Transfusion Requirements in Critical Care

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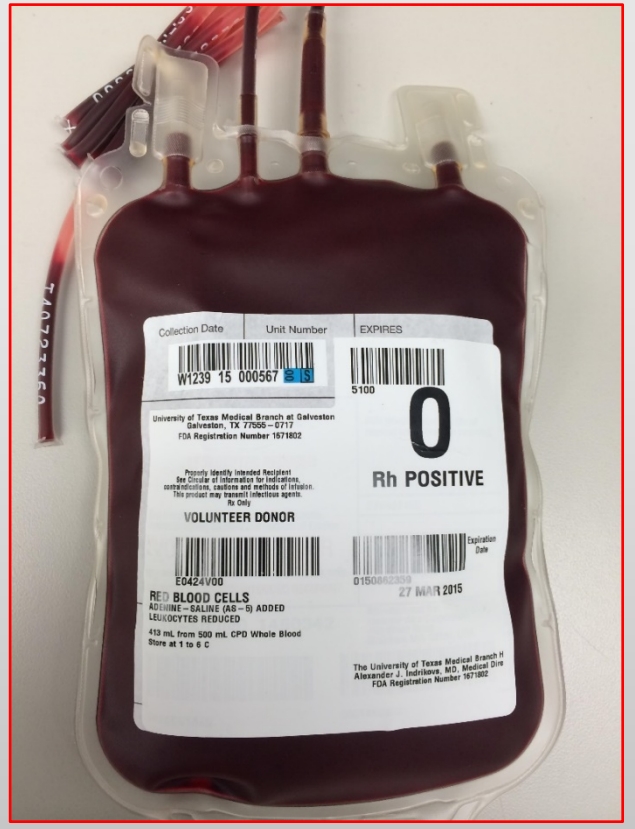
Disclosure

I have no conflict of interest in relation to this presentation.

Packed Red Blood Cells



Total amount: 350 cc

- RBCs: 200 cc.
- Plasma: 50 cc.
- Nutrient solution: 100 cc of CPDA-1 (citrate, phosphate, dextrose, adenine).

Anemia in Critically Ill Patients

- Anemia is common in critically ill patients.
- Severe anemia is associated with increased morbidity and mortality.
- 40% of patients admitted to ICU end up receiving PRBC.
- Majority of transfusions for anemia are not for acute hemorrhage.
- Unclear if PRBC transfusions improves survival in patients without active bleeding.
- *Transfusion is aimed to augment oxygen delivery and uptake.*

Carson et al; Transfusion 2002

Walsh et al; Transfusion 2004

Table 1

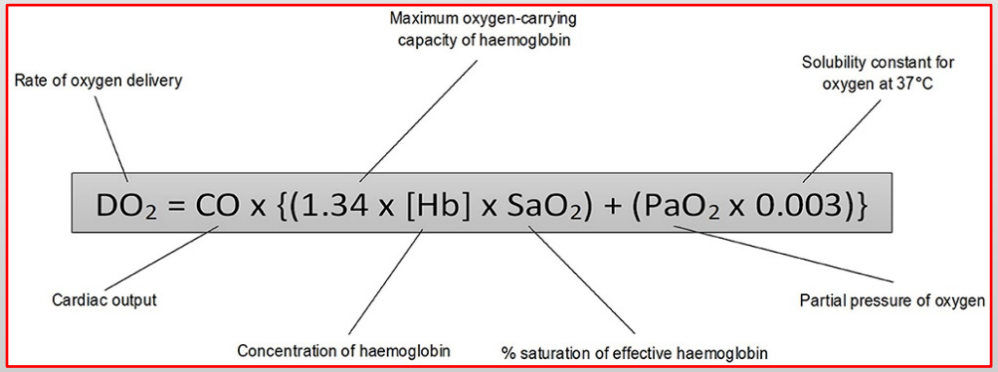
Causes of anemia in intensive care

Type of Anemia	Causes
Blood loss	Phlebotomy
	Gastrointestinal bleeding
	Trauma
	Surgery
Erythropoietin deficiencies	Inflammatory cytokines
	Renal insufficiency
	Drugs
	Decrease bone marrow response (functional deficiency)
Nutritional deficiencies	Low folate levels
	Low iron levels
	Low vitamin B levels (vitamin B12)
Hemolysis	Drug reactions
	Toxins
Coagulation abnormalities	Sepsis syndrome
	Thrombocytopenia
	Liver disease
	Viral infection Splenomegaly

Rawal et al; The Journal of Critical Care Medicine, 2016

Purpose of Transfusing PRBC

Oxygen Delivery

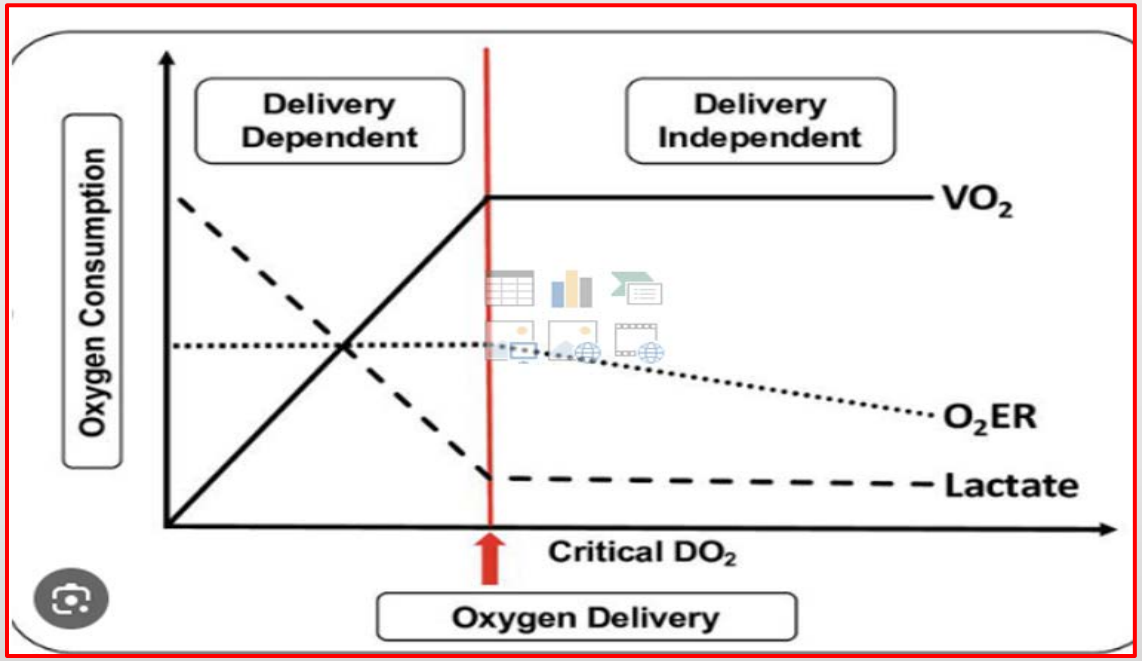


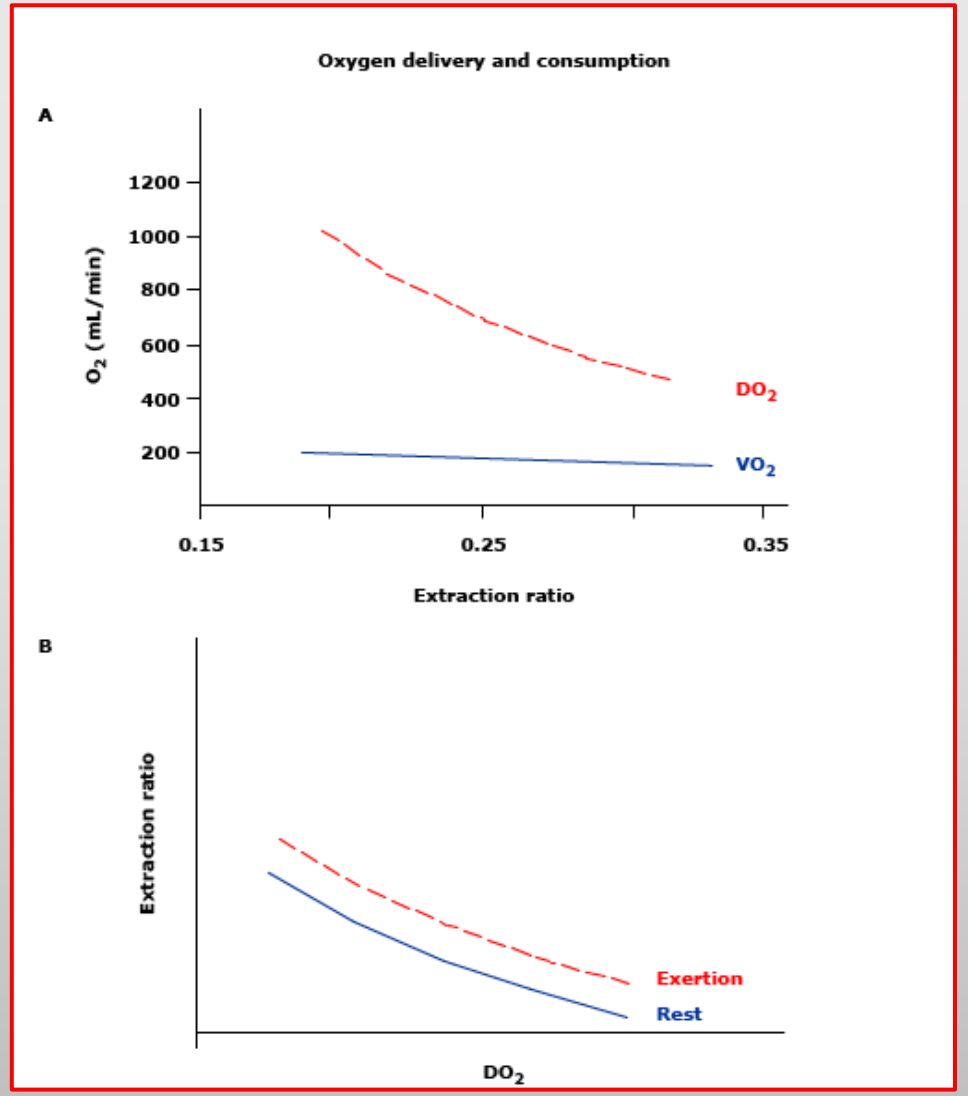
Oxygen consumption

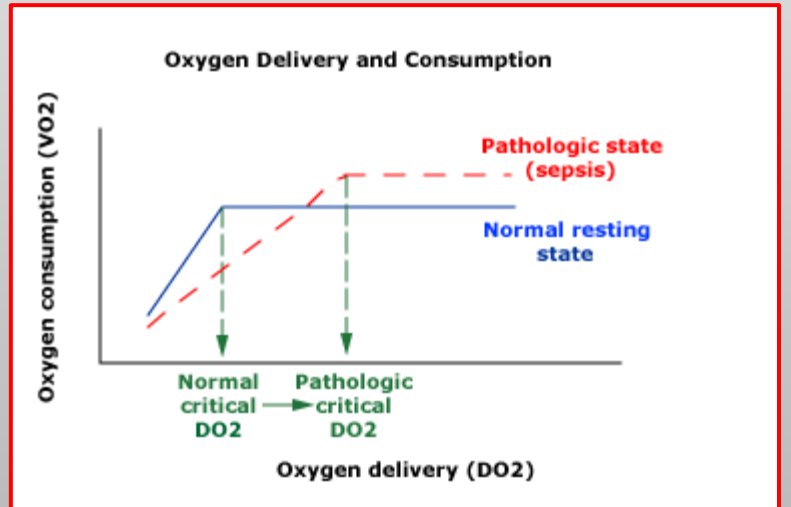
VO2= DO2 x O2 ER (extraction)

O2ER = (SaO2-SvO2) / SaO2

DO2 and VO2 Relationship

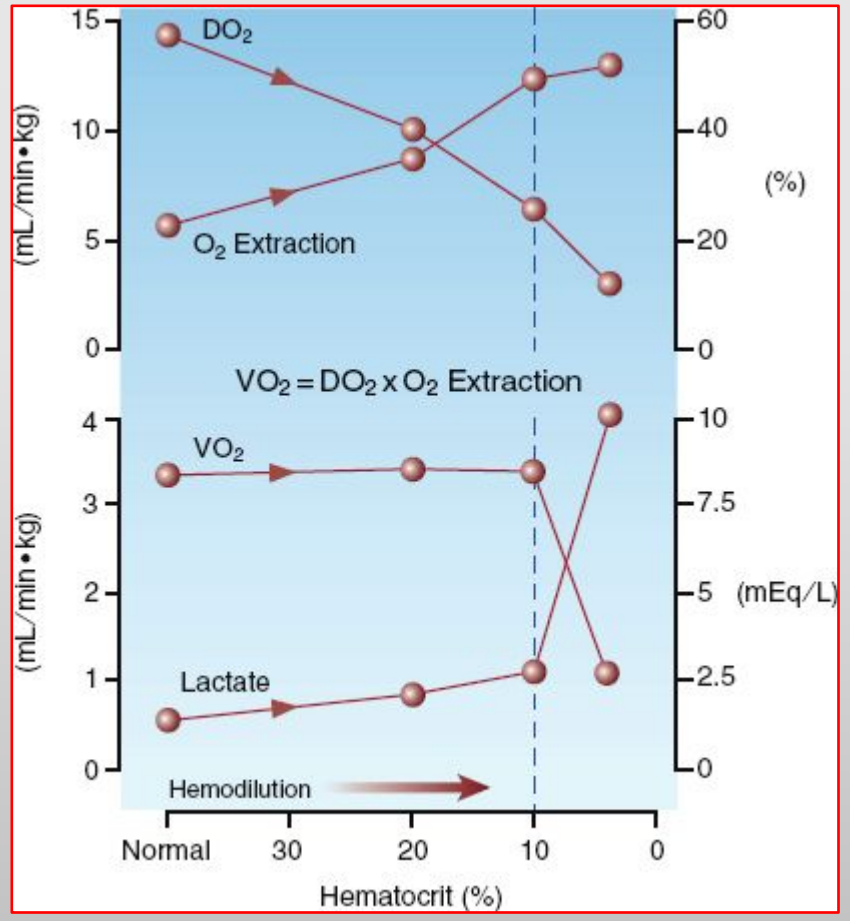






Oxygen Extraction Ratio: a Valid Indicator of Myocardial Metabolism in Anemia

Wilkerson et al; Journal of Surg Research 1987



Postural Pseudoanemia: Posture-dependent Change in Hematocrit

Jacob G et al; Mayo Clin Proc. 2005

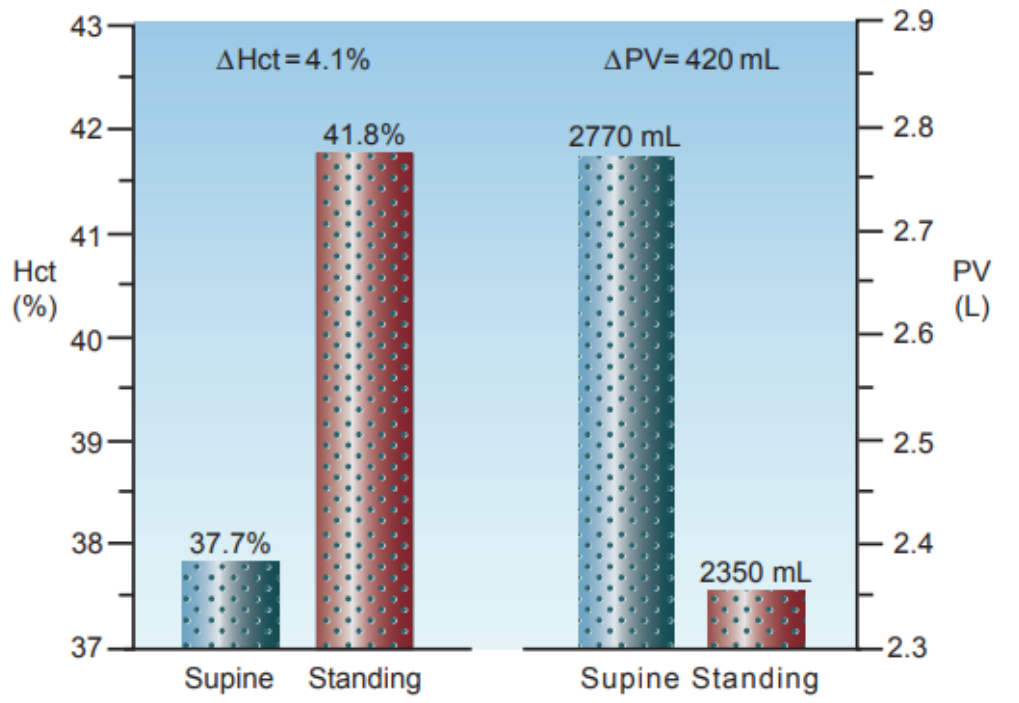


FIGURE 18.1 Postural changes in hematocrit (Hct) and plasma volume (PV) in a group of healthy adults. The numbers above the columns are mean values for each measurement. From Reference 5.

- Red cell mass: most accurate measure of the O2 carrying capacity of blood.
- Hct and Hb concentration: may not be an accurate measure of the O2 carrying capacity in critically ill patients.

Total circulating red cells versus hematocrit as a primary descriptor of oxygen transport by the blood.

Jones et al; Br J Hematol 1990

WHO criteria for Anemia: Males < 13gm/dL and Females < 12gm/dL.

Estimated total blood volume

- Males 66ml/Kg
- Females 60ml/Kg

40 year old male weighing 60 Kg with initial Hb 13 gm/dL.

I. Estimated total blood volume is 66ml x 60= 3960ml or 39.6dL.

II. Total Hb = 13x 39.6 =514.8 gm.

III. Received 4L of 0.9%NS, each 1L will roughly increase the intravascular volume by 280 ml.

IV. Estimated new blood volume: (286 mlx 4=1120ml or 11.2dL) + 39.6 dL= 50.8 dL.

V. Estimated new Hb = 514.8/50.8=10.1gm/dL.

Meeting Abstracts | September 1942

Anesthesia in Cases of Poor Surgical Risk: Some Suggestions for Decreasing the Risk

R. C. ADAMS; J. S. LUNDY

Anesthesiology September 1942, Vol. 3, 603–607.

https://doi.org/10.1097/00000542-194209000-00032

A Multicenter, Randomized, Controlled Clinical Trial of Transfusion Requirements in Critical Care (TRICC)

Hébert et al, NEJM 1999

N=838 critically ill patients with anemia

- Restrictive strategy: Target Hb 7-9 gm/dL.
- Liberal strategy: Target Hb 10 to 12 gm/dL.

Setting: 22 tertiary care and 3 community ICUs in Canada.

Exclusion:

- Actively bleeding.
- Hemodynamically unstable.

Primary outcome: 30-day mortality.

Primary Outcomes (Restrictive vs Liberal)

- 30-day mortality: 18.7% vs. 23.3% (P=0.11).

Secondary Outcomes

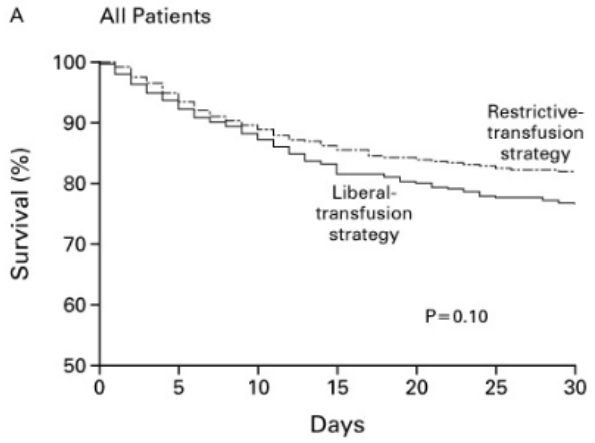
- Inpatient mortality: 22.2% vs. 28.1% (P=0.05).
- Multiple-organ dysfunction score: 3.2 vs. 4.2 (P=0.04).
- Change in organ dysfunction from baseline: 3.2 vs. 4.2 (P=0.04).

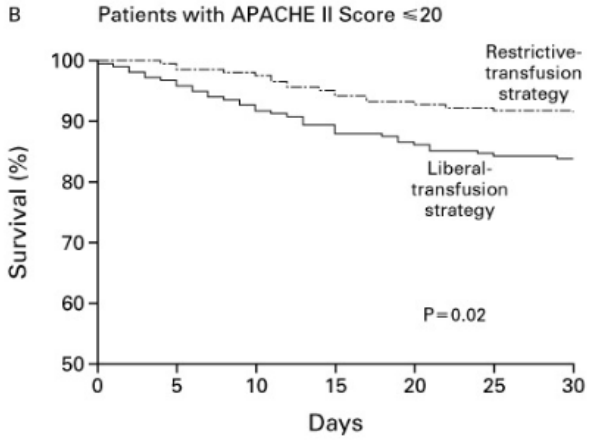
Significant survival benefit when adjusted for

- APACHE II ≤20 (8.7% vs 16.1%, P 0.03).
- Age <55 years (5.7% vs 13%, P 0.02).

No difference in survival when adjusted for

- Cardiac disease (20.5% vs 22.9%, P 0.69).
- Severe infections or septic shock.
- Trauma.





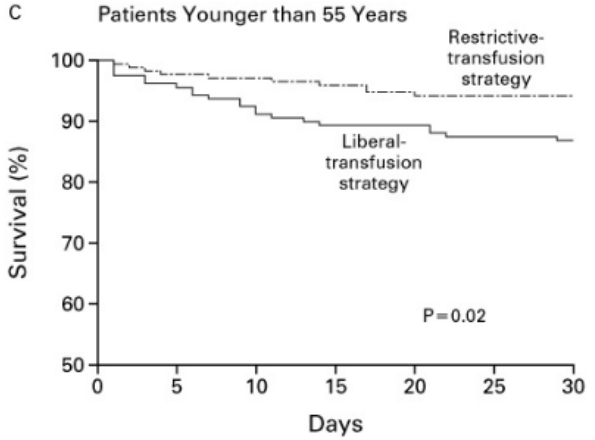


TABLE 3. COMPLICATIONS THAT OCCURRED DURING THE PATIENTS' STAYS IN THE INTENSIVE CARE UNIT.

COMPLICATION*	RESTRICTIVE-TRANSFUSION STRATEGY (N=418)	LIBERAL-TRANSFUSION STRATEGY (N=420)	ABSOLUTE DIFFERENCE BETWEEN GROUPS	95% CONFIDENCE INTERVAL†	P VALUE
	no. (%)		percent		
Cardiac	55 (13.2)	88 (21.0)	7.8	2.7 to 12.9	<0.01
Myocardial infarction	3 (0.7)	12 (2.9)	2.1	—	0.02
Pulmonary edema	22 (5.3)	45 (10.7)	5.5	1.8 to 9.1	<0.01
Angina	5 (1.2)	9 (2.1)	0.9	—	0.28
Cardiac arrest	29 (6.9)	33 (7.9)	0.9	−2.6 to 4.5	0.60
Pulmonary	106 (25.4)	122 (29.0)	3.7	−2.3 to 9.7	0.22
ARDS	32 (7.7)	48 (11.4)	3.8	−0.2 to 7.8	0.06
Pneumonia	87 (20.8)	86 (20.5)	−0.3	−5.8 to 5.1	0.92
Infectious	42 (10.0)	50 (11.9)	1.9	−2.4 to 6.1	0.38
Bacteremia	30 (7.2)	40 (9.5)	2.3	−1.4 to 6.1	0.22
Catheter-related sepsis	21 (5.0)	17 (4.0)	−1.0	−3.8 to 1.8	0.50
Septic shock	41 (9.8)	29 (6.9)	−2.9	−6.7 to 0.8	0.13
Hematologic‡	10 (2.4)	10 (2.4)	0	−2.1 to 2.1	1.00
Gastrointestinal§	13 (3.1)	19 (4.5)	1.4	−1.2 to 4.0	0.28
Neurologic¶	25 (6.0)	33 (7.9)	1.9	−1.6 to 5.3	0.28
Shock‖	67 (16.0)	55 (13.1)	−2.9	−7.7 to 1.8	0.23
Any complication	205 (49.0)	228 (54.3)	5.2	−1.5 to 12.0	0.12

Hébert et al, NEJM 1999

Efficacy of Red Blood Cell Transfusion in The Critically ill: a Systematic Review of the Literature

Marik et al; Critical Care Medicine 2008

Cohort studies that assessed the independent effect of RBC transfusion on patient outcomes.

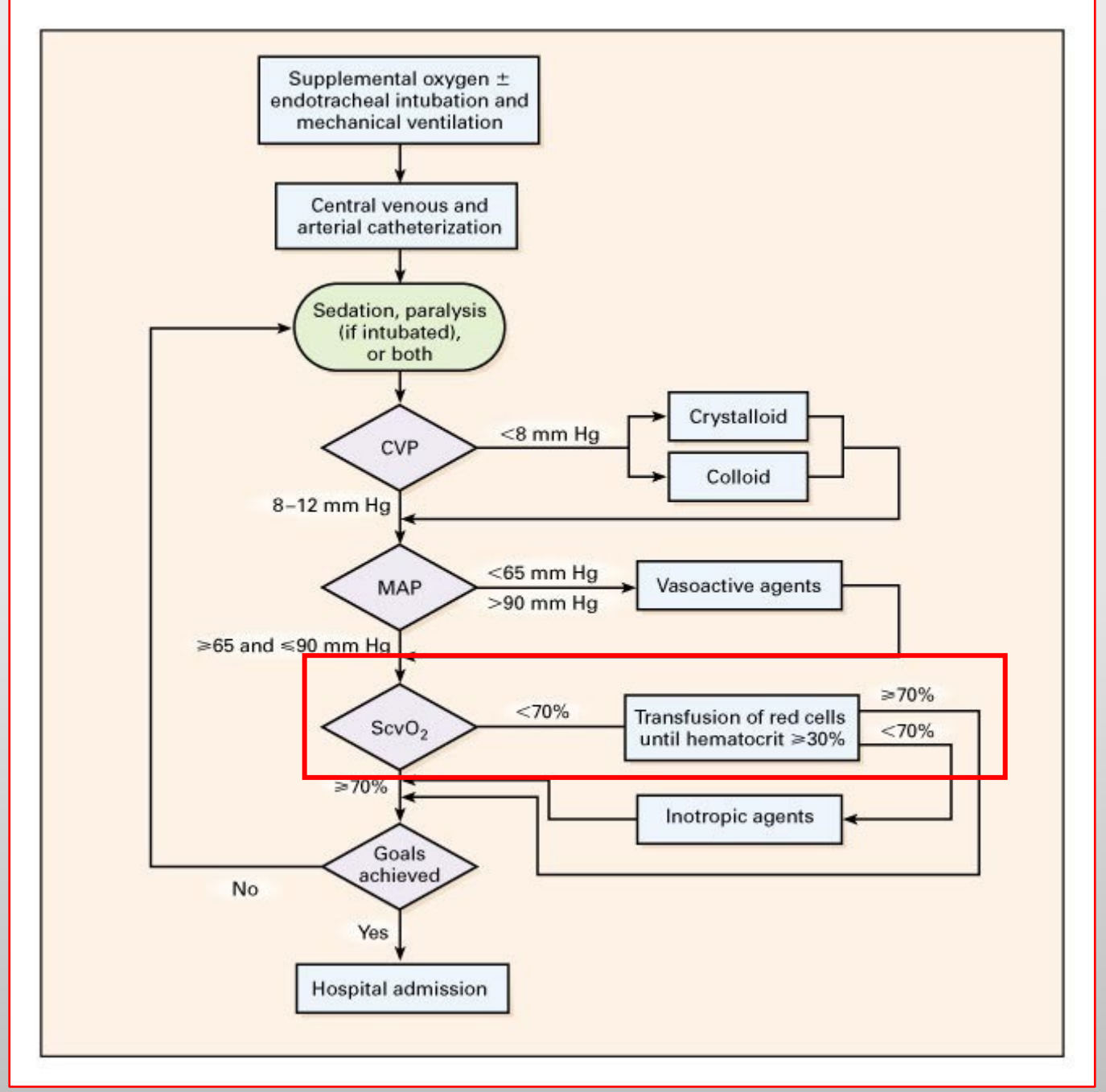
From 571 articles screened, 45 met inclusion criteria and were included for data extraction.

45 studies with a median patient of 687/ total 272,596.

Outcome measures:

- Mortality
- Infections
- Multiorgan dysfunction syndrome
- Acute respiratory distress syndrome

- 42 out of 45 studies: risks outweighed the benefits.
- 2 studies: risk was neutral
- 1 study: benefit> risk (elderly patients with acute MI with Hct< 30%).
- 17 studies: transfusion was independent predictor of death (OR1.7).
- 22 studies: independent risk factor for infection (OR 1.8).
- 3 studies: MODS
- 6 studies: ARDS (OR 2.5)



Rivers et al; NEJM 2001

Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock (TRISS)

Holst L, et al, NEJM 2014

N=998 ICU patients with septic shock.

- Restrictive: Target Hb 7g/dL
- Liberal: Target Hb 9g/dL

Setting: 32 ICUs in Denmark, Sweden, Norway, and Finland.

Primary outcome: 90-day mortality.

Primary Outcomes (Restrictive vs Liberal)

- Death by day 90: 43% vs. 45% (P=0.44).

Secondary Outcomes

- Days alive without vasopressor/ inotropic therapy: 73% vs. 75% P=0.93).
- Days alive without mechanical ventilation : 65% vs. 67% (P=0.49).
- Days alive without RRT: 85% vs. 83% (P=0.54).
- Days alive and out of hospital : 30% vs. 31% (P=0.89).
- Number of transfusions: 1545 vs. 3088 (P<0.001).
- Transfused in the ICU: 63.9% vs. 98.8% (P<0.001).

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Villanueva C et al, NEJM 2013

N=921 patients with acute UGIB.

- Restrictive strategy: Target Hb 7gm/dL
- Liberal strategy: Target Hb 9gm/dL

Single center, non-blinded, parallel group, randomized, controlled trial.

Setting: One center in Barcelona, Spain.

Primary outcome: All-cause mortality at 45 days.

Primary Outcome (Restrictive vs Liberal)

- All-cause mortality at 45 days: 5% vs. 9% (P=0.02, NNT 25).

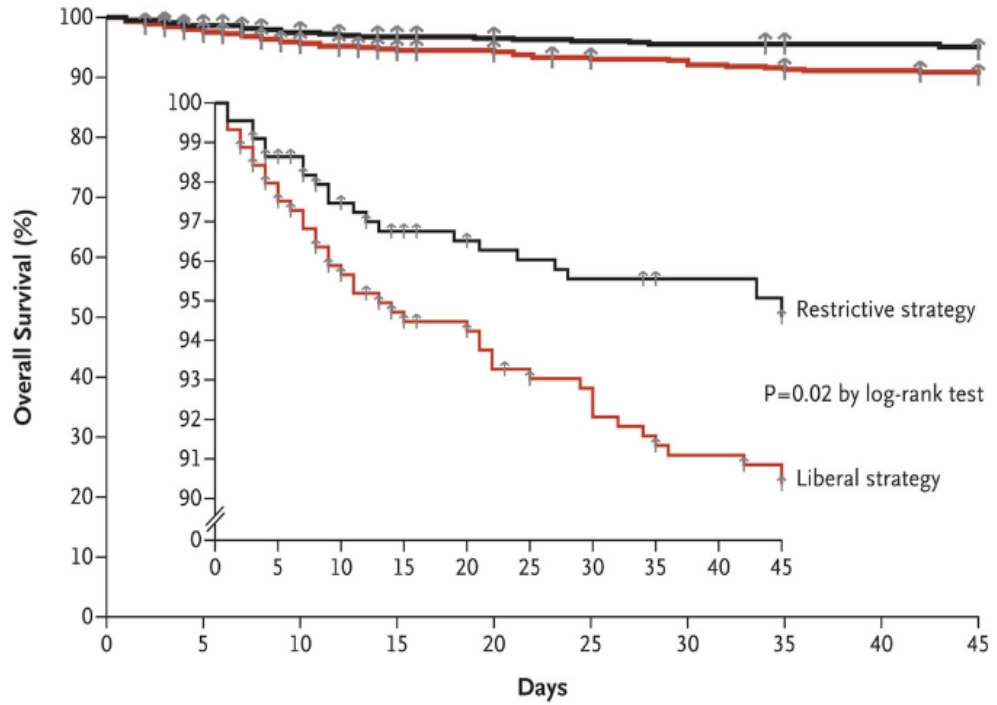
Secondary Outcomes

- Further bleeding associated with hemodynamic instability or Hgb drop ≥2 within 6 hours : 10% vs. 16% (P=0.01).
- RBC transfusions : 49% vs. 86% (P<0.001).
- 1.5 vs. 3.7 transfusions per patient (P<0.001).
- 1.2 vs. 2.9 transfusions during initial bleeding (P<0.001).

Mean LOS

- 9.6 vs. 11.5 days (P=0.01).

A Survival, According to Transfusion Strategy

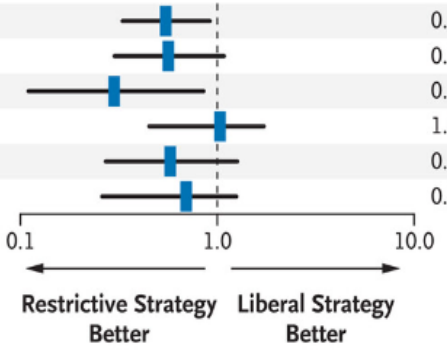


No. at Risk

Restrictive strategy	444	429	412	404	401	399	397	395	394	392
Liberal strategy	445	428	407	397	393	386	383	378	375	372

B Death by 6 Weeks, According to Subgroup

Subgroup	Restrictive Strategy	Liberal Strategy	Hazard Ratio (95% CI)	P Value
	no. of patients/total no. (%)			
Overall	23/444 (5)	41/445 (9)	0.55 (0.33–0.92)	0.02
Patients with cirrhosis	15/139 (11)	25/138 (18)	0.57 (0.30–1.08)	0.08
Child–Pugh class A or B	5/113 (4)	13/109 (12)	0.30 (0.11–0.85)	0.02
Child–Pugh class C	10/26 (38)	12/29 (41)	1.04 (0.45–2.37)	0.91
Bleeding from varices	10/93 (11)	17/97 (18)	0.58 (0.27–1.27)	0.18
Bleeding from peptic ulcer	7/228 (3)	11/209 (5)	0.70 (0.26–1.25)	0.26



Villanueva C et al, NEJM 2013

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

Carson JL, et al; NEJM 2011

N=2,016 high-risk adults undergoing hip surgery.

- Liberal: Target Hb 10gm/dL
- Restrictive: Target Hb 8 gm/dL

Setting: 47 clinical sites in the US and Canada.

Follow-up: 60 days.

Primary outcome: Death or inability to walk without assistance at 60-day follow-up.

Secondary outcomes: In-hospital MI, unstable angina, or death for any reason.

Primary Outcomes (Liberal vs Restrictive)

- Death or inability to walk 10 feet without assistance at 60 day follow-up: 35.2% vs. 34.7% (P=0.90).

Secondary Outcomes

- Death at 60 days: 7.6% vs. 6.6% (OR 1.17; 99% CI 0.75-1.83).
- Inability to walk 10 feet without assistance at 60 days 27.6% vs. 28.1%.
- MI, unstable angina, or in-hospital death 4.3% vs. 5.2% (OR 0.82; 99% CI 0.48-1.42).
- MI 2.3% vs. 3.8% (OR 0.60, 99% CI 0.30-1.19).
- Unstable angina 0.2% vs. 0.3% (OR 0.67, 99% CI 0.06-7.03).
- In-hospital death 2.0% vs 1.4% (OR 1.44, 99% CI 0.58-3.56).

Subgroup Analysis

- Primary outcome : 1.45 in men versus 0.91 in women (P=0.03).

Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery (TRICS III)

Mazer CD, et al; NEJM 2017

N=4,860 patients undergoing on-pump cardiac surgery.

- Restrictive: Target Hb 7.5 g/dL
- Liberal: Target Hb <8.5 (non-ICU) or 9.5 g/dL (ICU)

Duration of follow-up: 28 days.

International, open-label, randomized, controlled, noninferiority trial.

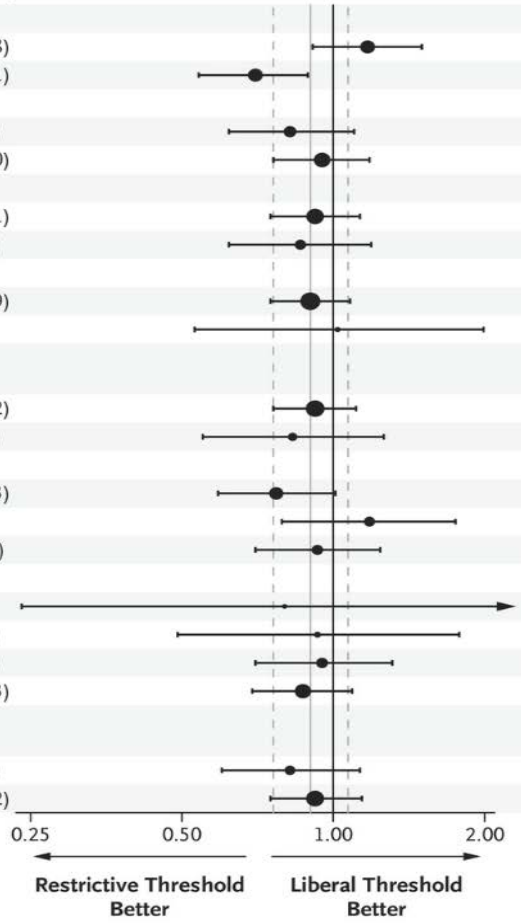
Primary outcome: Composite outcome of death from any cause, MI, stroke, or new renal failure requiring HD.

Primary Outcomes (Restrictive vs Liberal)

- Death from any cause, MI, stroke, or renal failure requiring HD during hospitalization or within 28 days: 11.4% vs. 12.5% (P<0.001 for noninferiority).
- Death: 3.0% vs. 3.6%.
- Stroke: 1.9% vs. 2.0%.
- Myocardial Infarction: 5.9% vs. 5.9%.
- New-onset renal failure with dialysis: 2.5% vs. 3.0%.

Characteristic	Restrictive Threshold (N=2430)	Liberal Threshold (N=2430)	Odds Ratio or Hazard Ratio (95% CI)
Primary outcome			
Composite-outcome event — no./total no. (%)	276/2428 (11.4)	303/2429 (12.5)	0.90 (0.76–1.07)
Death — no./total no. (%)	74/2427 (3.0)	87/2429 (3.6)	0.85 (0.62–1.16)
Stroke — no./total no. (%)	45/2428 (1.9)	49/2429 (2.0)	0.92 (0.61–1.38)
Myocardial infarction — no./total no. (%)	144/2428 (5.9)	144/2429 (5.9)	1.00 (0.79–1.27)
New-onset renal failure with dialysis — no./total no. (%)	61/2428 (2.5)	72/2429 (3.0)	0.84 (0.60–1.19)

Subgroup	No. of Patients	Restrictive Threshold	Liberal Threshold	Unadjusted Odds Ratio (95% CI)	P Value for Interaction
		no. of patients with event/total no. (%)			
Age					0.004
<75 yr	2426	152/1218 (12.5)	131/1208 (10.8)	1.17 (0.91–1.50)	
≥75 yr	2431	124/1210 (10.2)	172/1221 (14.1)	0.70 (0.54–0.89)	
Sex					0.45
Female	1719	99/876 (11.3)	113/843 (13.4)	0.82 (0.62–1.10)	
Male	3138	177/1552 (11.4)	190/1586 (12.0)	0.95 (0.76–1.18)	
Diabetes					0.75
No	3526	200/1783 (11.2)	211/1743 (12.1)	0.92 (0.75–1.13)	
Yes	1331	76/645 (11.8)	92/686 (13.4)	0.86 (0.62–1.19)	
Creatinine level					0.71
≤2.26 mg/dl	4685	253/2348 (10.8)	277/2337 (11.9)	0.90 (0.75–1.08)	
>2.26 mg/dl	172	23/80 (28.7)	26/92 (28.3)	1.02 (0.53–1.99)	
Chronic pulmonary disease					0.67
No	4057	229/2023 (11.3)	249/2034 (12.2)	0.92 (0.76–1.11)	
Yes	800	47/405 (11.6)	54/395 (13.7)	0.83 (0.55–1.26)	
Surgery category					0.22
Non-CABG	2247	111/1138 (9.8)	136/1109 (12.3)	0.77 (0.59–1.01)	
CABG only	1266	57/621 (9.2)	51/645 (7.9)	1.18 (0.79–1.75)	
CABG+ other	1344	108/669 (16.1)	116/675 (17.2)	0.93 (0.70–1.24)	
Left ventricular function					0.78
Very poor	84	6/46 (13.0)	6/38 (15.8)	0.80 (0.24–2.72)	
Poor	322	21/166 (12.7)	21/156 (13.5)	0.93 (0.49–1.78)	
Moderate	1441	88/731 (12.0)	89/710 (12.5)	0.95 (0.70–1.31)	
Good	3010	161/1485 (10.8)	187/1525 (12.3)	0.87 (0.69–1.09)	
Preoperative hemoglobin concentration					0.54
<12.0 g/dl	1149	84/593 (14.2)	93/556 (16.7)	0.82 (0.60–1.13)	
≥12.0 g/dl	3708	192/1835 (10.5)	210/1873 (11.2)	0.92 (0.75–1.14)	



Mazer CD, et al; NEJM 2017

Clinical Trials Evaluating Red Blood Cell Transfusion Thresholds: An Updated Systematic Review and With Additional Focus on Patients With Cardiovascular Disease

Carson et al; Am Heart J 2018

- Systemic review
- Objective: to evaluate transfusion thresholds in patients with cardiovascular disease.
- Included 37 trials that enrolled 19,049 patients.
- Enrolled patients undergoing cardiac surgery and with acute myocardial infarction.
- Primary outcome: 30 day mortality.

- 26 trials enrolling 15,681: no difference in patients the 30-day mortality.
- Cardiac surgery, mortality was comparable (risk ratio 0.99; 95% confidence interval 0.74-1.33).
- In 2 small trials (n=154) in patients with myocardial infarction, the mortality risk ratio was 3.88 (95% CI, 0.83-18.13) favoring the liberal strategy.

Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia (REALITY)

Ducrocq G et al; JAMA 2021

N: 668 patients with MI and Hb 7 to10 g/dL.

- Restrictive: Hb target 8 g/dL
- Liberal: Hb target 10g/dL

Duration of follow-up: 30 days.

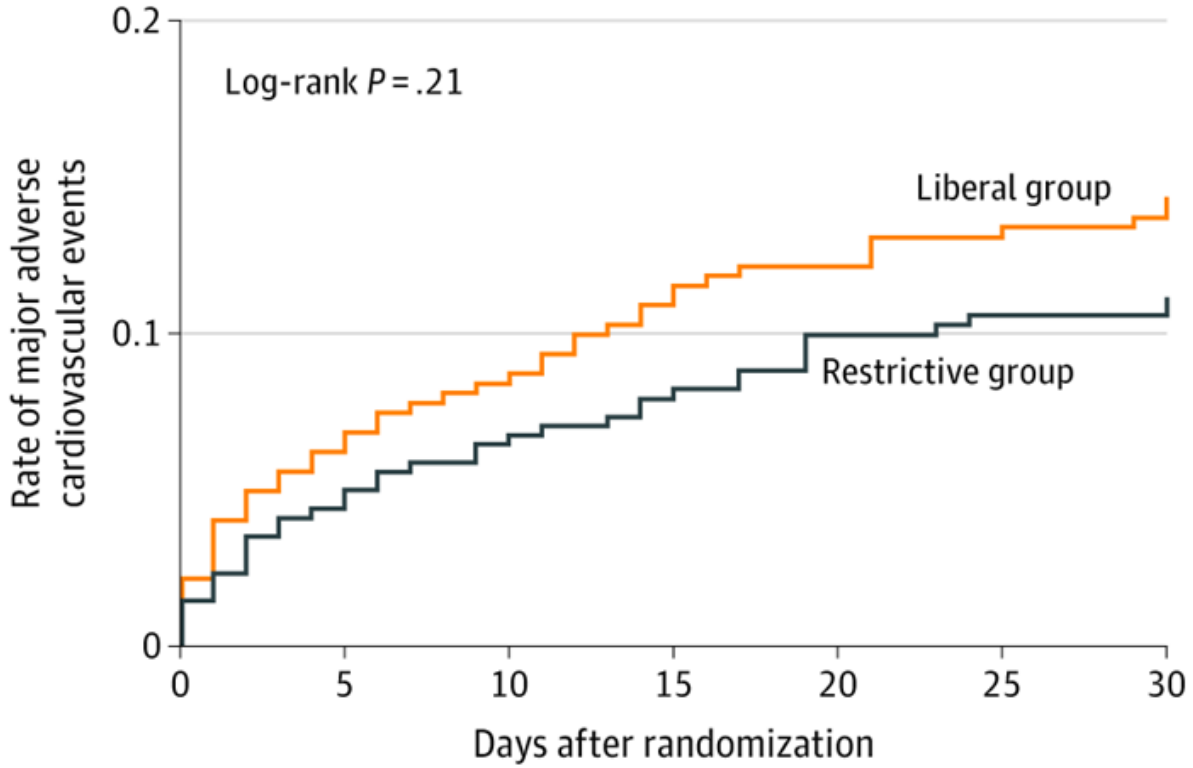
35 hospitals in France and Spain.

Primary Outcome: MACE (all-cause death, stroke, recurrent myocardial infarction, or emergency revascularization).

Primary Outcome (Restrictive vs Liberal).

- MACE 11% vs 14%.
- Relative risk of primary outcome: 0.79 (1-sided 97.5% CI, 0.00-1.19).
- All cause death: 5.6% vs 7.7%.
- Recurrent MI: 2.1% vs 3.1%.
- Emergency revascularization: 1.5% vs 1.9%.
- Non-fatal ischemic stroke: 0.6% in both groups.

Figure 2. Rate of Major Adverse Cardiovascular Events in a Study of the Effect of a Restrictive vs Liberal Blood Transfusion Strategy Among Patients With Acute Myocardial Infarction and Anemia



No. of patients at risk							
Liberal group	324	301	293	285	281	278	275
Restrictive group	342	326	319	314	307	305	305

Results shown are of analyses including the as-randomized population. All patients were followed up to the first event or 30 days. Major adverse cardiovascular events are a composite of all-cause death, stroke, recurrent myocardial infarction, or emergency revascularization prompted by ischemia.

Ducrocq G et al; JAMA 2021

Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia (TRIM)

Carson et al; NEJM 2023

N= 3504

- Restrictive: Target Hb 7-8 g/dL
- Liberal: Target Hb 10

Duration of follow-up: 30 days.

144 sites in the United States, Canada, France, Brazil, New Zealand, and Australia.

Primary outcome: Composite outcome of death and MI at 30 days.

Primary Outcomes (Restrictive vs Liberal)

- Death and recurrent MI: 16.9% vs. 14.5 % (P=0.07).

  Death: 9.9% vs 8.3%; Recurrent MI: 8.5% vs.7.2%.

Death, myocardial infarction, ischemia-driven unscheduled coronary revascularization, or readmission to the hospital or an ischemic cardiac condition: 19.6% vs. 17.4% (risk ratio, 1.13; 95% CI, 0.98 to 1.29).

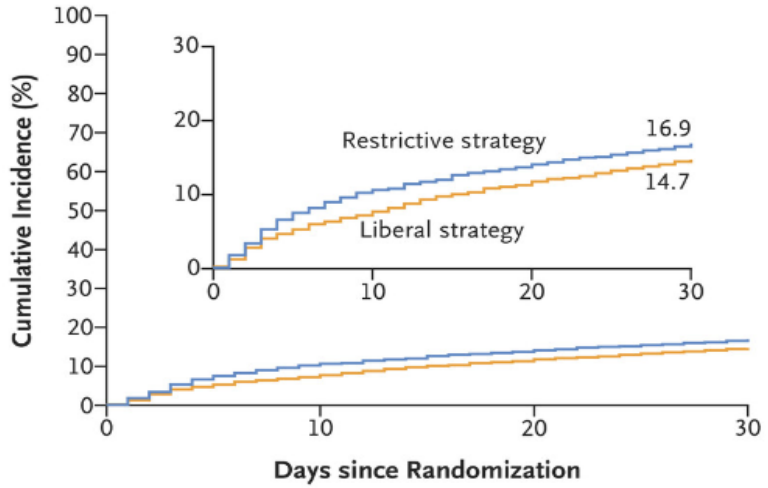
Cardiac death (5.5% and 3.2%; risk ratio, 1.74; 95% CI, 1.26 to 2.40).

Subgroup analysis

Type 1 myocardial infarction: risk ratio, 1.32; 95% CI, 1.04 to 1.67).

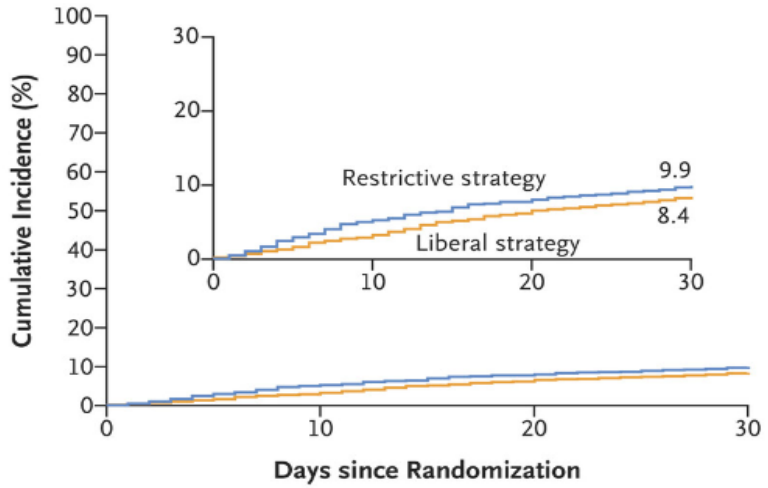
Type 2 myocardial infarction (risk ratio, 1.05; 95% CI, 0.85 to 1.29).

A Composite Outcome of Myocardial Infarction or Death



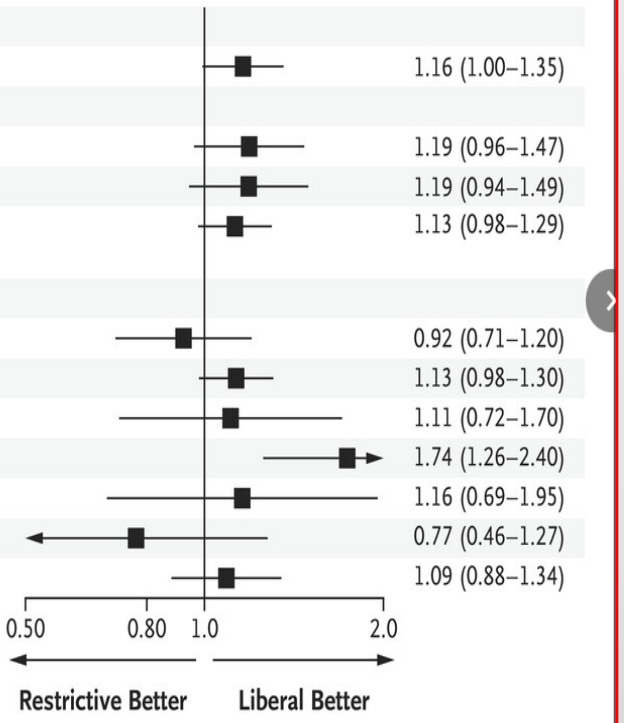
No. at Risk				
Restrictive strategy	1749	1565	1503	1439
Liberal strategy	1755	1605	1532	1467

B Death from Any Cause



No. at Risk				
Restrictive strategy	1749	1654	1605	1566
Liberal strategy	1755	1679	1621	1585

Outcome	Restrictive Strategy	Liberal Strategy	Risk Ratio (95% CI)
	no. of patients/total no. (%)		
Primary outcome			
Myocardial infarction or death	295/1749 (16.9)	255/1755 (14.5)	1.16 (1.00–1.35)
Secondary outcomes			
Death	173/1749 (9.9)	146/1755 (8.3)	1.19 (0.96–1.47)
Myocardial infarction	149/1749 (8.5)	126/1755 (7.2)	1.19 (0.94–1.49)
Death, myocardial infarction, revascularization, or rehospitalization	342/1749 (19.6)	305/1755 (17.4)	1.13 (0.98–1.29)
Other outcomes			
Heart failure	102/1749 (5.8)	111/1755 (6.3)	0.92 (0.71–1.20)
Death, myocardial infarction, or unstable angina	338/1749 (19.3)	300/1755 (17.1)	1.13 (0.98–1.30)
Unscheduled revascularization	43/1749 (2.5)	39/1755 (2.2)	1.11 (0.72–1.70)
Cardiac death	97/1749 (5.5)	56/1755 (3.2)	1.74 (1.26–2.40)
Stroke	30/1749 (1.7)	26/1755 (1.5)	1.16 (0.69–1.95)
Pulmonary embolism or deep venous thrombosis	26/1749 (1.5)	34/1755 (1.9)	0.77 (0.46–1.27)
Pneumonia or bacteremia	166/1749 (9.5)	153/1755 (8.7)	1.09 (0.88–1.34)



Carson et al; NEJM 2023

Red Blood Cell Transfusion does not Increase Oxygen Consumption in Critically ill Septic Patients

Fernandes CJ Jr. et al; Critical Care 2001

Table 2 Results from the group receiving red blood cell transfusion

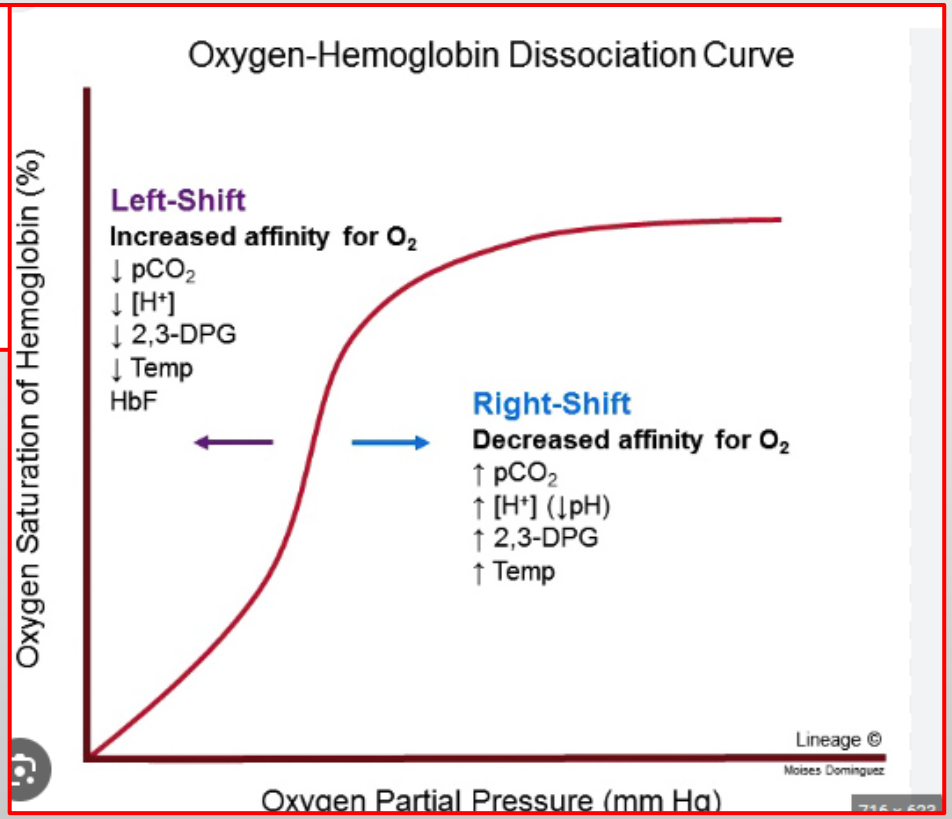
From: Red blood cell transfusion does not increase oxygen consumption in critically ill septic patients

Variable	Baseline	After infusion	*P*
HR (bpm)	109.4 ± 20.3	108.9 ± 21.7	NS
RAP (mmHg)	10.4 ± 3.7	10.7 ± 4.9	NS
MPAP (mmHg)	25.2 ± 5.0	26.9 ± 5.5	NS
WP (mmHg)	13.4 ± 3.8	13.2 ± 4.5	NS
MAP (mmHg)	76.8 ± 15.8	82.9 ± 17.2	NS
CI (L/min/m^2)	4.7 ± 0.7	4.7 ± 1.1	NS
LVSWI (g/min/m^2)	38.6 ± 12.6	41.1 ± 13.0	<0.05
SVRI (dyne/s/cm^5/m^2)	1050.3 ± 336.0	1148.3 ± 398.0	NS
PVRI (dyne/s/cm^5/m^2)	203.7 ± 58.0	238.8 ± 49.8	<0.05
DO_2 (ml/min/m^2)	607.3 ± 123.5	647.5 ± 167.7	NS
VO_2 (ml/min/m^2)			
Calorimetry	168.9 ± 63.1	162.5 ± 67.7	NS
Fick	142.2 ± 44.9	149.6 ± 41.9	NS
Hb (g%)	9.4 ± 0.5	10.1 ± 0.8	<0.05
Ht (%)	27.8 ± 1.7	29.8 ± 1.8	<0.05
pHi	7.19 ± 0.07	7.21 ± 0.16	NS
Lactate (mmol/l)	1.8 ± 0.5	1.7 ± 0.5	NS

The In Vitro Restoration of Red Cell 2,3-Diphosphoglycerate Levels in Banked Blood

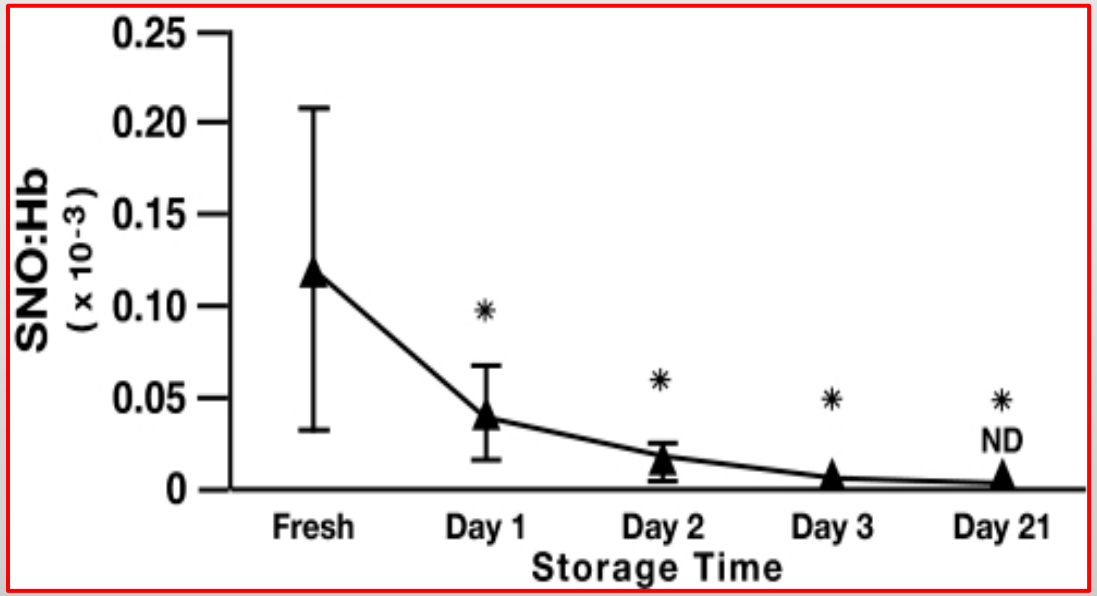
Oski et al; Blood 1971

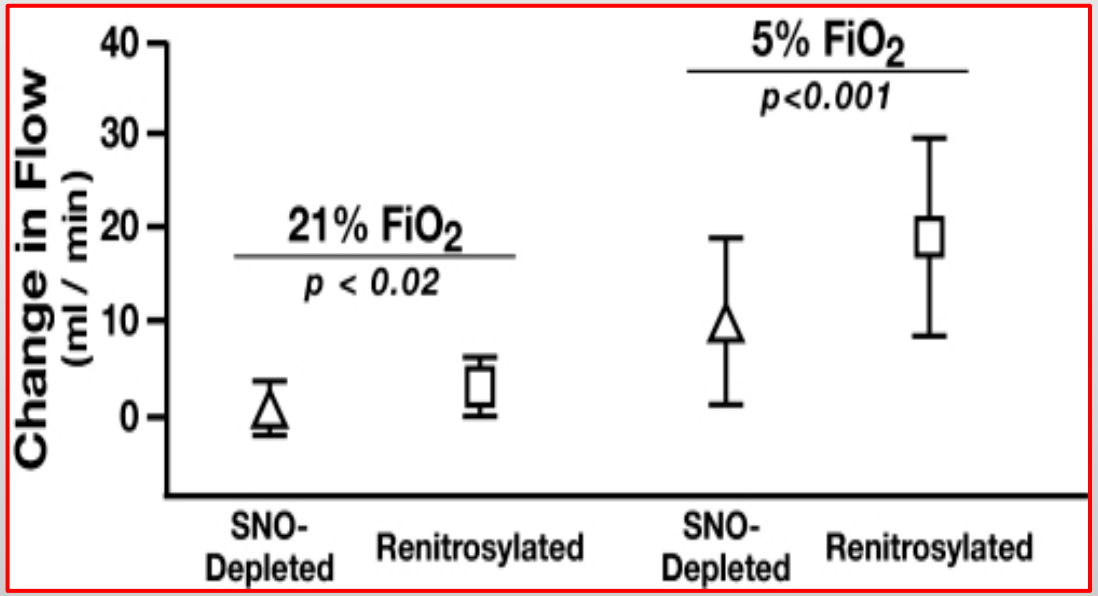
In blood stored under conventional blood bank conditions the 2,3-DPG level drops sharply and by 10 days of storage 2,3-DPG levels are only 20–25 per cent of their original level and by 21 days of storage they have fallen to 10 per cent of their initial content.[8-10] The addition of inosine to 2,3-DPG poor blood has been found to result in a partial restoration of 2,3-DPG levels and a decrease in the affinity of hemoglobin for oxygen.[10,11] The purpose



S-nitrosohemoglobin Deficiency: a Mechanism for Loss of Physiological Activity in Banked Blood

Reynolds JD et al; Proceedings of the National Academy of Sciences, 2007





Age of Transfused Blood in Critically Ill Adults (ABLE Study)

Lacroix J et al; NEJM 2015

- N= 2400
- Fresh Blood Group: 6.1±4.9 days
- Standard Group: 22.0±8.4 days

- 64 centers in Europe and Canada

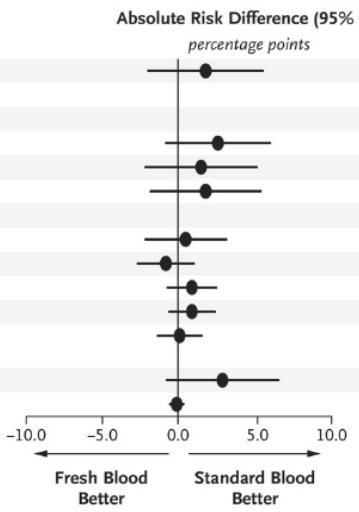
- Primary Outcome: 90 Day Mortality

Fresh vs. Standard

Primary Outcome: 37% vs 35% (absolute risk difference, 1.7 percentage points; 95% confidence interval [CI], –2.1 to 5.5)

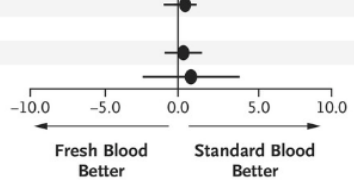
A Primary Outcome and Secondary Outcomes Related to Death and Major Illnesses

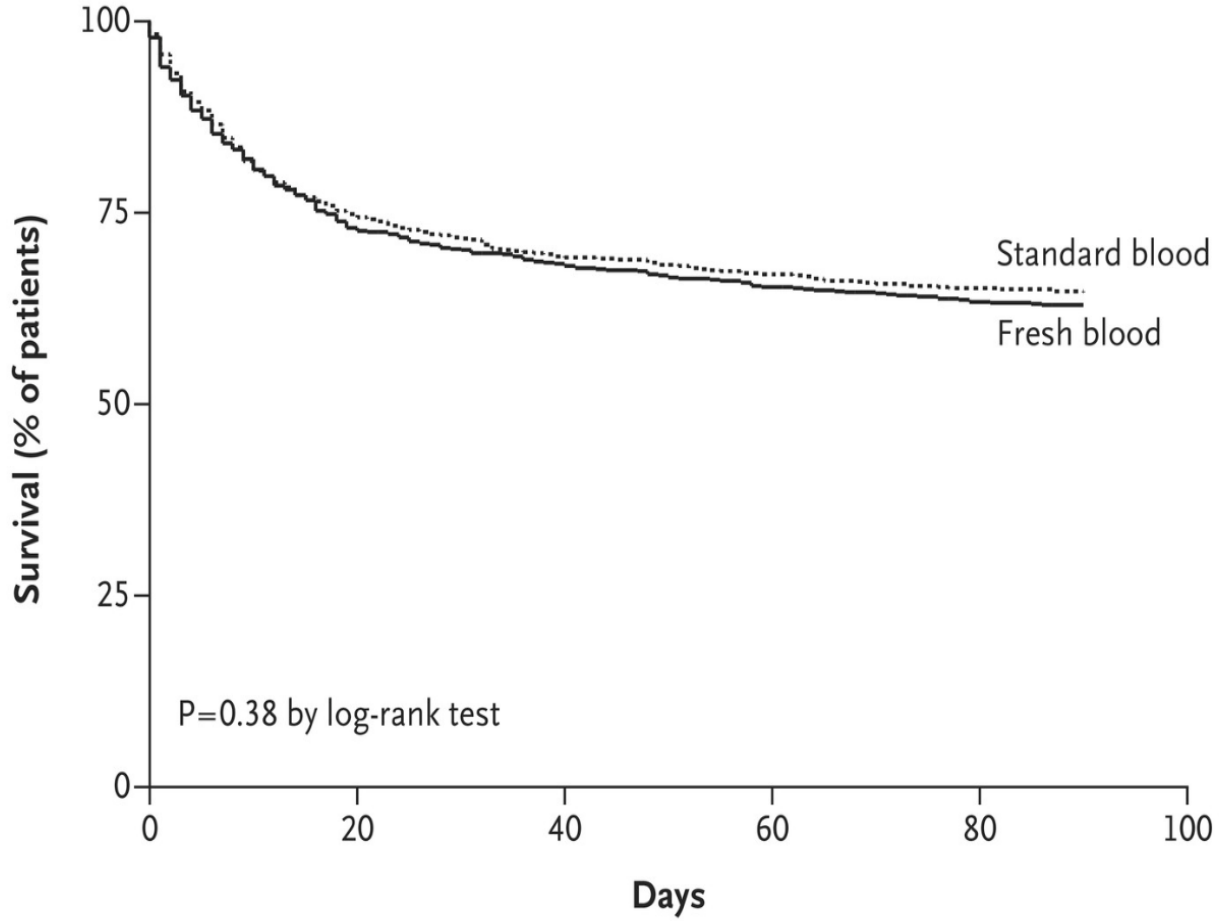
Outcome	Fresh Blood	Standard Blood	Absolute Risk Difference (95% CI)
	no. of patients/total no. (%)		*percentage points*
Primary outcome: death by day 90	448/1211 (37.0)	430/1219 (35.3)	1.7 (−2.1 to 5.5)
Secondary outcomes			
Death			
In ICU	324/1214 (26.7)	295/1217 (24.2)	2.5 (−1.0 to 5.9)
In hospital	403/1212 (33.3)	386/1211 (31.9)	1.4 (−2.3 to 5.1)
By day 28	371/1214 (30.6)	353/1225 (28.8)	1.7 (−1.9 to 5.4)
Major Illnesses			
Multiple organ dysfunction syndrome	162/1206 (13.4)	157/1207 (13.0)	0.4 (−2.3 to 3.1)
Acute respiratory distress syndrome	69/1206 (5.7)	80/1207 (6.6)	−0.9 (−2.8 to 1.0)
Cardiovascular failure	61/1206 (5.1)	51/1207 (4.2)	0.8 (−0.8 to 2.5)
Cardiac ischemia or infarction	54/1206 (4.5)	44/1207 (3.6)	0.8 (−0.7 to 2.4)
Deep-vein thrombosis or pulmonary embolism	43/1206 (3.6)	43/1207 (3.6)	0.0 (−1.5 to 1.5)
Nosocomial infection	411/1206 (34.1)	378/1207 (31.3)	2.8 (−0.9 to 6.5)
Acute transfusion reaction	4/1206 (0.3)	6/1207 (0.5)	−0.2 (−0.7 to 0.3)



B Other Secondary Outcomes

Outcome	Fresh Blood	Standard Blood	Mean Difference (95% CI)
	Mean (±SD)		*value*
MODS			
Highest score	6.4±3.2	6.2±3.2	0.2 (−0.1 to 0.4)
Delta score	1.4±1.8	1.4±1.9	−0.1 (−0.2 to 0.1)
Duration of supportive care (days)			
Mechanical ventilation	15.0±18.0	14.7±14.9	0.3 (−1.1 to 1.6)
Cardiac or vasoactive drugs	7.1±10.2	7.5±11.2	−0.4 (−1.2 to 0.5)
Extrarenal epuration	2.5±10.1	2.3±8.3	0.2 (−0.6 to 0.9)
Length of stay (days)			
In ICU	15.3±15.4	15.3±14.8	0.1 (−1.2 to 1.3)
In hospital	34.4±39.5	33.9±38.8	0.5 (−2.6 to 3.7)





Lacroix J et al; NEJM 2015

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 MI	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

Courtesy: Uptodate

Restrictive vs. Liberal Transfusions in these Patient Subgroups

- Elderly Critically Ill Patients.
- Oncologic and Hemato-Oncologic Critically Ill Patients.
- Critically Ill Patients Undergoing ECMO.
- Critically ill Adults with Acute Neurologic Injury (traumatic brain injury, subarachnoid hemorrhage, or stroke).

Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Vlaar AP et al; Intensive Care Med, 2020

- Should alternative RBC transfusion triggers (e.g. SvO2, acidosis, arrhythmia, electrocardiogram changes) guide transfusion in the non-bleeding critically ill patients?

  Answer: No

- Should iron be used to limit RBC transfusion in non-bleeding, critically ill adults with anemia?

  Answer: No

- Should erythropoietin be used to prevent transfusion in non-bleeding, critically ill adults with anemia?

  Answer: No

- Should combined erythropoietin and iron be used to prevent transfusion in critically ill, adult patients with anemia?

  Answer: No

- Should small-volume blood collection tubes vs. regular blood collection tubes be used for preventing anemia in non-bleeding critically ill patients?

  Answer: Yes

- Should blood conservation devices versus conventional sampling systems be used for blood sampling in non-bleeding critically ill patients?

  Answer: Yes

Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Vlaar AP et al; Intensive Care Med, 2020

Massive Transfusion

Definition:

- Massive transfusion:>/=10 units of WB or PRBCs in 24 hours, >/= 3 PRBC in 1 hour, >/= 4 blood products in 30 minutes.
- Ultra-massive transfusion: >/= 20 units of PRBCs within a 24- to 48-hour period.

Purpose of MT:

- Overcome tissue hypoperfusion.
- Tissue oxygen deficit.

Causes:

- Cardiac and vascular surgeries.
- Gastrointestinal and obstetrical hemorrhages.
- Liver transplants.
- Trauma.

Flow Rates in IV/IO Access

Gauge	Approximate Flow Rate to Gravity (mL/min)	Time to Infuse IL (min)
14G	250	4
16G	150	7
Cordis	130	8
18G	100	10
15G Humeral IO	80	13
16G Distal Port Triple Lumen	70	15
15G Tibial IO	70	15
20G	60	17
22G	35	29
18G Prox Port Triple Lumen	30	34

ABC Score for Massive Transfusion

Questions: Score of >/= 2 is considered positive.

1. SBP < 90
2. HR> 120
3. Penetrating trauma
4. Positive FAST examination

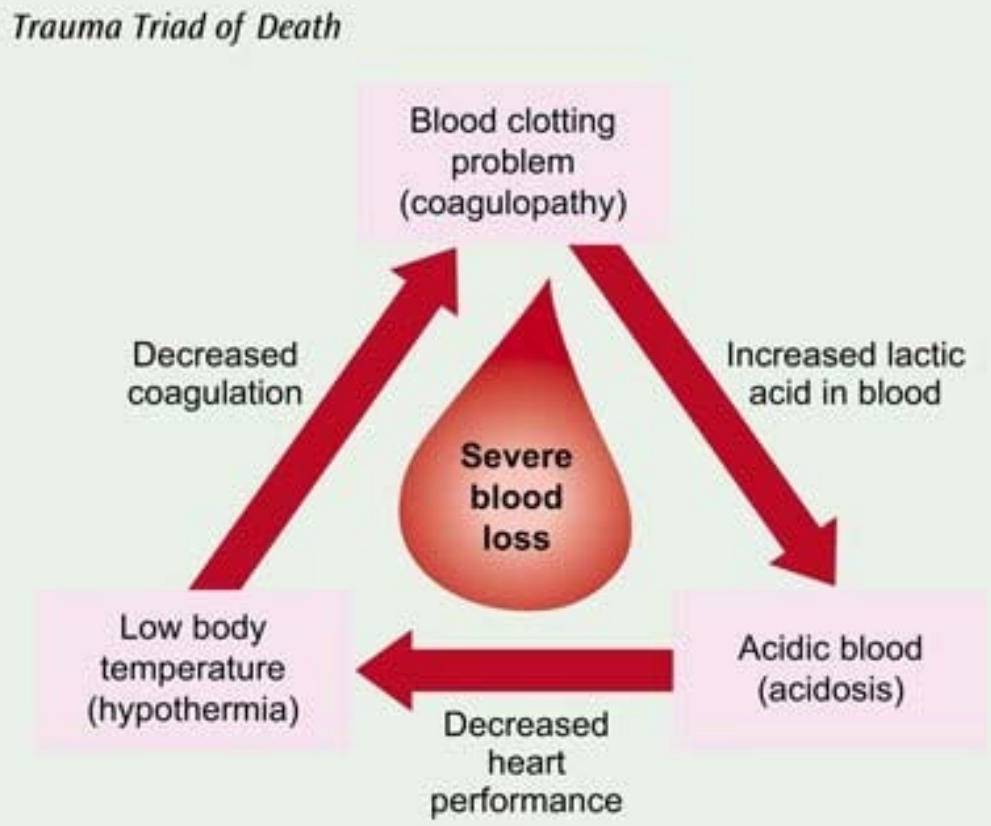
Sensitivity 75% and Specificity 86%

Nunez et al; Journal of Trauma 2009

NPV of 97% and PPV of 55%

Cotton et al; Journal of Trauma 2010

Resuscitation



- Hemorrhage control resuscitation (early use of platelets and plasma).
- Damage control resuscitation (1:1:1> PRBC: plasma: platelets).

Monitoring:

- ABG/VBG every 20 to 30 minutes to check for pH, blood gases, electrolytes, glucose and lactate.
- After every 5 units of PRBC transfused check Hb, PT, aPTT and fibrinogen levels or use TEG/ROTEM.

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients with Severe Trauma: the PROPPR Randomized Clinical Trial

Holcomb et al; JAMA 2015

- 680 trauma patients
- 12 level 1 trauma centers in North America
- 1:1:1 vs 1:1:2
- Primary outcome: All-cause mortality at 24 hours and 30 days
- Secondary outcomes: time to hemostasis, blood product volumes infused, complications

1:1:1 versus 1:1:2 (Median blood units 9 in both groups, Plasma 7 versus 5 and Platelets 12 vs 6)

- 24 hours mortality 12.7% vs 17% (P= 0.12)
- 30 days mortality 22.4% vs 26.1% (P=.26)
- Exsanguination 9.2% vs 14.6 % (P=0.03)
- Hemostasis achieved 86% vs 78% (P=0.006)
- Median time to hemostasis: 105 vs. 100 minutes (P=0.44)
- Rate of death due to exsanguination at 24 hours: 9.2% vs. 14.6% (P=0.03)
- No difference in complications: ARDS, MODS, VTE, sepsis, and transfusion-related complications

Effects of Tranexamic Acid on Death, Vascular Occlusive Events, and Blood Transfusion in Trauma Patients With Significant Hemorrhage (CRASH-2): a Randomized, Placebo-controlled Trial

Shakur et al; The Lancet. 2010

N=20,207 trauma patients with or at risk of significant hemorrhage.

- Tranexamic acid (n=10,093)
- Placebo (n=10,114)

Multicenter, randomized, placebo-controlled trial.

Setting: 274 hospitals in 40 countries.

Primary outcome: In-hospital death at 4 weeks.

Primary Outcomes

- Death in hospital within 4 weeks of injury.

  14.5% vs. 16.0% (RR 0.91, 95% CI 0.85–0.97; P=0.0035).

Secondary Outcomes

- Vascular occlusive events (MI, CVA, PE, DVT)

  1.7% vs. 2.0% (P=0.084)

Death due to Bleeding

- ≤1h from injury: 5.3% vs. 7.7% (RR 0.68, 95% CI 0.57-0.82; P<0.0001).
- 1-3h: 4.8% vs. 6.1% (RR 0.79, 95% CI 0.64-0.97; P<0.00001).
- >3h: 4.4% vs. 3.1% (RR 1.44, 95% CI 1.12-1.84; P<0.0001).

Resuscitation Goals

- A mean arterial pressure (MAP) within the range of 60 to 65 mm Hg.
- Hemoglobin level between 7 and 9 g/dL.
- International normalized ratio (INR) below 1.5.
- Fibrinogen levels within the range of 1.5 to 2 g/L.
- Platelet counts above 50,000 µL.
- pH between 7.35 and 7.45.
- Core temperature above 35 °C.


Thank you.