What is the Optimal Hematocrit for Surgical Patients? (And some other situations)

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Hgb & Hct: Use and Abuse

Educational Objectives

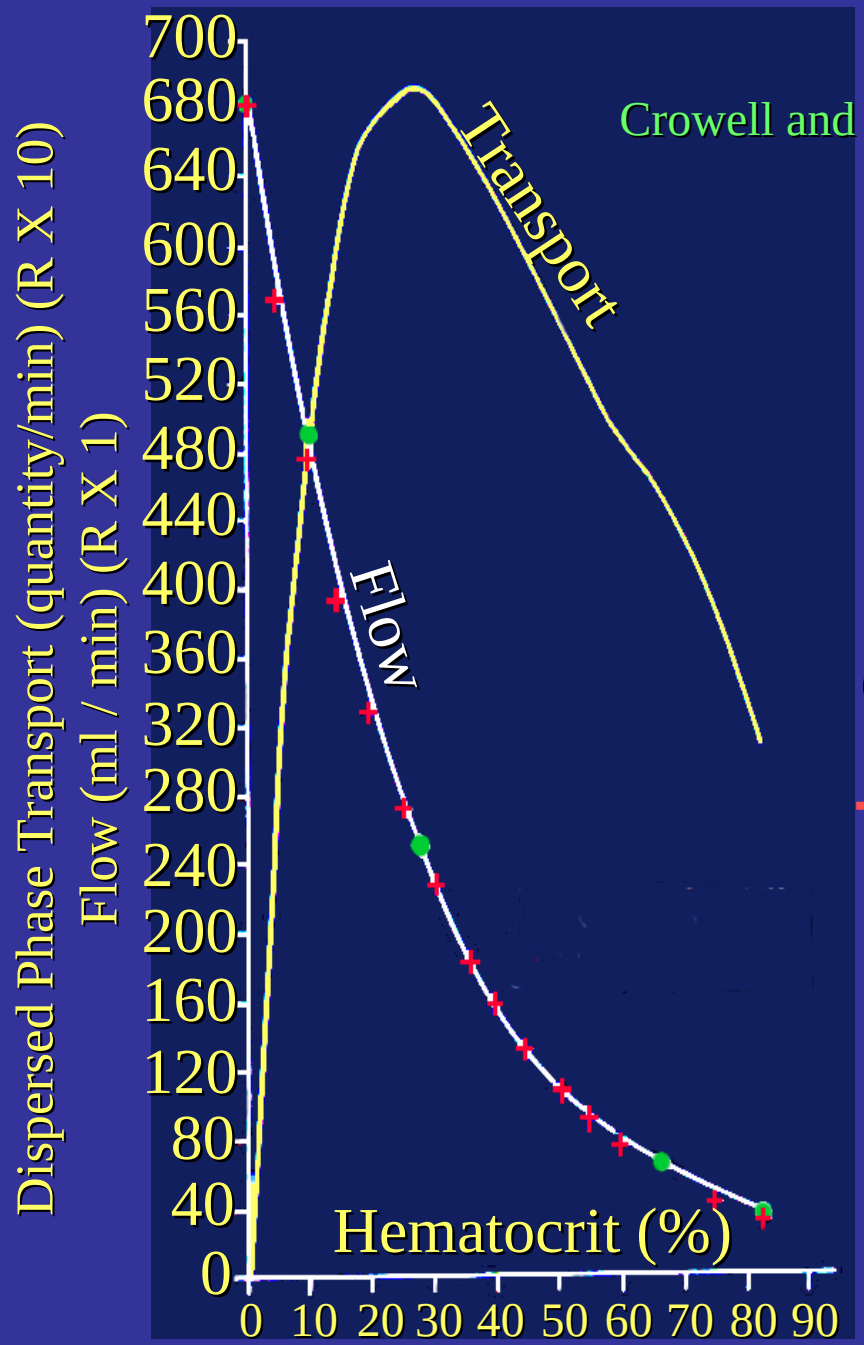
- Understand physiology of anemia / hemodilution
- Understand interactions between disease states and anemia
- Understand risks of anemia and transfusion

Baseline information

- No conflict of interest
- No off-label drug use
- Assume Hct=3X Hgb

Hgb and Hct Use and Abuse

- Physiology of Hemodilution
- Safe limits of anemia
  - Healthy vs Atherosclerotic Disease
- Transfusion as a problem
- Transfusion avoidance
- Conclusions



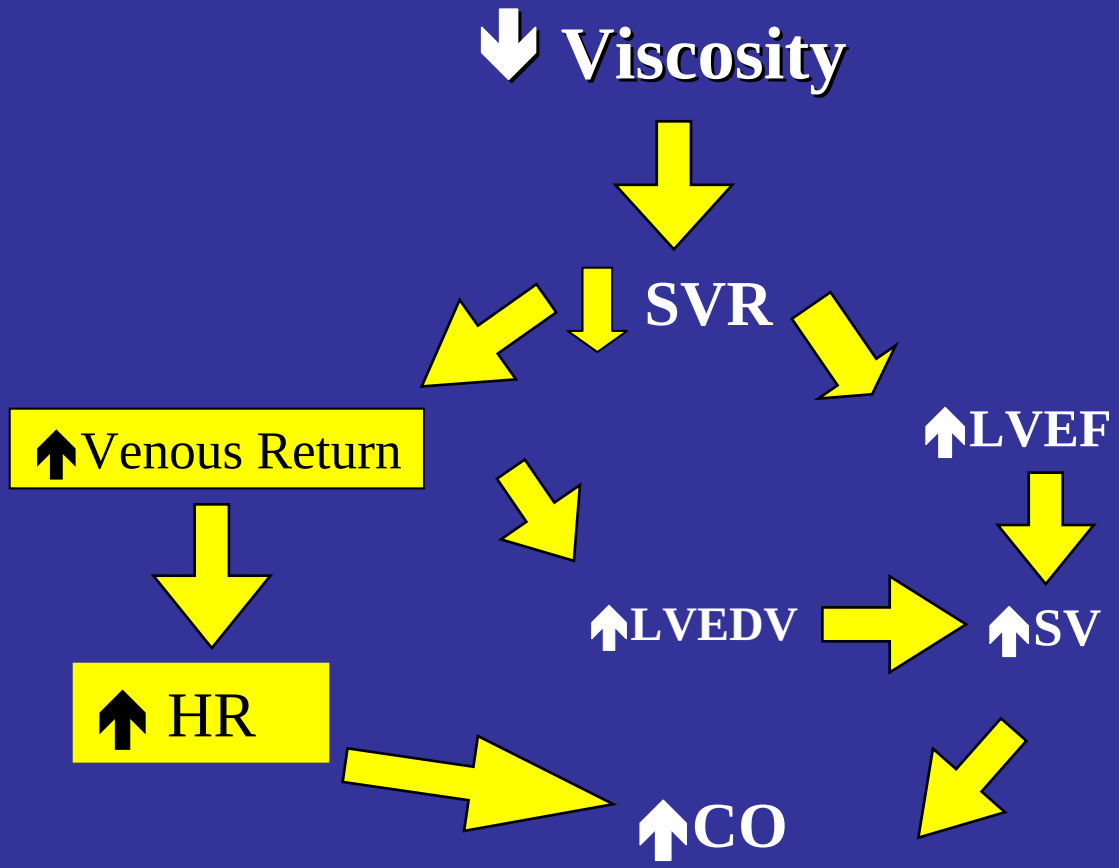
Crowell and Smith, ***J Appl Physiol*** 1967; 22:501

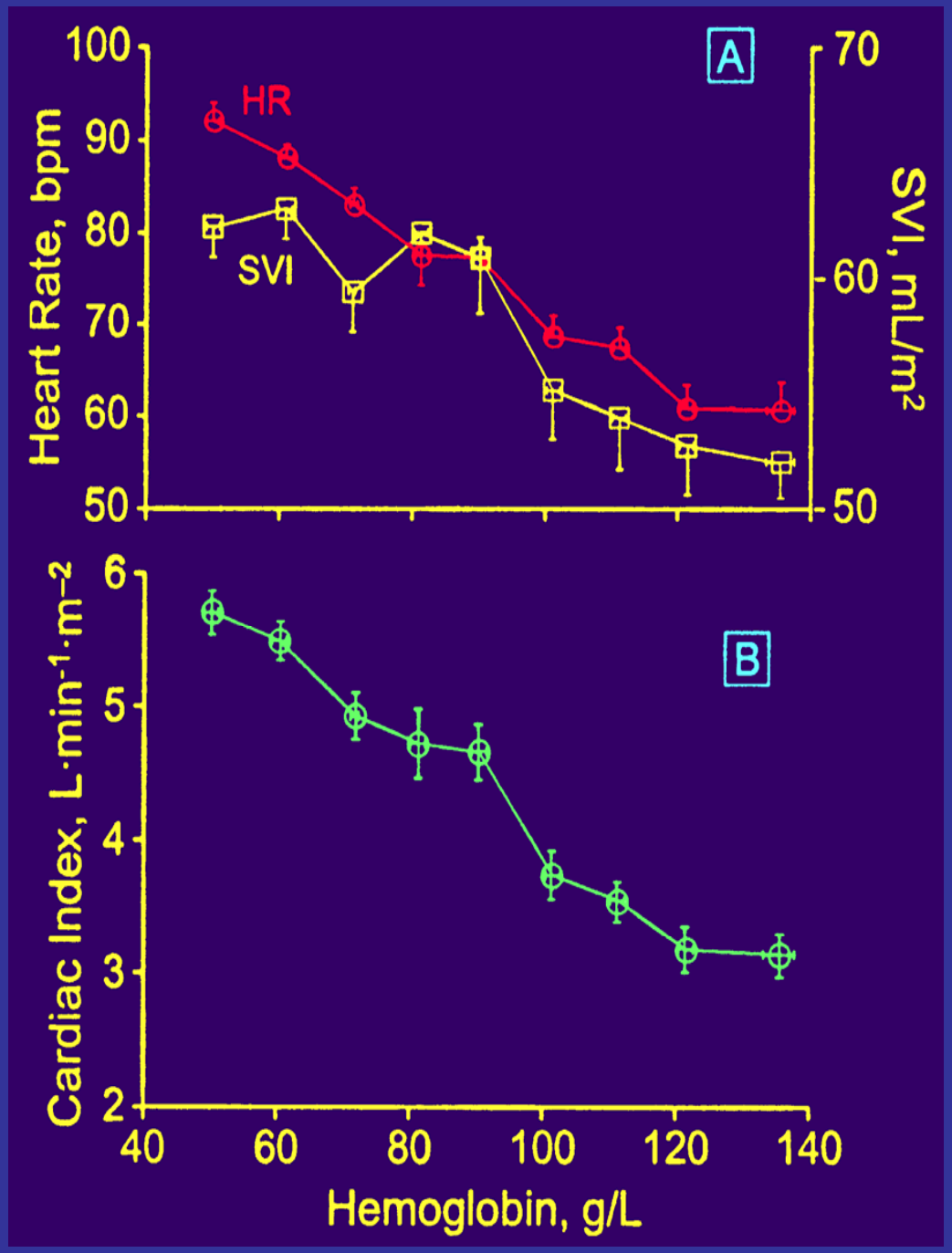
● Actual Values

+ Calculated Values

ISOVOLEMIC HEMODILUTION

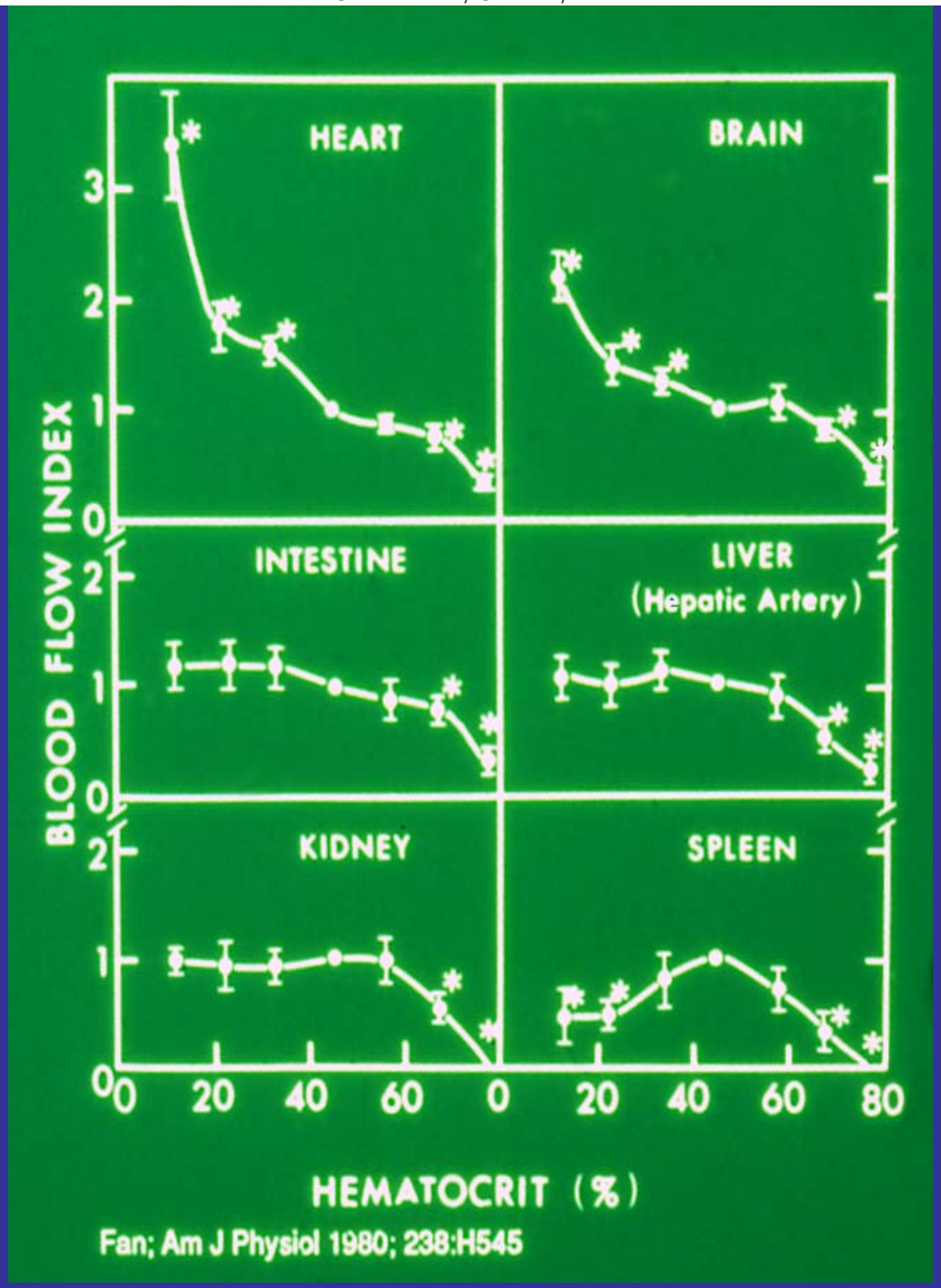
↑ CO is Largely Passive





Healthy Patients or Volunteers

RB Weiskopf, et al.
JAMA ***1998; 279(3):217-221***


HEART
BRAIN
INTESTINE
LIVER
(Hepatic Artery)
KIDNEY
SPLEEN
BLOOD FLOW INDEX
HEMATOCRIT (%)
0
20
40
60
80
Fan; Am J Physiol 1980; 238:H545

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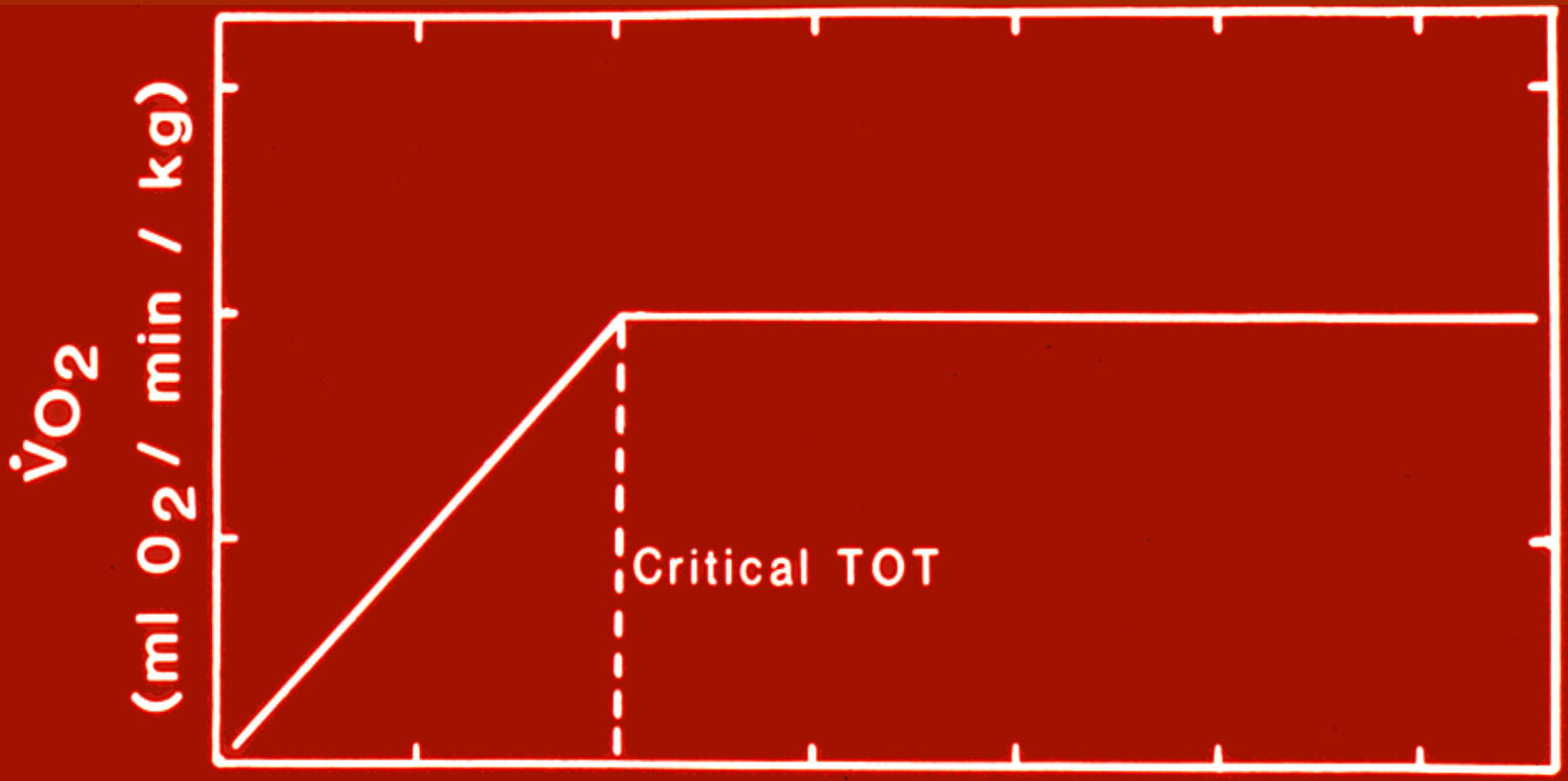
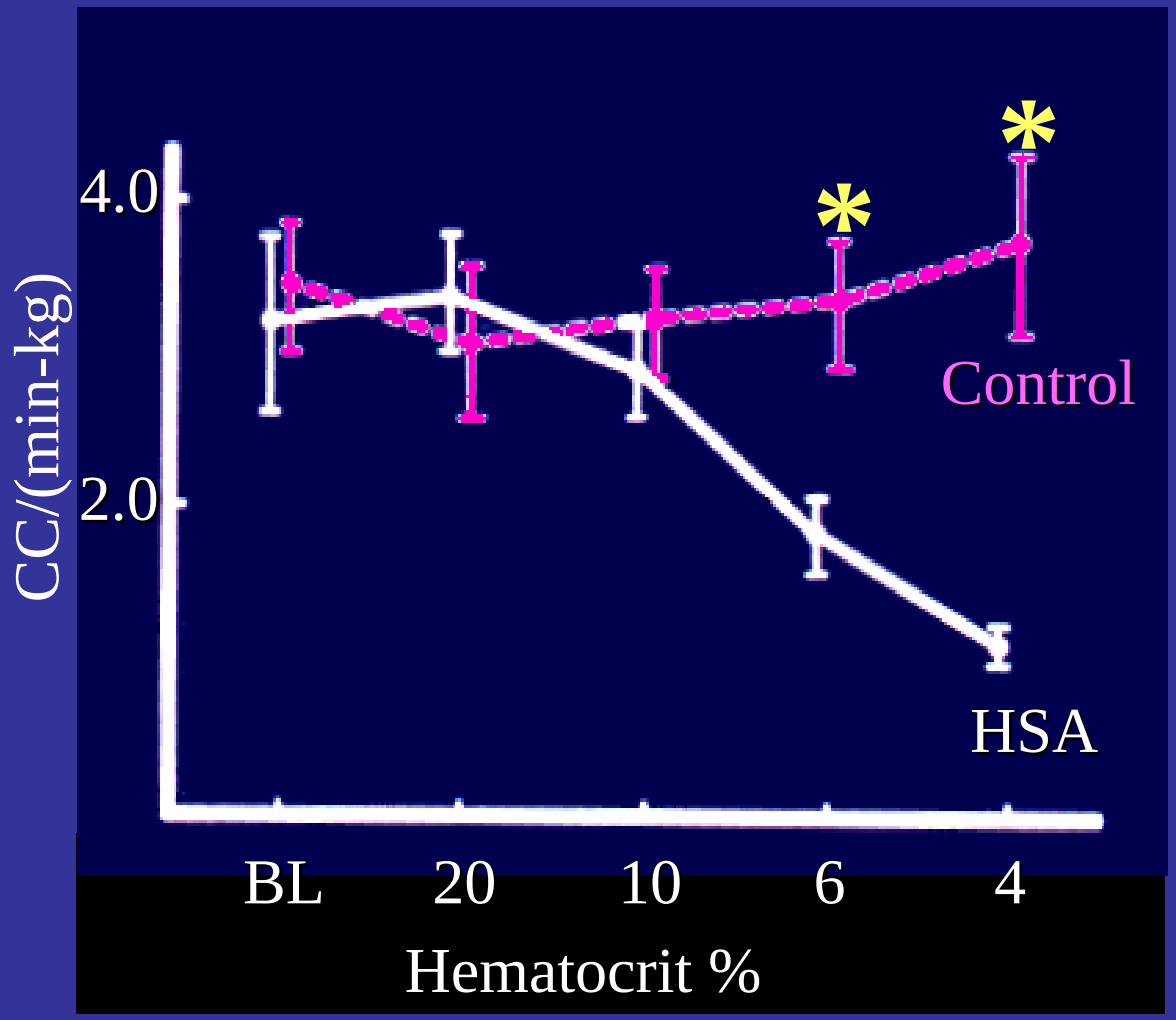


TOTAL OXYGEN TRANSPORT

(ml O_2 / min / kg)

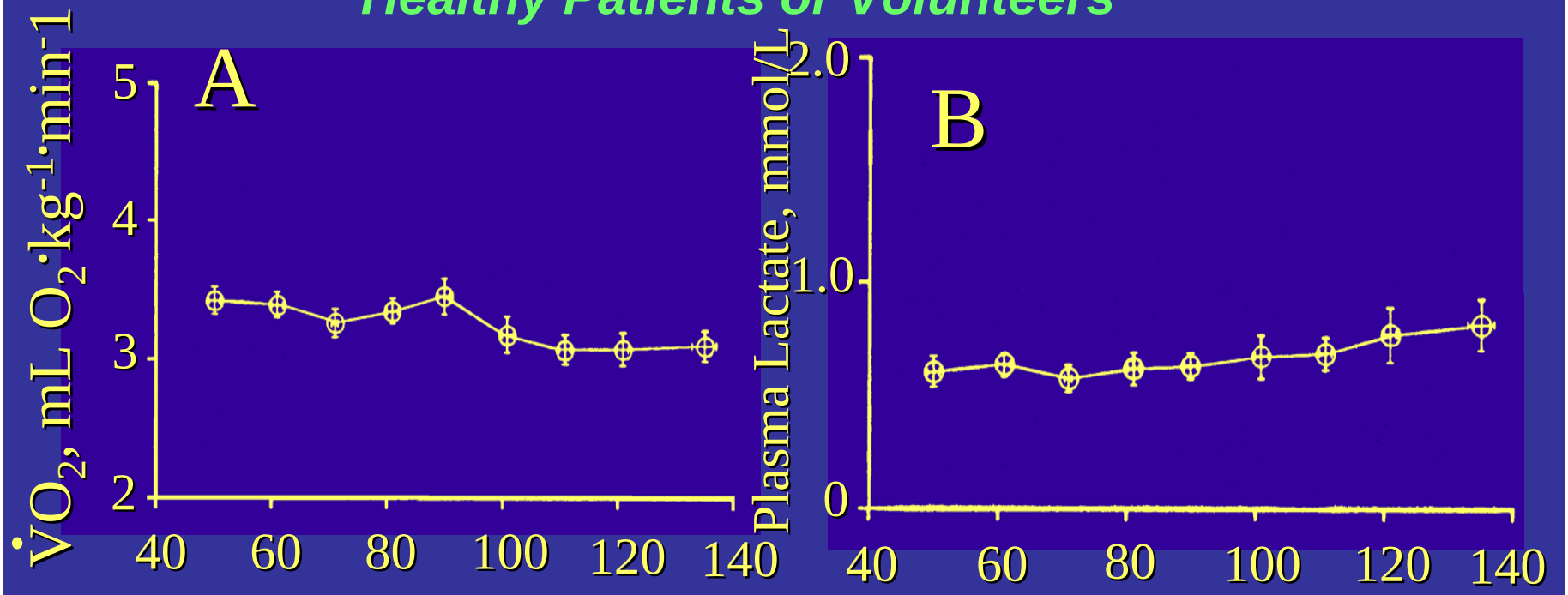
Hill, Perfusion 1987;2:39



Total O_2 consumption vs. hematocrit for the experimental (HSA) group. Control group data were obtained at equivalent volume-exchange points Difference between groups is significant ($P<0.05$) at hematocrits of 6 an 4%.

Wilkerson DK, ***J Surg Res*** 1987; 42:62

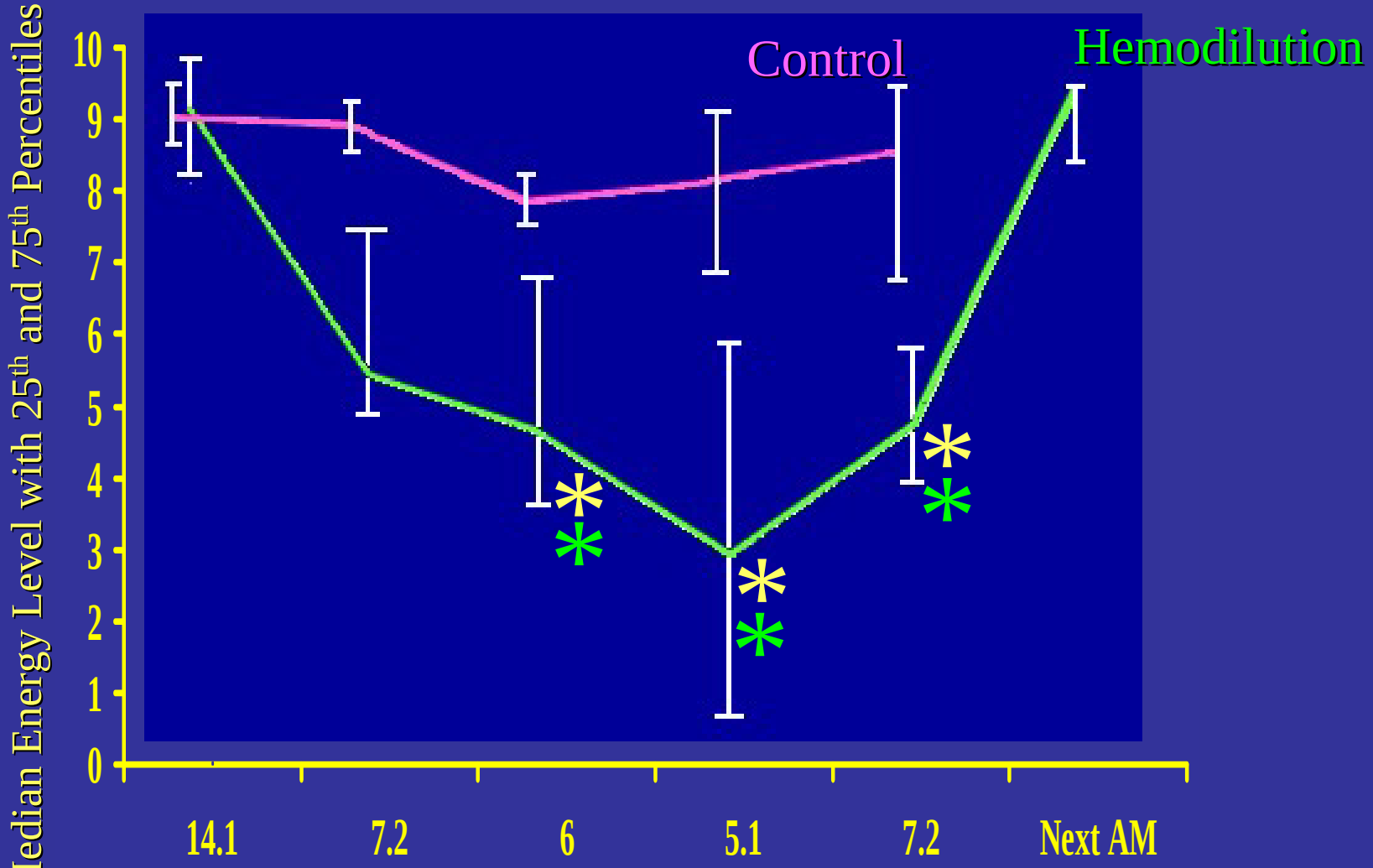
Healthy Patients or Volunteers



Acute isovolemic reduction of hemoglobin concentration to 50 g/L increased oxygen consumption (VO2) (A; P<0.001) but did not change plasma lactate concentration (B, P=0.9). Data are gathered into groups by increments of 10g/L and represented as mean (SE) (n=32).

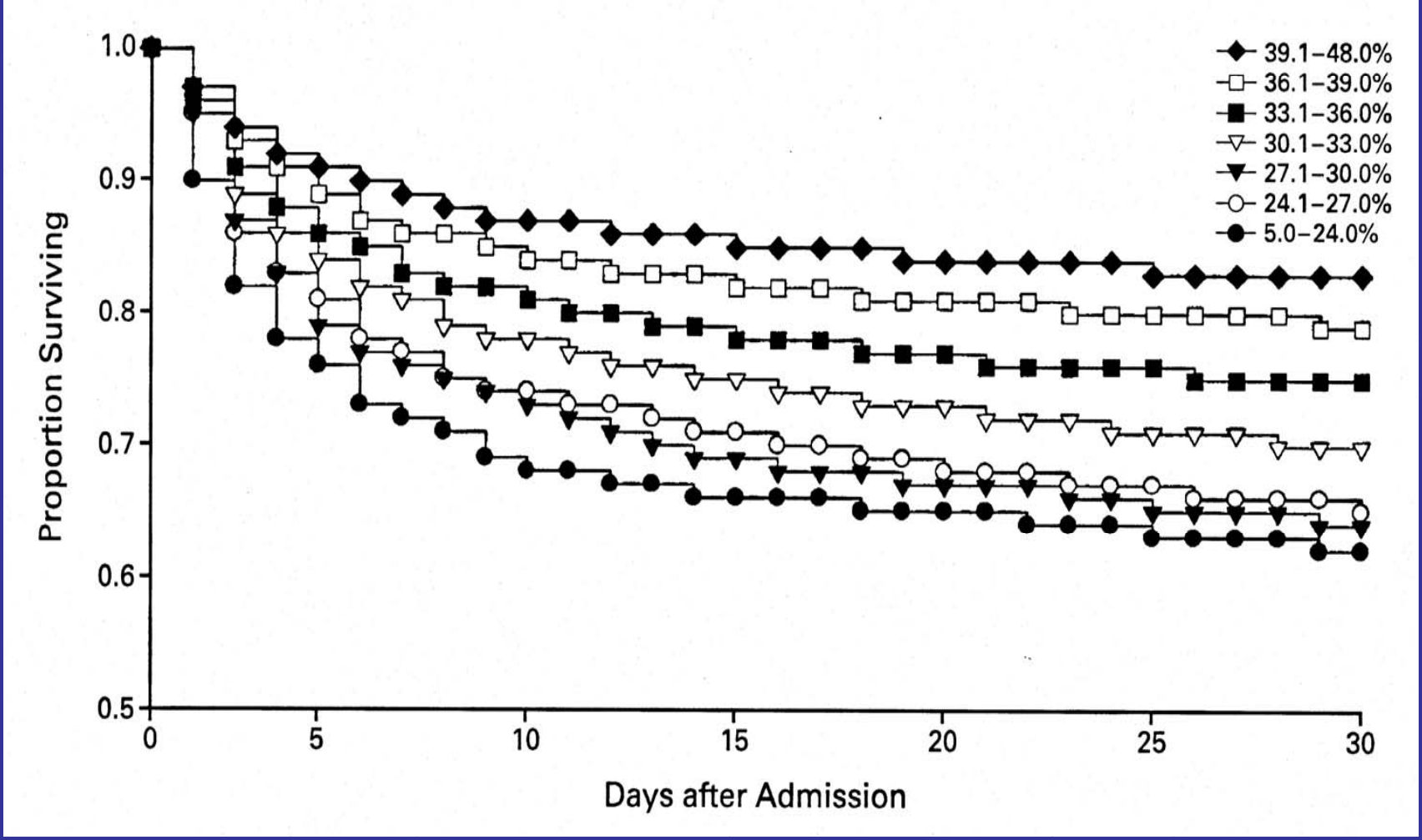
RB Weiskopf, et al. JAMA ***1998; 279(3):217-221***

*P<0.05 Change from 14.1 Baseline * P<0.05 Different from Control



Toy P, ***Transfusion*** 2000; 40:457

Elderly Pts (>65) with AMI

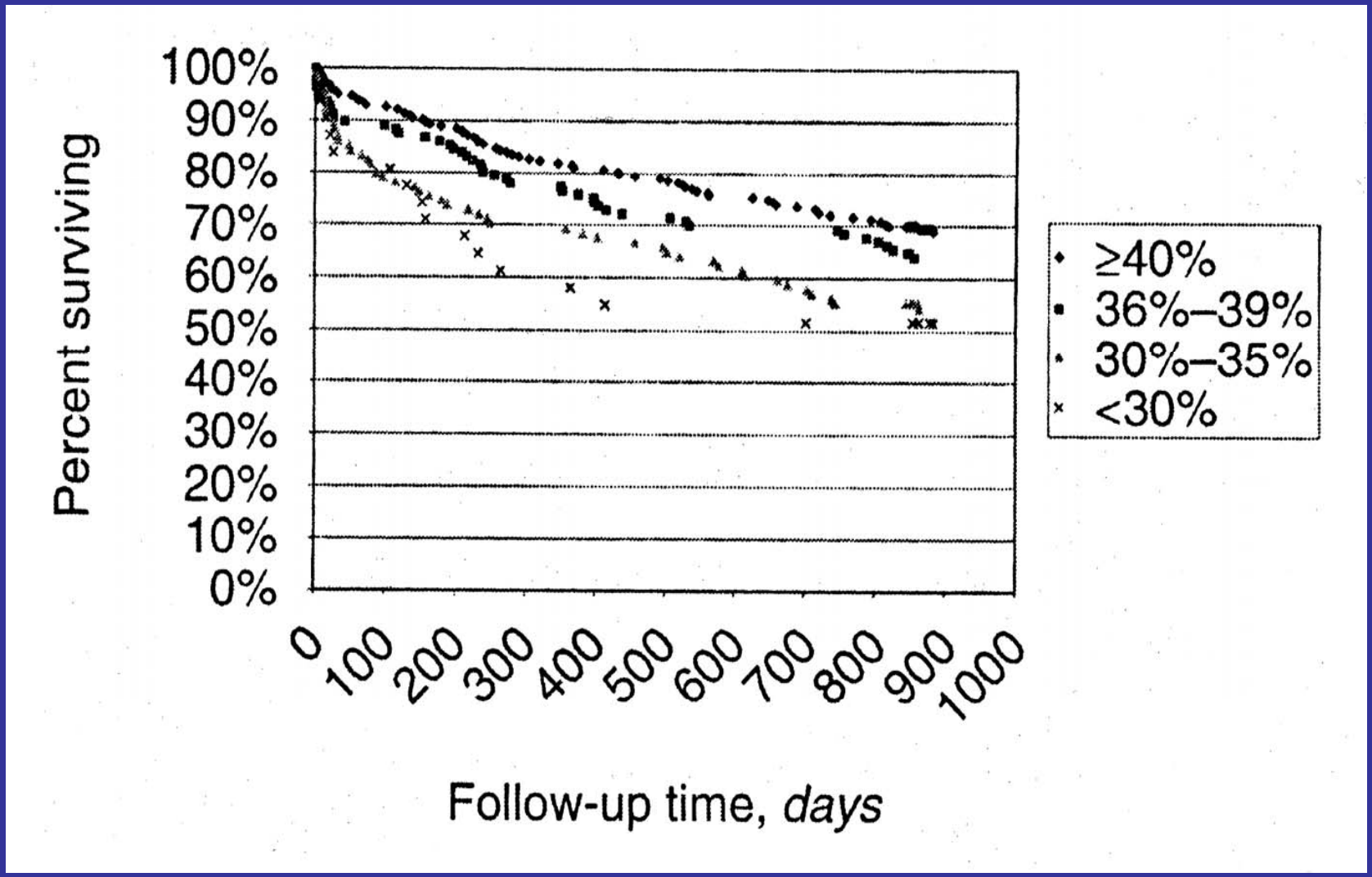


Wu, W-C, ***NEJM*** 2001 345:1230-6

Hgb in Chronic CHF

Silverberg DS, JACC 2000;35:1737-44

- Retrospective and prospective in chronic CHF
- Severity of CHF inversely proportional to pre-intervention Hct: 79% Hgb < 12 if NYHA Class IV
- Epo Rx to Hgb ≥ 12 g% improves LVEF, # hospitalizations (>90%), NYHA Class, decreases furosemide dose and rate of GFR decline



Kaplan-Meier Survival Curve for individuals with hematocrits levels of <30%, 30% to 35%, 36% to 39%, and ≥ 40%

Langston RD, ***Kidney Intl*** 2003 64:1398

Paul C. Hebert
Multiple papers on RBC transfusion

- *NEJM 1999;340:409-17:* 838 ICU Pts randomized to RBC transfusion at Hgb 7 or 9: restrictive strategy group had lower hospital mortality
  - Lower risk Pts had lower 30 d. mortal w/ restrictive strategy, as did Pts < 55 yrs old
  - No overall diff. in 30 d mortality
  - No mortality difference in Pts with CV disease

Paul Hebert – further analysis of Hgb 7 vs 9 trigger point (TRICC Trial)

- *Chest 2001;119:1850* – 713 Pts on mechanical ventilation: ND in weaning time even after adjustment for risk (APACHE Score)
- *J Trauma 2004;57:563-8* – 203 critically ill trauma patients: ND in 30 day mortality, multiple organ dysfunction, ICU or hospital LOS

The Cochrane Library 2005

(Last Updated 2003)

- Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion
- Searched for randomized trials involving transfusion triggers
- Investigated 6 outcomes: probability of tsfsn, volume of RBC tsfsn, Hct levels, cardiac events, 30 day mortality, and overall LOS
- Meta-analysis of 10 trials containing 1780 Pts

Cochrane Transfusion Trigger Database Results

Lower transfusion trigger (mean Hct diff of 6%) resulted in

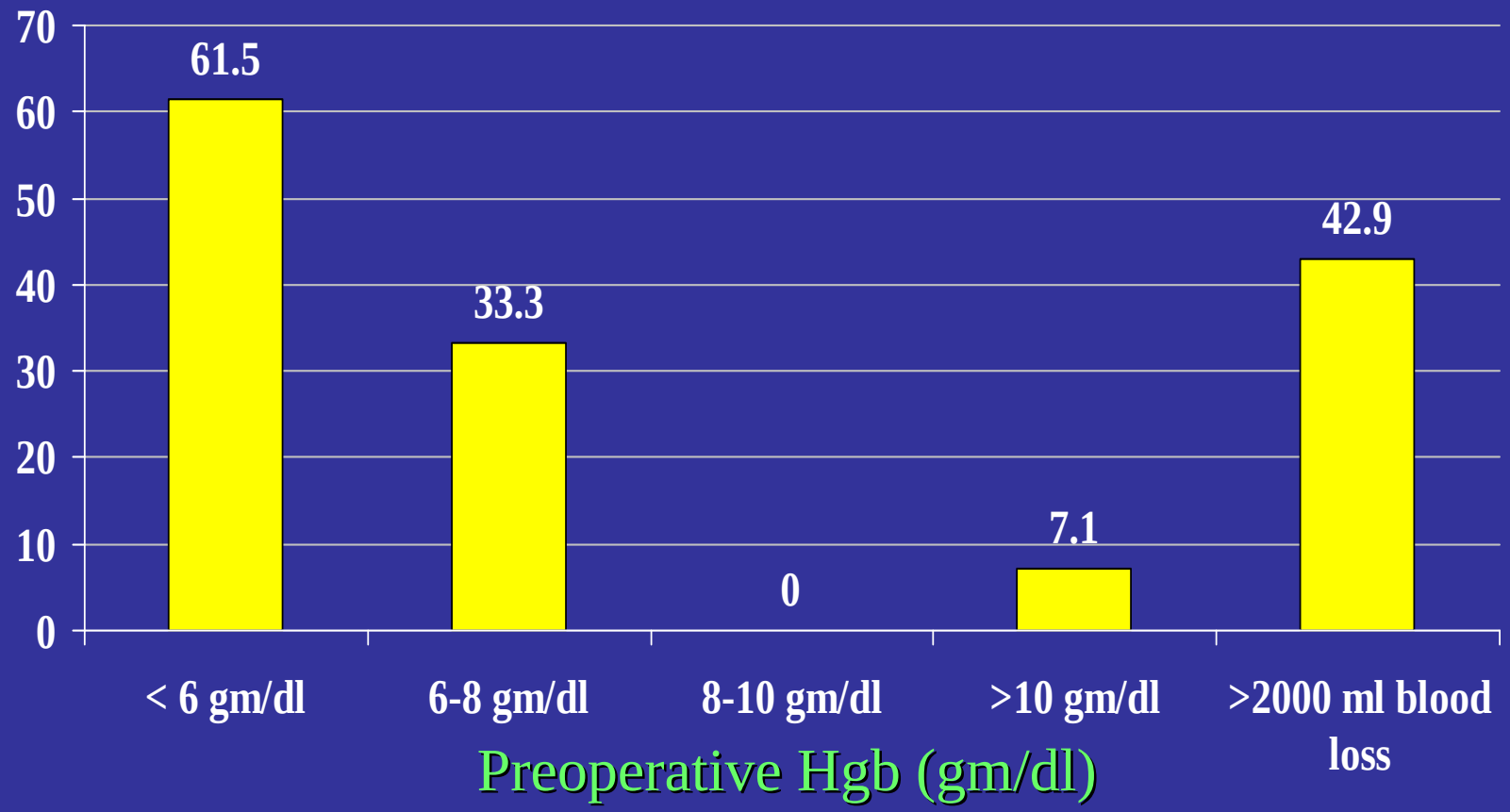
- Lower Hct and probability of transfusion (Duhh)
- No difference in mortality, cardiac morbidity, and LOS (but consider heterogeneity of Hcts)
- Noted disagreements in observational studies and RCTs, absence of RCT evidence in Pts with CV disease

Cochrane Transfusion Trigger Recommendations

- Limited data justifies additional RCTs
- Long term functional recovery data generally are lacking
- Suggest caution in Pts with CV disease (dearth of RCTs in this population)

Carson, LANCET

Hospital Mortality (%)



No mortality when Hgb >8.0 and blood loss < 500 ml

30-day Mortality in 1958 Jehovah Witnesses Undergoing Surgery

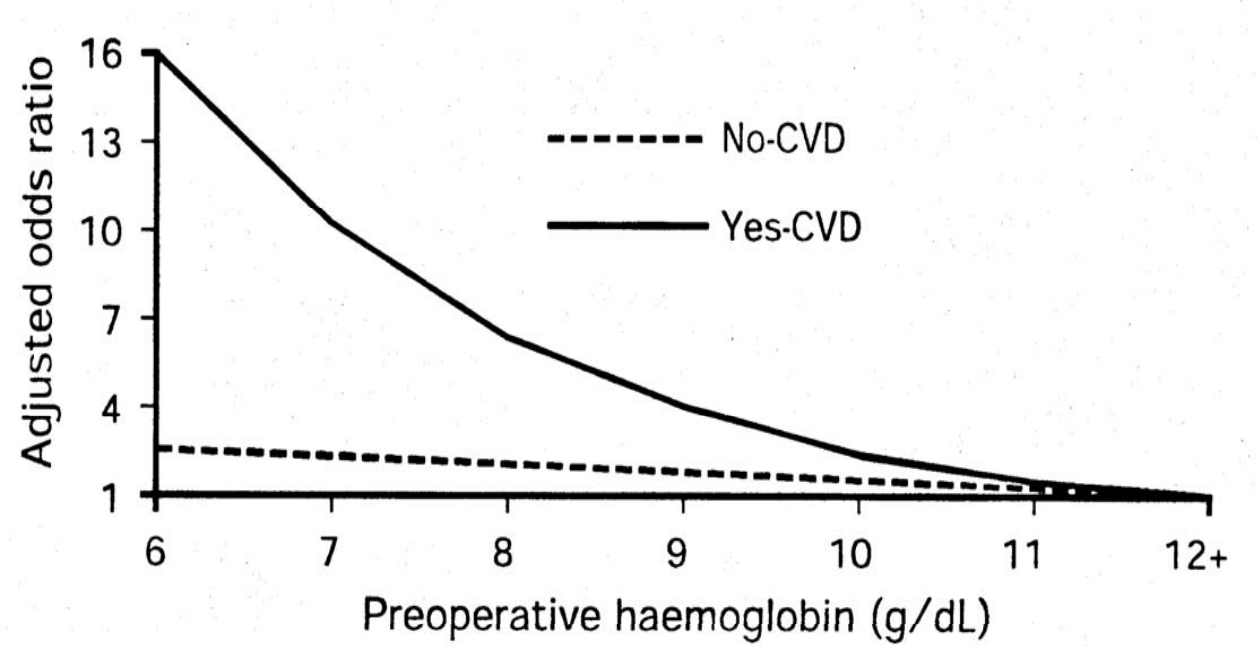


Figure: **Adjusted odds ratio for mortality by cardiovascular disease and preoperative haemoglobin**

Carson JL, ***Lancet*** 1996; 348:105

25 Healthy Dogs

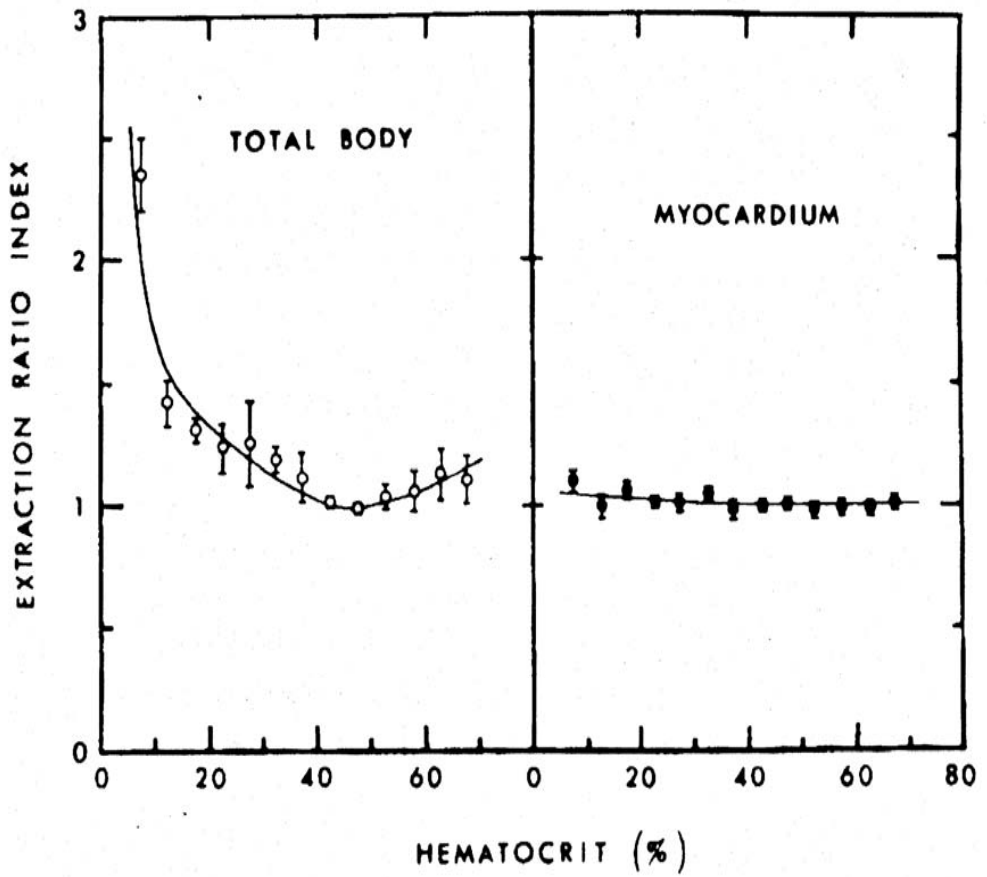
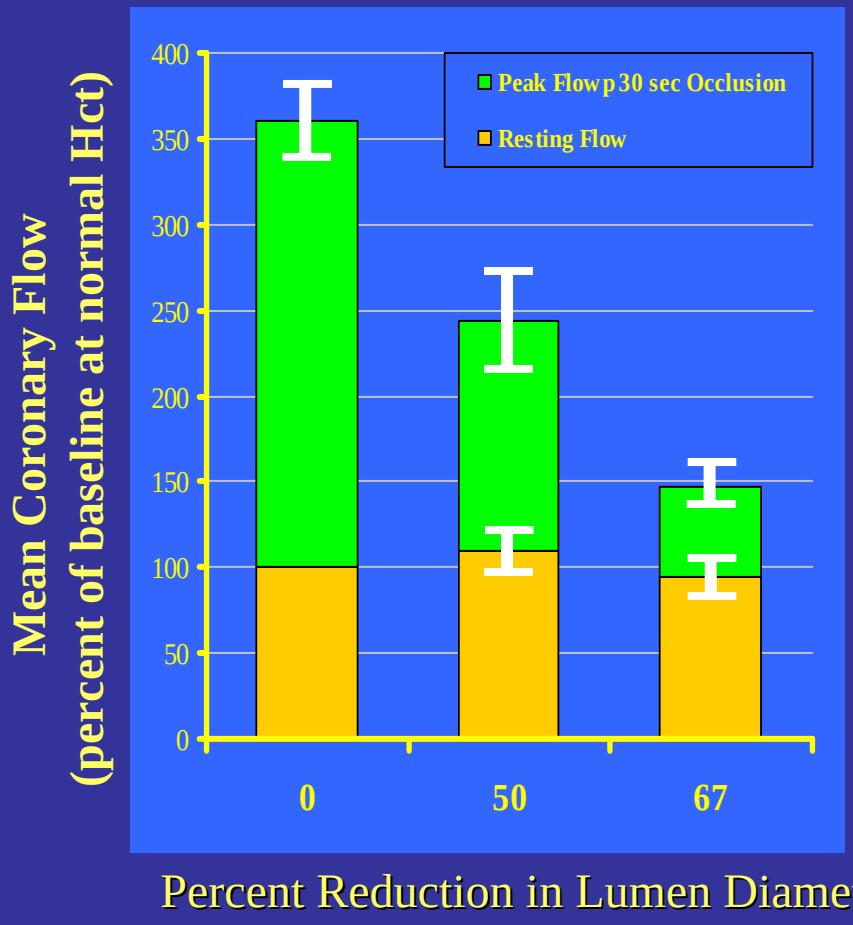


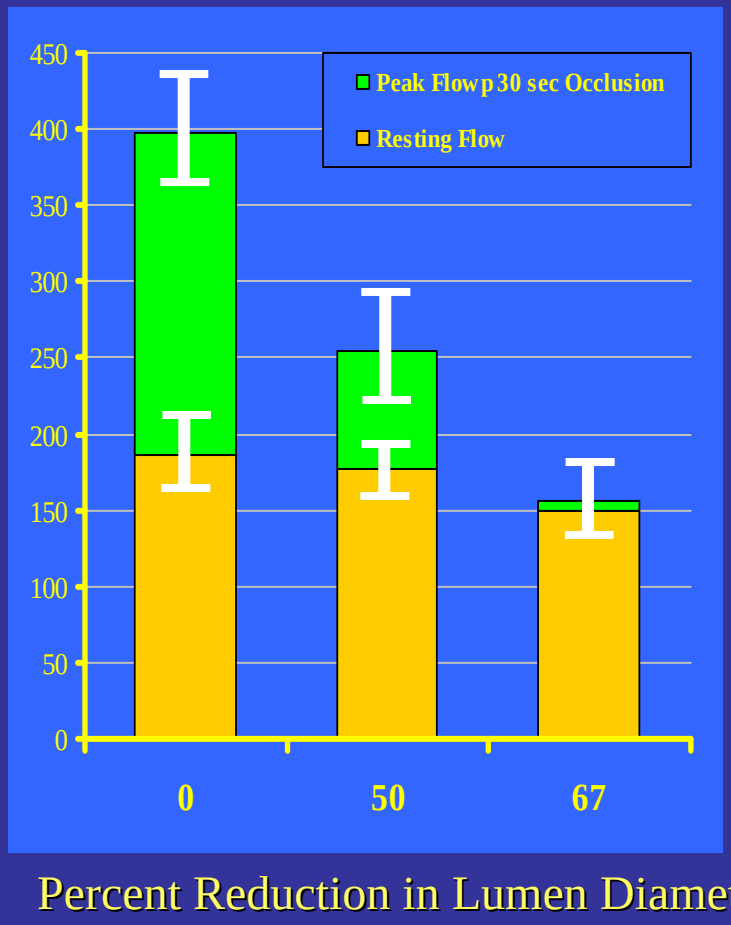
FIG. 9. Effects of hematocrit variations on oxygen extraction ratio in the total body (*left*) and in the myocardium (*right*). O_2 extraction ratio index is calculated by dividing extraction ratio by that obtained at hematocrit of 45%. Vertical bars denote SE.

Jan K-M, ***Am J Physiol*** 1977 233:H106

Hct Normal

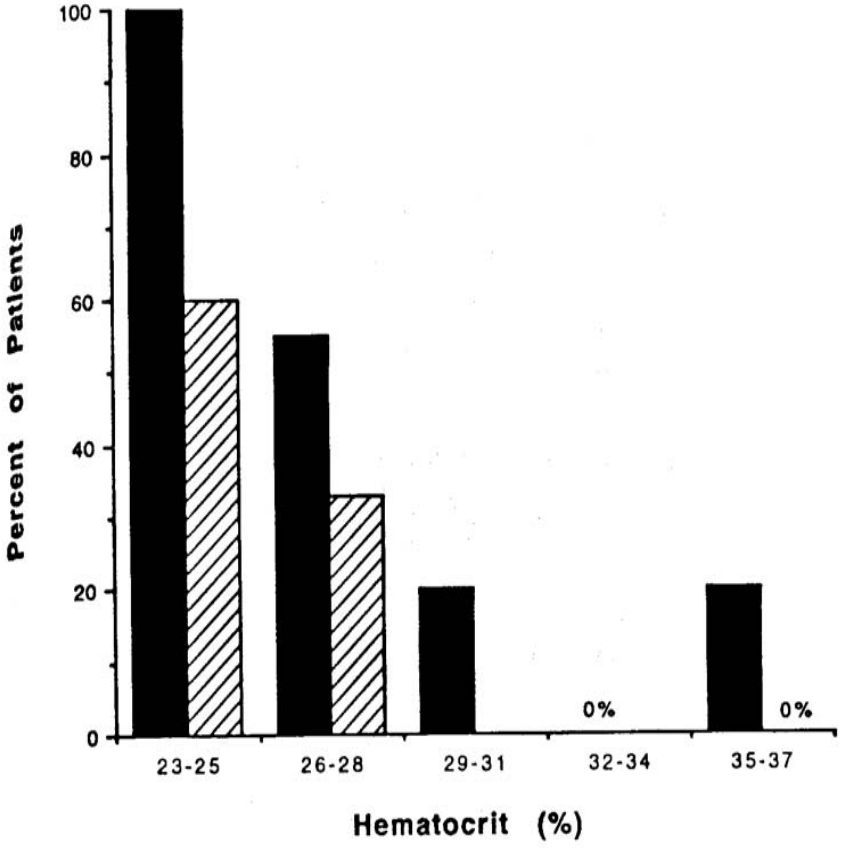


Hct 20



Geha, ***World J Surg*** 1978; 2:645

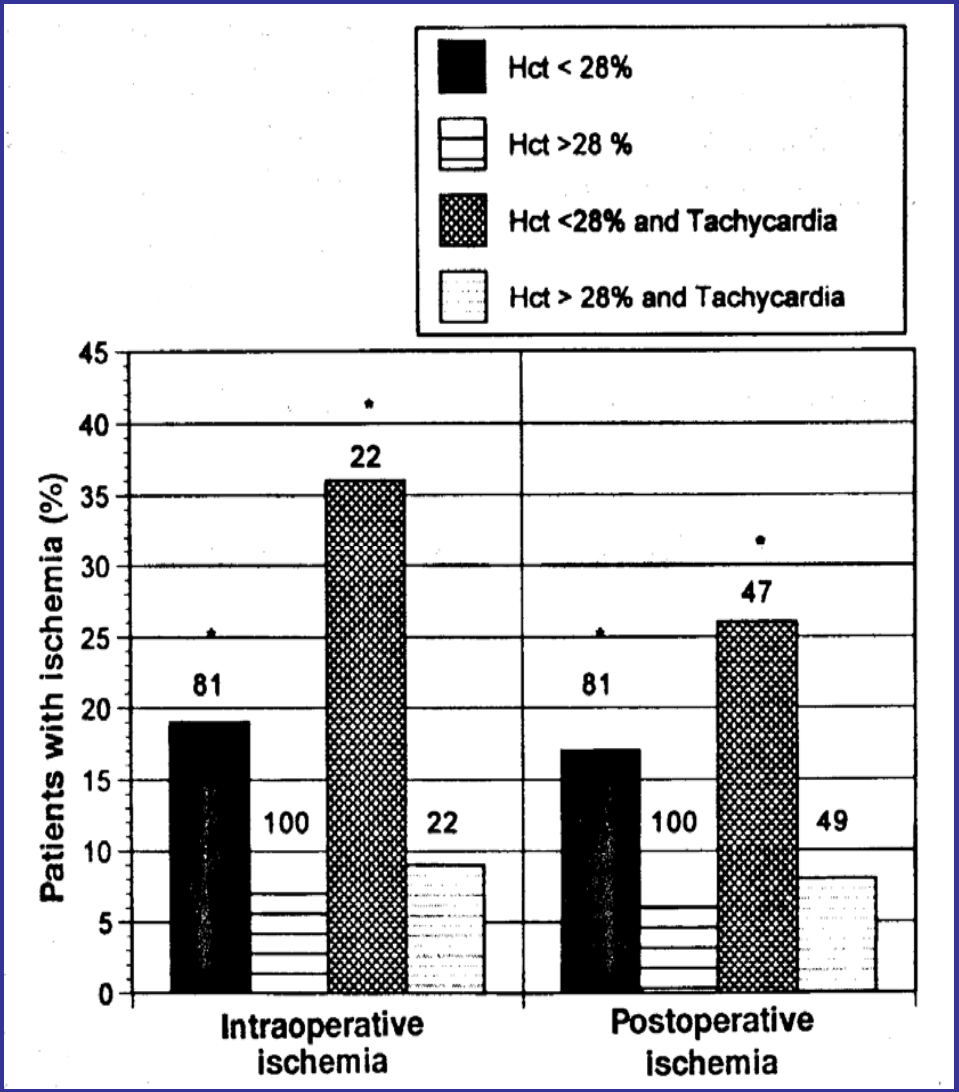
27 Leg Revascularization Patients



Incidence of postoperative myocardial ischemia and morbid cardiac events as related to hematocrit. *Solid bars* represent myocardial ischemia; *hatched bars* represent morbid cardiac events.

Nelson AH, *Crit Care Med* 1993; 21:860

199 Radical Prostatectomies



Hogue CW, *Transfusion* 1998; 38:924

Paul Hebert – TRICC Trial re-analysis

- Crit Care Med 2001;29:227 – 357 Pts with CV disease
  - Average Hgb 8.5±.6 vs 10.3±.7 (i.e., NOT 7 and 9)
  - Mortality same: ICU, hospital, 30- and 60-day
  - Less multiple organ dysfunction in restrictive group
  - Of 257 Pts with severe ischemic HD, ND in survival BUT this was the only group with lower survival (NS) in restrictive group (45% vs 36% at 30 days)

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RBC transfusion and mortality

Kuduvalli M, Eur J Cardio-Thorac Surg 2005;27:592

- 3024 consec. CABG Pts *retrospectively* analyzed
- 30 day and 1 year mortality as a function of lowest lab Hgb and presence/absence of RBC transfusion
- No standardization of transfusion
- Predictors of transfusion identified and corrected for by *propensity analysis*

RBCs and Mortality – cont

Kuduvalli M, Eur J C-T Surg 2005;27:592

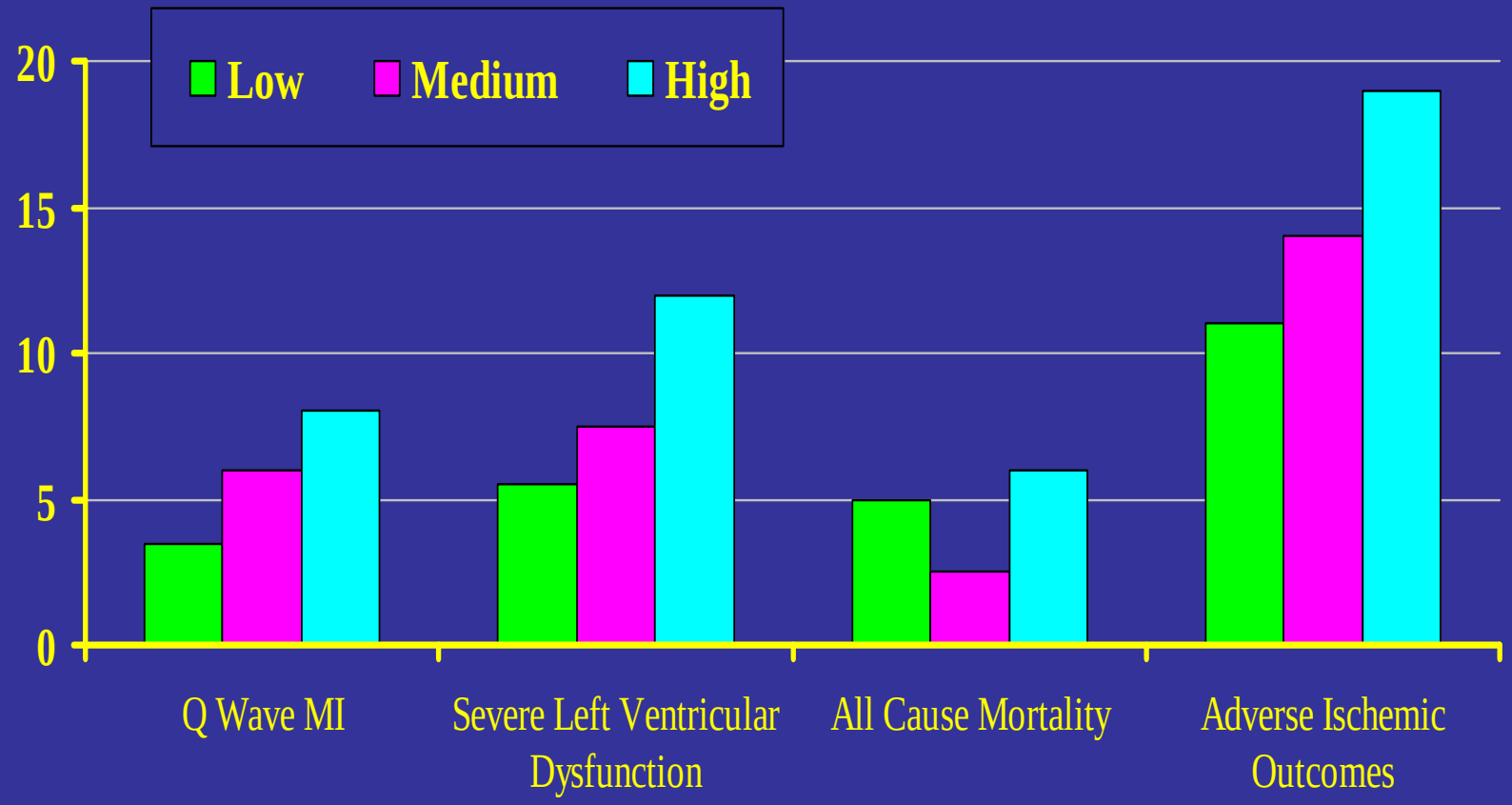
RBC transfusion predictors:

- Lowest lab Hgb (LLH)
- Lower BMI, higher age
- CPB use, # of grafts, extent of disease
- Females
- Redo CABG
- Renal dysfunction

Hazard Ratios:

- 1 yr any Transfusion: 3.0*
- Risk-adjusted 1 yr any Tx: 1.88*
- Risk-adj 1 yr excluding mortal 1st 30 days: 1.67*

2,202 CABG Pts @ ICU Admission



Frequency of Q-wave MI, severe left ventricular dysfunction (intraaortic balloon pump use), all-cause mortality, and combined (all three) adverse ischemic outcome by the IHCT group. Low, HCT ≤ 24%; Medium, HCT 25% to 33%; High, HCT ≥ 34%

Spiess BD, ***JTCVS*** 1998; 116:460

Taking a Good Thing Too Far

Besarab A, NEJM 1998;339:584-90

- 1233 Dialysis Pts with CHF or Isch HD
- Random assignment: Epo titrated to Hct 30 or 42
- Decreased mortality from increased Hct in both groups
- Risk ratio 1.3 for death or MI in higher Hct group, but 95% CI 0.9-1.9
- Study terminated on ethical grounds

Therapeutic Dilemma

Anemia is bad

- Increases mortality
- Decreases QOL
- Jeopardizes organ viability, especially in presence of limited vasodilatory reserve

Transfusion is bad

- Independent association with increased mortality and morbidity
- Immediate augmentation of $\mathbf{O_2}$ transport is limited (?)
- Immunosuppression and enhanced inflammation may be the culprit – leukoreduction role?
- Viral/bacteria/parasites