RP, Fergusson DA, et al. Restrictive or liberal red-cell transfusion for cardiac surgery. N Engl J Med 2017; 377:2133.

Thresholds for red blood cell transfusion in adults

Condition	Hemoglobin threshold for transfusion				
Symptomatic patient (eg, myocardial ischemia, hemodynamic instability)	10 g/dL*[1]				
Hospitalized patient					
Preexisting coronary artery disease	8 g/dL*				
Acute coronary syndromes, including acute MI	8 to 10 g/dL ^{¶[2]}				
ICU (hemodynamically stable)	7 g/dL* ^[3,4]				
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL* ^[5,6]				
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- Mazer CD, Whitlock RP, Fergusson DA, et al. Restrictive or liberal red-cell transfusion for cardiac surgery. N Engl J Med 2017; 377:2133.

Manish S. Patel, MD, Jeffrey L. Carson, MD

Summary Abstract

Rationale and Design for the Myocardial Ischemia and Transfusion (MINT) Randomized Clinical Trial

American Heart Journal

Available online 20 November 2022...

Jeffrey L. Carson, Maria Mori Brooks on-behalf-of-the-MINT-InvestigatorBackground

We will enroll 3500 patients with acute MI (type 1, 2, 4b or 4c) as defined by the Third Universal Definition of MI and a hemoglobin <10 g/dL at 144 centers in the United States, Canada, France, Brazil, New Zealand, and Australia. We randomly assign trial participants to a liberal or restrictive transfusion strategy. Participants assigned to the liberal strategy receive transfusion of RBCs sufficient to raise their hemoglobin to at least 10 g/dL. Participants assigned to the restrictive strategy are permitted to receive transfusion of RBCs if the hemoglobin falls below 8 g/dL or for persistent angina despite medical therapy. We will contact each participant at 30 days to assess clinical outcomes and at 180 days to ascertain vital status. The primary endpoint is a composite of all-cause death or recurrent MI through 30 days following randomization. Secondary endpoints include all-cause mortality at 30 days, recurrent adjudicated MI, and the composite outcome of all-cause mortality, nonfatal recurrent MI, ischemia driven unscheduled coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), or readmission to the hospital for ischemic cardiac diagnosis within 30 days. The trial will assess multiple tertiary endpoints.



AUTHORS' RECOMMENDATIONS

Numerous clinical trials have examined different transfusion thresholds in the perioperative and intensive care unit (ICU) settings and found that it is safe to withhold transfusion to 7 g/dL to 8 g/dL or for symptoms of anemia in the hemodynamically stable. Important outcomes such as myocardial infarction and functional recovery have been examined and have not been adversely impacted by using a restrictive transfusion approach. Patients with preexisting cardiovascular disease also tolerated lower transfusion thresholds. In patients with acute coronary syndrome, the optimal threshold is unknown, and these patients may be more vulnerable to the consequences of anemia. Thus it is necessary to rely on clinicaljudgment; a more liberal transfusion approach may be reasonable in this subgroup of patients. In preoperative patients, enough blood should be transfused to anticipate operative blood loss. Patients with symptoms of anemia should be transfused as needed. Ultimately, careful clinical assessment with thoughtful consideration of risks and benefits should guide the transfusion decision, not a specific hemoglobin concentration. No set of guidelines will apply to every patient.

orthopea 2022

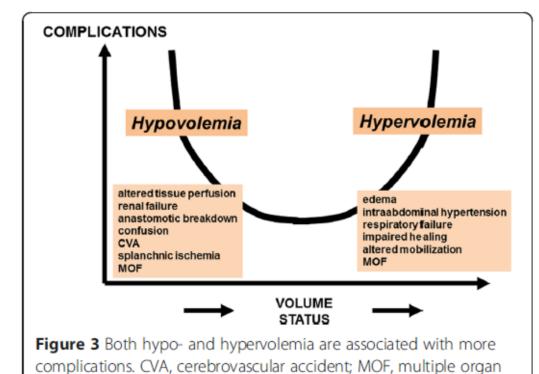
Editorial

M. C. Bellamy

Wet, dry or something else?

failure.

other fluid 1 fluid-1



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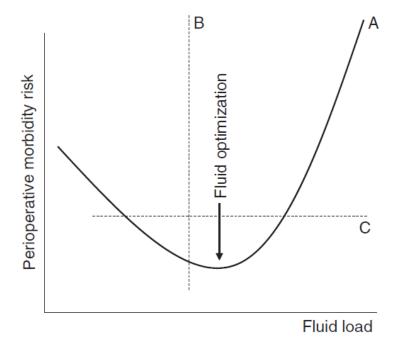
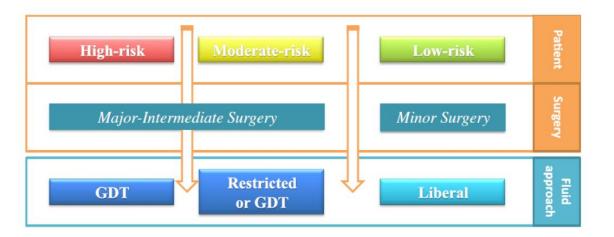
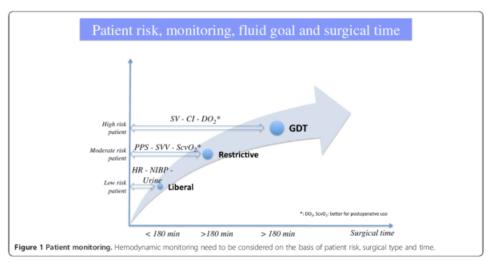


Fig 1 Curve A represents the hypothesized line of risk. Broken line B represents a division between patient groups in a 'wet *vs* dry' study. Broken line C represents a division between patient and groups in an 'optimized *vs* non-optimized' study



Liberal or restricted fluid administration; are we ready for a proposal of a restricted intraoperative BMC Anesthesiology 2014, 14:62 approach?

Giorgio Della Rocca, Luigi Vetrugno", Gabriella Tripi, Cristian Deana, Federico Barbariol and Livia Pompei



orthopea 2018

Perioperative cardiovascular monitoring of high-risk patients: a consensus of 12

Jean-Louis Vincent**, Paolo Pelosi*, Rupert Pearse*, Didier Payen*, Azriel Peref*, Andreas Hoeft*, Stefano Romagnoli*, V Marco Ranier⁸, Carole Ichal⁹, Patrice Forget¹⁰, Giorgio Della Rocca¹¹ and Andrew Rhodes¹²

Table 2 Options to optimize perioperative hemodynamic management in high-risk patients

Reactive

Correct hypotension, tachycardia.

Give fluids in the presence of suspected hypovolemia with increased pulse pressure variation (PPV), systolic pressure variation, stroke volume variation (SW), or pleth variability index (PVI).

Identify a reduction in cardiac output and react promptly with fluid

Identify a reduction in central venous oxygen saturation (ScvO₂) and react promptly with fluid challenge.

· Pro-active

Maintain arterial pressure and heart rate within acceptable ranges.

Maximize stroke volume.

Maintain PPV or SVV at less than 12% or PVI at less than 14%.

Maintain cardiac index (CI) or oxygen delivery (DO2) in a desired range (for example, CI of more than 4.5 L/minute/m2 and DO2 of more than 600 mL/minute/m²).

Maintain ScvO2 at more than 65%.

orthopea 2018

Critical Care (2015) 19:224

A GDT approach should be an "active" approach, the aim of which is not to "maximize" but to "optimize" the goal only in patients classified as fluid responders;

.... goals should be maintained for up to 6-8 postoperative hours.

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EVIEW Open Access

Clinical guidelines for perioperative hemodynamic management

of non cardiac surgical adult patients

REVIEW

Nicola BRIENZA 1 *, Giandomenico BIANCOFIORE 2, Franco CAVALIERE 3, Antonio CORCIONE 4, Andrea DE GASPERI 5, Rosanna C. DE ROSA 4, Roberto FUMAGALLI 6, Maria T. GIGLIO 1, Alessandro LOCATELLI 7, Ferdinando L. LORINI 8, Stefano ROMAGNOLI 9, Sabino SCOLLETTA 10, Luigi TRITAPEPE 11 Perioperative goal-directed therapy and postoperative complications in different kind of surgical procedures: an updated meta-analysis



Mariateresa Giglio¹*©, Giandomenico Biancofiore², Alberto Corriero³, Stefano Romagnoli⁴, Luigi Tritapepe⁵, Nicola Brienza⁶ and Filomena Puntillo⁶



use of large quantities of normal 0.9% saline is associated with an increased risk of hyperchloremic acidosis and possible harm. However, with the reduction in total IV fluid use in ERAS pathways, the significance of this is less clear. Balanced solutions such as Ringers lactate, Hartmann's solution or Plasmalyte avoid this problem. Post-

Study	BS Deaths	_	Sali Deaths							Risk Ratio with 95% CI	Weight (%)
Low	Deatils	Alive	Deatilis	Alive						WIGH 95/6 CI	(/0)
Young (2014) ³⁷	3	19	4	20						0.82 [0.21, 3.25]	2.0
Young (2015) ³⁸	87	1065	95	1015						0.88 [0.67, 1.17]	14.1
Semler (2017) ³⁴	87	433	83	371			-			0.92 [0.70, 1.20]	14.3
Semler (2018) ¹⁴	928	7014	975	6885			•			0.94 [0.87, 1.02]	18.4
Zampieri (2021) ³⁹	1381	3849	1439	3851			•			0.97 [0.91, 1.03]	18.6
Finfer (2021) ¹⁷	530	1903	530	1883			•			0.99 [0.89, 1.10]	18.1
Heterogeneity: T ² =0.	.00, I ² =12.	08%, H	² =1.14				4			0.96 [0.91, 1.01]	
Test of $\theta_i = \theta_i$: Q(5)=1	1.18, P=0.	95									
Non Low											
Waters (2001) ³⁶	1	32	1	32			-		>	1.00 [0.07, 15.33]	0.6
Verma (2016) ³⁵	5	28	2	32			\rightarrow	-	> 2	2.58 [0.54, 12.36]	1.6
Choosakul (2018) ³²	0	23	1	23	-	•			>	0.35 [0.01, 8.11]	0.4
Golla (2020) ³³	29	51	35	45			-	-		0.83 [0.57, 1.21]	11.5
Ramanan (2021) ²⁴	0	48	1	41	-	•			>	0.29 [0.01, 6.99]	0.4
Heterogeneity: T ² =0.	.24, I ² =24.	29%, H	² =1.32			-				0.93 [0.42, 2.10]	
Test of $\theta_i = \theta_j$: Q(4)=2	2.69, P=0.	51									
Overall							•			0.93 [0.76, 1.15]	
Heterogeneity: T ² =0.			² =8.65								
Test of $\theta_i = \theta_j$: Q(10)=											
Test of group differe	nces: Q _b (1	1)=0.00,	P=0.94								
				_	/8 1/4		/2 1	2	\neg		

Effect of Balanced Crystalloids Compared with Saline on 90-Day Mortality in C Patients by Risk of Bias.



Published January 18, 2022 NEJM Evid 2022; 1 (2) DOI: 10.1056/EVIDoa2100010

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults — A Systematic Review with Meta-Analysis

Naomi E. Hammond, Ph.D. ^{1,2}, Fernando G. Zampieri, Ph.D. ^{3,4}, Gian Luca Di Tanna, Ph.D. ⁵, Tessa Garside, Ph.D. ^{1,2}, Derick Adigbli, Ph.D. ^{1,2}, Alexandre B. Cavalcanti, M.D. Ph.D. ³, Flavia R. Machado, M.D., Ph.D. ⁶, Sharon Micallef, B.N. ¹, John Myburgh, Ph.D. ^{1,7}, Mahesh Ramanan, M.Med. ^{8,9}, Todd W. Rice, M.D. ¹⁰, Matthew W. Semler, M.D. ¹⁰, Paul J. Young, Ph.D. ^{1,1,1}, Balasubramanian Venkatesh, M.D. ^{1,1,3}, Simon Finfer, M.D. ^{1,1,4}, and Anthony Delaney, Ph.D. ^{1,2}

METHODS We systematically reviewed randomized clinical trials (RCTs) comparing the use of balanced crystalloids with saline in critically ill adults. The primary outcome was 90-day mortality after pooling data from low-risk-of-bias trials using a random-effects model. We also performed a Bayesian meta-analysis to describe the primary treatment effect in probability terms. Secondary outcomes included the incidence of acute kidney injury (AKI), new treatment with renal replacement therapy (RRT), and ventilator-free and vasopressor-free days to day 28.

RESULTS We identified 13 RCTs, comprising 35,884 participants. From six trials (34,450 participants) with a low risk of bias, the risk ratio (RR) for 90-day mortality with balanced crystalloids versus saline was 0.96 (95% confidence interval [CI], 0.91 to 1.01; $I^2 = 12.1\%$); using vague priors, the posterior probability that balanced crystalloids reduce mortality was 89.5%. The RRs of developing AKI and of being treated with RRT with balanced crystalloids versus saline were 0.96 (95% CI, 0.89 to 1.02) and 0.95 (95% CI, 0.81 to 1.11), respectively. Ventilator-free days (mean difference, 0.18 days; 95% CI, -0.45 to 0.81) and vasopressor-free days (mean difference, 0.19 days; 95% CI, -0.14 to 0.51) were similar between groups.

CONCLUSIONS The estimated effect of using balanced crystalloids versus saline in critically ill adults ranges from a 9% relative reduction to a 1% relative increase in the risk of death, with a high probability that the average effect of using balanced crystalloids is to reduce mortality. (PROSPERO number, CRD42021243399.)

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit The SPLIT Randomized Clinical Trial

JAMA. 2015;314(16):1701-1710. doi:10.1001/jama.2015.12334 Published online October 7, 2015. Corrected on November 3, 2015.

Paul Young, FCICM; Michael Bailey, PhD; Richard Beasley, DSc; Seton Henderson, FCICM; Diane Mackle, MN; Colin McArthur, FCICM; Shay McGuinness, FANZCA; Jan Mehrtens, RN; John Myburgh, PhD; Alex Psirides, FCICM; Sumeet Reddy, MBChB; Rinaldo Bellomo, FCICM; for the SPLIT Investigators and the ANZICS CTG

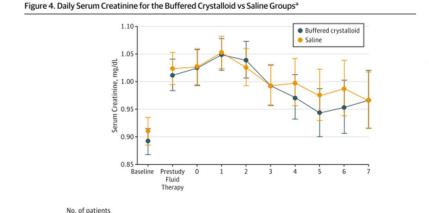
INTERVENTIONS Participating ICUs were assigned a masked study fluid, either saline or a buffered crystalloid, for alternating 7-week treatment blocks. Two ICUs commenced using 1 fluid and the other 2 commenced using the alternative fluid. Two crossovers occurred so that each ICU used each fluid twice over the 28 weeks of the study. The treating clinician determined the rate and frequency of fluid administration.

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit The SPLIT Randomized Clinical Trial

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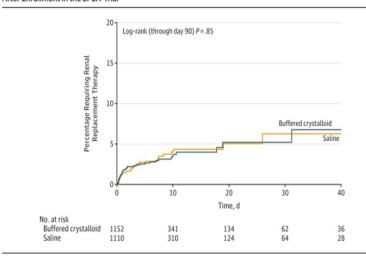
Buffered crystalloid

1133 847 481 992 478 297 200 144 112

947 442

a Day O is the day of enrollment. The baseline creatinine was defined as lowest serum creatinine in the hospital laboratory records for the 6 months prior to intensive care unit admission. The prestudy fluid therapy creatinine was defined as the most recent measurement of serum creatinine taken in the 24 hours prior to the commencement of study fluid. Censoring applied at hospital discharge or death. Serum creatinine values are approximated by a log-normal distribution so results are presented as geometric means. The error bars indicate 95% Cls.

Figure 2. Cumulative Incidence of Patients Requiring Renal Replacement Therapy Until Day 90 After Enrollment in the SPLIT Trial



Censoring applied at hospital discharge or death. The x-axis is truncated at 40 days because the number of participants still in follow-up beyond 40 days is small.

Buffered crystalloids or saline in the ICU — a SPLIT decision

Michael Joannidis and Lui G. Forni

NATURE REVIEWS | NEPHROLOGY

VOLUME 12 JANUARY 2016

during fluid therapy. Although some clinicians might choose to use buffered crystalloids in preference to 0.9% saline owing to the points outlined above, those who continue to use 0.9% saline can be reassured by the preliminary results of the SPLIT trial, together with the support of >150 years of clinical experience and the fact that >7,000 patients in ICUs have received 0.9% saline in other randomized controlled trials. Although the SPLIT trial might not bring both factions together, these data have certainly closed the gap by showing that administration of a relatively low volume of 0.9% saline to patients in the ICU with a relatively low severity of disease, does not elicit clinically significant harmazzi

Safety and efficacy of tetrastarches in surgery and trauma: a systematic review and meta-analysis of randomised controlled trials

Daniel Chappell^{1,*}, Philippe van der Linden², Javier Ripollés-Melchor^{3,4} and Michael F. M. James⁵

Methods: This systematic review and meta-analysis was registered at PROSPERO (CRD42018100379). We included 85 fully published articles from 1980 to June 2018 according to the protocol and three additional recent articles up to June 2020 in English, French, German, and Spanish reporting on prospective, randomised, and controlled clinical trials applying volume therapy with HES 130/0.4 or HES 130/0.42, including combinations with crystalloids, to patients undergoing surgery. Comparators were albumin, gelatin, and crystalloids only. A meta-analysis could not be performed for the two trauma studies as there was only one study that reported data on endpoints of interest.

Results: Surgical patients treated with HES had lower postoperative serum creatinine (P<0.001) and showed no differences in renal dysfunction, renal failure, or renal replacement therapy. Although there was practically no further difference in the colloids albumin or gelatin, the use of HES improved haemodynamic stability, reduced need for vasopressors (P<0.001), and decreased length of hospital stay (P<0.001) compared with the use of crystalloids alone Conclusions: HES was shown to be safe and efficacious in the perioperative setting. Results of the present meta-analysis suggest that when used with adequate indication, a combination of intravenous fluid therapy with crystalloids and volume replacement with HES as colloid has clinically beneficial effects over using crystalloids only.



Fluid Overload and Surgical Outcome

Another Piece in the Jigsaw

Dileep N. Lobo, DM, FRCS

In the 16th century, Philippus Theophrastus Aureolus Bombastus von Hohenheim, better known as Paracelsus, said, "Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy." The key to better intravenous fluid therapy is to give the right amount of the right fluid at the right time and to try and maintain the patient in a state of zero fluid balance as much as possible.

Annals of Surgery • Volume 249, Number 2, February 2009



Standards clinici per il Patient Blood Management e per il management della coagulazione e dell'emostasi nel perioperatorio Position paper della Società Italiana di Anestesia, Analgesia, Rianimazione e Terapia Intensiva (SIAARTI)

Cinnella G*, Pavesi Mo, De Gasperi AA, Ranucci MS, Mirabella L*

Clinical Standards for Patient Blood Management and Perioperative Hemostasis and Coagulation Management Position Paper of the Italian Society of Anesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI)

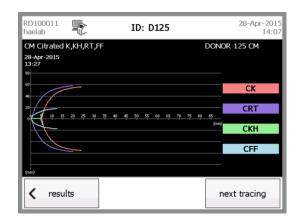
Gilda CINNELLA, Marco PAVESI, andrea DE GASPERI, Marco RANUCCI, Lucia MIRABELLA

Minerva Anestesiologica 2019 Feb 13 DOI: 10.23736/S0375-9393.19.12151-7

Dotazioni raccomandate per il monitoraggio della funzione emostatico-coagulativa ^{2,3,25}:

- **a. Tutti gli Ospedali devono avere** a disposizione un <u>monitoraggio standard</u> inclusivo di: PT / INR, aPTT, <u>conta piastrinica</u>, <u>fibrinogeno</u>.
- b. Gli Ospedali che trattano chirurgie a rischio molto alto dovrebbero avere:
 - la disponibilità di <u>monitoraggio point-of-care mediante test visco-elastici</u> (TEG/ROTEM). In questo ambito, esistono linee-guida, metanalisi e documenti di consenso che confermano l'efficacia di un monitoraggio basato su test viscoelastici nella riduzione delle necessità trasfusionali e nel contenimento del sanguinamento.
 - <u>test pre-operatori di funzione piastrinica</u> (Multiplate, VerifyNow, PlateletWorks, Platelet mapping) danno un valore aggiunto come previsto dalle linee guida SCA-STS, per definire la tempistica della chirurgia in pazienti sotto inibitori piastrinici del recettore P2Y12 (clopidogrel, prasugrel, ticagrelor)
- c. Ospedali con trauma center: Gli Ospedali che trattano routinariamente il trauma devono avere la disponibilità di monitoraggio point-of-care mediante test visco-elastici (TEG-ROTEM). In questo ambito, esistono documenti di consenso che confermano l'efficacia di un monitoraggio basato su test viscoelastici nella riduzione delle necessità trasfusionali e nel contenimento del sanguinamento
- d. . **Per tutte le altre tipologie di intervento ad alto rischio di sanguinamento** la disponibilità di test viscoelastici è consigliata. Peraltro, al di fuori della cardiochirurgia e della chirurgia epatica, le evidenze in letteratura sono scarse.

Viscoelastic devices 2019









Cartridge-based systems, which have been introduced by both manufacturers (TEG6S® and ROTEM sigma), will make these VCA much more widely available, particularly the more complicated assay modifications such as Fibtem® or PlateletMapping® (http://www.rotem.de/en/,

Viscoelastic methods of blood clotting assessment – a multidisciplinary review

REVIEW published: 14 September 2015 doi: 10.3389/fmed.2015.00062

Jan Benes 1,2*, Jan Zatloukal 1 and Jakub Kletecka

TABLE 2 | List and comparison of the most important variables describing the VEM-derived curve.

Variable	ROTEM [®]	TEG [®]
Clotting time (2 mm amplitude)	CT (clotting time) Normal (EXTEM) = 42-74 s Normal (INTEM) = 137-246 s	R (reaction time) Normal (citrate/ kaolin) = 3-8 min
Clot formation/ kinetics (20 mm amplitude)	CFT (clot formation time) Normal (EXTEM) = 46-148 s Normal (INTEM) = 40-100 s	K (kinetics) Normal (citrate/kaolin) = 1-3 min
Clot strengthening (angle of clot formation)	Alfa angle (slope of tangent at 2 mm amplitude) Normal (EXTEM) = 63-81° Normal (INTEM) = 71-82°	Alfa angle (slope between r and k points) Normal (citrate/kaolin) = 55-78°
Amplitude/ maximal firmness	MCF (maximum clot firmness) Normal (EXTEM) = 49-71 mm Normal (INTEM) = 52-72 mm Normal (FIBTEM) = 9-25 mm A5, A10, etc amplitudes at dedicated time-points predicting the final clot firmness	MA (maximal amplitude) Normal (citrate/ kaolin) = 51-69 mm
Lysis	LI30, LI60, ML	CL30, CL60, CL

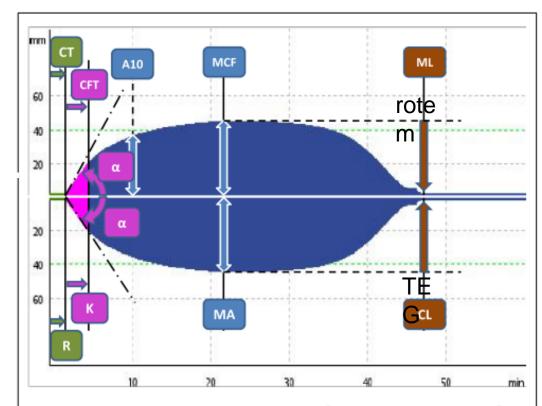


FIGURE 2 | The typical tracings of ROTEM® (upper panel) and TEG® devices (lower panel) with the most prominent parameters of both methods with the comparison (see also Table 2).



Viscoelastic methods of blood clotting assessment - a multidisciplinary review

published: 14 September 2015 doi: 10.3389/fmed.2015.00062

Jan Benes 1,2*, Jan Zatloukal 1 and Jakub Kletecka 1

ROTEM

TEG



Wikkelsø A, Wetterslev J, Møller AM, Afshari A.

Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding.

Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD007871.

DOI: 10.1002/14651858.CD007871.pub3.

Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding (Review)

Wikkelsø A, Wetterslev J, Møller AM, Afshari A

statistically significant effect of TEG or ROTEM compared to any comparison on the proportion of participants transfused with pooled red blood cells (PRBCs) (RR 0.86, 95% CI 0.79 to 0.94; I² = 0%, 10 studies, 832 participants, low quality of evidence), fresh frozen plasma (FFP) (RR 0.57, 95% CI 0.33 to 0.96; I² = 86%, 8 studies, 761 participants, low quality of evidence), platelets (RR 0.73, 95% CI 0.60 to 0.88; I² = 0%, 10 studies, 832 participants, low quality of evidence), and overall haemostatic transfusion with FFP or platelets (low quality of evidence). Meta-analyses also showed fewer participants with dialysis-dependent renal failure.

We found no difference in the proportion needing surgical reinterventions (RR 0.75, 95% CI 0.50 to 1.10; $I^2 = 0\%$, 9 st low quality of evidence) and excessive bleeding events or massive transfusion (RR 0.38, 95% CI 0.38 to 1.77; $I^2 = 349$ ies, 280 participants, low quality of evidence). The planned subgroup analyses failed to show any significant differences.

We graded the quality of evidence as low based on the high risk of bias in the studies, large heterogeneity, low number of events, imprecision, and indirectness. TSA indicates that only 54% of required information size has been reached so far in regards to mortality, while there may be evidence of benefit for transfusion outcomes. Overall, evaluated outcomes were consistent with a benefit in favour of a TEG-or ROTEM-guided transfusion in bleeding patients.

Authors' conclusions

There is growing evidence that application of TEG- or ROTEM-guided transfusion strategies may reduce the need for blood products, and improve morbidity in patients with bleeding. However, these results are primarily based on trials of elective cardiac surgery involving cardiopulmonary bypass, and the level of evidence remains low. Further evaluation of TEG- or ROTEM-guided transfusion in acute settings and other patient categories in low risk of bias studies is needed.

Drinker's guide to viscoelastic testing

