# Patient Blood Management

PATIENT BLOOD MANAGEMENT
ASST OVEST MILANESE

Presidente del Convegno
Ivo Beverina

Comitato Scientifico
Bruno Brando
Erika Borotto
Chiara Novelli

## dalla teoria alla pratica

# Hemoglobin -guided versus clinically-guided transfusion

Andrea De Gasperi

- Grants for lectures and partecipations to Advisory Boards from

  - Aferetica
  - Astellas
  - Fresenius
  - Edwards
  - Gilead
  - Grifols
  - Kedrion
  - MSD
  - Novartis
  - Pfizer
  - Thermofisher

| Ministero della Salute<br>*Istituto Superiore di Sanità*<br>*Centro Nazionale Sangue* | **LINEE GUIDA PER IL PROGRAMMA DI PATIENT BLOOD MANAGEMENT** | **LG CNS 05**<br>**Rev. 0**<br>**27.10.2016** |
|---|---|---|

**Considerato** che il Patient Blood Management si prefigge l'obbiettivo di prevenire o ridurre in modo significativo l'utilizzo degli emocomponenti e dei medicinali plasmaderivati, mediante i cosiddetti "tre pilastri del PBM": I) ottimizzare l'eritropoiesi del paziente; II) ridurre al minimo il sanguinamento; III) sfruttare e ottimizzare la riserva fisiologica individuale per la tolleranza all'anemia;

| | ***Raccomandazioni da adottare nel periodo pre-operatorio, intra-operatorio e post-operatorio*** |
|---|---|
| 3 | La soglia trasfusionale da adottare per la terapia con concentrati eritrocitari (omologhi o autologhi) in altre categorie di pazienti è stabilita in collaborazione con un esperto di medicina trasfusionale. |

# Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care*

Lena M. Napolitano, MD; Stanley Kurek, DO; Fred A. Luchette, MD; Howard L. Corwin, MD;

The efficacy of RBC transfusion in hemodynamically stable trauma and critically ill patients with anemia has not been demonstrated in most clinical settings. Historically, the decision to transfuse has been guided by an Hb concentration, "transfusion trigger." A

*Vox Sanguinis* (2010) **98**, 2–11

REVIEW


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

The historical and empirical '10/30 rule', which has biased many decades of transfusion practice, was first proposed by Adams and Lundy in 1942 as one of many perioperative suggestions ai[8] ving outcome in surgical patients with poor anaesthesia risk [8]. Too often the 'rule' has been cited inappropriately and applied too broadly.

8 Adam RC, Lundy JS: Anesthesia in cases of poor risk. Some suggestions for decreasing the risk. *Surg Gynecol Obstet* 1942; **74**:1011–1101

JAMA | Special Communication

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

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

*JAMA*. 2016;316(19):2025-2035.

## First Recommendation

The AABB recommends a restrictive RBC transfusion threshold in which the transfusion is not indicated until the hemoglobin level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients, rather than a liberal threshold when the hemoglobin level is 10 g/dL (strong recommendation, moderate quality evidence). For patients undergoing orthopedic surgery or cardiac surgery and those with preexisting cardiovascular disease, the AABB recommends a restrictive RBC transfusion threshold (hemoglobin level of 8 g/dL; strong recommendation, moderate quality evidence). The restrictive hemoglobin transfusion threshold of 7 g/dL is likely comparable with 8 g/dL, but RCT evidence is not available for all patient

| Source | Transfusion Threshold No. of Deaths | Transfusion Threshold Total No. | Transfusion Threshold No. of Deaths | Transfusion Threshold Total No. | RR (95% CI) | Weight, % |
|---|---|---|---|---|---|---|
| **Restrictive threshold, hemoglobin <8 to 9 g/dL** | | | | | | |
| Lotke et al,[75] 1999 | 0 | 62 | 0 | 65 | Not estimable | |
| Blair et al,[53] 1986 | 0 | 26 | 2 | 24 | 0.19 (0.01-3.67) | 0.4 |
| Foss et al,[63] 2009 | 5 | 60 | 0 | 60 | 11.00 (0.62-194.63) | 0.4 |
| Carson et al,[58] 1998 | 1 | 42 | 1 | 42 | 1.00 (0.06-15.47) | 0.4 |
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| Cooper et al,[61] 2011 | 2 | 23 | 1 | 21 | 1.83 (0.18-18.70) | 0.6 |
| Carson et al,[56] 2013 | 7 | 55 | 1 | 55 | 7.00 (0.89-55.01) | 0.7 |
| Parker,[78] 2013 | 5 | 100 | 3 | 100 | 1.67 (0.41-6.79) | 1.5 |
| Bracey et al,[54] 1999 | 3 | 215 | 6 | 222 | 0.52 (0.13-2.04) | 1.6 |
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| Jairath et al,[72] 2015 | 14 | 257 | 25 | 382 | 0.83 (0.44-1.57) | 5.8 |
| Carson et al,[60] 2011 | 43 | 1009 | 52 | 1007 | 0.83 (0.56-1.22) | 10.5 |
| Subtotal | 121 | 2321 | 122 | 2451 | 1.05 (0.78-1.40) | 34.2 |
| Heterogeneity: $\tau^2 = 0.02$; $\chi^2_{12} = 13.14$; $P = .36$; $I^2 = 9\%$ | | | | | | |
| Tests for overall effect: $z$ score = 0.31; $P = .76$ | | | | | | |
| **Restrictive threshold, hemoglobin <7 g/dL** | | | | | | |
| DeZern et al,[87] 2016 | 1 | 59 | 2 | 30 | 0.25 (0.02-2.69) | 0.6 |
| Hébert et al,[70] 1995 | 8 | 33 | 9 | 36 | 0.97 (0.42-2.22) | 3.8 |
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| Murphy et al,[76] 2015 | 26 | 1000 | 19 | 1003 | 1.37 (0.76-2.46) | 6.5 |
| Villanueva et al,[84] 2013 | 19 | 416 | 34 | 417 | 0.56 (0.32-0.97) | 7.2 |
| Hébert et al,[69] 1999 | 78 | 418 | 98 | 420 | 0.80 (0.61-1.04) | 14.7 |
| Holst et al,[71] 2014 | 168 | 502 | 175 | 496 | 0.95 (0.80-1.13) | 18.0 |
| Subtotal | 349 | 2900 | 375 | 2865 | 0.94 (0.74-1.19) | 65.8 |
| Heterogeneity: $\tau^2 = 0.05$; $\chi^2_8 = 16.09$; $P = .04$; $I^2 = 50\%$ | | | | | | |
| Tests for overall effect: $z$ score = 0.53; $P = .59$ | | | | | | |
| **Overall** | 470 | 5221 | 497 | 5316 | 0.97 (0.81-1.16) | 100 |
| Heterogeneity: $\tau^2 = 0.04$; $\chi^2_{21} = 29.75$; $P = .10$; $I^2 = 29\%$ | | | | | | |
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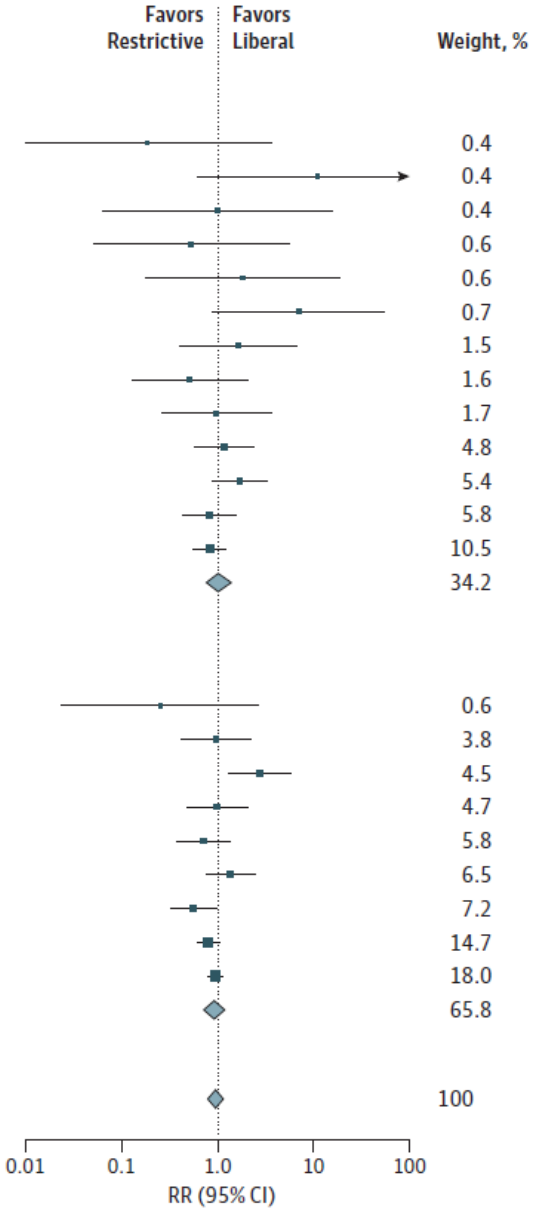

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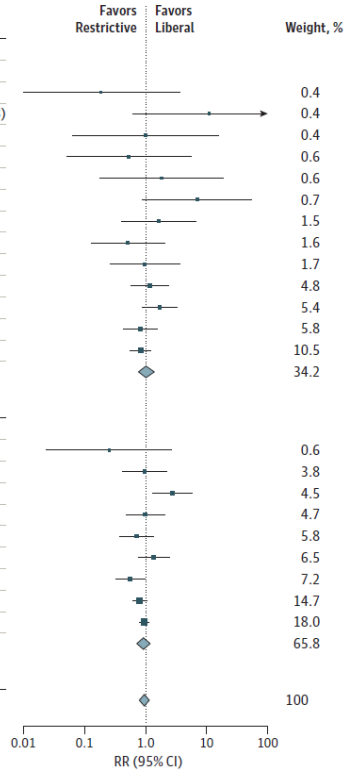


*JAMA*. 2016;316(19):2025-2035.

As in the AABB's previous guideline,[28] 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] However, small RCTs are known

*JAMA*. 2016;316(19):2025-2035.

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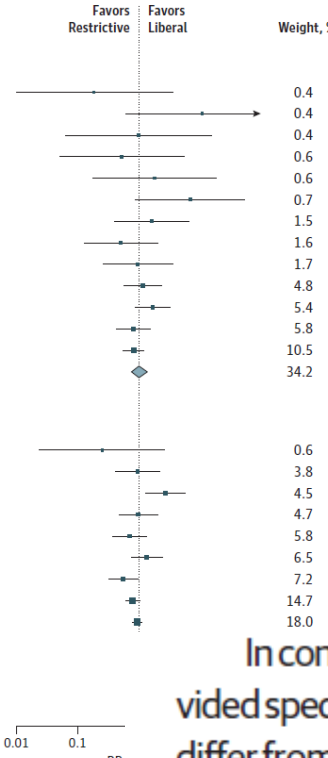



In contrast to the AABB recommendations, several guidelines provided specific guidance for patients with acute coronary syndrome that differ from guideline to guideline. The British Committee for Standards in Haematology recommended hemoglobin level be maintained at 8 g/dL to 9 g/dL.[104] The National Comprehensive Cancer Network recommended a hemoglobin transfusion goal of greater than 10 g/dL.[106] The National Blood Authority of Australia recommended that a hemoglobin level greater than 8 g/dL be maintained to possibly reduce mortality but that higher levels are uncertain.[103] The European Society of Cardiology recommended transfusion for patients with a hemoglobin level of less than 7 g/dL unless the patient is not hemodynamically stable.[100] The American College of Physicians recommended a hemoglobin transfusion threshold of 7 g/dL to 8 g/dL in hospitalized patients who have either coronary heart disease or acute coronary syndrome.[105]

**106.** Rogers GM, Gela D, Cleeland C, et al. *NCCN Guidelines Version 2.2014 Cancer- and Chemotherapy-Induced Anemia. NCCN Clinical Practice Guidelines in Oncology*. Fort Washington, PA: National Comprehensive Cancer Network; 2013.

# Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis

| *BMJ* 2016;352:i1351 | doi: 10.1136/bmj.i1351

Annemarie B Docherty,[1,2] Rob O'Donnell,[2] Susan Brunskill,[3] Marialena Trivella,[3] Carolyn Doree,[4] Lars Holst,[5] Martyn Parker,[6] Merete Gregersen,[7] Juliano Pinheiro de Almeida,[8] Timothy S Walsh,[1,2] Simon J Stanworth[3,9]

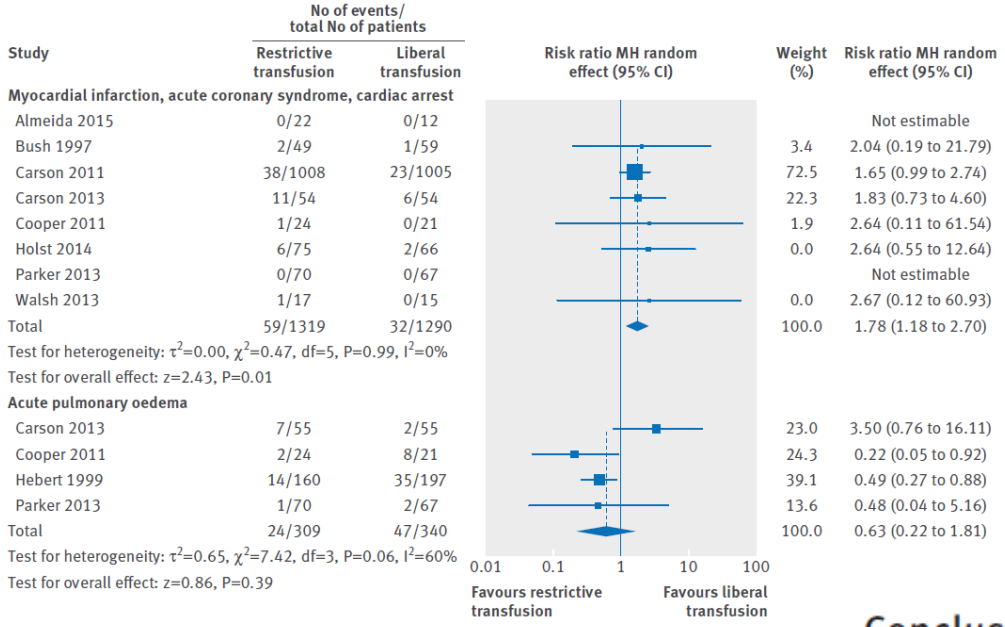



Fig 3 | Forest plot showing risk ratios for adverse cardiovascular events and risk of bias assessment for e

## Conclusion

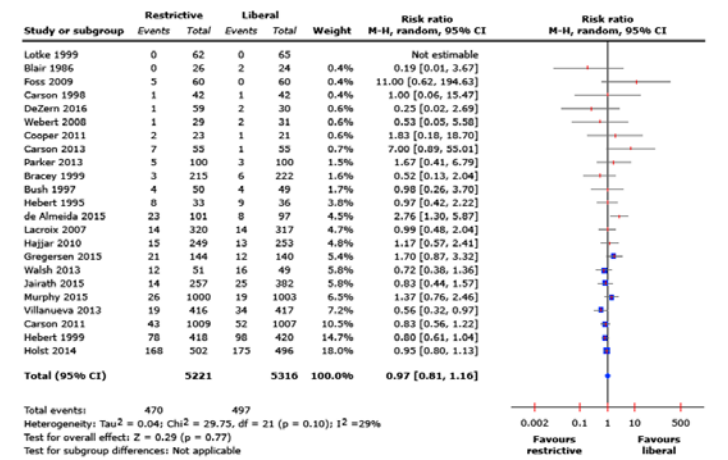
This review of available evidence suggests that for anaemic patients with cardiovascular disease, the use of restrictive transfusion thresholds (typically a haemoglobin level of 70-80 g/L) is associated with higher rates of acute coronary syndrome than more liberal transfusion thresholds (typically 90-100 g/L). No

## Thresholds for red blood cell transfusion in adults

| Condition | Hgb threshold for transfusion |
|---|---|
| Symptomatic patient (eg, myocardial ischemia, tachycardia) | 10 g/dL*[1,2] |
| Hospitalized patient | |
| Preexisting coronary artery disease | 8 g/dL*[2] |
| Acute coronary syndromes | 8 to 10 g/dL¶[2,3] |
| Heart failure | 7 to 8 g/dL¶ |
| Intensive care unit (hemodynamically stable) | 7 g/dL*[4,5] |
| Gastrointestinal bleeding (hemodynamically stable) | 7 g/dL*[6] |
| Non-cardiac surgery | 8 g/dL*[1] |
| Cardiac surgery | 7 to 8 g/dL*[7] |
| 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.

**Meta-analysis of outcomes with restrictive versus liberal transfusion thresholds: mortality at 30 days**



| Study or subgroup | Restrictive Events | Restrictive Total | Liberal Events | Liberal Total | Weight | Risk ratio M-H, random, 95% CI |
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| Lotke 1999 | 0 | 62 | 0 | 65 | | Not estimable |
| Blair 1986 | 0 | 26 | 2 | 24 | 0.4% | 0.19 [0.01, 3.67] |
| Foss 2009 | 5 | 60 | 0 | 60 | 0.4% | 11.00 [0.62, 194.63] |
| Carson 1998 | 1 | 42 | 1 | 42 | 0.4% | 1.00 [0.06, 15.47] |
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| Holst 2014 | 168 | 502 | 175 | 496 | 18.0% | 0.95 [0.80, 1.13] |
| **Total (95% CI)** | | **5221** | | **5316** | **100.0%** | **0.97 [0.81, 1.16]** |
| Total events: | 470 | | 497 | | | |

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 29.75$, df = 21 (p = 0.10); $I^2 = 29\%$
Test for overall effect: Z = 0.29 (p = 0.77)
Test for subgroup differences: Not applicable

# Transfusion Requirements in Surgical Oncology Patients

## *A Prospective, Randomized Controlled Trial*

Juliano Pinheiro de Almeida, M.D., Jean-Louis Vincent, M.D., Ph.D.,

**Methods:** In a randomized, controlled, parallel-group, double-blind (patients and outcome assessors) superiority trial in the intensive care unit of a tertiary oncology hospital, the authors evaluated whether a restrictive strategy of erythrocyte transfusion (transfusion when hemoglobin concentration <7 g/dl) was superior to a liberal one (transfusion when hemoglobin concentration <9 g/dl) for reducing mortality and severe clinical complications among patients having major cancer surgery. All adult patients with cancer having major abdominal surgery who required postoperative intensive care were included and randomly allocated to treatment with the liberal or the restrictive erythrocyte transfusion strategy. The primary outcome was a composite endpoint of mortality and morbidity.

**Results:** A total of 198 patients were included as follows: 101 in the restrictive group and 97 in the liberal group. The primary composite endpoint occurred in 19.6% (95% CI, 12.9 to 28.6%) of patients in the liberal-strategy group and in 35.6% (27.0 to 45.4%) of patients in the restrictive-strategy group

# Transfusion Requirements in Surgical Oncology Patients

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**Results:** A total of 198 patients were included as follows: 101 in the restrictive group and 97 in the liberal group. The primary composite endpoint occurred in 19.6% (95% CI, 12.9 to 28.6%) of patients in the liberal-strategy group and in 35.6% (27.0 to 45.4%) of patients in the restrictive-strategy group ($P = 0.012$). Compared with the restrictive strategy, the liberal transfusion strategy was associated with an absolute risk reduction for the composite outcome of 16% (3.8 to 28.2%) and a number needed to treat of 6.2 (3.5 to 26.5).

**Conclusion:** A liberal erythrocyte transfusion strategy with a hemoglobin trigger of 9 g/dl was associated with fewer major postoperative complications in patients having major cancer surgery compared with a restrictive strategy. **(ANESTHESIOLOGY 2015; 122:29-38)**

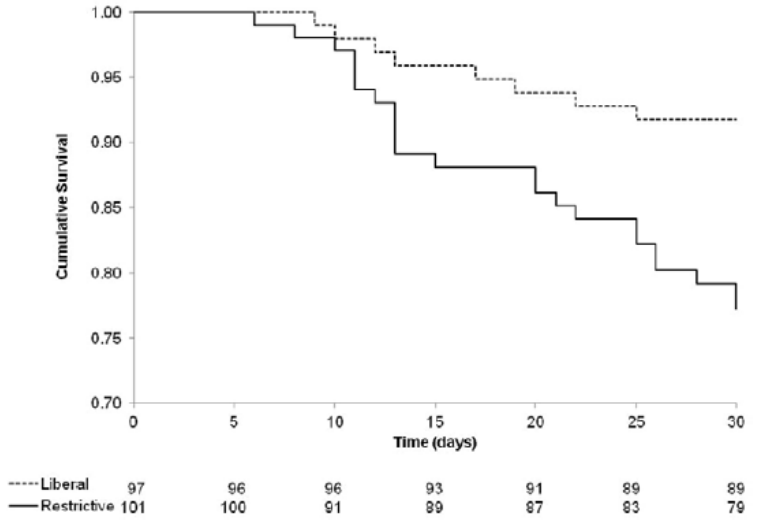



**Fig. 2.** Kaplan–Meier curves showing the probability of 30-day survival in patients randomized to a restrictive strategy of erythrocyte transfusion (transfusion when hemoglobin concentration <7 g/dl) and those randomized to a liberal strategy (transfusion when hemoglobin concentration <9 g/dl). The *P* value was calculated with the use of the log-rank test.

# Transfusion Requirements in Surgical Oncology Patients

## *A Prospective, Randomized Controlled Trial*

Juliano Pinheiro de Almeida, M.D., Jean-Louis Vincent, M.D., Ph.D.,

**Table 3.** Outcome Measures

| Variable, % (95% CI) | Liberal Strategy (N = 97) | Restrictive Strategy (N = 101) | *P* Value |
|---|---|---|---|
| Primary outcome | | | |
| Death or severe complication at 30 d | 19.6 (12.9–28.6) | 35.6 (27.0–45.4) | 0.012 |
| Secondary outcomes | | | |
| Mortality from all causes at 30 d | 8.2 (4.2–15.4) | 22.8 (15.7–31.9) | 0.005 |
| Acute respiratory distress syndrome | 0 (0–3.8) | 2.0 (0.5–6.9) | 0.498 |
| Septic shock | 13.4 (8.0–21.6) | 21.8 (14.9–30.8) | 0.122 |
| Acute kidney injury | 45.4 (35.8–55.3) | 43.6 (34.3–53.3) | 0.799 |
| Renal replacement therapy | 2.1 (0.6–7.2) | 3.0 (1.0–8.4) | 1.00 |
| Cardiovascular complications | 5.2 (2.2–11.5) | 13.9 (8.4–21.9) | 0.038 |
| Myocardial infarction | 0 (0–3.8) | 1.0 (0.2–5.4) | 1.00 |
| Stroke or transient ischemic attack | 0 (0–3.8) | 3.0 (1.0–8.4) | 0.247 |
| Mesenteric ischemia | 0 (0–3.8) | 1.0 (2.0–5.4) | 1.00 |
| Peripheral arterial ischemia | 1.0 (0.2–5.6) | 2.0 (0.5–6.9) | 1.00 |
| Unexpected cardiac arrest | 1.0 (0.2–5.6) | 4.0 (1.6–9.7) | 0.369 |
| Congestive heart failure | 2.1 (0.6–7.2) | 5.0 (2.1–11.1) | 0.445 |
| Pulmonary embolism | 1.0 (0.2–5.6) | 1.0 (2.0–5.4) | 1.00 |
| Reoperation | 10.3 (5.7–18.0) | 16.8 (10.8–25.3) | 0.181 |
| New infection | 21.6 (14.6–30.8) | 30.7 (22.5–40.3) | 0.148 |
| Source of infection | | | |
| Abdomen | 5.2 (2.2–11.5) | 14.9 (9.2–23.1) | 0.024 |
| Lung | 7.2 (3.5–14.2) | 7.9 (4.1–14.9) | 0.851 |
| Urinary tract | 3.1 (1.1–8.7) | 3.0 (1.0–8.4) | 1.00 |
| Wound | 4.1 (1.6–10.1) | 3.0 (1.0–8.4) | 0.717 |
| Mediastinum | 1.0 (0.2–5.6) | 2.0 (0.5–6.9) | 1.00 |
| Blood stream | 4.1 (1.6–10.1) | 3.0 (1.0–8.4) | 0.717 |
| Unidentified | 1.0 (0.2–5.6) | 0 (0–3.7) | 0.490 |
| Need for mechanical ventilation during ICU stay | 30.9 (22.6–40.7) | 39.6 (30.1–49.4) | 0.202 |
| Duration of mechanical ventilation, median IQR, d | 2 (1–3) | 2 (1–2) | 0.803 |
| Need for vasopressor during ICU stay | 58.8 (48.8–68.0) | 56.4 (46.7–65.7) | 0.740 |
| Duration of vasopressor, median IQR, d | 2 (2–4) | 2 (1–4) | 0.476 |
| ICU readmission | 15.5 (9.6–24.0) | 17.8 (11.6–26.4) | 0.656 |
| ICU length of stay, median IQR, d | 4 (3–7) | 4 (3–8) | 0.758 |
| Hospital length of stay, median IQR, d | 13 (10–20) | 14 (10–22) | 0.686 |
| 60-d mortality from all causes | 11.3 (6.5–19.2) | 23.8 (16.5–32.9) | 0.022 |

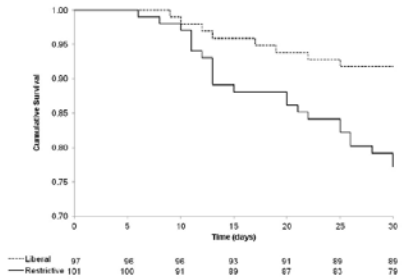



**Fig. 2.** Kaplan–Meier curves showing the probability of 30-day survival in patients randomized to a restrictive strategy of erythrocyte transfusion (transfusion when hemoglobin concentration <7 g/dl) and those randomized to a liberal strategy (transfusion when hemoglobin concentration <9 g/dl). The *P* value was calculated with the use of the log-rank test.

# Transfusion Requirements in Surgical Oncology Patients

## *A Prospective, Randomized Controlled Trial*

Juliano Pinheiro de Almeida, M.D., Jean-Louis Vincent, M.D., Ph.D.,

**Methods:** In a randomized, controlled, parallel-group, double-blind (patients and outcome assessors) superiority trial in the intensive care unit of a tertiary oncology hospital, the authors evaluated whether a restrictive strategy of erythrocyte transfusion (transfusion when hemoglobin concentration <7 g/dl) was superior to a liberal one (transfusion when hemoglobin concentration <9 g/dl) for reducing mortality and severe clinical complications among patients having major cancer surgery. All adult patients with cancer having major abdominal surgery who required postoperative intensive care were included and randomly allocated to treatment with the liberal or the restrictive erythrocyte transfusion strategy. The primary outcome was a composite endpoint of mortality and morbidity.

**Results:** A total of 198 patients were included as follows: 101 in the restrictive group and 97 in the liberal group. The primary composite endpoint occurred in 19.6% (95% CI, 12.9 to 28.6%) of patients in the li in the restrictive-strategy group ($P = 0.012$). Compared with the restrictive absolute risk reduction for the composite outcome of 16% (3.8 to 28.2%

**Conclusion:** A liberal erythrocyte transfusion strategy with a hemo postoperative complications in patients having major cancer surgery

2015; 122:29-38)

Another possible explanation for the different finding is that patients with cancer receiving restrictive transfusions may be more susceptible to altered oxygen delivery and impaired tissue oxygenation during the postoperative period, leading to higher rates of complications and death. Jhanji *et al.*[22] reported that patients having major abdominal surgery who had impaired microvascular flow after surgery experienced a higher rate of postoperative complications than did patients with normal microvascular flow (measured with sublingual capillaroscopy). Abnormalities in microvascular flow can occur when hemoglobin levels decrease less than 8.0 g/dl. In a study of patients with trauma with an average hemoglobin of 7.5 g/dl and impaired capillary perfusion, Weinberg *et al.*[23] demonstrated that erythrocyte transfusion improved microvascular flow. However, no

# Should Transfusion Trigger Thresholds Differ for Critical Care Versus Perioperative Patients? A Meta-Analysis of Randomized Trials

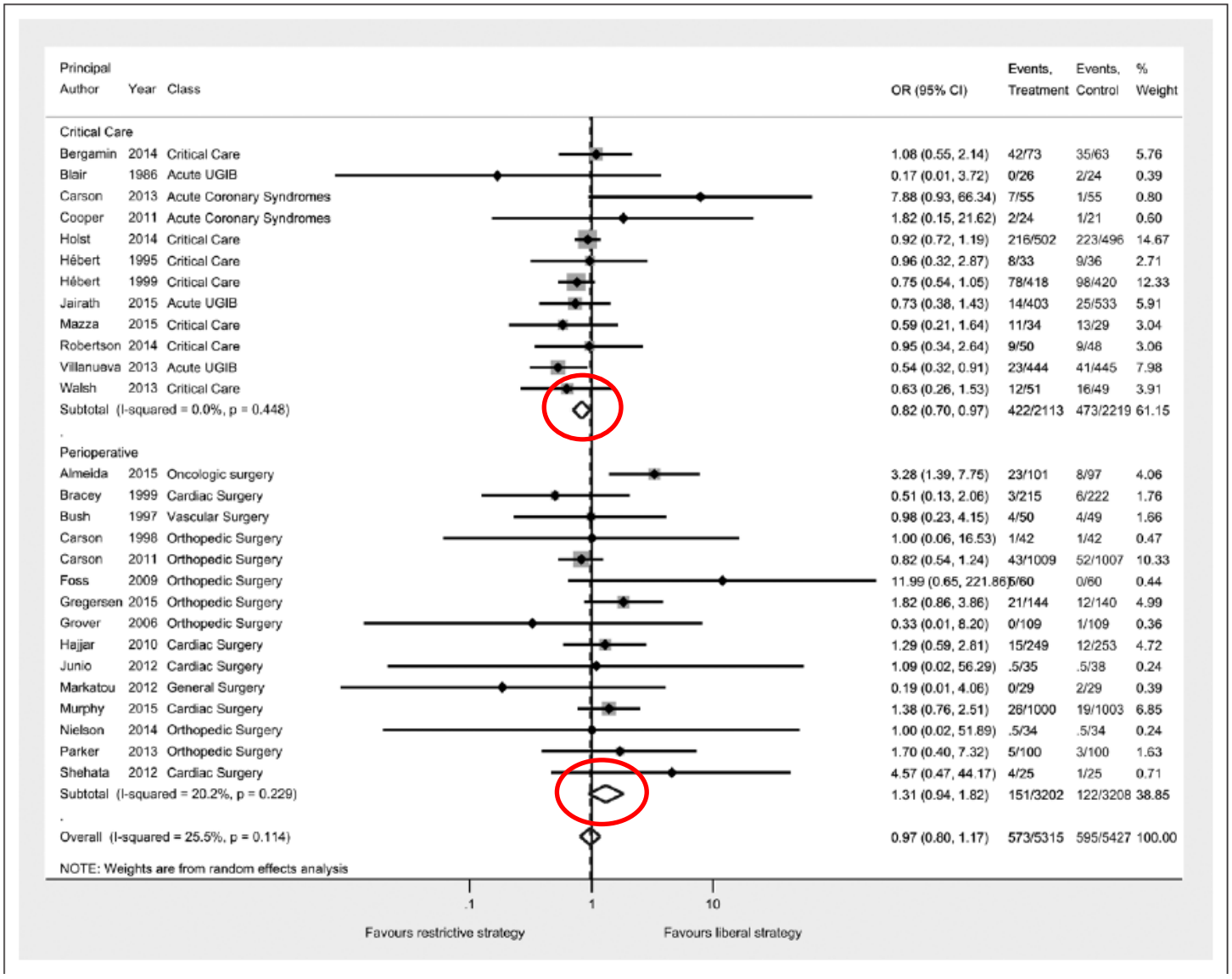
Matthew A. Chong, MD[1]; Rohin Krishnan, BSc[1]; Davy Cheng, MD, FRCPC[1]; Janet Martin, PharmD, MSc(HTA)[1,2]

Twenty-seven randomized controlled trials (10,797 patients) were included. In critical care patients, restrictive transfusion resulted in significantly reduced 30-day mortality compared with liberal transfusion (odds ratio, 0.82; 95% CI, 0.70–0.97). In surgical patients, a restrictive transfusion strategy led to the opposite direction of effect for mortality (odds ratio, 1.31; 95% CI, 0.94–1.82). The subgroup interaction test was significant ($p = 0.04$), suggesting that the effect of restrictive transfusion on mortality is statistically different for critical care (decreased risk) versus surgical patients (potentially increased risk or no difference). Regarding secondary outcomes, for critically ill patients, a restrictive strategy resulted in reduced risk of stroke/transient ischemic attack, packed RBC exposure, transfusion reactions, and hospital length of stay. In surgical patients, restrictive transfusion resulted in reduced packed RBC exposure.

**Conclusions:** The safety of restrictive transfusion strategies likely differs for critically ill patients versus perioperative patients. Further trials investigating transfusion strategies in the perioperative setting are necessary. (*Crit Care Med* 2018; 46:252–263)

# Should Transfusion Trigger Thresholds Differ for Critical Care Versus Perioperative Patients? A Meta-Analysis of Randomized Trials

Matthew
Janet Ma



# Should Transfusion Trigger Thresholds Differ for Critical Care Versus Perioperative Patients? A Meta-Analysis of Randomized Trials

Matthew A. Chong, MD[1]; Rohin Krishnan, BSc[1]; Davy Cheng, MD, FRCPC[1]; Janet Martin, PharmD, MSc(HTA)[1,2]

## Major Findings

Evidence suggests that the safety of restrictive transfusion thresholds differs for critically ill patients versus perioperative patients. In critical care patients, a restrictive transfusion strategy (transfusion trigger ~7–8 g/dL in the majority of studies) significantly reduced mortality, stroke/TIA, transfusion reactions, allogeneic blood exposure, and hospital length of stay. In contrast, for perioperative patients, current evidence suggests that a restrictive transfusion strategy may increase the risk of mortality, although the overall results were not statistically significant and lack of power prevents definitive conclusions.

| Ministero della Salute<br>*Istituto Superiore di Sanità*<br>*Centro Nazionale Sangue* | **LINEE GUIDA PER IL PROGRAMMA DI PATIENT BLOOD MANAGEMENT** | **LG CNS 05**<br>**Rev. 0**<br>**27.10.2016** |
|---|---|---|

**Considerato** che il Patient Blood Management si prefigge l'obbiettivo di prevenire o ridurre in modo significativo l'utilizzo degli emocomponenti e dei medicinali plasmaderivati, mediante i cosiddetti "tre pilastri del PBM": I) ottimizzare l'eritropoiesi del paziente; II) ridurre al minimo il sanguinamento; III) sfruttare e ottimizzare la riserva fisiologica individuale per la tolleranza all'anemia;

| | ***Raccomandazioni da adottare nel periodo pre-operatorio, intra-operatorio e post-operatorio*** |
|---|---|
| 3 | La soglia trasfusionale da adottare per la terapia con concentrati eritrocitari (omologhi o autologhi) in altre categorie di pazienti è stabilita in collaborazione con un esperto di medicina trasfusionale. |
| 4 | Nei pazienti ospedalizzati e clinicamente stabili, in caso di necessità di trasfusione di concentrati eritrocitari (omologhi o autologhi), è trasfusa una sola unità alla volta; la scelta relativa ad un'ulteriore trasfusione deve essere supportata da una attenta rivalutazione clinica del paziente. |

**Single-unit transfusions and hemoglobin trigger: relative impact on red cell utilization**

TRANSFUSION 2017;57;1163–1170

*William W. Yang,[1] Rajiv N. Thakkar,[3] Eric A. Gehrie,[2] Weiyun Chen,[4] and Steven M. Frank[5]*

Historically, back in the 1980s and 1990s, physicians were trained to give two-unit RBC transfusions, and single-unit transfusions were thought to be unnecessary.[13] Now it is recognized that single RBC units are often adequate to treat the signs and symptoms of anemia,[14] but this practice has not been fully adopted.

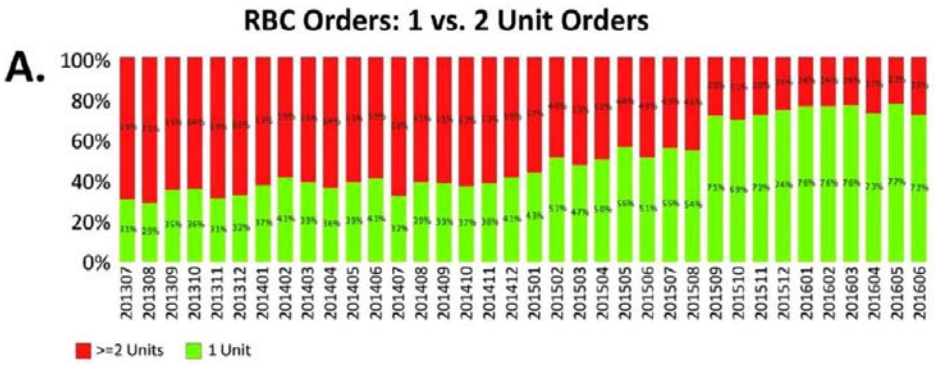
TRANSFUSION 2017;57;1163–1170

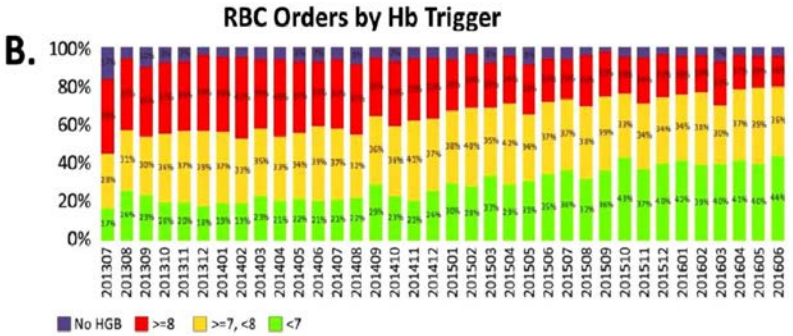
# Single-unit transfusions and hemoglobin trigger: relative impact on red cell utilization

*William W. Yang,[1] Rajiv N. Thakkar,[3] Eric A. Gehrie,[2] Weiyun Chen,[4] and Steven M. Frank[5]*

despite this interest in PBM, the optimal methods to efficiently reduce unnecessary RBC transfusions are not well defined. The most common method is to focus on an evidence-based, restrictive Hb trigger, which is the Hb concentration at which RBC transfusion is initiated. The second method, which is less commonly discussed, is to reduce the amount of blood that is given by encouraging single-unit RBC transfusions when patients are hemodynamically stable and not actively bleeding. In this way, the optimal dose of blood can be titrated to achieve an evidence-based Hb target, which has been defined as the Hb concentration after the transfusion is completed.[12]

TRANSFUSION 2017;57;1163–1170




blood at a specific Hb threshold. The longstanding practice tradition of giving 2-unit RBC transfusions to stable anemic patients has been questioned before, and most recently by the AABB Choosing Wisely recommendations. For hospitals that are just starting PBM programs, we believe that a "Why give 2 when 1 will do?" policy is an important component of the program that should be used in combination with an evidence-based Hb trigger transfusion policy. These methods, when used as part of a comprehensive PBM program, have the potential to reduce unnecessary transfusions along with their associated risks and costs.

# Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology

*First update 2016*

*Eur J Anaesthesiol* 2017; **34:**332–395

Sibylle A. Kozek-Langenecker, Aamer B. Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa,

### 1.3.1. Transfusion triggers

We recommend a target haemoglobin concentration of 7 to 9 g $dl^{-1}$ during active bleeding. **1C**

### 1.5. Monitoring tissue perfusion

We recommend repeated measurements of a combination of haematocrit (Hct)/haemoglobin, serum lactate, and base deficit to monitor tissue perfusion, tissue oxygenation and the dynamics of blood loss during acute bleeding. These parameters can be extended by measurement of cardiac output, dynamic parameters of volume status [e.g. stroke volume variation (SVV), pulse pressure variation (PPV)], $CO_2$ gap and central venous oxygen saturation. **1C**

# Indications for and Adverse Effects of Red-Cell Transfusion

N Engl J Med 2017;377:1261-72.

Jeffrey L. Carson, M.D., Darrell J. Triulzi, M.D., and Paul M. Ness, M.D.

in making decisions about transfusion, other clinical factors, including hemodynamic status, rate of bleeding, symptoms, and overall status of the patient, be considered in addition to the hemoglobin concentration. Physiological or laboratory biomarkers for guiding decisions about transfusion have not been established.

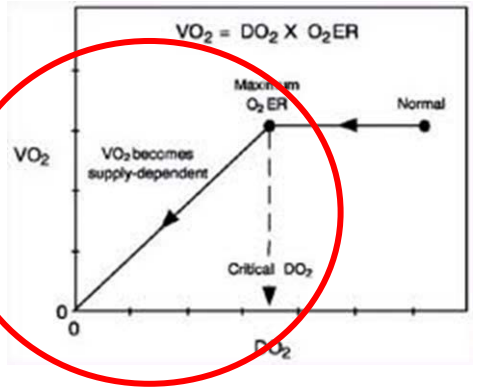
*British Journal of Anaesthesia* **107** (S1): i41–i59 (2011)
doi:10.1093/bja/aer350

# What is really dangerous: anaemia or transfusion?

A. Shander[1,2,3,4*], M. Javidroozi[1], S. Ozawa[5] and G. M. T. Hare[6,7]

Acute haemorrhage can result in hypovolaemia and circulatory collapse (shock) due to the lost volume. Exsanguination occurs mostly in combat injury or trauma[61] and remains a leading cause of maternal mortality across the world.[62] Other aetiologies (e.g. gastrointestinal or internal bleeding due to rupture vessels) also occur.[63 64] Unless the circulatory volume is resuscitated and bleeding is controlled, the condition most often will result in imminent death. Volume loss can normally be managed using i.v. fluids,[65] but the resultant acute severe anaemia can be more challenging to manage, particularly in massively bleeding cases commonly complicated by coagulopathy and transfusion of large amounts of blood.[66]

(Anesth Analg 2017;124:1547–54)




Anemia, defined as a hemoglobin (Hb) concentration below normal, results in a decreased blood oxygen ($O_2$)-carrying capacity ($CaO_2$) because of a lower Hb concentration. Blood transfusion is often used to treat acute anemia with the goal of increasing blood $CaO_2$ and oxygen delivery ($DO_2$).

**Table 1** Equations for oxygen transport and utilization

| | |
|---|---|
| Arterial oxygen content | $CaO_2 = (Hb \times 1{\cdot}34 \times SaO_2) + (PaO_2 \times 0{\cdot}003)$ |
| Oxygen delivery | $DO_2 = CO \times CaO_2$ |
| Oxygen consumption | $VO_2 = CO \times (CaO_2 - CvO_2)$ |
| | $VO_2 = CO \times ([Hb \times 1{\cdot}34 \times (SaO_2 - SvO_2)] + [(PaO_2 - PvO_2) \times 0{\cdot}003])$ |
| Oxygen extraction | $EO_2 = VO_2/DO_2$ |

CO, cardiac output; Hb, haemoglobin; $PaO_2$, arterial oxygen pressure; $PvO_2$, venous oxygen pressure; $SaO_2$, arterial oxygen saturation; $SvO_2$, venous oxygen saturation.

**Impact of anemia and red blood cell transfusion on organ function**

*M. R. Nowrousian*

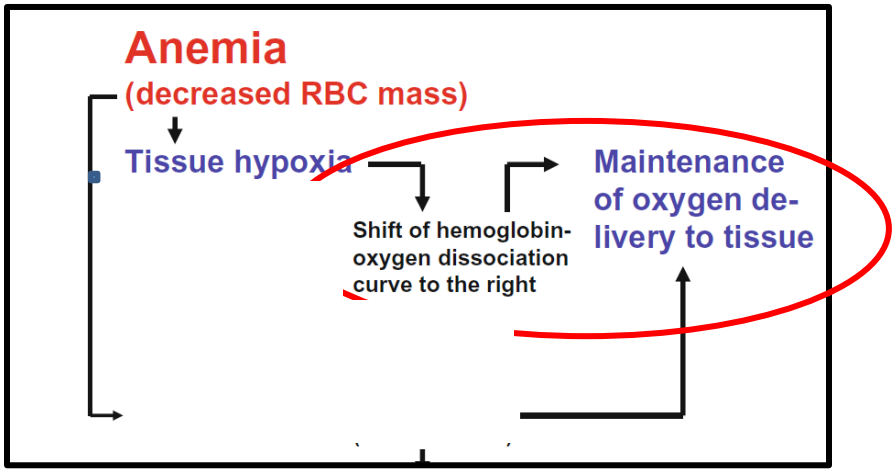
The immediate effect of anemia is a decreased oxygen-carrying capacity of the blood and, consequently, a decreased supply of oxygen to various organs. The resultant tissue hypoxia evokes a number of compensatory mechanisms and a series of physiological and metabolic abnormalities that are responsible for the clinical signs and symptoms of anemia and cause limitations in physical and mental well-being of patients and their quality of life (QOL). Recent clinical studies show that anemia has much greater impacts on tissue and organ functions than previously thought.

**Impact of anemia and red blood cell transfusion on organ function**

*M. R. Nowrousian*

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).

In conditions of rest and at Hb levels above 10 g/dl, the shift in Hb-oxygen dissociation curve and shunting of blood are usually sufficient to compensate for tissue hypoxia, but in nonresting conditions and at Hb levels of 10 g/dl or less, additional mechanisms, particularly those of the cardiovascular system are required to meet the oxygen need of tissues (Varat et al. 1972; Metivier et al. 2000).



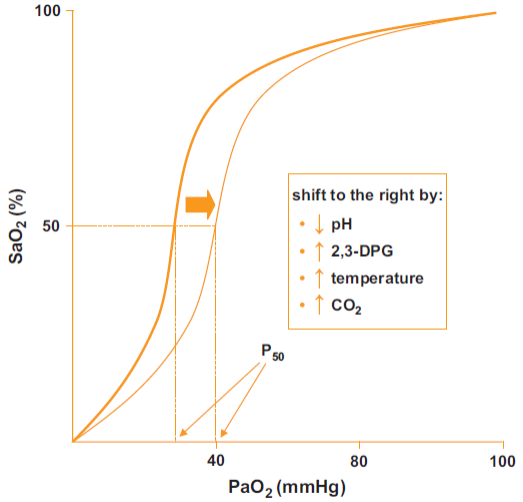




**Figure 2.** Oxyhaemoglobin dissociation curve. Changes in parameters leading to a rightwards shift are given (box). P50 = Oxygen tension at which haemoglobin is 50% saturated. 2,3-DPG = 2,3-diphosphoglycerate.

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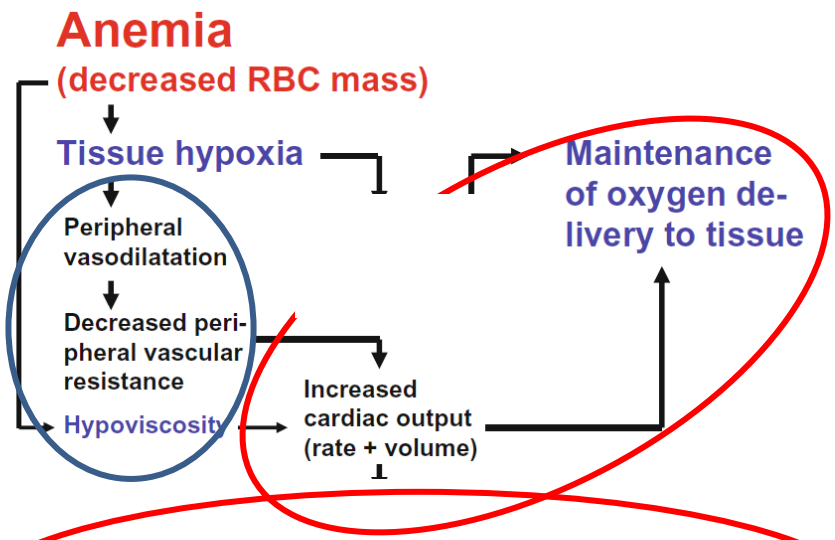


Increased cardiac output is the most important compensatory mechanism in response to anemia. Indeed, cardiac output inversely correlates with Hb or hematocrit level. The two possibly most important mechanisms involved in increased cardiac output are: 1) reduced blood viscosity, and 2) increased sympathetic stimulation of the cardiovascular effectors. While blood viscosity exerts its effects predominantly on preload and afterload as major determinants of cardiac output, sympathetic stimulation primarily increases heart rate and contractility, as well as venomotor tone.

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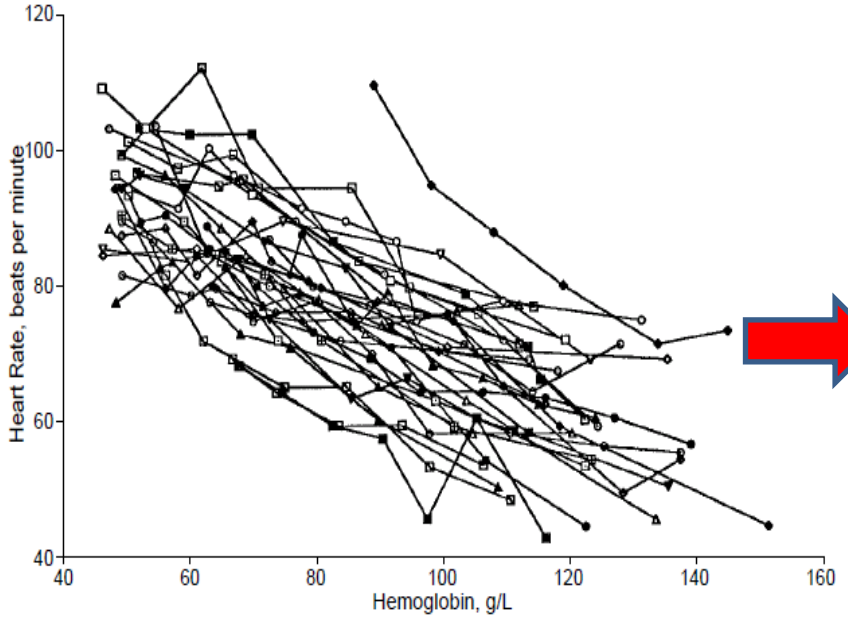
CO, cardiac output; Hb, haemoglobin; $PaO_2$, arterial oxygen pressure; $PvO_2$, venous oxygen pressure; $SaO_2$, arterial oxygen saturation; $SvO_2$, venous oxygen saturation.

# 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




**Interventions.—**Aliquots of blood (450-900 mL) were removed to reduce blood Hb concentration from 131 (2) g/L to 50 (1) g/L [mean (SE)]. Isovolemia was maintained with 5% human albumin and/or autologous plasma. Cardiovascular parameters, arterial and mixed venous oxygen content, oxyhemoglobin saturation, and arterial blood lactate were measured before and after removal of each aliquot of blood. Electrocardiogram and, in a subset, Holter monitor were monitored continuously.

**Main Outcome Measures.—**"Critical" oxygen delivery ($To_2$) as assessed by oxygen consumption ($\dot{V}o_2$), plasma lactate concentration, and ST changes on electrocardiogram.

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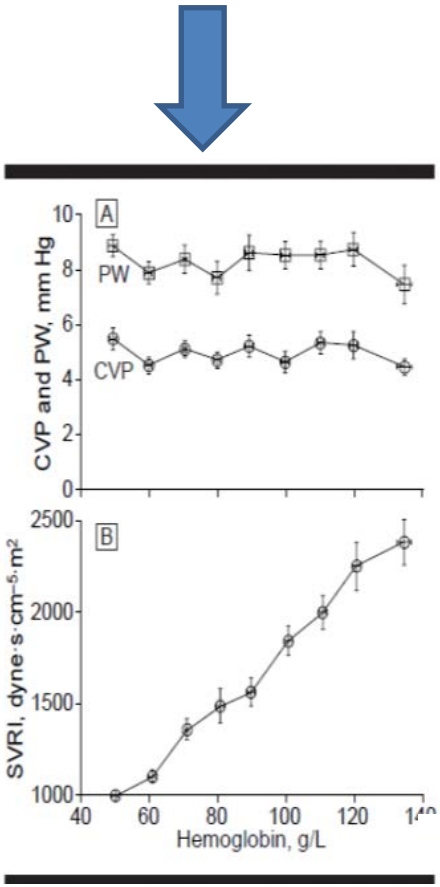


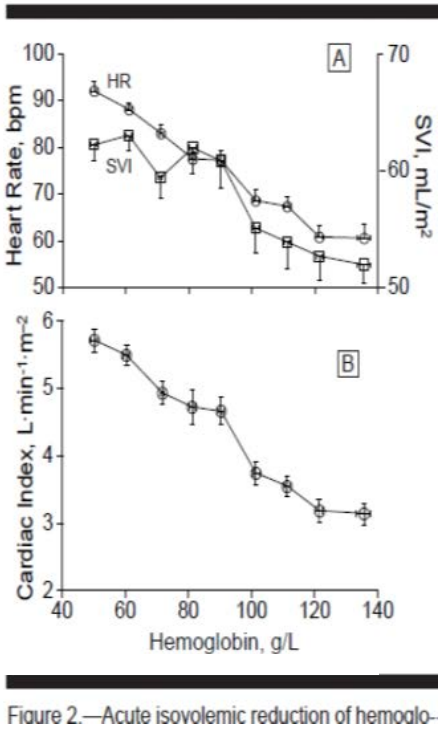


Figure 2.—Acute isovolemic reduction of hemoglo-

**Impact of anemia and red blood cell transfusion on organ function**

*M. R. Nowrousian*

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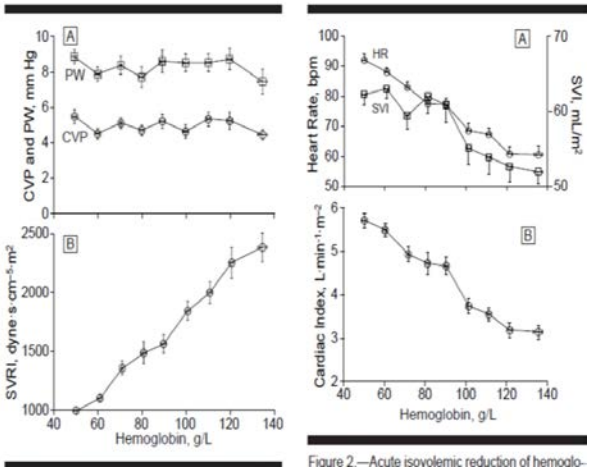


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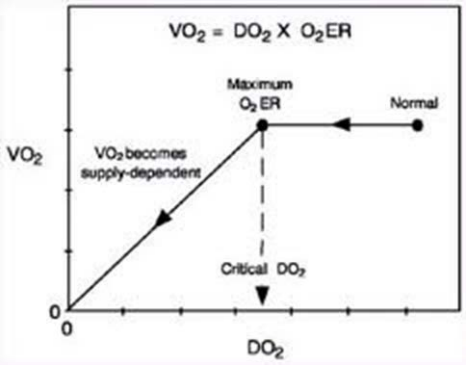


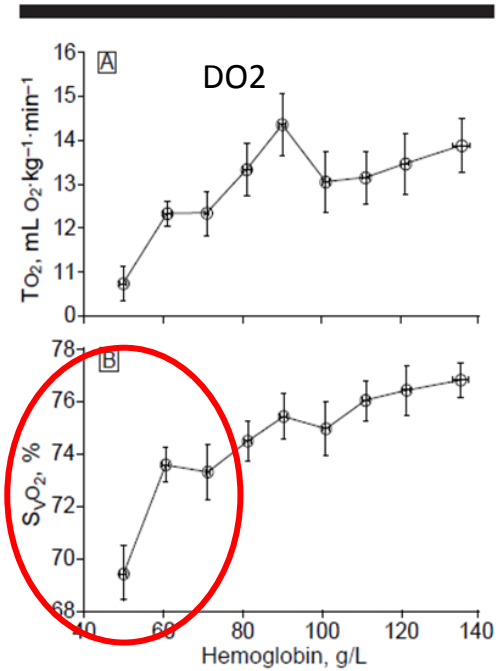


Figure 4.—Acute isovolemic reduction of hemoglobin concentration to 50 g/L decreased oxygen transport rate ($T_{O_2}$) (A; $P<.001$) and mixed venous oxyhemoglobin saturation ($S_vO_2$)(B; $P<.001$). Data are gathered into groups by hemoglobin increments of 10 g/L and represented as mean (SE) (N=32).

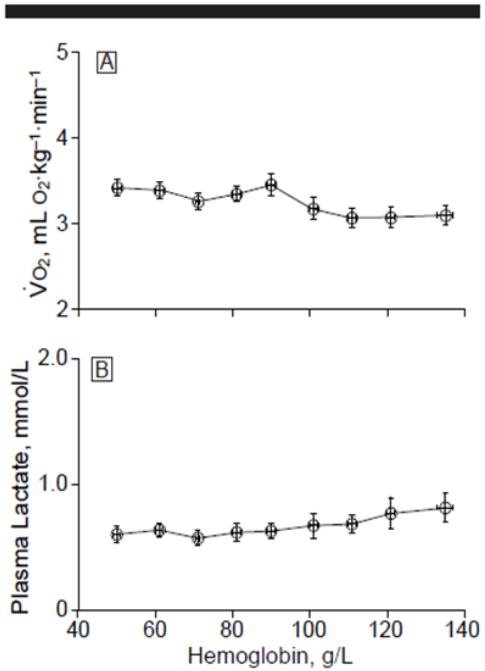


Figure 5.—Acute isovolemic reduction of hemoglobin concentration to 50 g/L increased oxygen consumption ($\dot{V}O_2$) (A; $P<.001$) but did not change plasma lactate concentration (B; $P=.09$). Data are gathered into groups by hemoglobin increments of 10 g/L and represented as mean (SE) (N=32).

*Critical Care* 2010, 14:213

# Venous oxygen saturation as a physiologic transfusion trigger

Benoit Vallet*, Emmanuel Robin and Gilles Lebuffe

Venous oxygen saturation is a clinical tool which integrates the whole body oxygen uptake-to-delivery ($VO_2$-$DO_2$) relationship. In the clinical setting, in the absence of pulmonary artery catheter (PAC)-derived mixed venous oxygen saturation ($SvO_2$), the central venous oxygen saturation ($ScvO_2$) is increasingly being used as a reasonably accurate surrogate [1]

## Comparison of central-venous to mixed-venous oxygen saturation during changes in oxygen supply/demand.

K Reinhart, T Rudolph, D L Bredle, L Hannemann and S M Cain

*Chest* 1989;95;1216-1221

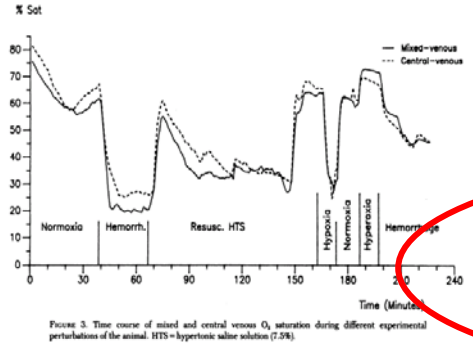


FIGURE 3. Time course of mixed and central venous $O_2$ saturation during different experimental perturbations of the animal. HTS = hypertonic saline solution (7.5%).

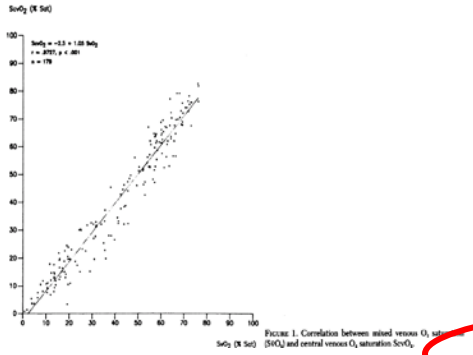

FIGURE 1. Correlation between mixed venous $O_2$ saturation ($S\bar{v}O_2$) and central venous $O_2$ saturation $ScvO_2$.

**Table 1—*Mean Values and Correlations for Mixed and Central Venous Fiberoptic Catheters under Various Conditions**

| Condition | $S\bar{v}O_2$ | $ScvO_2$ | r | n | $\lvert S\bar{v}O_2\text{-}ScvO_2\rvert$ |
|---|---|---|---|---|---|
| Total | 53 ± 16 | 52 ± 15 | 0.96 | 29531 | 3.7 ± 2.9 |
| Control | 59 ± 14 | 57 ± 15 | 0.98 | 14167 | 2.8 ± 2.0 |
| Hemorrhage | 33 ± 14 | 37 ± 12 | 0.94 | 1490 | 6.0 ± 3.1 |

$ScvO_2$ was expected to be slightly lower than $S\bar{v}O_2$ during steady-state conditions, due to a relatively large contribution of highly saturated venous renal effluent to the inferior vena cava.[15] Our data in Table 1 are in general agreement with this expectation. In nonshock patients[12,14] and healthy volunteers[16] similar differences between mixed and central venous saturations have been reported. During hypoxia and hemorrhagic shock, a redistribution of blood flow away from renal and splanchnic beds to the heart and brain would tend to reverse this difference.[17,18] Such redistribution is consistent with the somewhat higher $ScvO_2$ saturations we observed in both hemorrhage and hypoxia (Table

*Critical Care* 2010, 14:213

Benoit Vallet*, Emmanuel Robin and Gilles Lebuffe

## Conclusion

Physiologic transfusion triggers should progressively replace arbitrary Hb-based transfusion triggers [19]. The same conclusions were drawn by Orlov *et al.* in a recent trial using a global oxygenation parameter for guiding RBC transfusion in 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, $SvO_2$ or $ScvO_2$) 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.

*Eur J Anaesthesiol* 2017; **34**:332–395

**Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology**

*First update 2016*

### 1.3.1. Transfusion triggers

We recommend a target haemoglobin concentration of 7 to 9 g $dl^{-1}$ during active bleeding. **1C**

Continuous haemoglobin monitoring can be used as a trend monitor. **C**

# Noninvasive Hemoglobin Monitoring: How Accurate Is Enough?

(Anesth Analg 2013;117:902–7)

Mark J. Rice, MD, Nikolaus Gravenstein, MD, and Timothy E. Morey, MD

The essential purpose of noninvasive Hb technology in the operating room is to assist clinicians in deciding whether to transfuse. For that reason, we suggest that not only should noninvasive Hb devices and the gold standard method produce statistically similar results, they should also lead to comparable clinical decisions.

The principal measures were the accuracy (mean difference), precision (standard deviation [SD] of mean difference), and 95% LOA of noninvasive Hb measurements compared to invasive central laboratory measurements.

J.M. Ehrenfeld, M. Cannesson (eds.), *Monitoring Technologies in Acute Care Environments*,
DOI 10.1007/978-1-4614-8557-5_36, © Springer Science+Business Media New York 2014





**Table 36.1** Commercially available noninvasive hemoglobin devices

| Device | Technology | Availability as of Nov 2012 |
|---|---|---|
| Pulse CO-Oximetry (e.g., Pronto, Radical-7) (Masimo Corp.) | Multiple wavelength Pulse CO-Oximetry | FDA cleared, CE marked |
| Pronto-7 (Masimo Corp.) | Rainbow 4D spectrophotometry | FDA cleared, CE marked |
| OrSense (e.g., MBM200) | Occlusion spectroscopy | CE marked |
| Haemospect | Transcutaneous reflection spectroscopy | CE marked |

# Accuracy of non-invasive continuous total hemoglobin measurement by Pulse CO-Oximetry in severe traumatized and surgical bleeding patients

Werner Baulig[1] · Burkhardt Seifert[2] · Donat R. Spahn[3] · Oliver M. Theusinger[3]

J Clin Monit Comput (2017) 31:177–185

Masimo Radical-7™ Pulse CO-Oximeter (Masimo Radical 7 Type RDS-1 Pulse Co-Oximeter and accessories, Masimo Corp., Irvine, CA, USA), a multi-wavelength spectrophotometric technique became commercially available on the medical market for transcutaneous continuous monitoring of the Hb concentration (SpHb). The method of the *Radical-7 device* is based on the measurement of the differential optical density of seven different wavelengths of light passed through tissue.

J.M. Ehrenfeld, M. Cannesson (eds.), *Monitoring Technologies in Acute Care Environments*,
DOI 10.1007/978-1-4614-8557-5_36, © Springer Science+Business Media New York 2014





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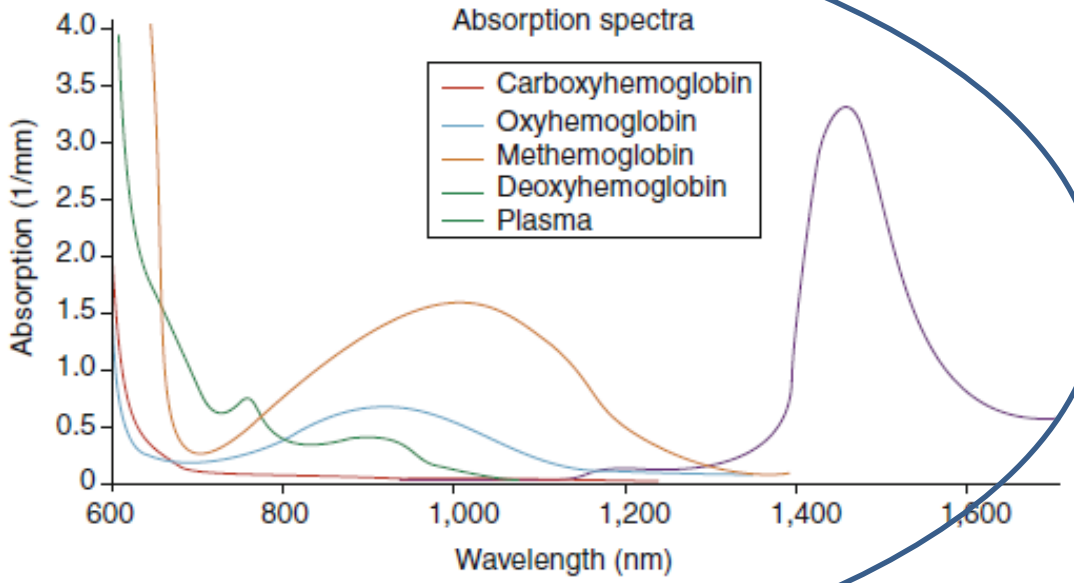


**Fig. 36.1** Pulse CO-Oximetry uses multiple wavelengths of light to distinguish between different species of hemoglobin

(Anesth Analg 2010;111:1424–6)

# The Accuracy of Noninvasive and Continuous Total Hemoglobin Measurement by Pulse CO-Oximetry in Human Subjects Undergoing Hemodilution

Mark R. Macknet, MD, Martin Allard, MBChB, FRCA, Richard L. Applegate, II, MD, and James Rook, DO

By providing additional and continuous data, SpHb monitoring may facilitate transfusion management. To reflect the tHb clinically, how accurate does the SpHb need to be? We propose that being within ≤1.5 g/dL of the tHb value would be sufficiently accurate.

# Comparison of the Accuracy of Noninvasive Hemoglobin Monitoring by Spectrophotometry (SpHb) and HemoCue® with Automated Laboratory Hemoglobin Measurement

Anesthesiology 2011; 115:548–54



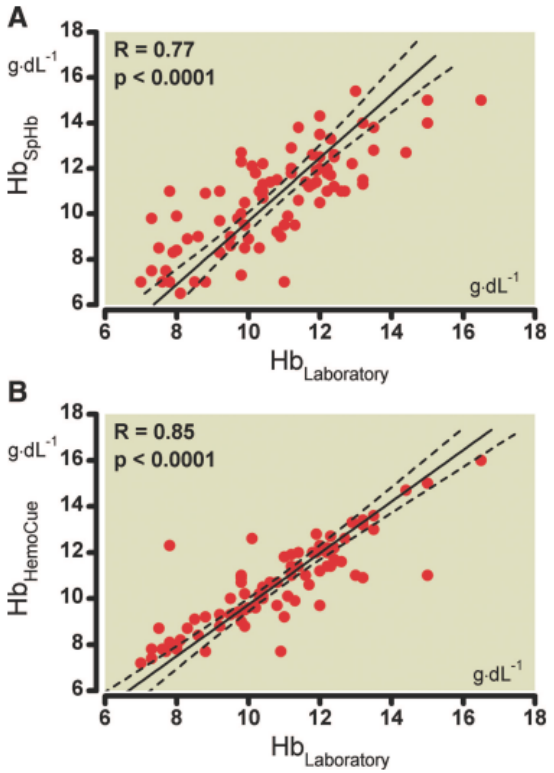


Fig. 2. Representation of linear regression between hemoglo-

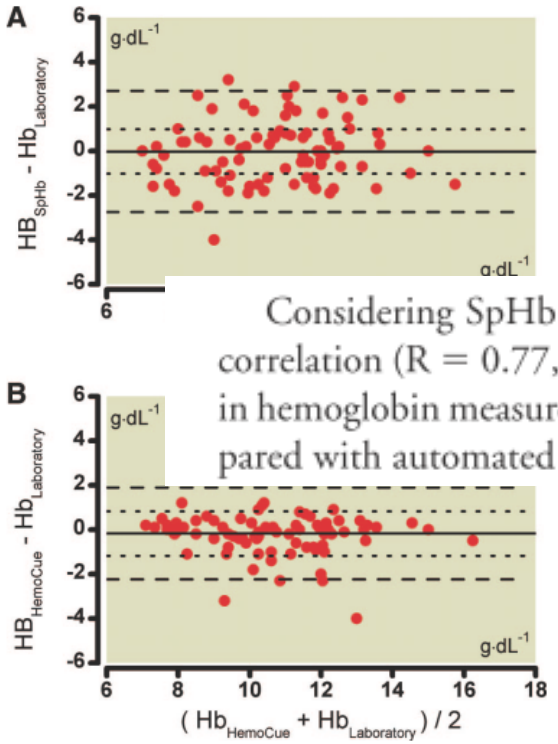


Fig. 3. Bland and Altman representation of comparison analysis between hemoglobin$_{SpHb}$ and hemoglobin$_{Laboratory}$ (*A*) and be-

Considering SpHb monitoring, we showed a significant correlation ($R = 0.77$, $P < 0.001$) and a nonsignificant bias in hemoglobin measurement of $-0.02 \pm 1.39\ g \cdot dl^{-1}$ compared with automated analysis in the laboratory (figs. 2 and

# Comparison of the Accuracy of Noninvasive Hemoglobin Monitoring by Spectrophotometry (SpHb) and HemoCue® with Automated Laboratory Hemoglobin Measurement

Anesthesiology 2011; 115:548–54

Lionel Lamhaut, M.D.,* Roxana Apriotesei, M.D.,† Xavier Combes, M.D., Ph.D.,* Marc Lejay, M.D.,† Pierre Carli, M.D.,‡ Benoît Vivien, M.D., Ph.D.*

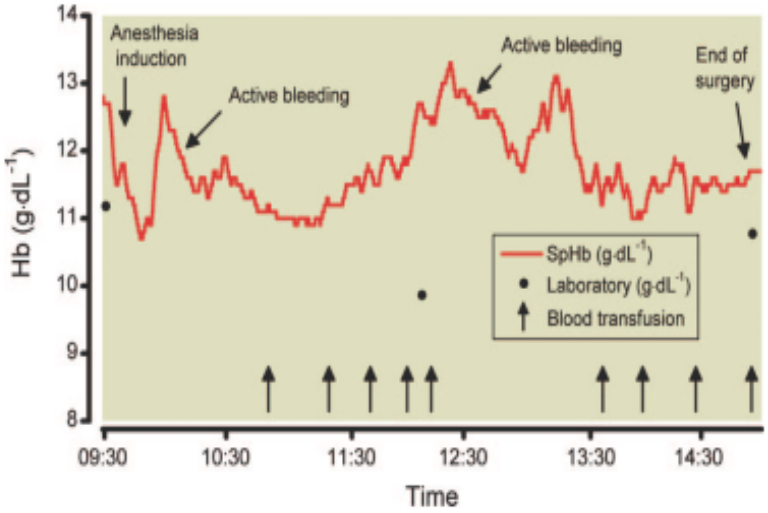


**Fig. 1.** Trend of continuous hemoglobin measurement displayed by the Radical-7® Pulse CO-Oximeter monitor during nephrectomy and cavectomy performed in a 50-yr-old patient. Hemoglobin measurements performed on the automated analyzer in the laboratory and blood transfusion are plotted on the graphic. Hemoglobin = hemoglobin value SpHb = continuous hemoglobin assessment by Radical-7®

more than the absolute and instantaneous hemoglobin value displayed by the Radical-7® Pulse CO-Oximeter, continuous measurement allows the physician to focus on the hemoglobin trend and detect either a slow decrease or a significant rapid drop in hemoglobin, and therefore decide the appropriate time to perform an invasive measurement of hemoglobin.

the main benefits of SpHb monitoring are the noninvasiveness (no blood sample is required) and the continuous online assessment of hemoglobin concentration (fig. 1). Indeed, continuous online monitoring of SpHb enables the instantaneous detection of a hemoglobin drop, whereas the physician had not yet scheduled an invasive hemoglobin measurement, either by a point of care device (result in 1 min) or by analysis in the hematology laboratory (delayed result). In this situation, by the time

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The essential purpose of noninvasive Hb technology in the operating room is to assist clinicians in deciding whether to transfuse. For that reason, we suggest that not only should noninvasive Hb devices and the gold standard method produce statistically similar results, they should also lead to comparable clinical decisions. To that end, a test of decision making around the relevant Hb concentration range of 6 to 10 g/dL should be used. It is our opinion that the published accuracy data from the Masimo Radical-7 device, especially in the aforementioned critical range, does not guide clinicians to make transfusion decisions.

# Noninvasive Hemoglobin Monitoring: How Accurate Is Enough?

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## WHAT ACCURACY IS REQUIRED?

guidelines[15] from 2006 state that transfusion of RBCs should typically not be done when the Hb is >10 g/dL, and almost always for an Hb <6 g/dL. Thus, between 6 and 10 g/dL is where an operating room noninvasive Hb device needs to be accurate within 1 g/dL. Below 6 g/dL, accuracy is probably not as critical because within this range, transfusion would almost universally be recommended. Similarly, with an Hb >10 g/dL, the patient would rarely be transfused, so accuracy is again not as crucial.

**A new perspective on best transfusion practices**

Aryeh Shander[1,2], Irwin Gross[3], Steven Hill[4], Mazyar Javidroozi[1], Sharon Sledge

*Blood Transfus 2013; 11: 193-202* DOI 10.2450/2012.0195-12


A shift from Hb-based transfusion triggers towards so-called "physiological" triggers indicative of tissue oxygenation status and ischaemia is the key to establishing better transfusion practices. Some suggested emerging technology is non-invasive monitoring of Hb levels, which can provide the patient's Hb and its trend in real-time. However, more clinical data are needed to establish the value of this approach.

of elevation of at least 0.1 mV in an electrocardiogram, new wall motion abnormality in trans-oesophageal or trans-thoracic echocardiography, mixed venous oxygen partial pressure <32 mmHg, oxygen extraction ratio >40%, mixed venous oxygen saturation <60%, or >10% decrease in $VO_2$. Normovolaemia is assumed for

….the physician without physiology practices a sort of popgun pharmacy, hitting now the malady and again the patient, he himself not knowing which.

William Osler