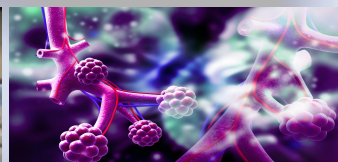


Gestion Périopératoire du patient à risque : **Vers une stratégie intégrée**

Emmanuel FUTIER, MD, PhD

Département de Médecine Périopératoire, Anesthésie Réanimation
Hôpital Estaing et Hôpital Gabriel Montpied, CHU de Clermont-Ferrand
Université Clermont Auvergne, CNRS UMR 6293, INSERM U1103, GReD

 @efutier

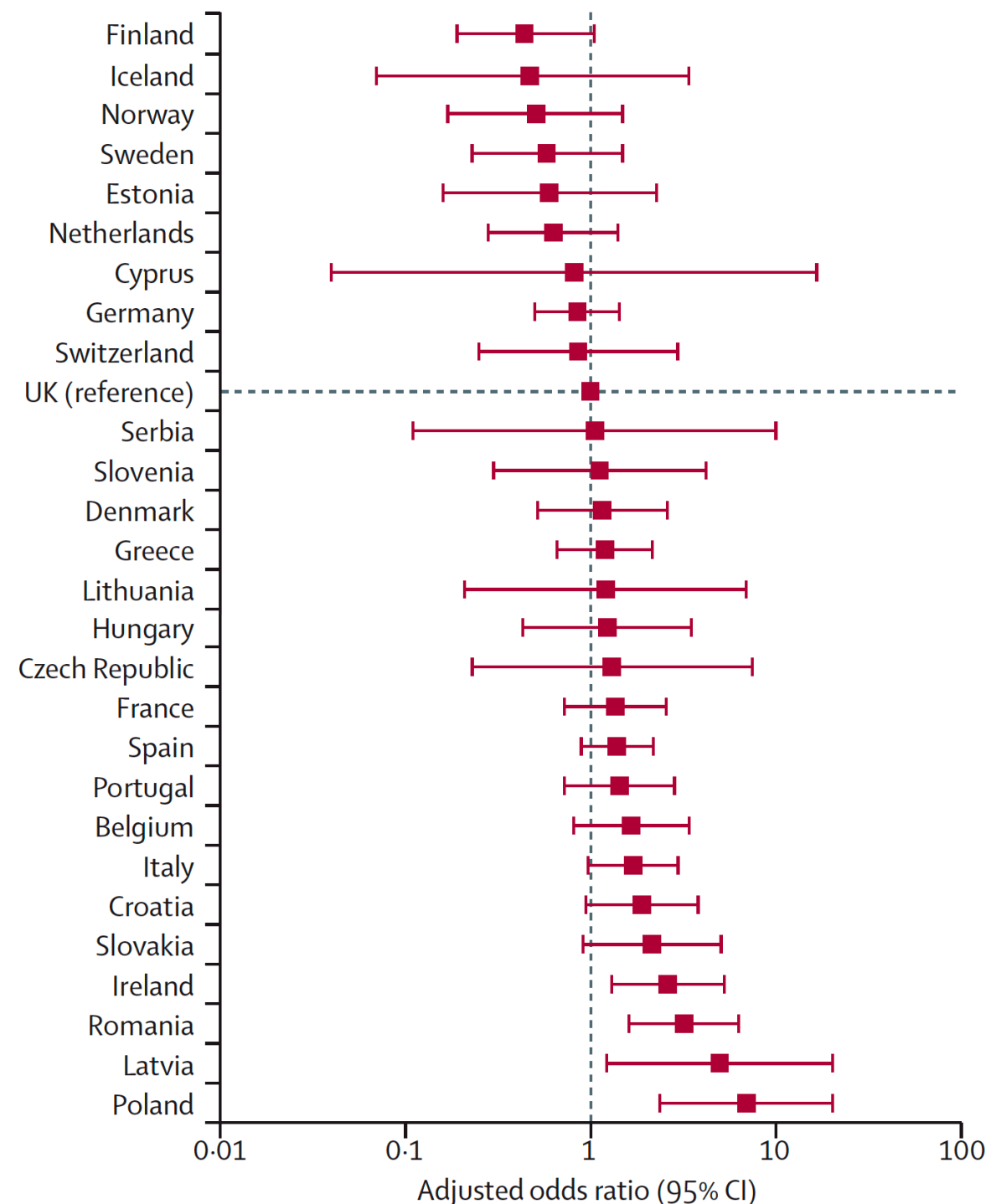


Mortality after surgery in Europe: a 7 day cohort study

*Rupert M Pearce, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology**

European Surgical Outcomes Study (EuSOS)

- International multicenter observational 7 day cohort study (April 2011) - 498 hospitals (28 European nations)
- N= 46 539 patients undergoing elective or non-elective inpatient surgery
- Primary endpoint: In-hospital mortality



Mortality after surgery in Europe: a 7 day cohort study

*Rupert M Pearce, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology**

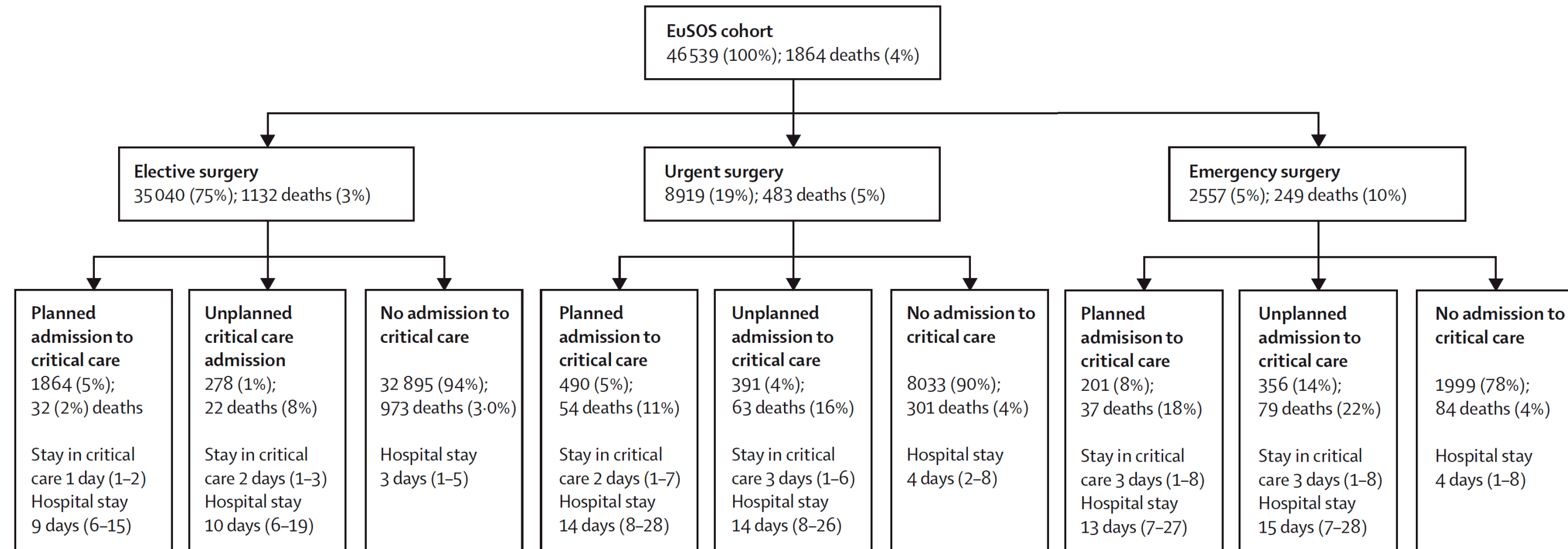
	Number of patients	Median days in hospital (IQR)	Percentage died in hospital (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
France	2278	3.0 (1.0–6.0)	3.2% (2.5–3.9)	0.90 (0.70–1.16)	1.36 (0.72–2.56)

Table 2: Relation between country and in-hospital mortality

(adjusted for age, ASA score, urgency of surgery, grade of surgery (minor, intermediate, major), surgical specialty, and the presence of either metastatic disease or cirrhosis)

Mortality after surgery in Europe: a 7 day cohort study

*Rupert M Pearse, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology**



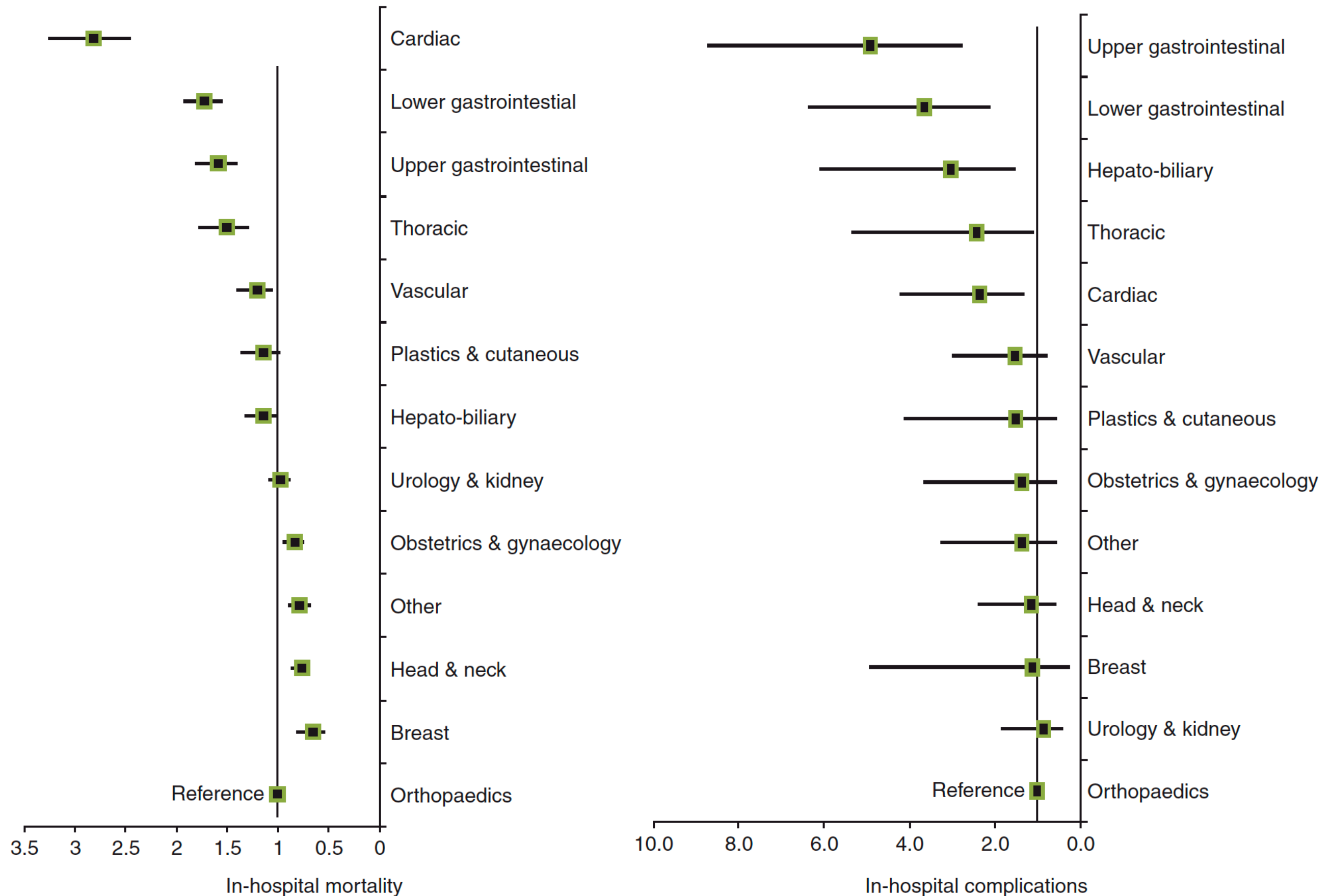
Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high- income countries

The International Surgical Outcomes Study group

ISOS study

- A prospective international 7-day cohort study of outcomes in >44 000 patients following elective adult inpatient surgery from 27 countries (474 hospitals) between April and August 2014
- Primary outcome measure: In-hospital postoperative complications
 - 1 in 6 patients experienced a complication before hospital discharge
 - 1 in 35 patients subsequently died without leaving the hospital (mortality 2.8%)

Adjusted risk (odds ratio) of complications and in-hospital mortality



	N = 44 814	Severity of complications			Mortality for patients who developed complications N = 207
		Mild	Moderate	Severe	
Infectious complications					
Superficial surgical site	1320 (2.9)	681/1320 (51.6)	517/1320 (39.2)	122/1320 (9.2)	17/1320 (1.3)
Deep surgical site	566 (1.3)	120/566 (21.2)	250/566 (44.2)	196/566 (34.6)	28/566 (4.9)
Body cavity	340 (0.8)	97/340 (28.5)	136/340 (40.0)	107/340 (31.5)	24/340 (7.0)
Pneumonia	708 (1.6)	240/708 (33.9)	325/708 (45.9)	143/708 (20.2)	55/708 (7.8)
Urinary tract	681 (1.5)	294/681 (43.2)	333/681 (48.9)	54/681 (7.9)	13/681 (1.9)
Bloodstream	417 (0.9)	140/417 (33.6)	162/417 (38.8)	115/417 (27.6)	48/417 (11.5)
Total infectious complications	4032	1572/4032 (39.0)	1723/4032 (42.7)	737/4032 (18.3)	104/4032 (2.6)
Cardiovascular complications					
Myocardial infarction	139 (0.3)	45/139 (32.4)	43/139 (30.9)	51/139 (36.7)	26/139 (18.7)
Arrhythmia	1222 (2.7)	468/1222 (38.3)	568/1222 (46.5)	186/1222 (15.2)	74/1222 (6.1)
Pulmonary oedema	330 (0.7)	127/330 (38.4)	141/330 (42.8)	62/330 (18.8)	34/330 (10.3)
Pulmonary embolism	78 (0.2)	17/78 (21.8)	33/78 (42.3)	28/78 (35.9)	5/78 (6.4)
Stroke	111 (0.2)	31/111 (27.9)	28/111 (25.2)	52/111 (46.9)	18/111 (16.2)
Cardiac arrest	153 (0.3)	N/A	N/A	153/153 (100.0)	91/153 (59.5)
Total cardiovascular complications	2033	688/2033 (33.8)	813/2033 (40.0)	532/2033 (26.2)	141/2033 (6.9)
Other complications					
Gastrointestinal bleed	201 (0.4)	95/201 (47.3)	66/201 (32.8)	40/201 (19.9)	24/201 (11.9)
Acute kidney injury	778 (1.7)	423/778 (54.4)	203/778 (26.1)	152/778 (19.5)	76/778 (9.8)
Postoperative bleed	1362 (3.0)	N/A	1147/1362 (84.2)	215/1362 (15.8)	55/1362 (4.0)
ARDS	142 (0.3)	46/142 (32.4)	41/142 (28.9)	55/142 (38.7)	34/142 (23.9)
Anastomotic leak	208 (0.5)	52/208 (25.0)	62/208 (29.8)	94/208 (45.2)	21/208 (10.1)
All others	2934 (6.5)	1342/2925 (45.9)	1200/2925 (41.0)	392/2925 (13.4)	83/2925 (2.8)
Total other complications	5625	1958/5625 (34.8)	2719/5625 (48.3)	948/5625 (16.9)	158/5625 (2.8)
Total number of complications	11 690	4218/11 690 (36.1)	5255/11 690 (45.0)	2217/11 690 (19.0)	207/7508 (2.8)

ORIGINAL

Critical care admission following elective surgery was not associated with survival benefit: prospective analysis of data from 27 countries

Brennan C. Kahan¹, Desponia Koulenti^{2,3}, Kostoula Arvaniti⁴, Vanessa Beavis⁵, Douglas Campbell⁵, Matthew Chan⁶, Rui Moreno⁷, Rupert M. Pearce^{8,9*}  and The International Surgical Outcomes Study (ISOS) group

Table 3 Crude and risk-adjusted mortality for patients according to admission directly to critical care after surgery

	Mortality amongst patients admitted to standard ward after surgery (<i>n</i> = 39,566)	Mortality amongst patients admitted to critical care after surgery (<i>n</i> = 4317)	Risk-adjusted odds ratio (95% CI)	<i>p</i> value for interaction
Overall	99 (0.3%)	103 (2.4%)	3.01 (2.10–5.21)	–
Low and middle income countries	25 (0.2%)	29 (2.8%)	4.68 (2.56–8.57)	–
High income countries	74 (0.3%)	74 (2.3%)	2.50 (1.65–3.78)	0.07

- Risk adjusted OR for mortality 3.01 (95% CI 2.10–5.21; *p* < 0.001)
(Adjustment for age, gender, current smoker, ASA score, severity of surgery (minor, intermediate, major surgical procedure), presence of ischaemic heart disease, heart failure, diabetes mellitus, COPD/asthma, cirrhosis, and stroke)
- No significant effect of critical care measure in the high-risk (ASA III or IV and undergoing major surgery) subgroup of patients



Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial

Lancet 2008; 371: 1839–47

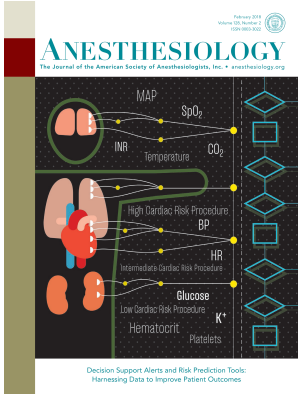
POISE study

- N=8351 patients with, or at risk of, atherosclerotic disease undergoing non-cardiac surgery
- Clinically significant hypotension defined as systolic arterial pressure (SAP) < 90 mmHg

	Adjusted odds ratio (95% CI)	Frequency of risk factor n (%)	PAR* (95% CI)
Death			
Intraoperative and postoperative predictors			
Clinically significant hypotension	4.97 (3.62–6.81)	1029 (12.3%)	37.3% (29.5–45.8)
Myocardial infarction without ischaemic symptoms	3.45 (2.20–5.41)	271 (3.3%)	10.6% (6.4–17.0)
Significant bleeding	1.67 (1.14–2.44)	553 (6.6%)	9.4% (4.3–19.5)
Stroke	18.97 (9.93–36.25)	60 (0.7%)	8.0% (5.0–12.5)
Clinically significant bradycardia	2.13 (1.37–3.32)	351 (4.2%)	7.9% (3.9–15.3)
Myocardial infarction with ischaemic symptoms	3.31 (1.78–6.15)	144 (1.7%)	4.2% (1.9–9.2)
Stroke			
Intraoperative and postoperative predictors			
Clinically significant hypotension	2.14 (1.15–3.96)	1029 (12.3%)	14.7% (5.2–35.4)
Significant bleeding	2.18 (1.06–4.49)	553 (6.6%)	10.1% (3.0–28.5)
New clinically significant atrial fibrillation	3.51 (1.45–8.52)	200 (2.4%)	6.9% (2.1–20.4)
Total explained	..	..	51.8% (37.1–66.2)

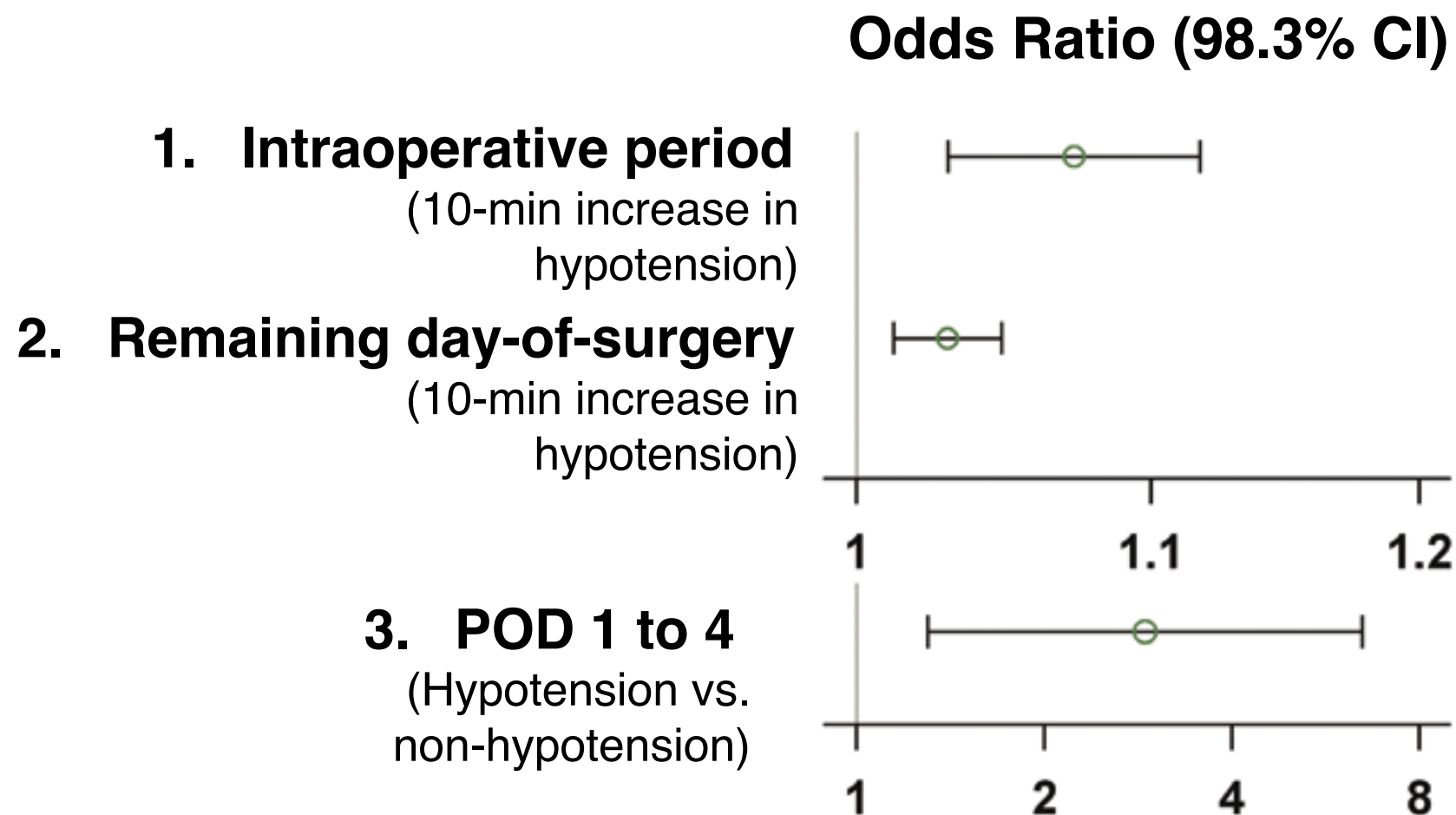
Period-dependent Associations between Hypotension During and for 4 Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death

A Substudy of the POISE-2 Trial



N= 9,765 of 10,010 patients, 42% experienced hypotension

- Clinically important hypotension defined as SBP < 90 mmHg requiring treatment
- **Primary endpoint:** composite of 30-day myocardial infarction and death



Goal-Directed Therapy *versus* Standard of care

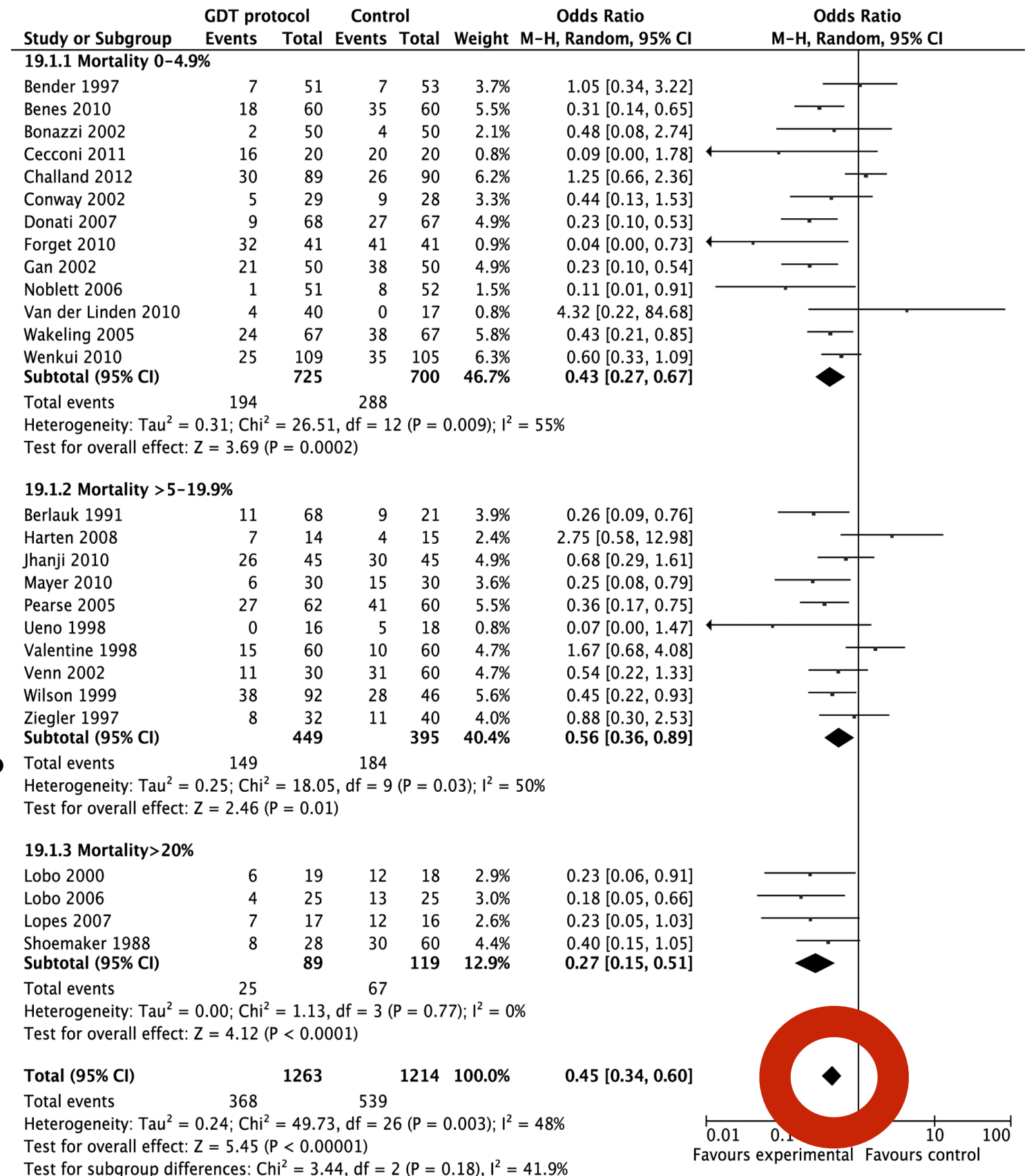
Effect on different patient risk groups

- 27 RCTs
- Postoperative Morbidity
(OR 0.45, 95% CI 0.34 to 0.60; $P < 0.00001$)

- Mortality $< 5\%$

- Mortality 5-20%

- Mortality $> 20\%$



Goal-Directed Therapy *versus* Standard of care

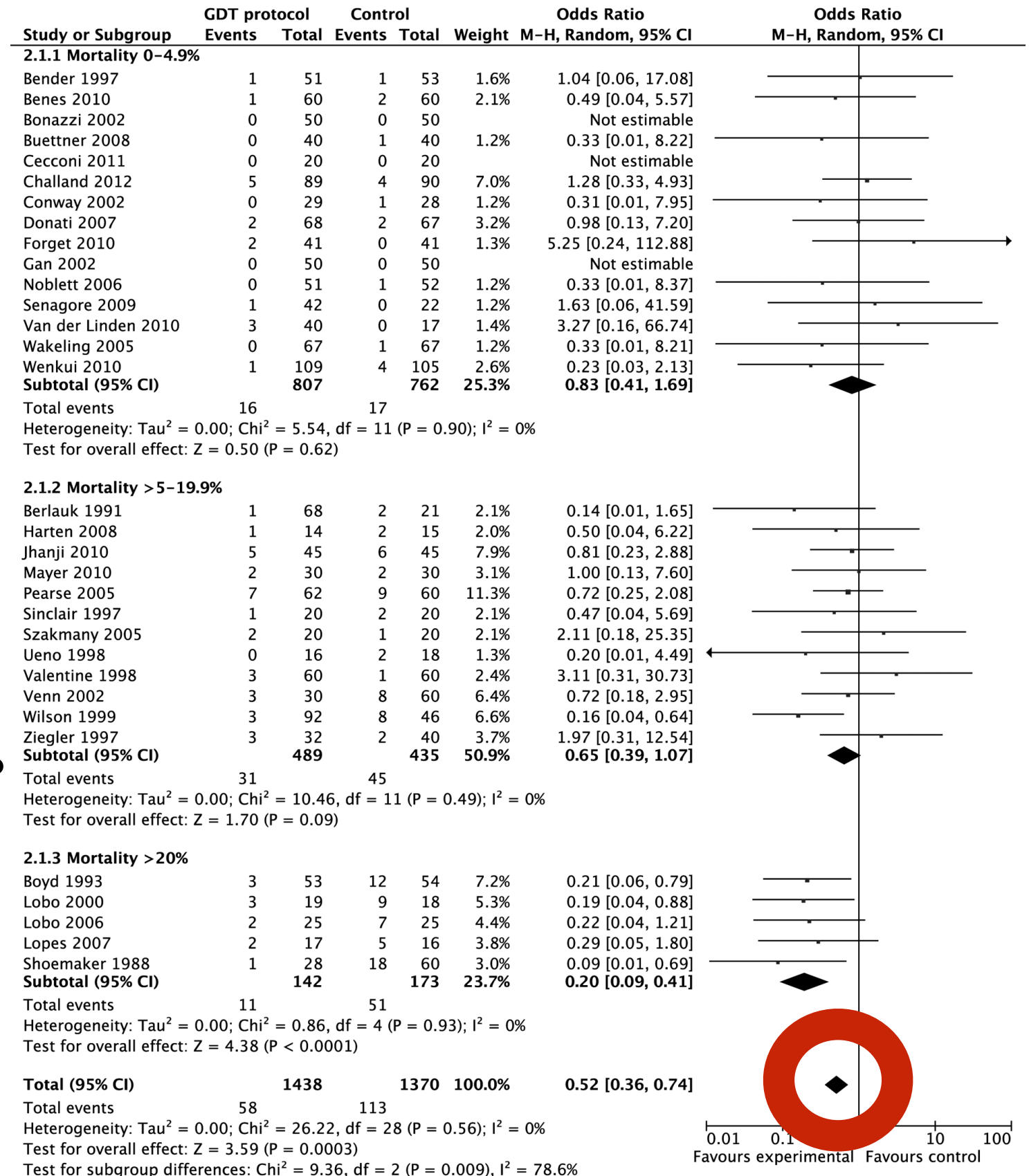
Effect on different patient risk groups

- 32 RCTs
- Postoperative Mortality
(OR 0.52, 95% CI 0.36 to 0.74; P =0.003)

- Mortality <5%

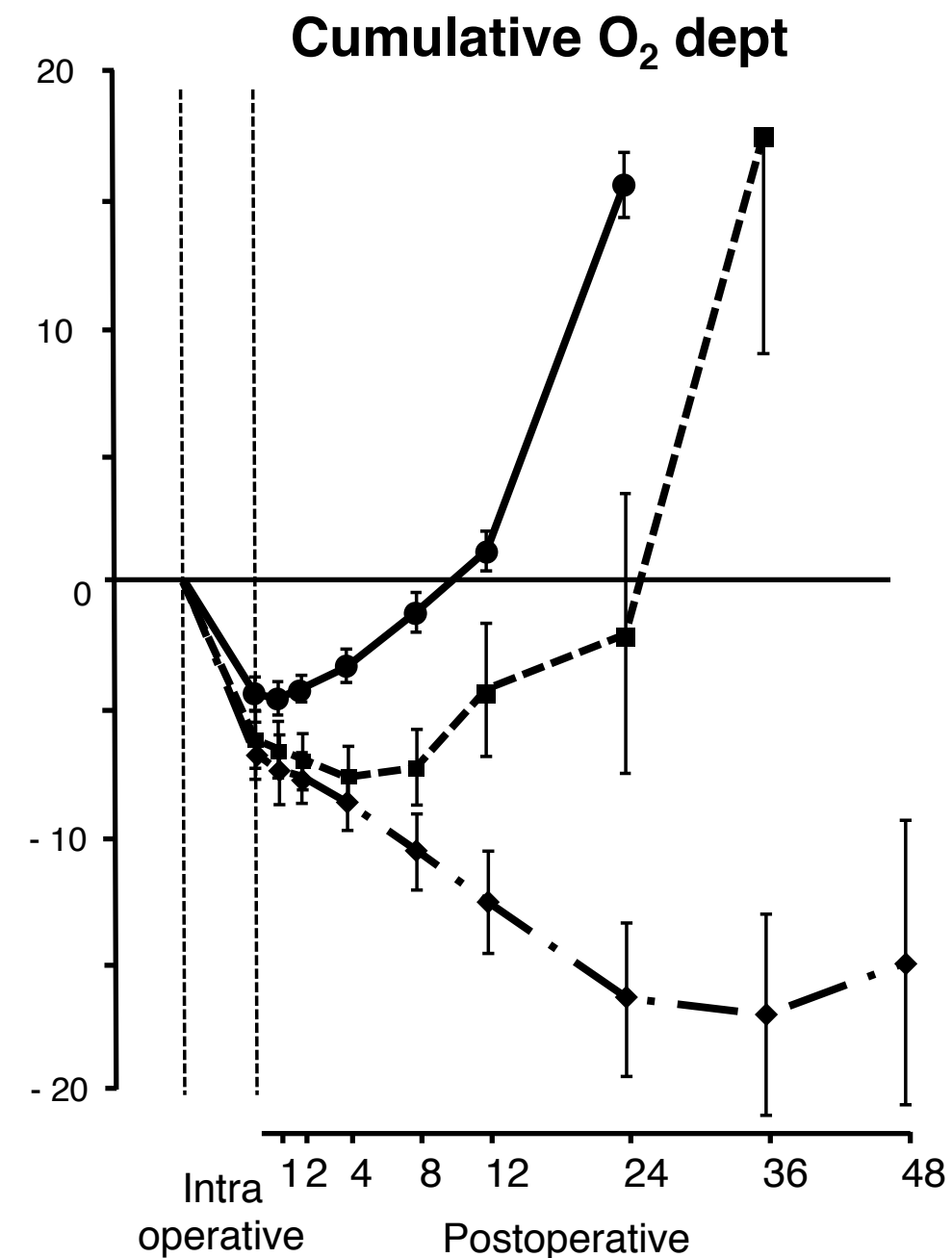
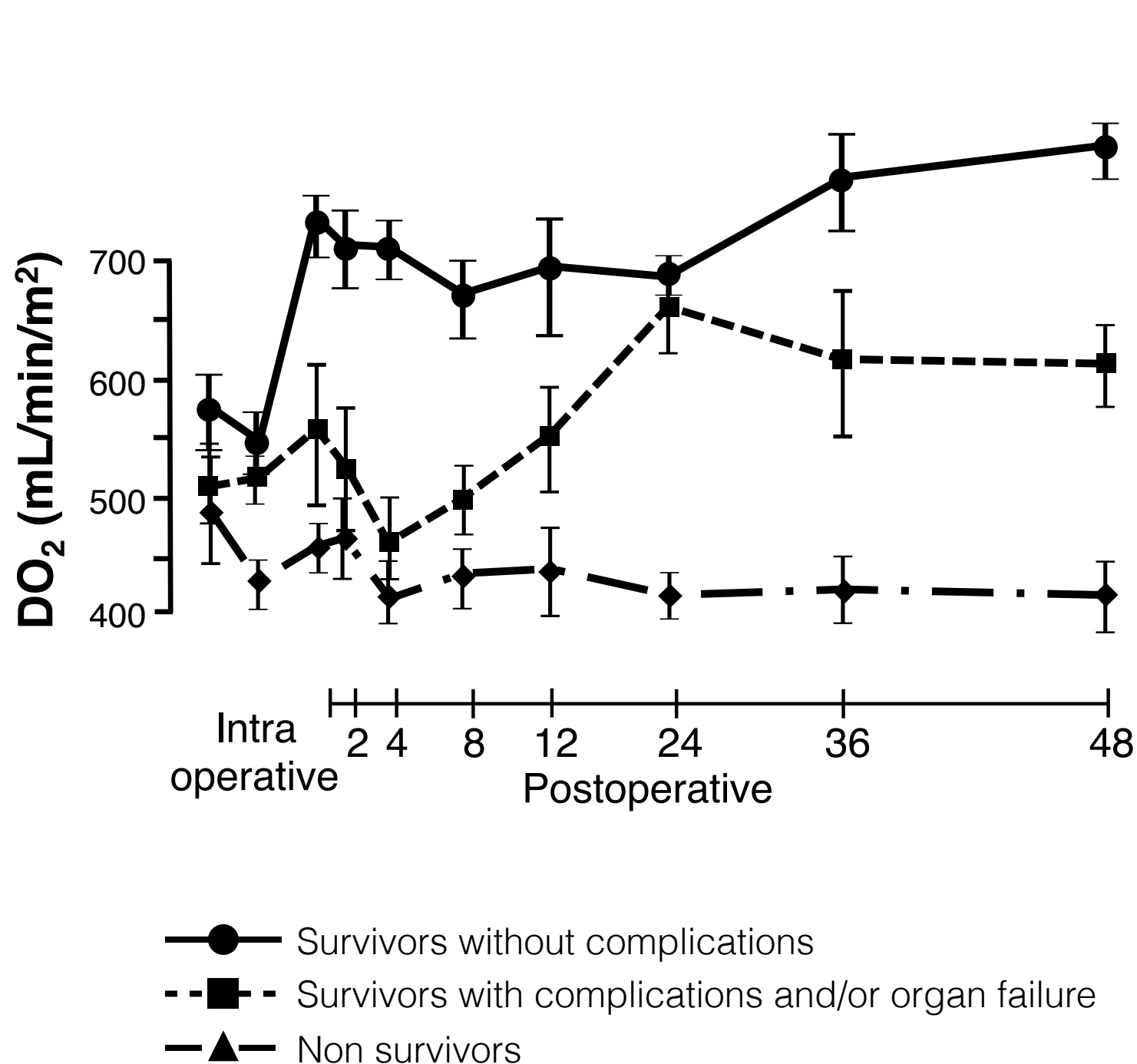
- Mortality 5-20%

- Mortality >20%



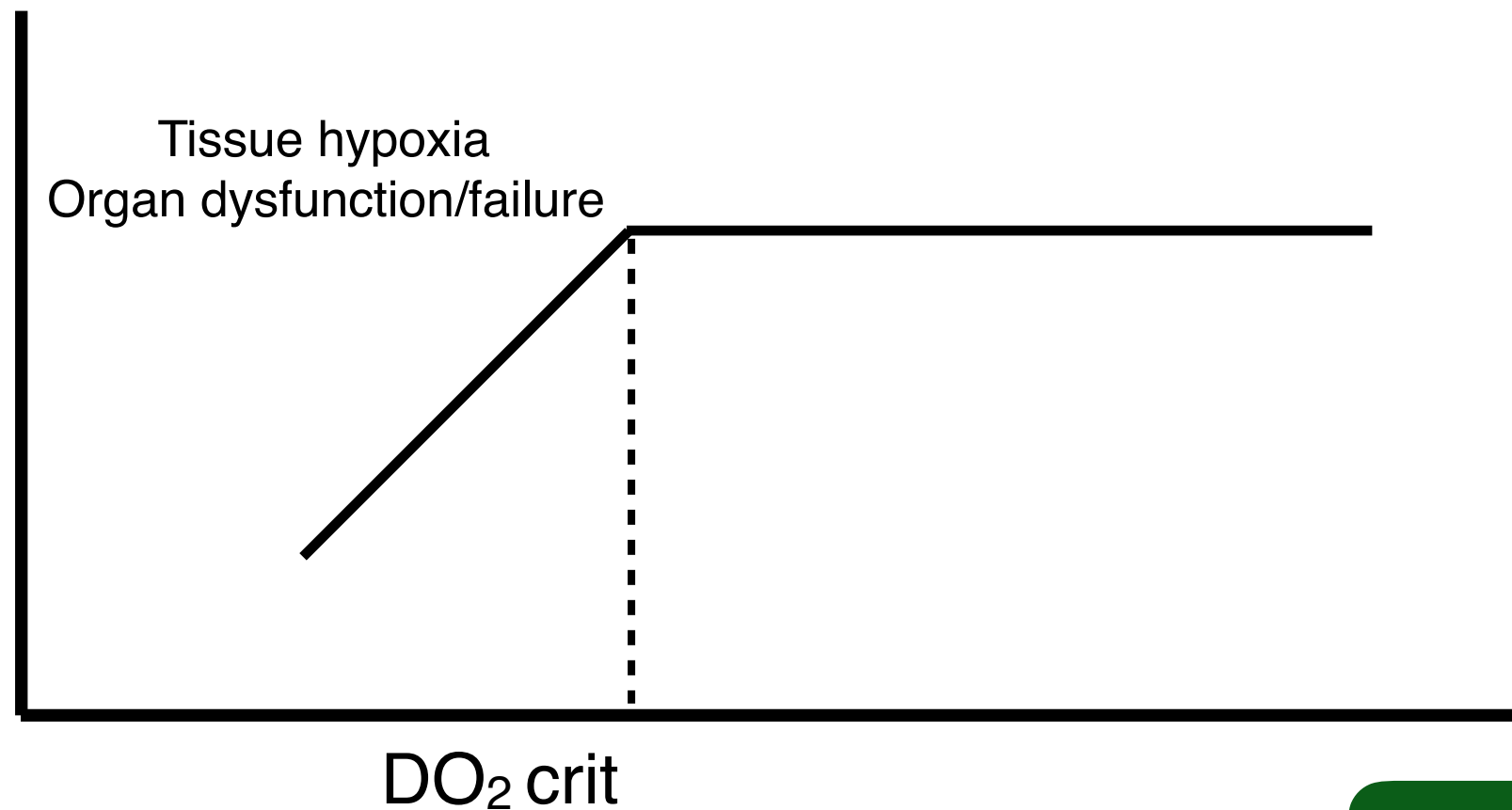
Role of Oxygen Debt in the Development of Organ Failure Sepsis, and Death in High-Risk Surgical Patients

William C. Shoemaker, M.D.; Paul L. Appel, M.P.A.; and
Harry B. Kram, M.D.



Oxygen Supply-Demand Relationship

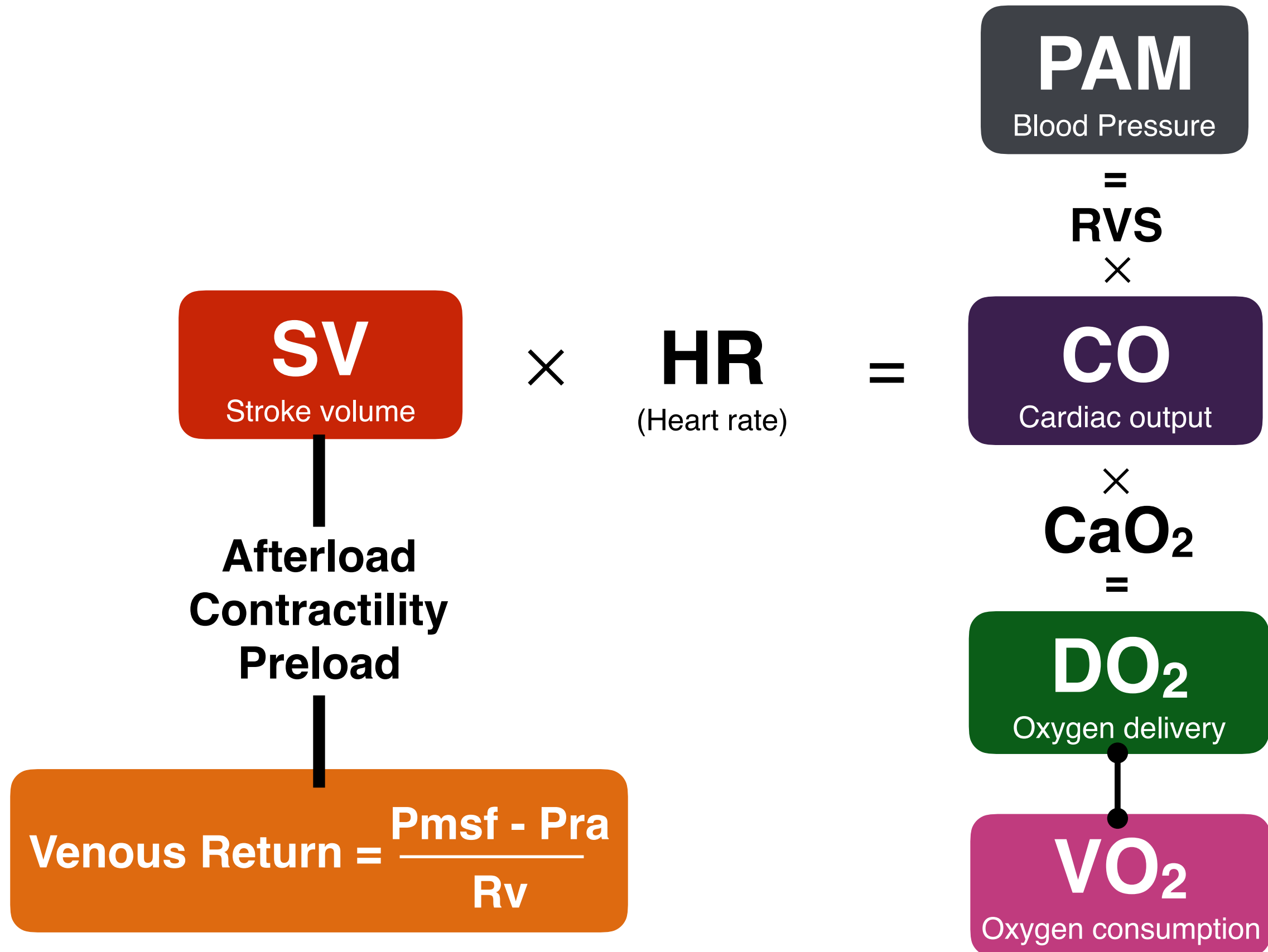
VO_2
Oxygen consumption



DO_2
Oxygen delivery

Hemodynamic Optimization in High-Risk Surgical Patients

A multimodal Treatment Strategy



DO₂
Oxygen delivery

=

CO
(Cardiac Output)

×

CaO₂
(Oxygen Content)

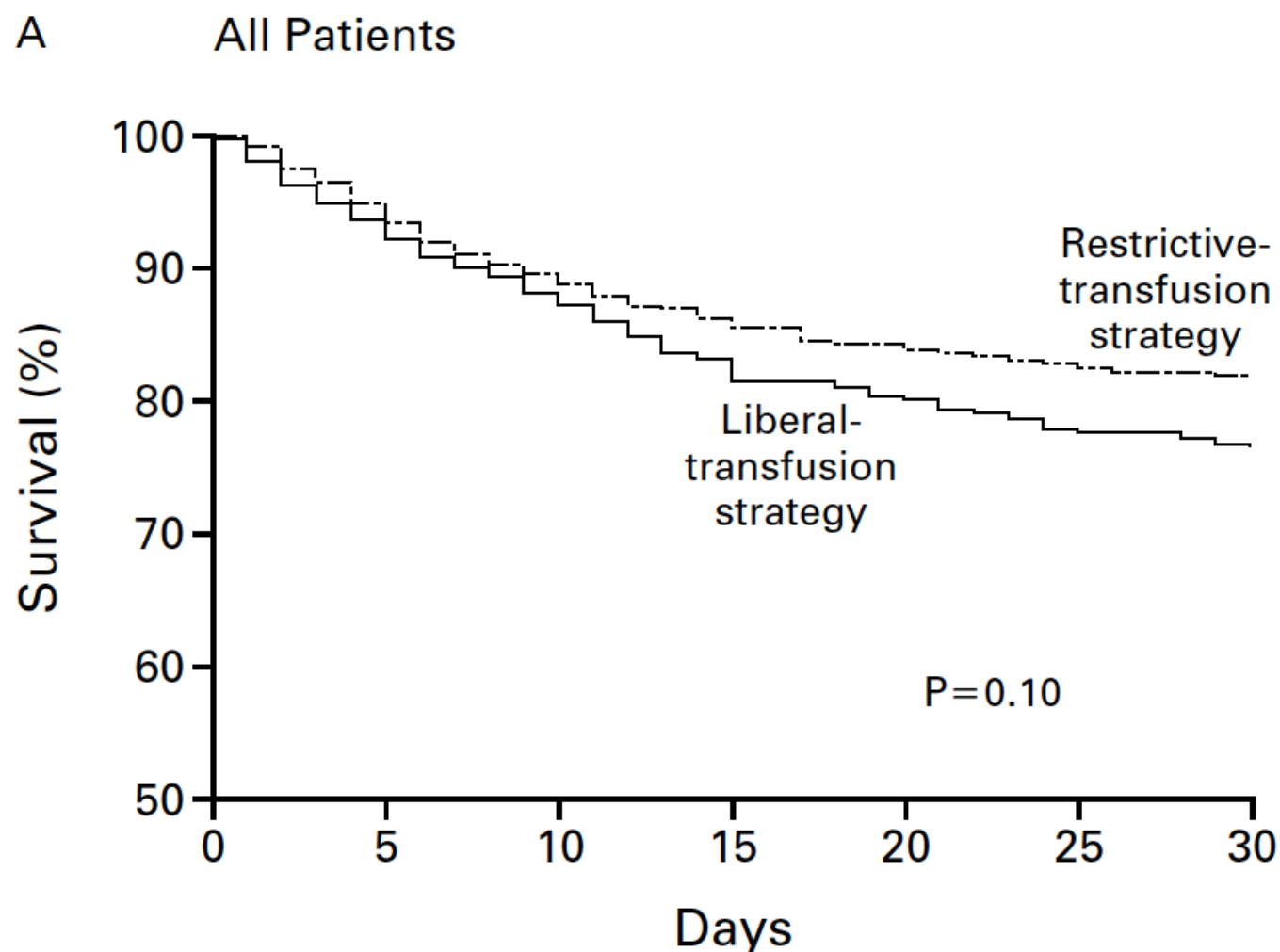
$$\begin{array}{ccccccc} \text{CaO}_2 & = & \text{Hb} & \times & \text{SaO}_2 & \times & 1.34 \\ \text{(Oxygen Content)} & & \text{(Hemoglobin)} & & \text{(O}_2 \text{ Saturation)} & & \end{array}$$



N Engl J Med 1999;340:409-17

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D.,
CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.Sc.,
ELIZABETH YETISIR, M.Sc., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS
FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*



Outcome	RESTRICTIVE-TRANSFUSION STRATEGY (N=418)	LIBERAL-TRANSFUSION STRATEGY (N=420)
No. of organs failing — no. (%)	7-9 g/dl	10-12 g/dl
0	100 (23.9)	82 (19.5)
1	136 (32.5)	149 (35.5)
2	109 (26.1)	108 (26.0)
3	51 (12.2)	63 (15.0)
>3	22 (5.3)	18 (4.3)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MARCH 12, 2015

VOL. 372 NO. 11

Liberal or Restrictive Transfusion after Cardiac Surgery

Gavin J. Murphy, F.R.C.S., Katie Pike, M.Sc., Chris A. Rogers, Ph.D., Sarah Wordsworth, Ph.D., Elizabeth A. Stokes, M.Sc., Gianni D. Angelini, F.R.C.S., and Barnaby C. Reeves, D.Phil., for the TITRe2 Investigators*

TITRe2 trial

N=2006 patients

Outcome	Restrictive Transfusion Threshold (N = 1000)	Liberal Transfusion Threshold (N = 1003)	Estimated Treatment Effect	
	7.5 g/dl versus 9 g/dl		Odds Ratio or Hazard Ratio (95% CI)	P Value
Acute kidney injury	140/989 (14.2)	122/989 (12.3)		
Stage 1	49/989 (5.0)	40/989 (4.0)		
Stage 2	39/989 (3.9)	35/989 (3.5)		
Stage 3	50/989 (5.1)	46/989 (4.7)		

ORIGINAL ARTICLE

Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery

TRICS III study

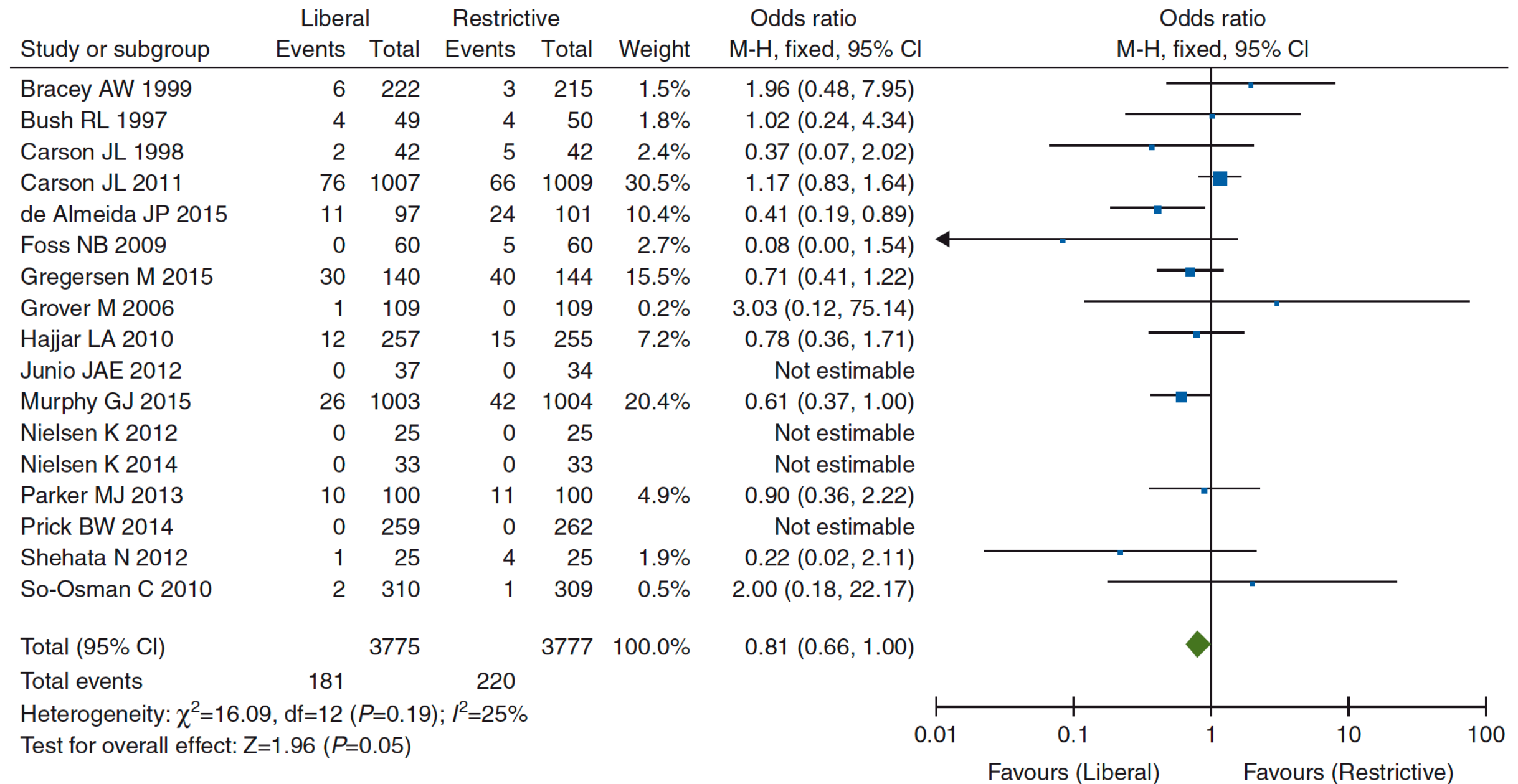
- International, open-label, randomized, controlled, noninferiority trial
- N= 5243 adults undergoing cardiac surgery with an EuroSCORE I of 6 or more
- Liberal (Hb <9.5 g/dl) vs restrictive (Hb <7.5 g/dl) transfusion strategy intraoperatively or postoperatively
- **Primary outcome:** composite of death from any cause, nonfatal myocardial infarction, stroke, or new-onset renal failure with dialysis from the start of surgery until either hospital discharge or 28 days after surgery

Table 3. Primary and Secondary Outcomes in the Per-Protocol Population.

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)

Liberal *versus* Restrictive Transfusion Strategy in the Perioperative Setting

Fig 2. Forest plot of all-cause mortality in the perioperative setting



All-cause mortality was reduced in patients randomized to receive a liberal transfusion strategy: OR 0.81; 95% CI 0.66-1.00; P for effect=0.05; NNT=97

REVIEW

Venous oxygen saturation as a physiologic transfusion trigger

Benoit Vallet*, Emmanuel Robin and Gilles Lebuffe

SRLF recommendations	ScvO ₂ <70%		ScvO ₂ ≥ 70%		Kruskal-Wallis test (p <.05)
	Yes (n = 15)	No (n = 13)	Yes (n = 18)	No (n = 7)	
ScvO ₂ preBT	57.4 [48.2–62.0]	58.0 [55.3–65.0]	76.9 [72.0–80.8]	75.7 [75.0–86.4]	p < 0.001
ScvO ₂ postBT	68.7* [63.0–75.6]	67.8* [60.7–72.0]	78.7 [70.0–84.2]	74.0* [65.0–76.7]	p < 0.01
Hb preBT	7.4 [7.1–7.9]	7.8 [7.4–8.7]	7.5 [7.3–8.1]	8.1 [7.5–8.2]	Ns
Hb postBT	9.4** [8.7–9.7]	10.0** [9.4–10.6]	10.1** [9.3–10.6]	9.8* [9.4–10.7]	Ns

$$\text{DO}_2 = \text{CO} \times \text{CaO}_2$$

Oxygen delivery = (Cardiac Output) × (Oxygen Content)

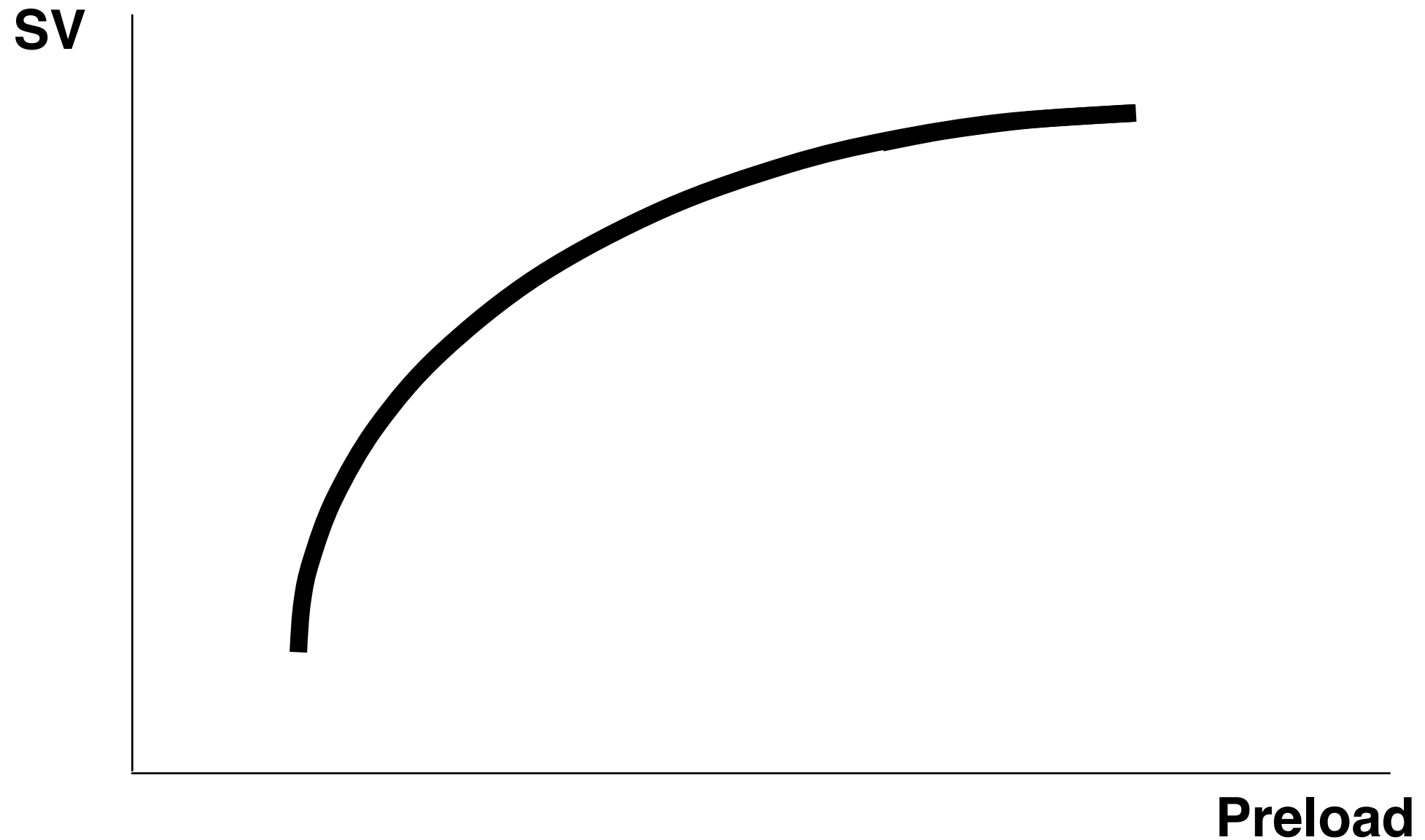
Fluid challenge



DO₂
Oxygen delivery

$$= \left(\underset{\text{(Stroke Volume)}}{SV} \times \underset{\text{(Heart Rate)}}{HR} \right) \times \underset{\text{(Oxygen Content)}}{CaO_2}$$

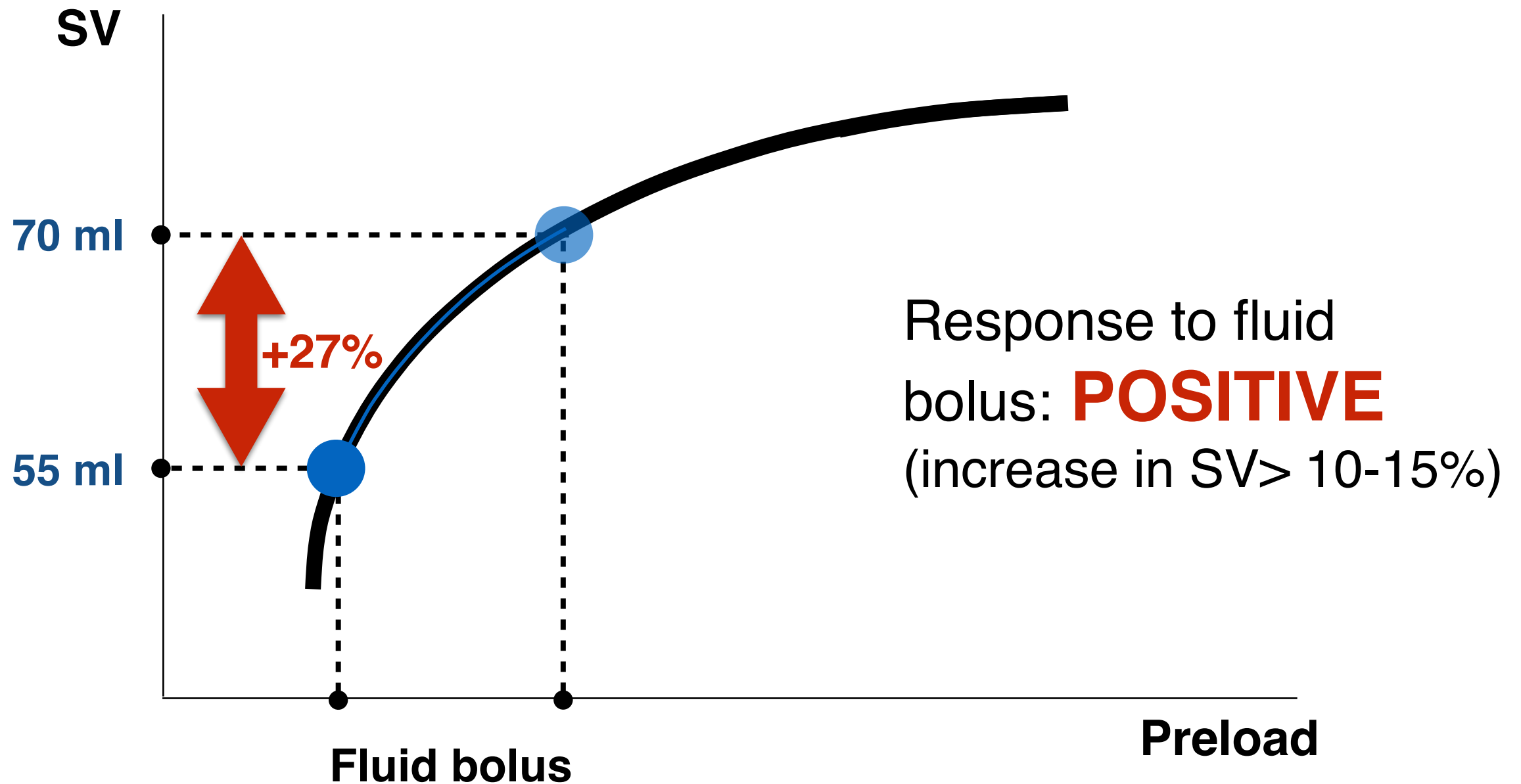
Cardiac output optimization



$$CO = \textcolor{red}{SV} \times HR$$

Cardiac output optimization

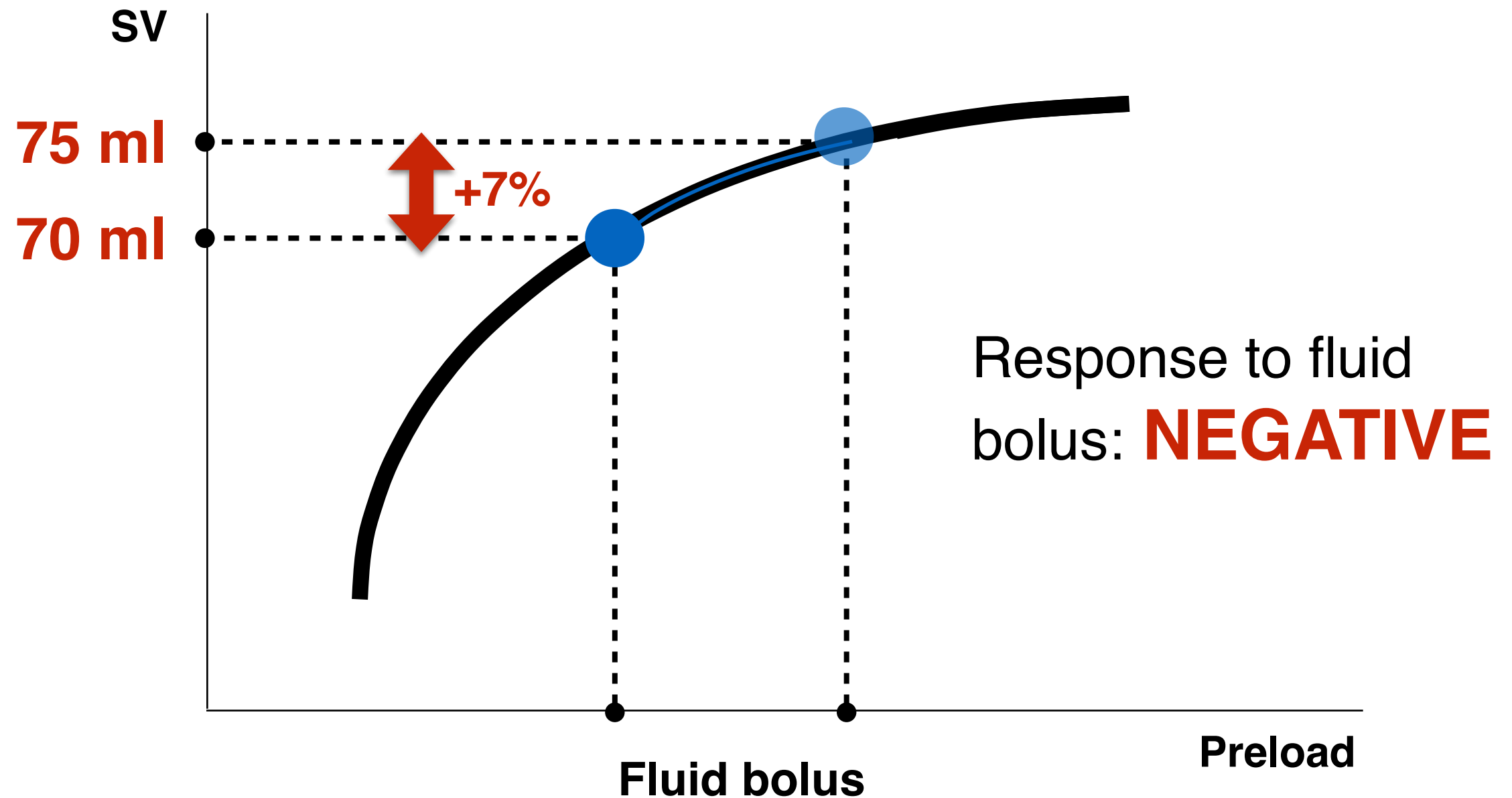
Fluid Titration



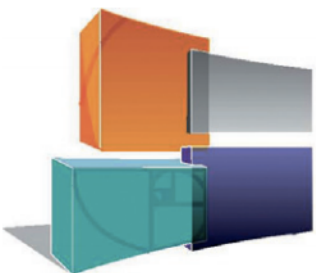
$$CO = SV \times HR$$

Cardiac output optimization

Fluid Titration



$$CO = SV \times HR$$



SFAR

Société Française d'Anesthésie et de Réanimation

RFE SFAR-ADARPEF

Ann Fr Anesth Reanim. 2013; 32:e151-8

Stratégie du remplissage vasculaire périopératoire

Guidelines for perioperative haemodynamic optimization

B. Vallet ^{a,*}, Y. Blanloeil ^b, B. Cholley ^c, G. Orliaguet ^d, S. Pierre ^e, B. Tavernier ^a

4.1. Recommandation 1

- Chez les patients chirurgicaux considérés « à haut risque », **il est recommandé de titrer le remplissage vasculaire peropératoire** en se guidant sur une **mesure du volume d'éjection systolique (VES)** dans le but de réduire la morbidité postopératoire, la durée de séjour hospitalier, et le délai de reprise d'une alimentation orale des patients de chirurgie digestive (**GRADE 1+**).
- Par patients « à haut risque », nous entendons les patients qui, de par leur terrain ou la nature même de leur intervention, sont exposés à un risque accru de complications postopératoires.

Intraoperative fluids: how much is too MUCH?

M. Doherty^{1*} and D.J. Buggy^{1,2}



Perioperative morbidity

Hypoperfusion

Hypovolemia
Organ dysfunction

Fluid excess

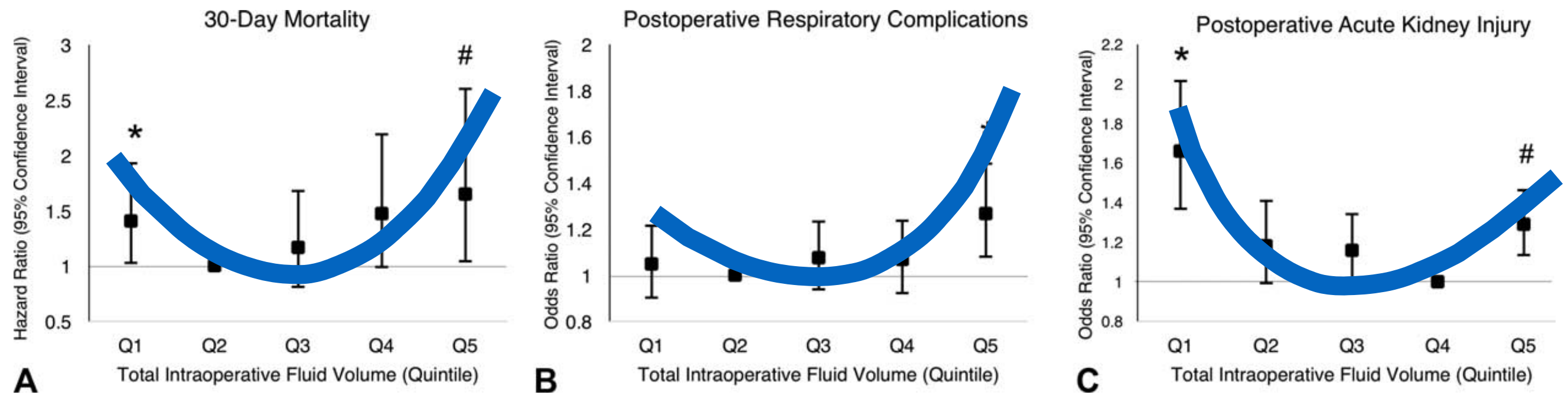
Tissue Oedema
Glycocalyx dysfunction
Hypoxemia
Organ dysfunction

Fluid Load

Effects of Intraoperative Fluid Management on Postoperative Outcomes

Christina H. Shin, Dustin R. Long, Duncan McLean, Stephanie D. Grabitz, Cand. Med, Karim Ladha, MD, MSc,z Fanny P. Timm, Cand. Med, Tharusan Thevathasan, Alberto Pieretti, Cristina Ferrone, Andreas Hoeft, Thomas W. L. Scheeren, Boyd Taylor Thompson, Tobias Kurth and Matthias Eikermann, MD, PhD

- Data from 92,094 adult patients undergoing noncardiac surgery with endotracheal intubation
- Primary exposure variable: Total intraoperative volume of crystalloid and colloid
- **Primary outcome:** 30-day survival.
- **Secondary outcomes:** Respiratory complications within 3 postoperative days (pulmonary edema, reintubation, pneumonia, or respiratory failure) and AKI



ORIGINAL ARTICLE

Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery

P.S. Myles, R. Bellomo, T. Corcoran, A. Forbes, P. Peyton, D. Story, C. Christophi, K. Leslie, S. McGuinness, R. Parke, J. Serpell, M.T.V. Chan, T. Painter, S. McCluskey, G. Minto, and S. Wallace, for the Australian and New Zealand College of Anaesthetists Clinical Trials Network and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

RELIEF trial

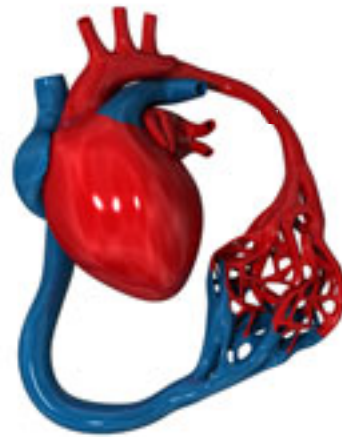
Outcome	Restrictive Fluid (N = 1490)	Liberal Fluid (N = 1493)	Hazard or Risk Ratio (95% CI) [†]	P Value
Secondary outcomes[§]				
Composite septic outcome or death — no./total no. (%) [¶]	323/1481 (21.8)	295/1487 (19.8)	1.10 (0.96–1.27)	0.19
Surgical-site infection — no./total no. (%)	245/1481 (16.5)	202/1487 (13.6)	1.22 (1.03–1.45)	0.02
Sepsis — no./total no. (%)	157/1481 (10.6)	129/1487 (8.7)	1.22 (0.98–1.52)	0.08
Anastomotic leak — no./total no. (%)	49/1481 (3.3)	35/1487 (2.4)	1.41 (0.92–2.16)	0.12
Pneumonia — no./total no. (%)	54/1481 (3.6)	57/1487 (3.8)	0.95 (0.66–1.37)	0.79
Acute kidney injury — no./total no. (%) ^{**}	124/1443 (8.6)	72/1439 (5.0)	1.71 (1.29–2.27)	<0.001
Renal-replacement therapy — no./total no. (%)	13/1460 (0.9)	4/1462 (0.3)	3.27 (1.01–13.8)	0.048
Pulmonary edema — no./total no. (%)	20/1481 (1.4)	32/1487 (2.2)	0.63 (0.36–1.09)	0.10
Unplanned admission to ICU — no./total no. (%)	161/1487 (10.8)	145/1491 (9.7)	1.11 (0.90–1.38)	0.32
Median duration of mechanical ventilation (IQR) — hr ^{§§}	17 (5–65)	14 (3–31)	NA	0.07
Median score on quality-of-recovery scale (IQR) ^{¶¶}	106 (89–121)	107 (90–122)	NA	0.31
Median duration of stay in HDU or ICU (IQR) — days	1.8 (1.0–3.1)	1.4 (0.9–2.9)	NA	0.13
Median duration of hospital stay (IQR) — days	6.4 (3.6–10.6)	5.6 (3.6–10.5)	NA	0.26
Death — no. (%) [‡]				
At 90 days	31 (2.1)	18 (1.2)	1.73 (0.97–3.10)	0.06
At 12 mo	95 (6.5)	96 (6.6)	1.03 (0.78–1.36)	0.86

Objectives of IV fluid therapy

↑ **Preload**



↑ **Cardiac output**



↑ **O₂ delivery (DO₂)**



↓ **Tissue hypoperfusion**

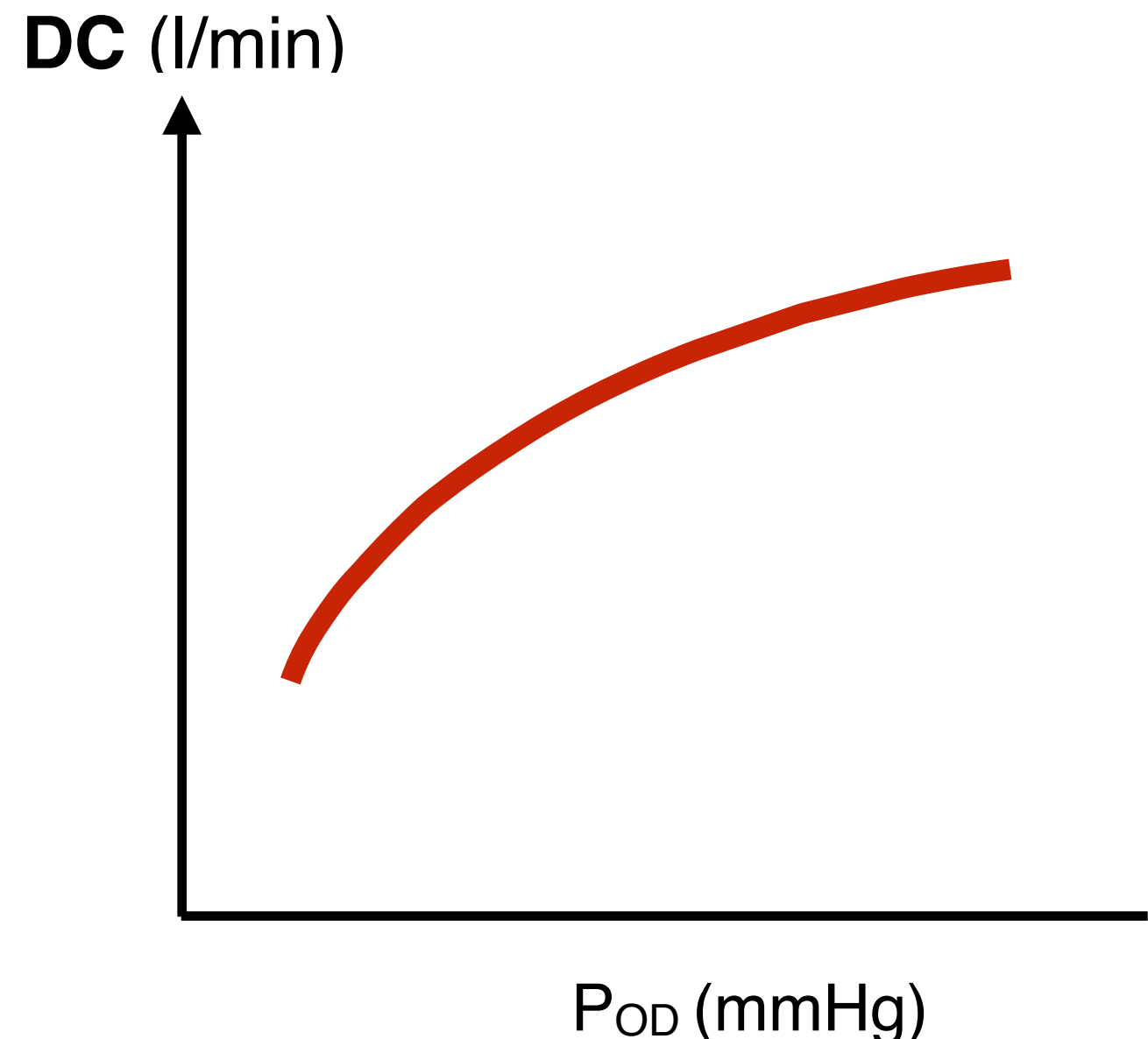
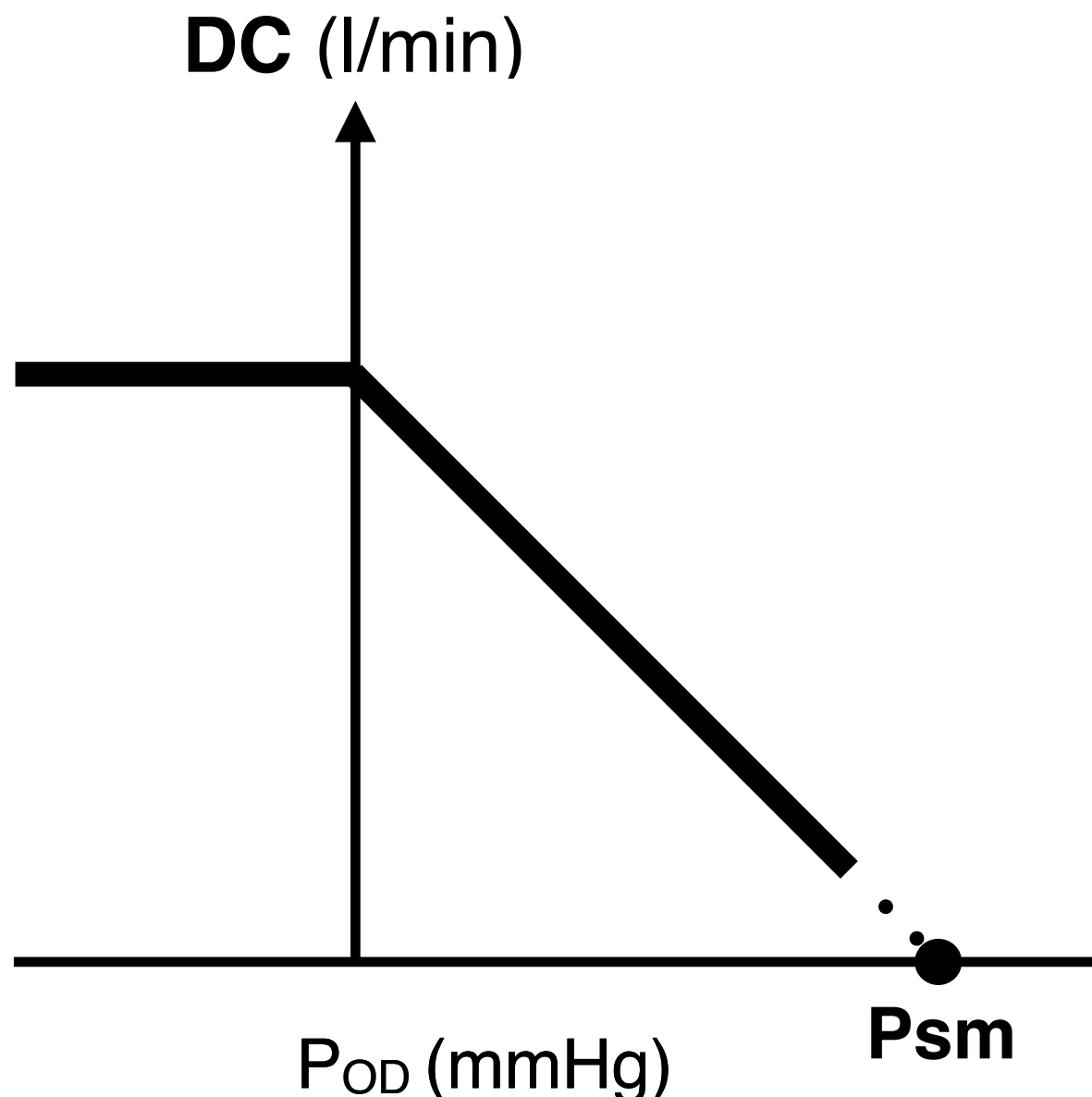
Retour veineux — Débit cardiaque

Le débit cardiaque est déterminé par :

Retour Veineux

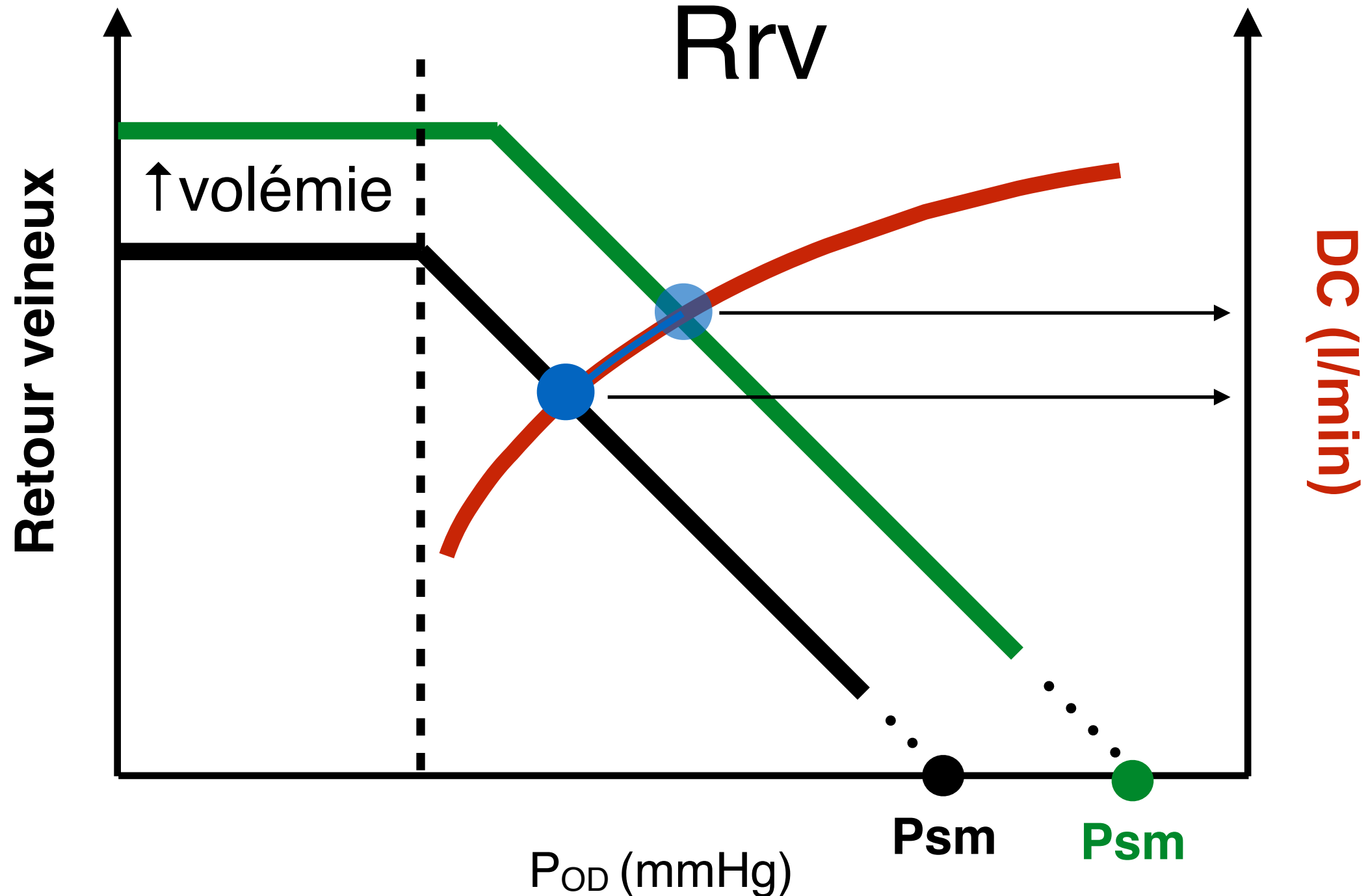
et

Fonction Cardiaque

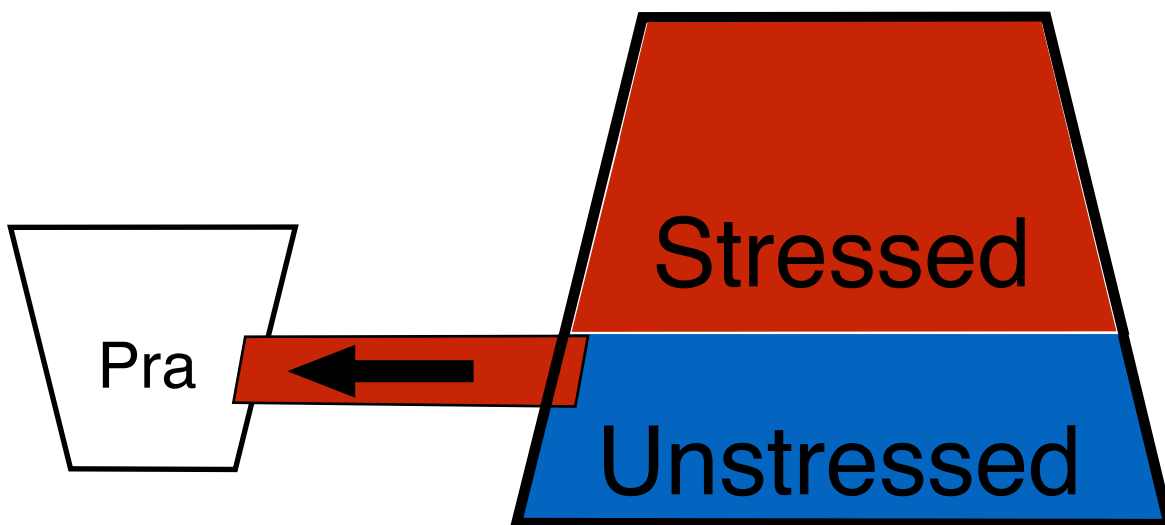
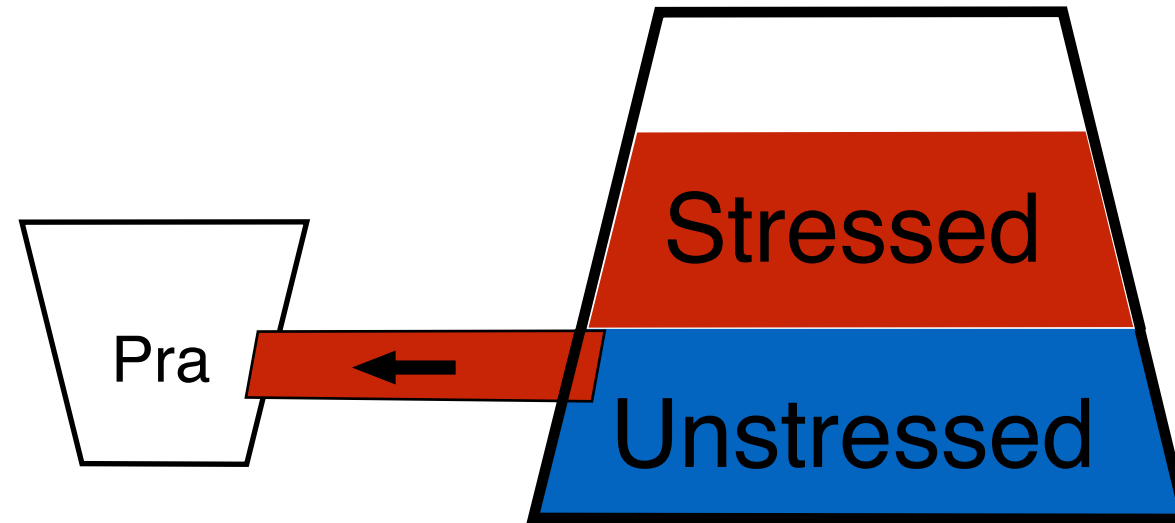


Retour veineux — Débit cardiaque

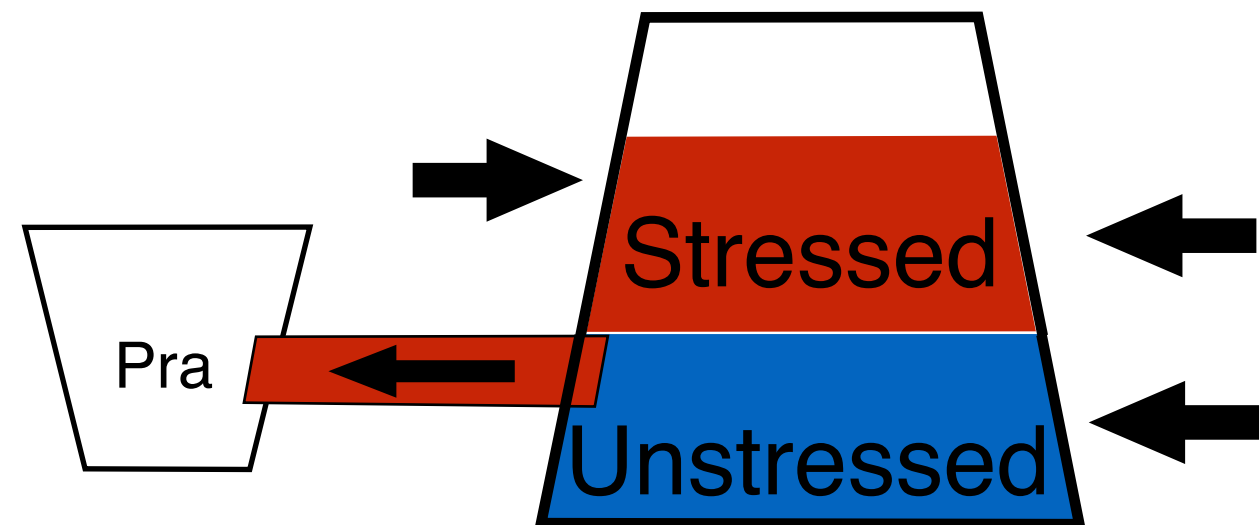
$$R_v = \frac{(P_{sm} - P_{OD})}{R_{rv}}$$



Stressed vs Unstressed Volume



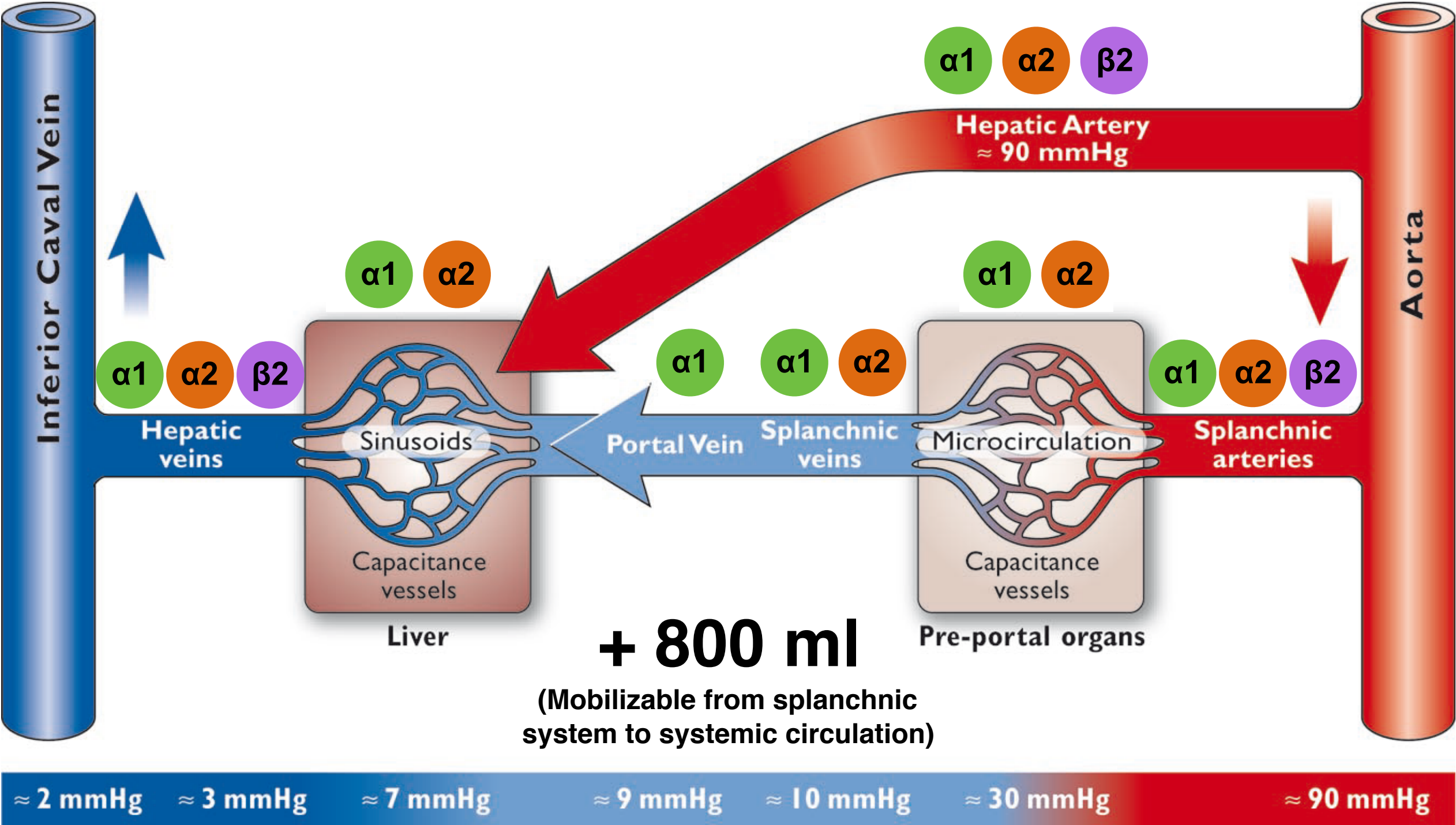
Fluid load



Vasopressor

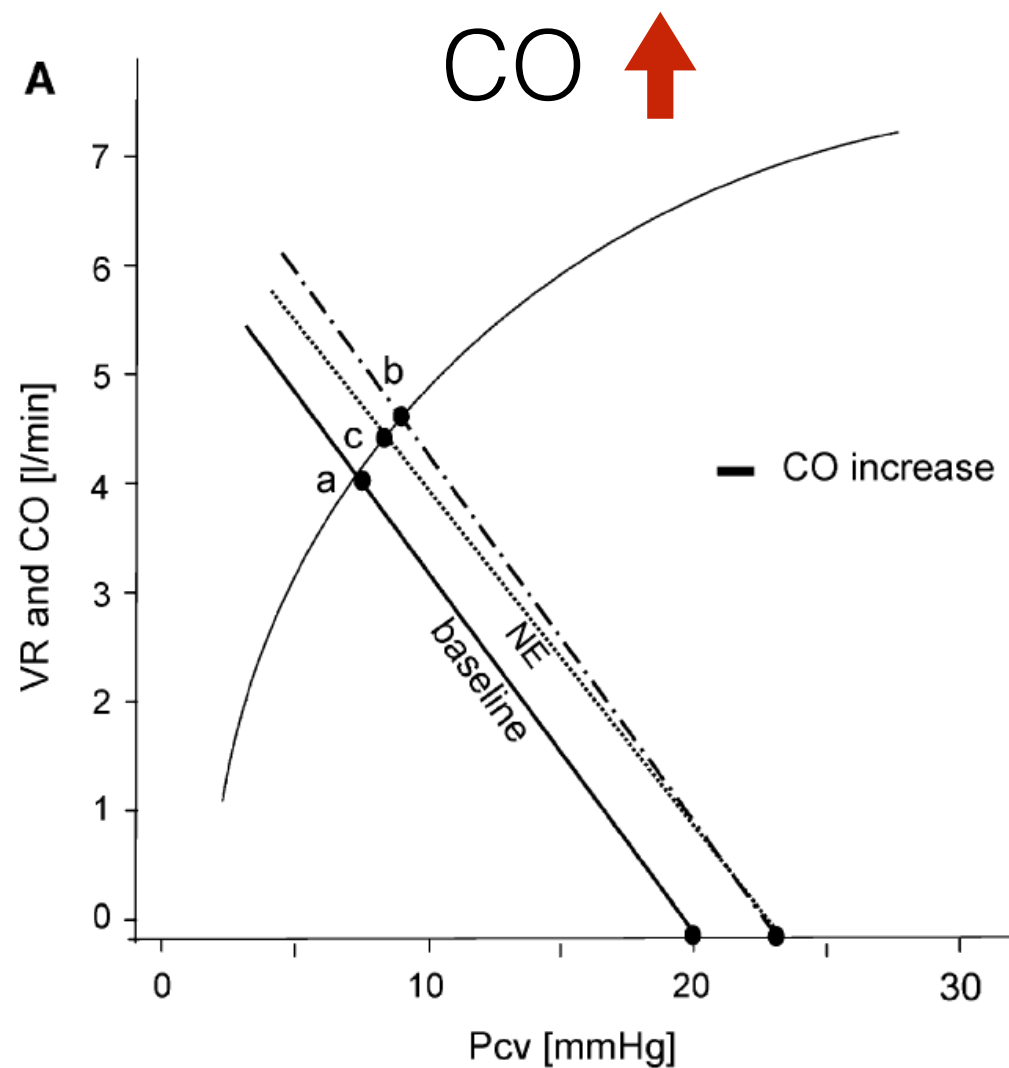
Catecholamine-induced Changes in the Splanchnic Circulation Affecting Systemic Hemodynamics

Simon Gelman, M.D., Ph.D.*, Phillip S. Mushlin, M.D., Ph.D.†



Cardiac Output Response to Norepinephrine in Postoperative Cardiac Surgery Patients: Interpretation With Venous Return and Cardiac Function Curves*

Jacinta J. Maas, MD; Michael R. Pinsky, MD, MCCM; Rob B. de Wilde, PhD; Evert de Jonge, MD, PhD; Jos R. Jansen, MS, PhD



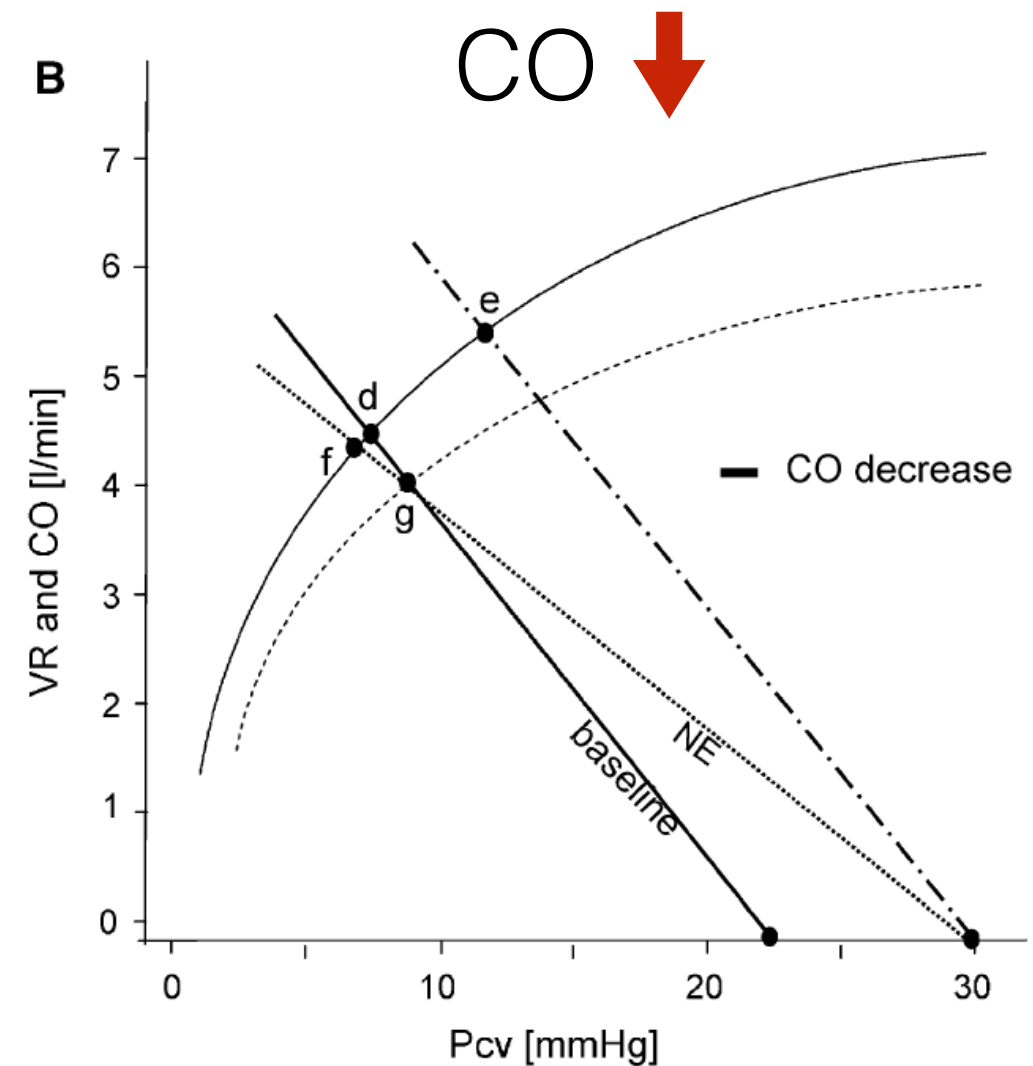
$$R_v = \frac{(P_{sm} - P_{od})}{R_{rv}}$$

Cardiac Output Response to Norepinephrine in Postoperative Cardiac Surgery Patients: Interpretation With Venous Return and Cardiac Function Curves*

Jacinta J. Maas, MD; Michael R. Pinsky, MD, MCCM; Rob B. de Wilde, PhD; Evert de Jonge, MD, PhD; Jos R. Jansen, MS, PhD

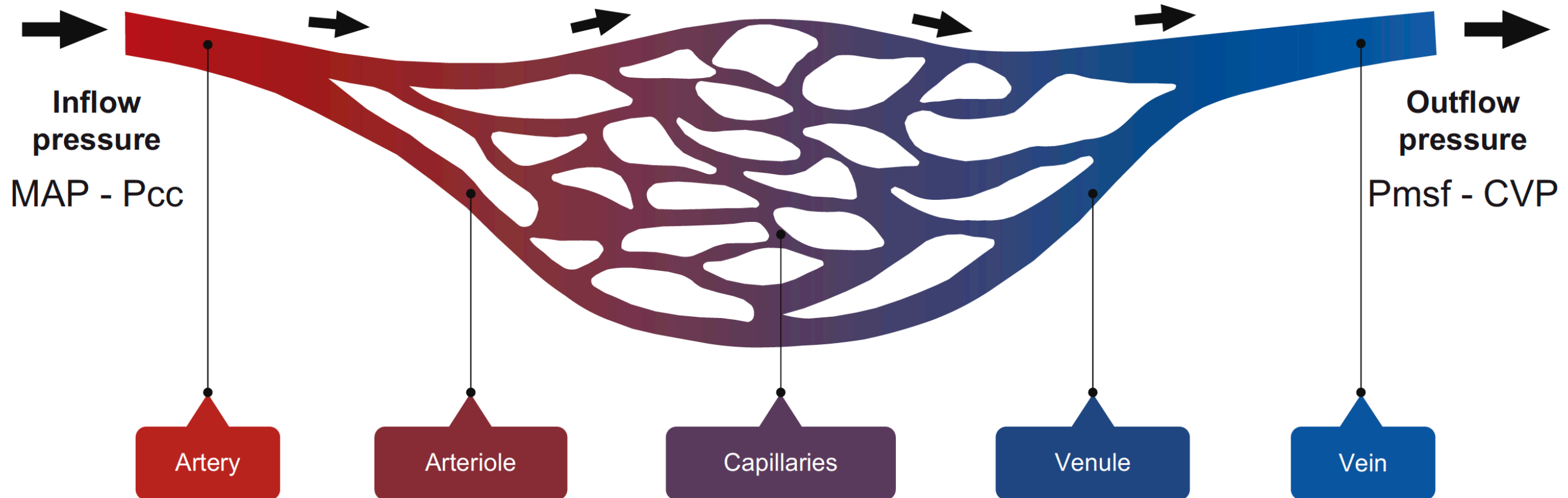
$$R_v = \frac{(P_{sm} - P_{OD})}{R_{rv}}$$

Diagram illustrating the formula for Venous Return (R_v). A red downward arrow is positioned above R_v , and a red upward arrow is positioned above the numerator $(P_{sm} - P_{OD})$. A red upward arrow is positioned below the denominator R_{rv} .



$$\begin{array}{ccccccc} \text{PAM} & = & (& \text{CO} & \times & \text{SVR} &) & + & \text{CVP} \\ \text{Blood Pressure} & & & \text{(Cardiac Output)} & & \text{(Vascular resistance)} & & & \text{(Central Venous Pressure)} \end{array}$$

Tissue Perfusion



Mean perfusion pressure (MPP)
 $MPP = MAP - CVP$

Perfusion pressure for different organs

Organs	Inflow pressure	Outflow pressure (whichever is higher)	Perfusion pressure
Brain	MAP	CVP or intracranial pressure (ICP)	MAP-CVP or ICP
Heart	Diastolic BP	CVP or intrathoracic pressure (ITP)	Diastolic BP-CVP or ITP
Kidney	MAP	CVP or intraabdominal pressure (IAP)	MAP-CVP or IAP
Bowel	MAP	CVP or intraabdominal pressure (IAP)	MAP-CVP or IAP

Relationship between Intraoperative Mean Arterial Pressure and Clinical Outcomes after Noncardiac Surgery

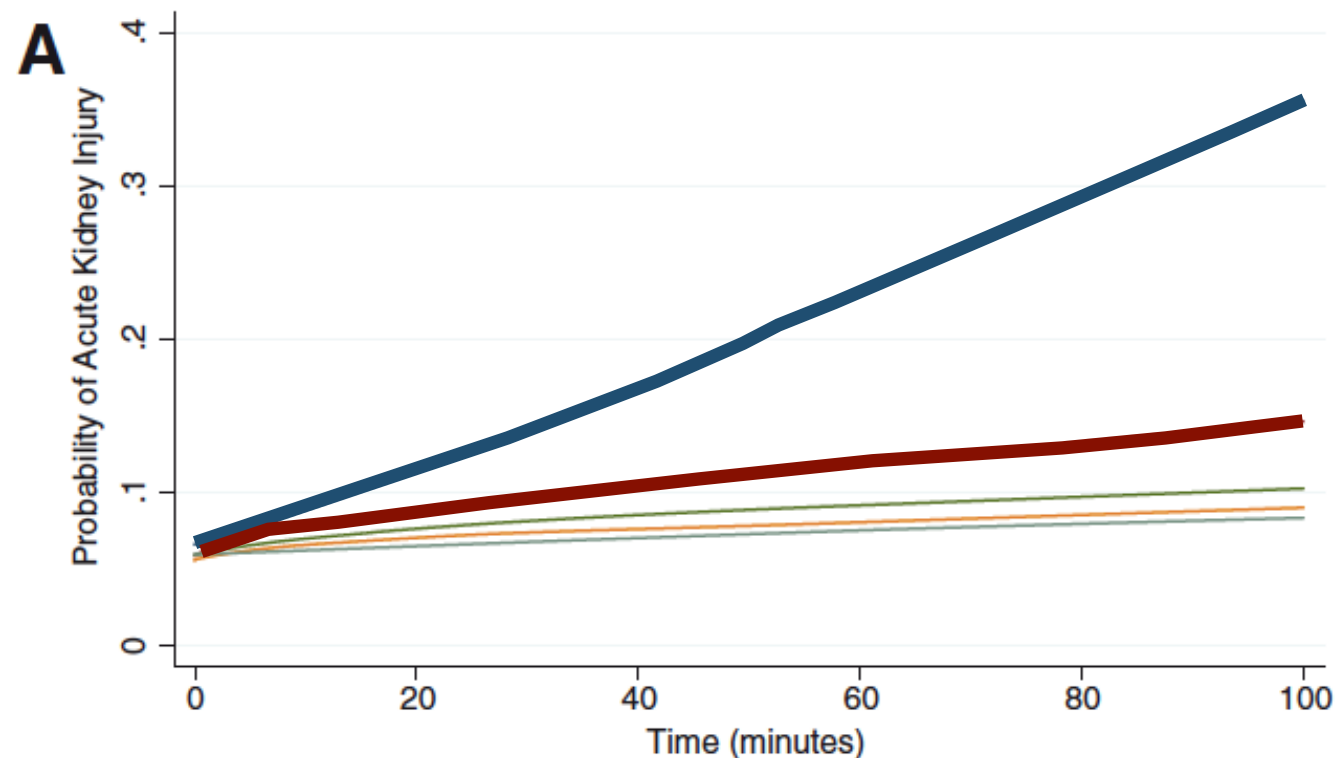
Toward an Empirical Definition of Hypotension

Michael Walsh, M.D.,* Philip J. Devereaux, M.D., Ph.D.,† Amit X. Garg, M.D., Ph.D.,‡ Andrea Kurz, M.D.,§ Alparslan Turan, M.D., || Reitze N. Rodseth, M.D.,# Jacek Cywinski, M.D.,** Lehana Thabane, Ph.D.,†† Daniel I. Sessler, M.D.‡‡

Data from 33,330 patients who underwent non-cardiac surgery (Cleveland, Ohio)

AKI

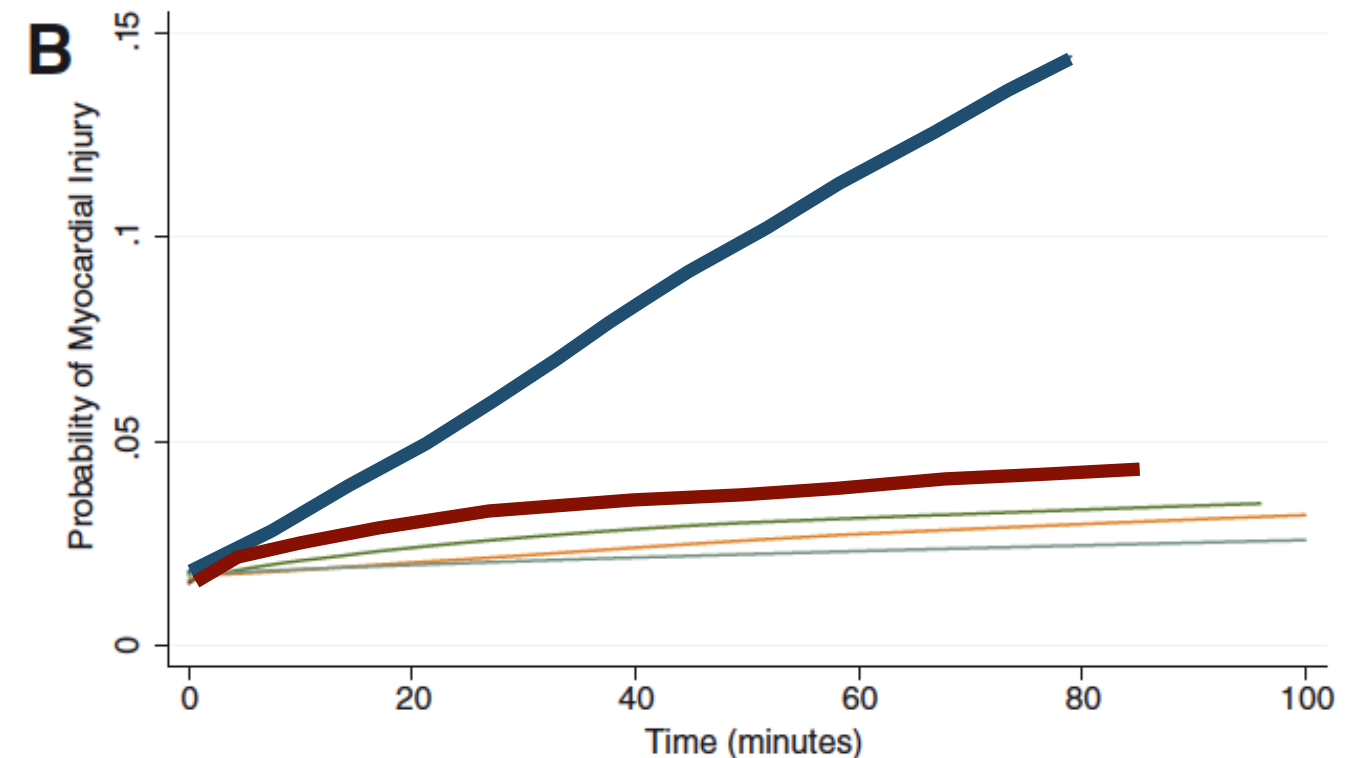
(serum creatinine >1.5-fold or 0.3 mg/dl from baseline)



— MAP < 55 mmHg — MAP 55 to 59 mmHg — MAP 60 to 64 mmHg
— MAP 65 to 69 mmHg — MAP 70 to 74 mmHg

Myocardial injury

(serum troponin T ≥ 0.04 $\mu\text{g/l}$)

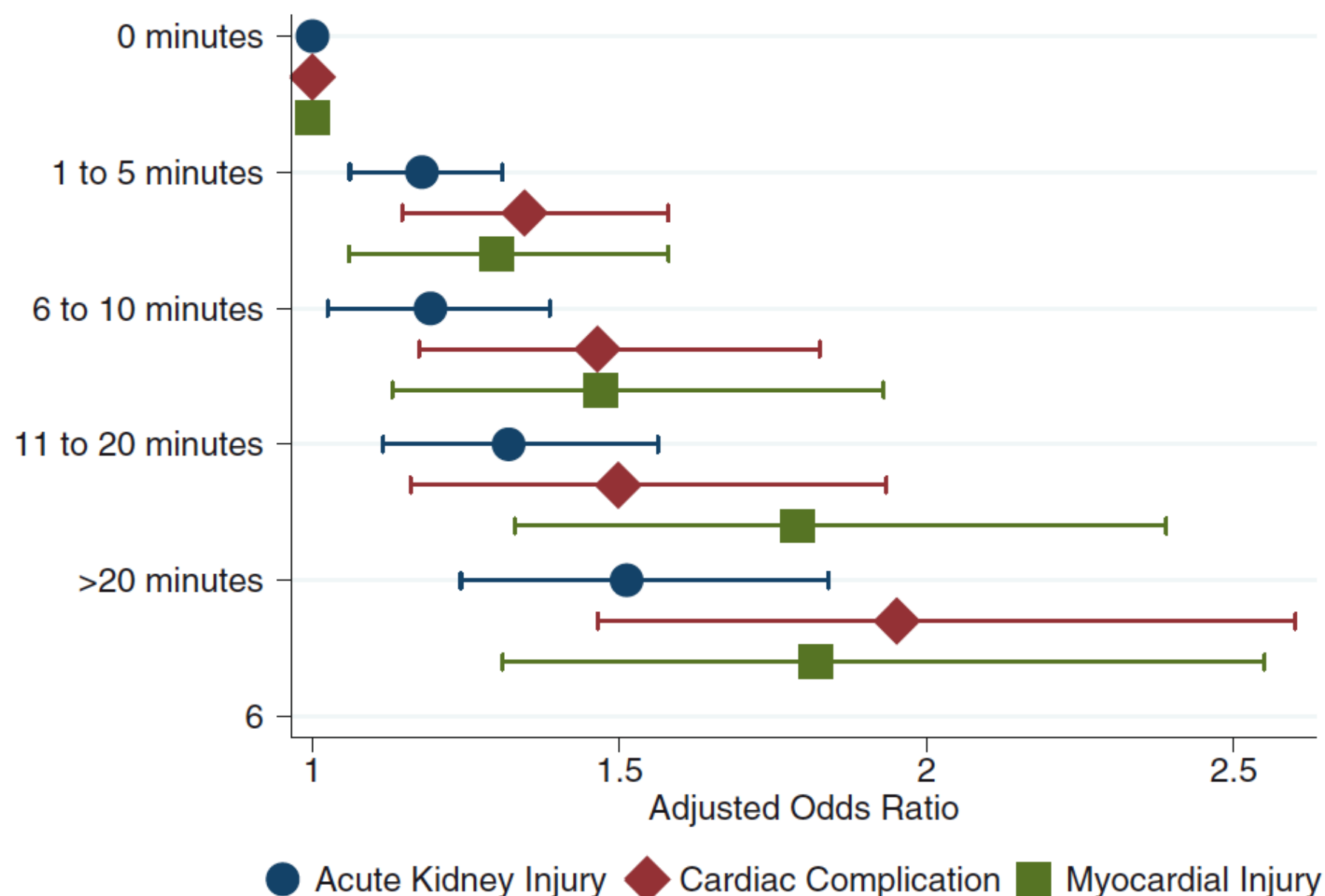


Relationship between Intraoperative Mean Arterial Pressure and Clinical Outcomes after Noncardiac Surgery

Toward an Empirical Definition of Hypotension

Michael Walsh, M.D.,* Philip J. Devereaux, M.D., Ph.D.,† Amit X. Garg, M.D., Ph.D.,‡ Andrea Kurz, M.D.,§ Alparslan Turan, M.D., || Reitze N. Rodseth, M.D.,# Jacek Cywinski, M.D.,** Lehana Thabane, Ph.D.,†† Daniel I. Sessler, M.D.‡‡

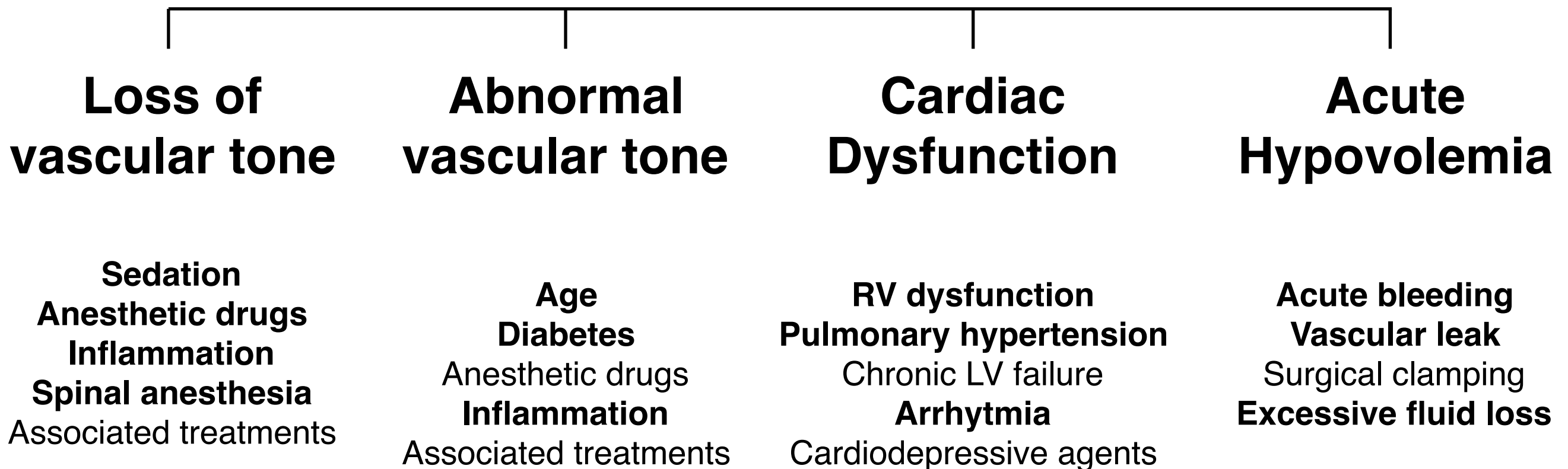
Data from 33,330 patients who underwent non-cardiac surgery (Cleveland, Ohio)



Arterial Hypotension: different mechanisms

$$\text{MAP} = \left(\begin{array}{c} \text{CO} \\ \text{Cardiac output} \end{array} \times \begin{array}{c} \text{SVR} \\ \text{Vascular resistance} \end{array} \right) + \text{CVP}$$

Decrease in SVR and/or CO



Arterial Hypotension: different treatments

$$\text{MAP} = \left(\begin{array}{c} \text{CO} \\ \text{Cardiac output} \end{array} \times \begin{array}{c} \text{SVR} \\ \text{Vascular resistance} \end{array} \right) + \text{CVP}$$



AND/OR



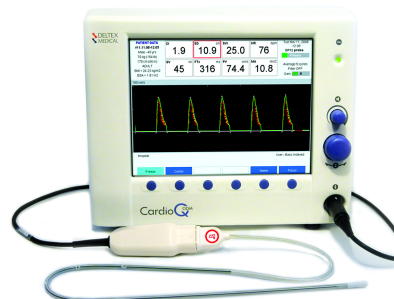
AND/OR



IV or inhaled

Fluid challenge

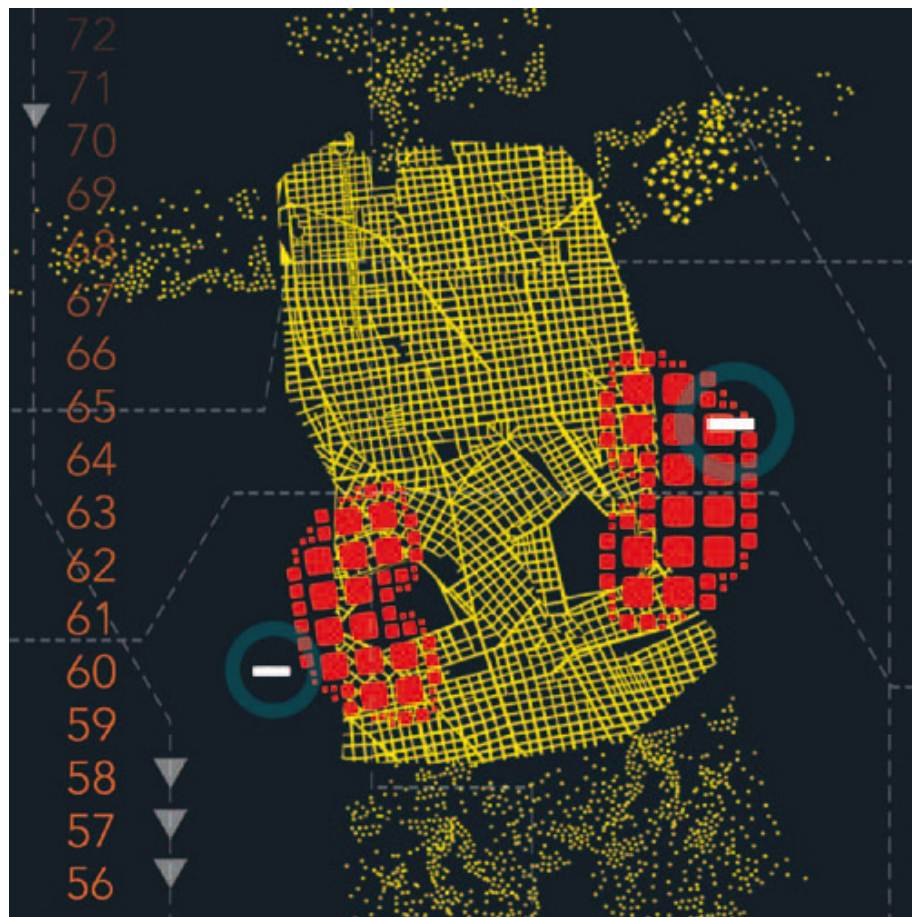
Vasoactive drug



Intraoperative Hypotension and Patient Outcome

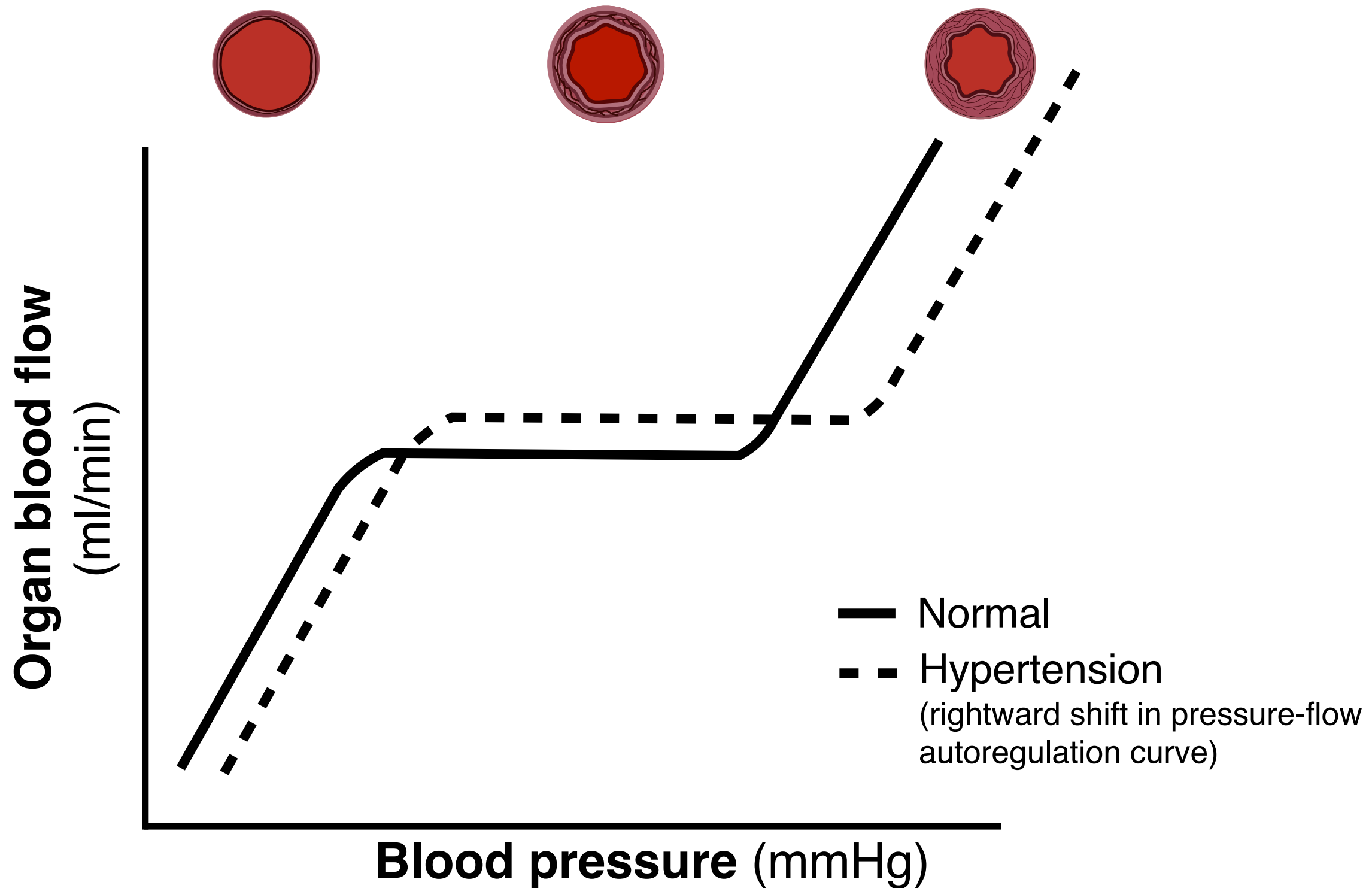
Does “One Size Fit All?”

Kenneth Brady, M.D.,* Charles W. Hogue, M.D.†

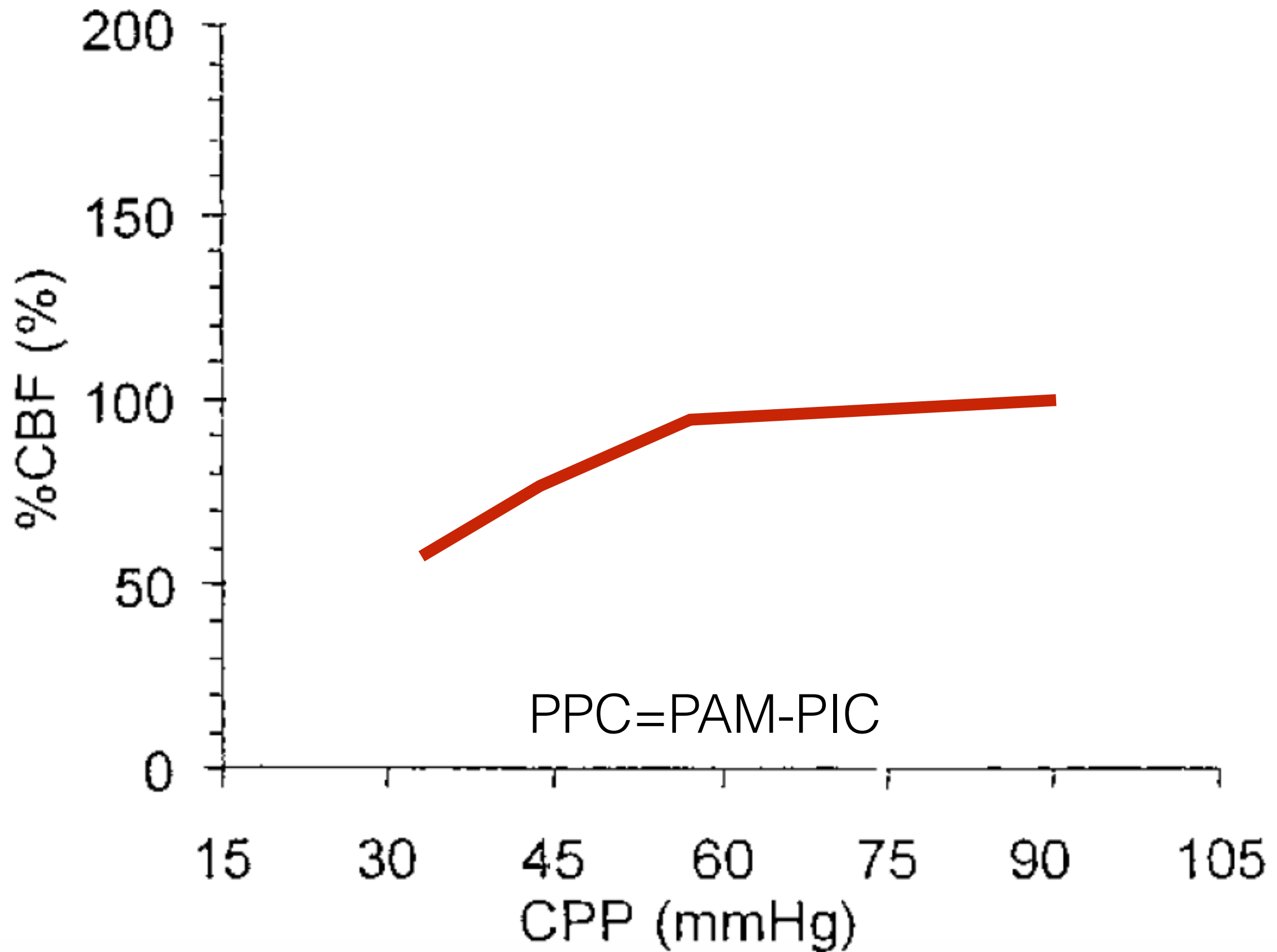


“... we believe that the combined data suggest that a single blood pressure target derived from group summary data cannot be extrapolated to be optimal for all patients, or, ‘one size does not fit all.’”

Organ Pressure-Flow Autoregulation



Organs may be more susceptible to ischemia at low BP in patients with preexisting hypertension



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

IMPORTANCE Perioperative hypotension is associated with an increase in postoperative morbidity and mortality, but the appropriate management strategy remains uncertain.

OBJECTIVE To evaluate whether an individualized blood pressure management strategy tailored to individual patient physiology could reduce postoperative organ dysfunction.

DESIGN, SETTING, AND PARTICIPANTS The Intraoperative Norepinephrine to Control Arterial Pressure (INPRESS) study was a multicenter, randomized, parallel-group clinical trial conducted in 9 French university and nonuniversity hospitals. Adult patients (n = 298) at increased risk of postoperative complications with a preoperative acute kidney injury risk index of class III or higher (indicating moderate to high risk of postoperative kidney injury) undergoing major surgery lasting 2 hours or longer under general anesthesia were enrolled from December 4, 2012, through August 28, 2016 (last follow-up, September 28, 2016).

INTERVENTIONS Individualized management strategy aimed at achieving a systolic blood pressure (SBP) within 10% of the reference value (ie, patient's resting SBP) or standard management strategy of treating SBP less than 80 mm Hg or lower than 40% from the reference value during and for 4 hours following surgery.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of systemic inflammatory response syndrome and dysfunction of at least 1 organ system of the renal, respiratory, cardiovascular, coagulation, and neurologic systems by day 7 after surgery. Secondary outcomes included the individual components of the primary outcome, durations of ICU and hospital stay, adverse events, and all-cause mortality at 30 days after surgery.

RESULTS Among 298 patients who were randomized, 292 patients completed the trial (mean [SD] age, 70 [7] years; 44 [15.1%] women) and were included in the modified intention-to-treat analysis. The primary outcome event occurred in 56 of 147 patients (38.1%) assigned to the individualized treatment strategy vs 75 of 145 patients (51.7%) assigned to the standard treatment strategy (relative risk, 0.73; 95% CI, 0.56 to 0.94; $P = .02$; absolute risk difference, -14%, 95% CI, -25% to -2%). Sixty-eight patients (46.3%) in the individualized treatment group and 92 (63.4%) in the standard treatment group had postoperative organ dysfunction by day 30 (adjusted hazard ratio, 0.66; 95% CI, 0.52 to 0.84; $P = .001$). There were no significant between-group differences in severe adverse events or 30-day mortality.

CONCLUSIONS AND RELEVANCE Among patients predominantly undergoing abdominal surgery who were at increased postoperative risk, management targeting an individualized systolic blood pressure, compared with standard management, reduced the risk of postoperative organ dysfunction.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01536470

JAMA. doi:10.1001/jama.2017.14172
Published online September 27, 2017.

← Editorial

+ Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The INPRESS Study Group investigators are listed at the end of this article.

Corresponding Author: Emmanuel Futier, MD, PhD, Département de Médecine Périopératoire, Anesthésie Réanimation, Hôpital Estaing, 1 place Lucie Aubrac, 63003 Clermont-Ferrand, France (efutier@chu-clermontferrand.fr).

Section Editor: Derek C. Angus, MD, MPH, Associate Editor, JAMA (angusdc@upmc.edu).



INPRESS study

- **Individualized treatment strategy**
Continuous IV norepinephrine to maintain SBP within $\pm 10\%$ of the reference value
- **Standard treatment strategy**
IV ephedrine administered for any drop in SBP below 80 mm Hg or lower than 40% from the reference value

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

INPRESS study

- Prospective multicenter randomized clinical trial
- N=298 patients at increased risk of postoperative complications undergoing major abdominal surgery
- Individualized vs standard BP treatment strategy
- Primary endpoint: composite of SIRS and organ dysfunction by day 7 after surgery

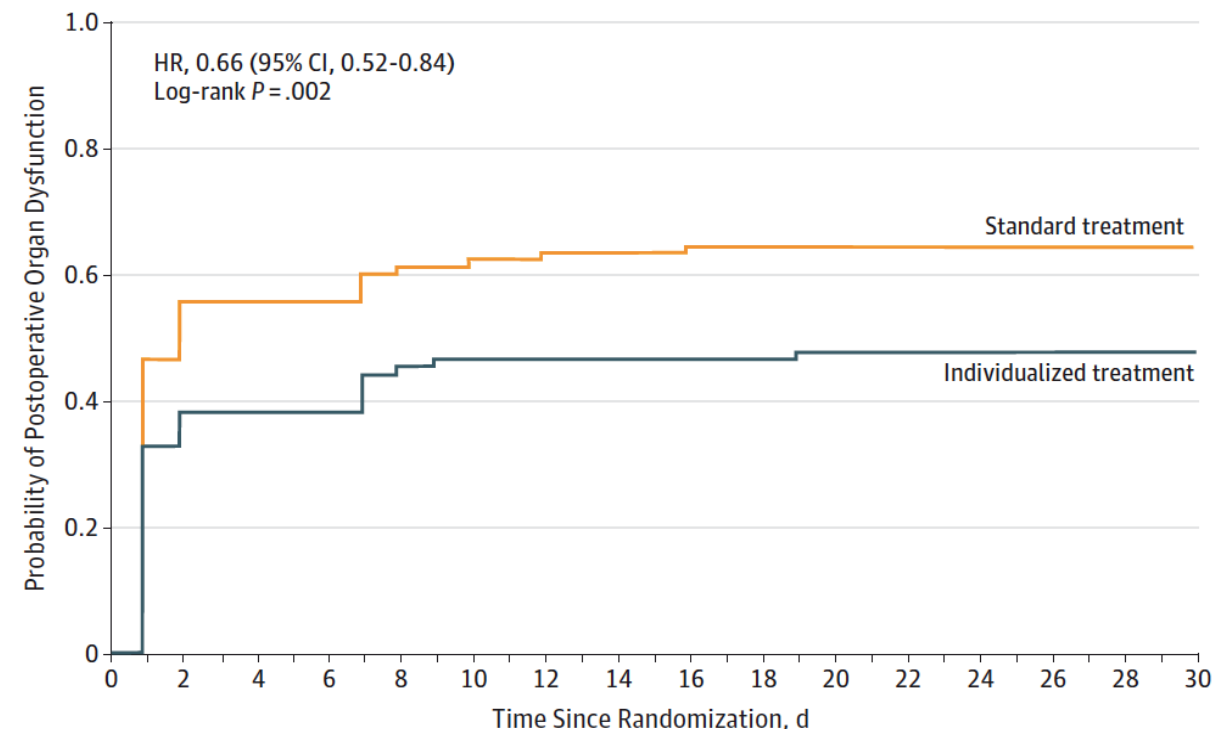


Table 3. Primary and Secondary Outcomes and Adverse Events

Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	Between-Group Absolute Difference, % (95% CI)	Unadjusted Relative Risk (95% CI)	P Value	Adjusted Relative Risk (95% CI) ^a	P Value
Primary Outcome							
Primary composite outcome, No. (%) ^b	56 (38.1)	75 (51.7)	−14 (−25 to −2)	0.74 (0.57 to 0.95)	.02	0.73 (0.56 to 0.94)	.02
Secondary Outcomes							
Complications within 7 d							
Acute kidney injury according to RIFLE criteria, No. (%) ^d							
Risk	23 (15.7)	36 (24.8)	−9 (−18 to 0)	0.63 (0.39 to 1.00)	.05	0.73 (0.47 to 1.14)	.17
Injury	16 (10.9)	26 (17.9)	−7 (−15 to 1)	0.61 (0.34 to 1.08)	.09	0.61 (0.34 to 1.08)	.09
Failure	9 (6.1)	9 (6.2)	0 (−6 to 5)	0.99 (0.40 to 2.41)	.98	0.97 (0.40 to 2.34)	.95
Use of renal replacement therapy, No. (%)	4 (2.7)	5 (3.5)	0 (−5 to 3)	0.79 (0.22 to 2.88)	.72	0.81 (0.22 to 2.97)	.76

Renal dysfunction (RIFLE stage of Risk or higher):
48 patients (32.7%) in the individualized treatment group and 71 patients (49.0%) in the standard treatment group (absolute risk difference, −16%; 95% CI, −27% to −5%; adjusted relative risk, 0.70; 95% CI, 0.53 to 0.92; P = .01).

Table 2. Clinical Management of Patients During the Intervention Period, Including During Surgery and for 4 Hours Following Surgery^a

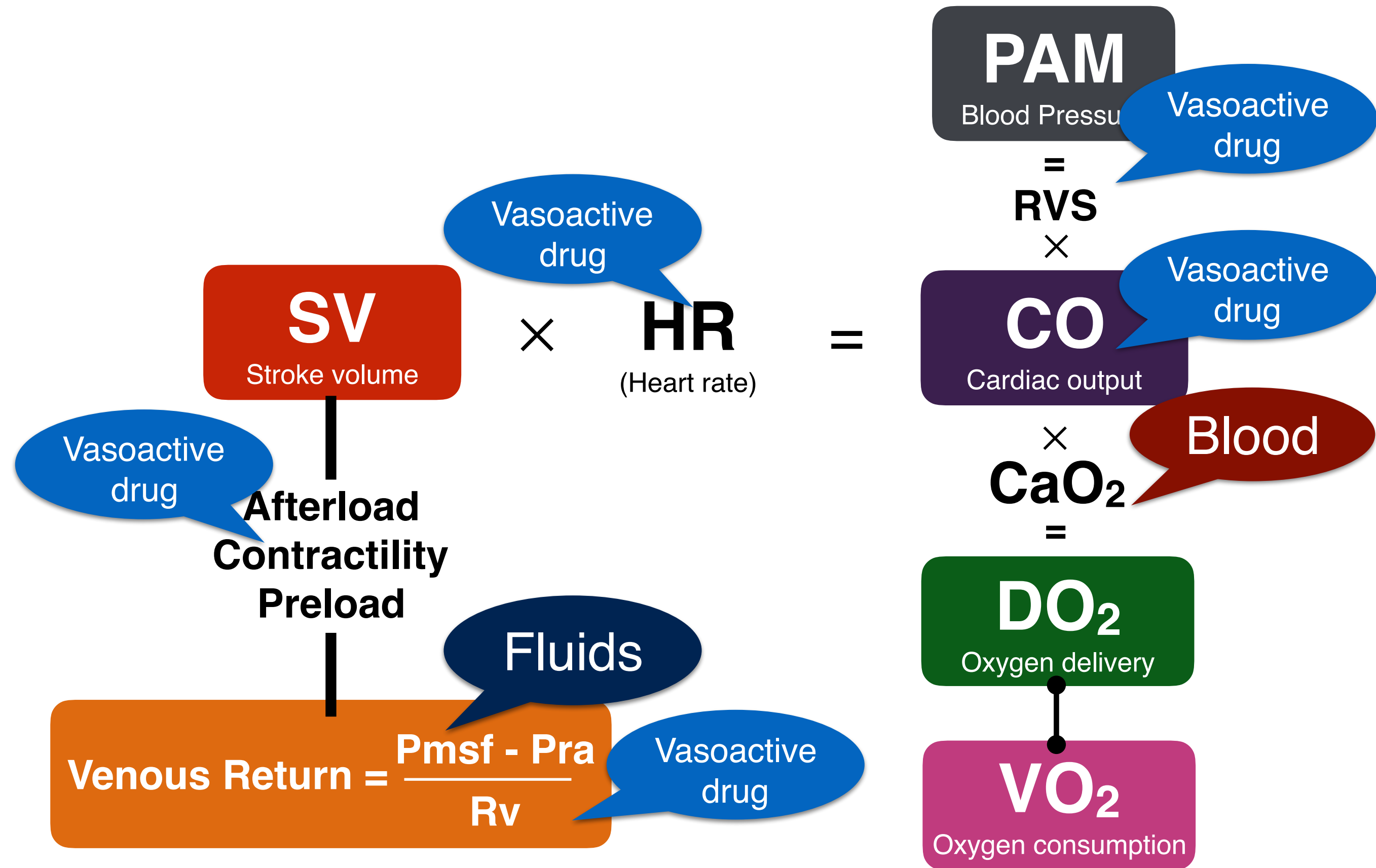
Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	P Value
Cumulative volume of crystalloid, median (IQR), mL	2275 (1600-3000)	2500 (1825-3225)	.09
During surgery	1500 (1000-2000)	2000 (1500-2500)	<.001
During 4 h following surgery	750 (500-1000)	600 (500-1000)	.54
Cumulative volume of colloid, median (IQR), mL	1000 (500-1500)	1000 (500-1750)	.25
During surgery	875 (500-1500)	1000 (500-1500)	.12
During 4 h following surgery	500 (300-500)	500 (400-1500)	.43
Use of blood products			
Patients, No. (%)	39 (26.5)	34 (23.4)	.54
No. of units/patient, mean (SD)	2.5 (1.4)	2.8 (1.7)	.28

Additional fluids (6% 130/0.4 HES) using a protocolized hemodynamic algorithm

Conclusion

Hemodynamic Optimization in High-Risk Surgical Patients

A multimodal Treatment Strategy

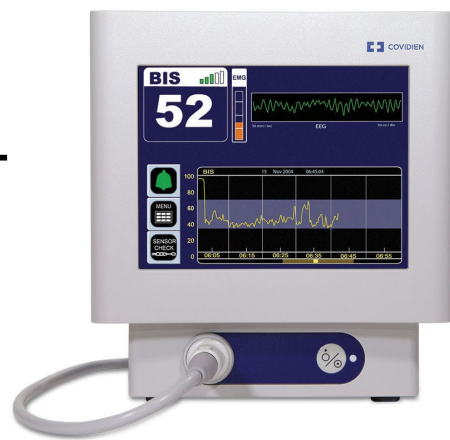


Monitorage Hémodynamique Multimodal



PAM
FC

+



BIS
Entropie

+



SpO₂

+



Hb

+



DC
VES
ScvO₂

Stratégie de monitoring en fonction du niveau de risque

		Risque lié à la chirurgie		
		Faible	Modéré	Élevé
Risque lié au patient	Faible	Rien	VES/DC • Non-invasif Clearsight, CNAP Doppler oesophagien • Semi-invasif Vigileo, Pulsioflex, Most-Care	VES/DC • Non-invasif Doppler oesophagien • Semi-invasif Vigileo, Pulsioflex, Most-Care
	Modéré	VES/DC • Non-invasif Clearsight, CNAP Doppler oesophagien • Semi-invasif Vigileo, Pulsioflex, Most-Care	VES/DC • Non-invasif Doppler oesophagien • Semi-invasif Pulse contour Vigileo, Pulsioflex, Most-Care	VES/DC, PVC • Non-invasif Doppler oesophagien • Semi-invasif Pulse contour Vigileo, Pulsioflex, Most-Care
	Élevé	VES/DC • Semi-invasif Vigileo, Pulsioflex, Most-Care	VES/DC, PVC, ScvO₂ • Semi-invasif Vigileo, Pulsioflex, Most-Care) • Invasif Thermodilution Transpulmonaire (VolumeView, Picco2)	VES/DC, PVC, SvO₂/ScvO₂ • Invasif Thermodilution - Transpulmonaire (VolumeView, Picco2) - Pulmonaire (Swan Ganz)

FIN

Merci pour votre attention