UNIVERSITEIT GENT

FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

Goal Directed Perfusion:
basic concepts and some examples

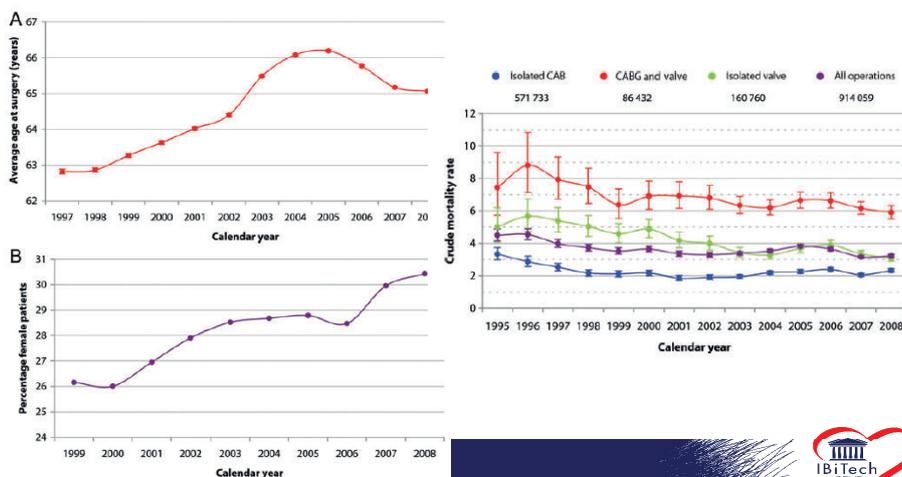Filip De Somer, Ph.D.

University Hospital Ghent

Belgium

ORIGINAL ARTICLE

The European Association for Cardio-Thoracic Surgery (EACTS) database: an introduction

Stuart J. Head[a], Neil J. Howell[b], Ruben L.J. Osnabrugge[a], Ben Bridgewater[c], Bruce E. Keogh[d], Robin Kinsman[e], Peter Walton[e], Jan F. Gummert[f], Domenico Pagano[b] and A. Pieter Kappetein[a,*]

Acute risk change for cardiothoracic admissions to intensive care: A new measure of quality in cardiac surgery

Tim G. Coulson, BM, BSc,[a,c] Michael Bailey, PhD, MSc,[b] Christopher M. Reid, PhD,[c] Lavinia Tran, PhD, BBiomedsci,[c] Daniel V. Mullany, MBBS, MMedSc, FCICM, FANZCA,[d] Julian A. Smith, MS, FRACS,[e] and David Pilcher, MBBS, MRCP, FRACP, FCICM[a,c,f]

Background: Quality of cardiac surgical care may vary between institutions. Mortality is low and large numbers are required to discriminate between hospitals. Measures other than mortality may provide better comparisons.

Objectives: To develop and assess the Acute Risk Change for Cardiothoracic Admissions to Intensive Care (ARCTIC) index, a new performance measure for cardiothoracic admissions to intensive care units (ICUs).

Methods: The Australian and New Zealand Society of Cardiac and Thoracic Surgeons database and Australian and New Zealand Intensive Care Society Adult Patient Database were linked. Logistic regression was used to generate a predicted risk of death first from preoperative data using the previously validated Allprocscore and second on admission to an ICU using Acute Physiology and Chronic Health Evaluation III score. Change in risk as a percentage (ARCTIC) was calculated for each patient. The validity of ARCTIC as a marker of quality was assessed by comparison with intraoperative variables and postoperative morbidity markers.

Results: Sixteen thousand six hundred eighty-seven patients at 21 hospitals from 2008 to 2011 were matched. An increase in ARCTIC score was associated with prolonged cardiopulmonary bypass time ($P = .001$), intraoperative blood product transfusion ($P < .001$), reoperation ($P < .001$), postoperative renal failure ($P < .0001$), prolonged ventilation ($P < .0001$), and stroke ($P = .001$).

Conclusions: The ARCTIC index is associated with known markers of perioperative performance and postoperative morbidity. It may be used as an overall marker of quality for cardiac surgery. Further work is required to assess ARCTIC as a method to discriminate between cardiac surgical units. (J Thorac Cardiovasc Surg 2014;■:1-6)
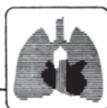

How do we know that blood flow meet the metabolic needs of a patient?

By retrospective analysis of organ function, blood markers and morbidity

"What we need is a multivariate online analysis of risk during cardiopulmonary bypass" *Charles Wildevuur*

Which parameters?

accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:
Roger C. Bone, M.D., F.C.C.P., Chairman
Robert A. Balk, M.D., F.C.C.P.
Frank B. Cerra, M.D.
R. Phillip Dellinger, M.D., F.C.C.P.

Alan M. Fein, M.D., F.C.C.P.
William A. Knaus, M.D.
Roland M. H. Schein, M.D.
William J. Sibbald, M.D., F.C.C.P.

- Body temperature: >38°C or <36°C
- Heart rate: >90 min^{-1}
- Hyperventilation: RR >20 min^{-1} or $PaCO_2$ <32mmHg
- WBC: >12000 μL^{-1} or <4000 μL^{-1}

PIRO concept

|	
Predisposition: Premorbid illness with reduced probability of short term survival. Cultural or religious beliefs, age, gender.	Age, gender, EF, eGFR, diabetes, REDO
Insult: Culture and sensitivity (infection) or infection pathogens; detection of disease amenable to source control.	Surgery, transfusion, hemodynamics, ischemia, emboli
Response: SIRS, other signs of sepsis, shock, CRP.	↗ Creatinine, ↘ diuresis, delirium, ↗ bilirubin, ↘ PaO2
Organ: Organ dysfunction as number dysfunction of failing organs or composite score (e.g. MODS, SOFA, RIFLE).	AKI, stroke, MCS, RRT, ECMO

Cardiopulmonary bypass related injury

| Perioperative:	No AKI	AKI			
CABG	2,080 (70.9)	1,228 (64.7)	Ref		
Valve	488 (16.6)	286 (15.1)	1.18	(0.98–1.41)	0.080
CABG/valve	364 (12.4)	385 (20.4)	2.31	(1.92–2.76)	<0.001
Off-pump surgery	210 (7.2)	76 (4.0)	0.43	(0.32–0.58)	<0.001
Number of valves, mean ± SD	0.32 ± 0.52	0.39 ± 0.56	1.53	(1.36–1.73)	<0.001
Number of anastomoses, mean ± SD	2.74 ± 1.67	2.86 ± 1.66	1.02	(0.98–1.06)	0.433
Pump time (minutes), mean ± SD	110 ± 54	124 ± 55	1.01	(1.01–1.01)	<0.001
Pump time >120 (minutes)	1,093 (37.3)	879 (46.3)	2.07	(1.81–2.36)	<0.001
Cross-clamp time (minutes), mean ± SD	69.7 ± 40.3	77.4 ± 38.6	1.01	(1.01–1.01)	<0.001
Cardioplegia time (minutes), mean ± SD	20.1 ± 7.6	20.7 ± 6.6	1.02	(1.01–1.03)	<0.001
Blood cardioplegia	2,439 (83.2)	1,644 (86.6)	1.22	(1.01–1.46)	0.038
Cold cardioplegia	1,482 (50.6)	802 (42.2)	0.88	(0.77–1.01)	0.068
Cardioplegia hot shot	2,558 (87.2)	1,692 (89.1)	1.11	(0.90–1.36)	0.333
Retrograde autologous priming (RAP)	1,722 (58.7)	1,140 (60.0)	0.85	(0.75–0.98)	0.023
Volume of fluids on bypass (mL), mean ± SD	1,925 ± 2,151	2,213 ± 2,494	1.00	(1.00–1.00)	<0.001
Prime volume (mL), mean ± SD	1,150 ± 535	1,190 ± 559	1.00	(1.00–1.00)	<0.001
Blood prime units, mean ± SD	0.09 ± 0.46	0.20 ± 0.65	1.56	(1.36–1.79)	<0.001
Number of pRBCs units, mean ± SD	0.51 ± 1.24	0.87 ± 1.76	1.33	(1.26–1.40)	<0.001
Highest blood temperature, mean ± SD	37.5 ± 0.41	37.5 ± 0.70	1.00	(0.92–1.09)	0.911
Lowest venous saturation, mean ± SD	69.87 ± 6.27	69.82 ± 6.35	1.00	(0.99–1.01)	0.549
Total volume of heparin > 50,000 units	1,031 (35.2)	700 (36.9)	0.97	(0.84–1.11)	0.619
Last potassium on bypass, mean ± SD	5.58 ± 3.32	5.58 ± 3.54	1.00	(0.98–1.01)	0.795
Nadir hematocrit on bypass, mean ± SD	23.24 ± 3.29	22.56 ± 3.39	0.91	(0.90–.93)	<0.001
Nadir hematocrit < 20 on bypass	332 (11.3)	320 (16.9)	1.62	(1.34–1.97)	<0.001
Ultrafiltration (hemoconcentration on bypass)	136 (4.6)	139 (7.3)	1.74	(1.31–2.30)	<0.001
Return to bypass	219 (7.5)	204 (10.7)	1.61	(1.28–2.03)	<0.001
Aprotinin use	1,157 (39.5)	936 (49.4)	2.08	(1.82–2.37)	<0.001

Brown 2012

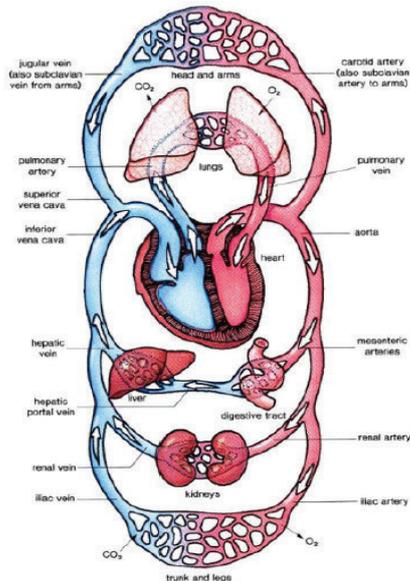# CardioRenal interrelationship in heart failure
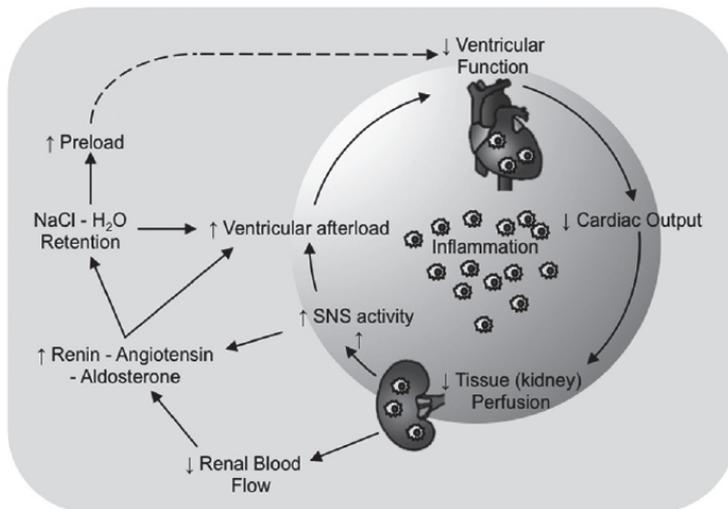
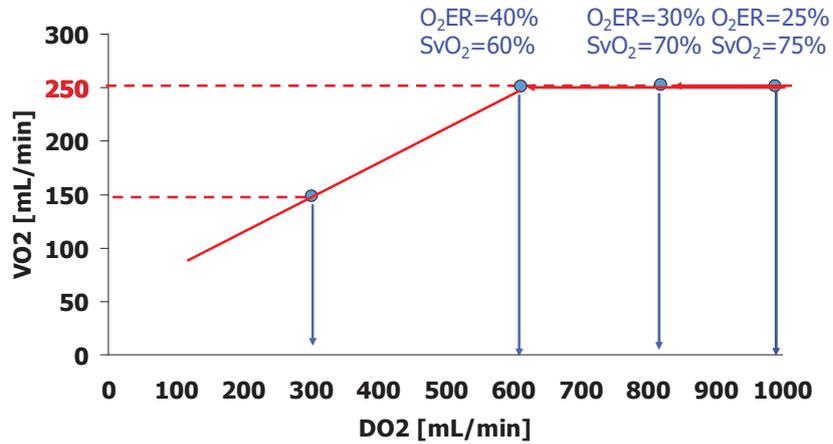Boudoulas 2017

Causes
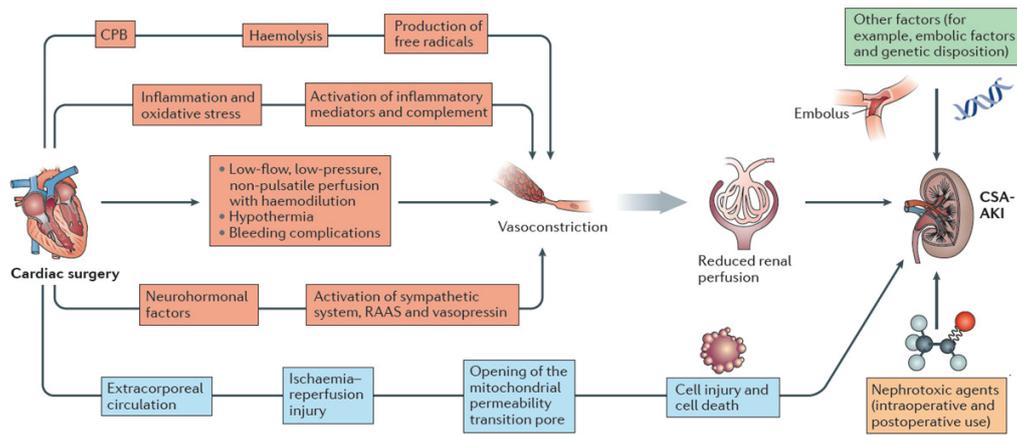
Wang 2017

- Changes based on metabolic needs
- Usually in the range of 2.8 to 3.0 L/min/mq
- May increase up to 15 L/min/m²
- CO with arterial oxygen content, determines the oxygen delivery (DO2)
- Guaranty oxygen need (VO2)
- Pulsatile flow

- Hematocrit: 40 – 50%
- Normal cardiac function
- Normal vascular volume

Darling 1999

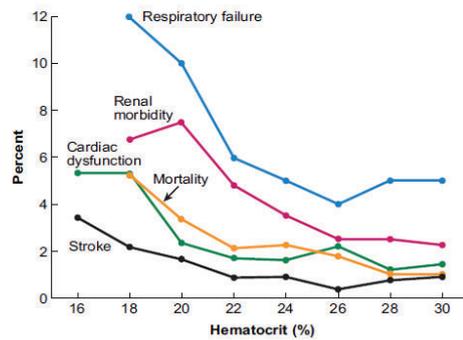# DO$_2$ and VO$_2$

Intraoperative anemia

Hematocrit on Cardiopulmonary Bypass and Outcome After Coronary Surgery in Nontransfused Patients

Marco Ranucci, MD, Daniela Conti, MD, Serenella Castelvecchio, MD, Lorenzo Menicanti, MD, Alessandro Frigiola, MD, Andrea Ballotta, MD, and Gabriele Pelissero, MD

Departments of Cardiothoracic and Vascular Anesthesia and Intensive Care Unit and Cardiac Surgery, and Scientific Directorate, IRCCS Policlinico S. Donato, Milan, Italy

Background. Preoperative anemia and the lowest registered hematocrit value on cardiopulmonary bypass are recognized risk factors for morbidity and mortality after coronary operations. A low hematocrit often results in blood transfusions with all of the associated possible complications. The relative contribution of these three factors to long-term outcome is still not well established. This study aimed to identify the role of preoperative anemia and hemodilution during cardiopulmonary bypass as determinants of morbidity and mortality after coronary operations.

Methods. A consecutive series of 3,003 patients was analyzed. They had all undergone isolated coronary operations without receiving blood transfusions during their hospital stay. The preoperative hematocrit and the lowest hematocrit on cardiopulmonary bypass were analyzed in a multivariable model as predictors of major morbidity and operative mortality.

Results. After adjustment for the other explanatory variables, both the preoperative hematocrit and the low-est hematocrit on cardiopulmonary bypass were found to be independent risk factors for major morbidity, but not for operative mortality. However, low values of preoperative hematocrit were not associated with an increased morbidity, provided that the lowest hematocrit on cardiopulmonary bypass was maintained above 28%. Median values of the lowest hematocrit on cardiopulmonary bypass below 25% were associated with an increased major morbidity rate.

Conclusions. Excessive hemodilution during cardiopulmonary bypass is a risk factor for major morbidity even in the absence of blood transfusions. Techniques that aim to reduce the fall in hematocrit during cardiopulmonary bypass, including blood cardioplegia, may be useful, especially in patients with a low preoperative hematocrit.

Hemodilution and CPB
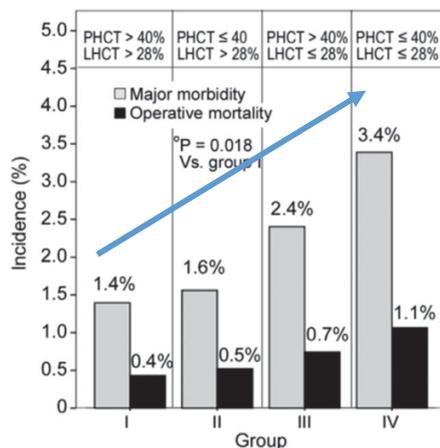
Haematocrit during CPB
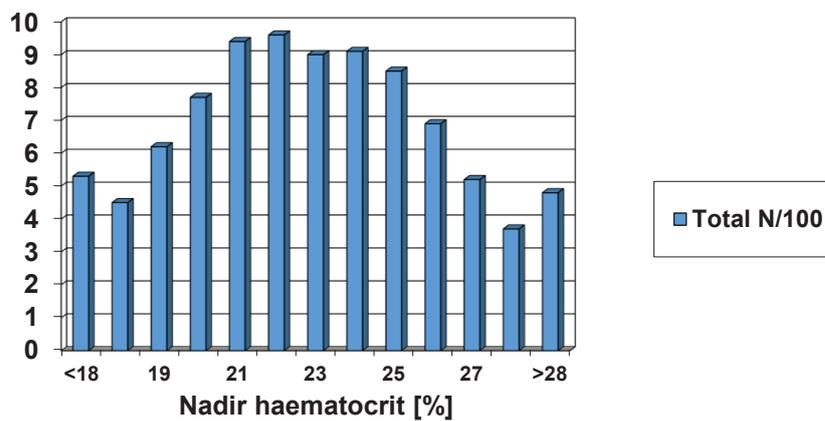
Karkouti 2005

Hematocrit during CPB

Loor 2013

Fig 2. Receiver operating characteristic curve for the three variables being identified as independent risk factors for acute renal failure. —— = lowest hematocrit on CPB; - - - - = pump flow indexed; —— = oxygen delivery indexed. (CPB = cardiopulmonary bypass; DO_2 = two determinants of oxygen delivery; HCT = hematocrit.)

Ranucci 2005

De Cuyper 2024

A Heart microvascular PO$_2$

B Kidney microvascular PO$_2$

C Intestinal microvascular PO$_2$

Ht = 8.7 ± 3.5 %

Ht = 38.5 ± 8.0 %

Ht = 17.5 ± 7.3 %

Van Bommel 2008

Microcirculation

De Backer 2007

Results –
Systemic variables

Cardiac Index
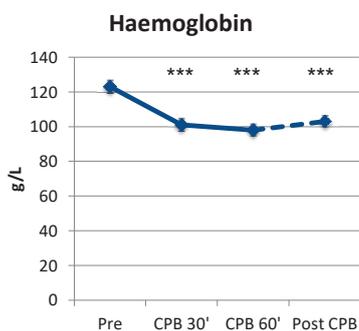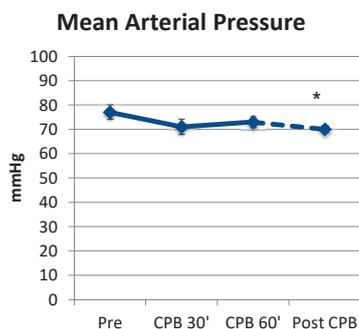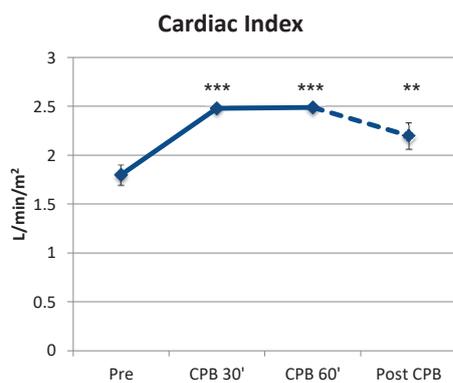
* p < 0.05, ** p < 0.01, ** p < 0.001

Lannemyr 2017

Mean Arterial Pressure

Haemoglobin

Systemic and renal oxygen delivery
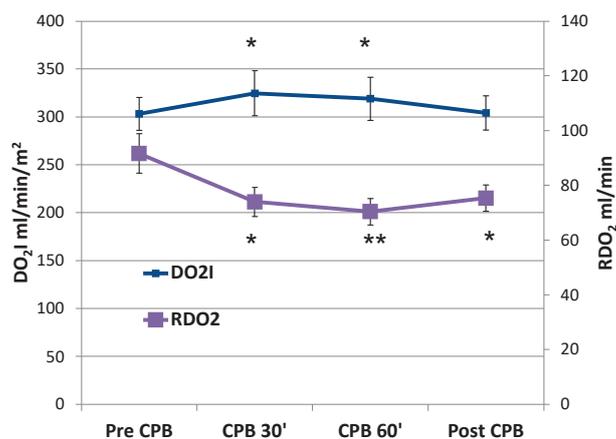
* p < 0.05, ** p < 0.01 vs Pre

Lannemyr 2017

Renal oxygen extraction
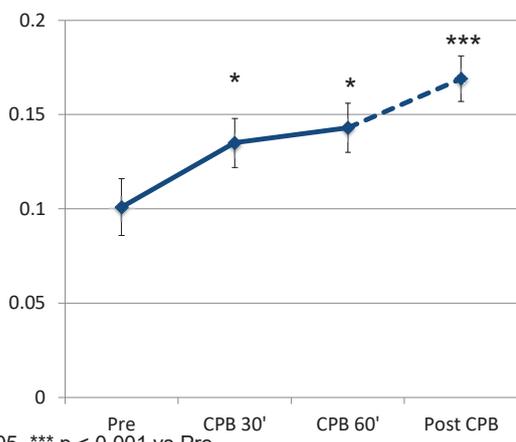
NAG - Excretion
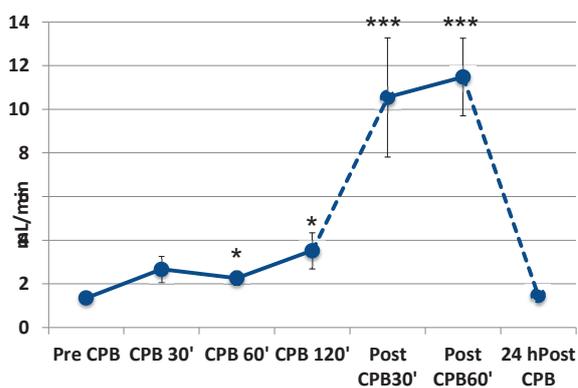
* p < 0.05, *** p < 0.001 vs Pre

Lannemyr 2017

Oxygen Pressure Field Theory: Krogh Cylinder Model

Capillary radius: $r = 5\mu$
Capillary X-section : $A = \pi r^2 = 78.5 \mu^2$

Cylinder radius: $R = 10$
Cylinder X-section: $A = \pi R^2 = 314 \mu^2$

Ratio: $\dfrac{\text{Capillary X-section}}{\text{Cylinder X-section}} = 1/4$

Highest ptO2: 79 mmHg → OPF Range: 79 ~ 1 mmHg ← Lowest ptO2: 1 mmHg

Blood Flow

$paO2 = 80$ mmHg

$pvO2 = 40$ mmHg

Avg. ptO2 = 20 mmHg

Avg. ptO2 = 10 mmHg

O2 radial vectors
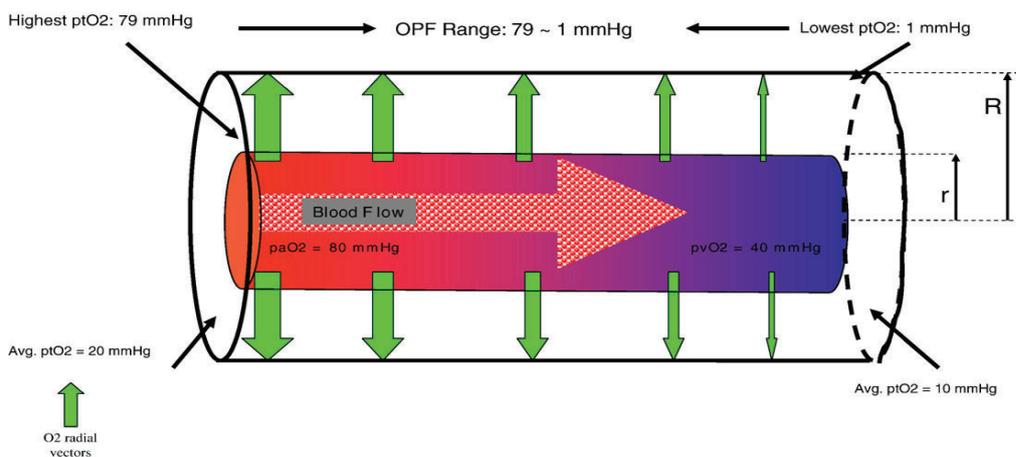
Grist 2008

Impact of velocity

Axial Vectors & Oxygenation of the Lethal Corner:
Room Air paO2 & Normal Intracapillary Blood Flow Velocity
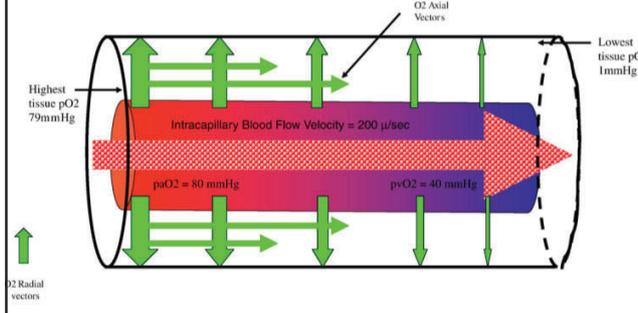
Axial Vectors & Oxygenation of the Lethal Corner:
Room Air paO2 & Slow Intracapillary Blood Flow Velocity

20% of oxygen supply venous end
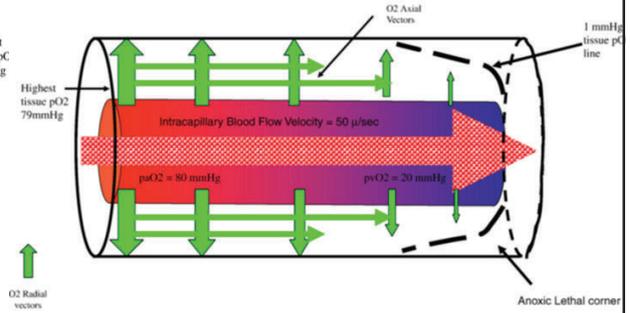
80% of oxygen supply venous end

Improve diffusion component

Axial Vectors & Oxygenation of the Lethal Corner:
Hyperoxia & Slow Intracapillary Blood Flow Velocity
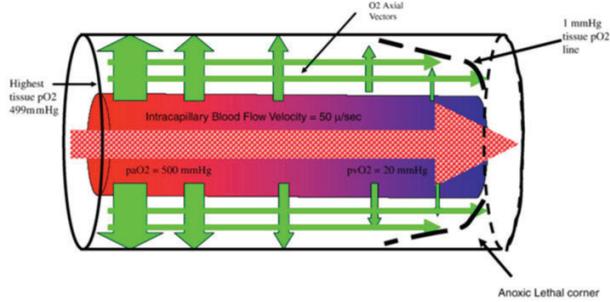
Axial kick is the use of elevated paO2 to increase the driving gradient of axial vectors in an attempt to oxygenate an anoxic lethal corner

Improve diffusion component
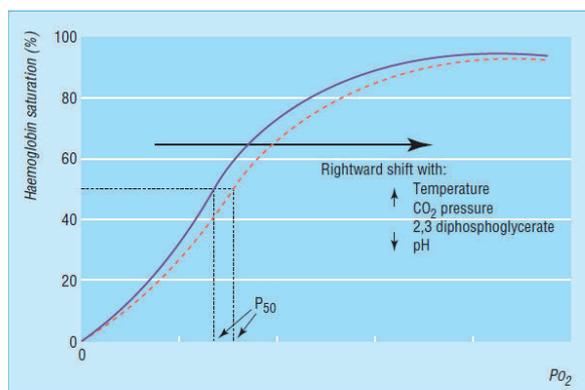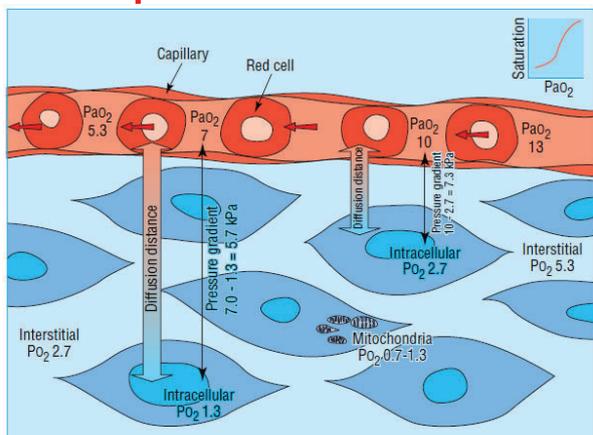
Effect of oxygen tension gradient and diffusion distance on availability of oxygen to cells

Oxygen-haemoglobin dissociation curve. The curve shifts to the right with increased temperature, acidosis, and 2,3-diphosphoglycerate concentrations

Leach 1998
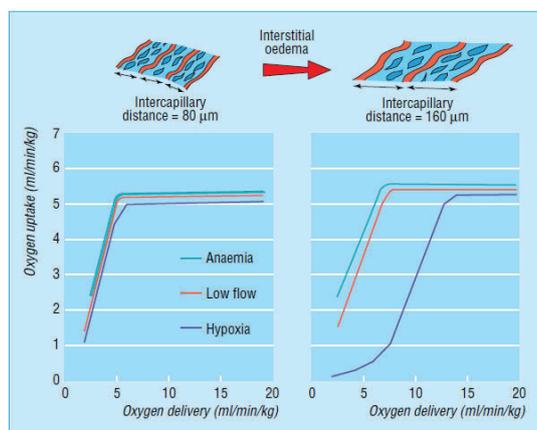
CO$_2$ removal
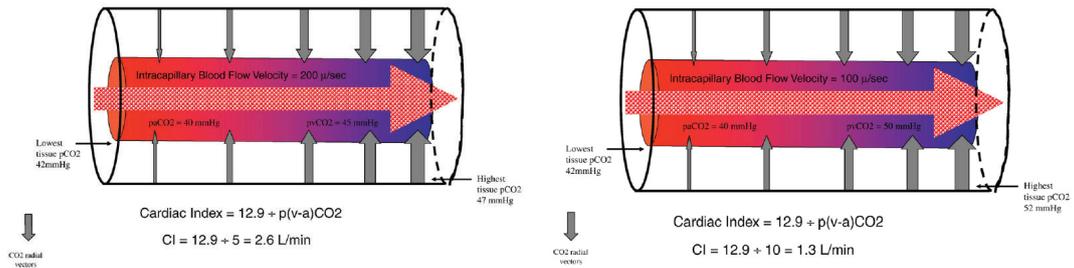
Congestion and microcirculation

A Original Krogh concept

Krogh Cylinder

B Current understanding of complexity

Ellsworth 2009

arteriole
capillary
venule
convection
diffusion

Ellsworth 1994

Regulating mechanisms

C Dilation

MAP

Arteriole
T=0 min MAP 90 mmHg
T=1 min MAP 60 mmHg
T=3 min MAP 30 mmHg

Venule
T=0 min
T=1 min
T=3 min

Atasever 2011
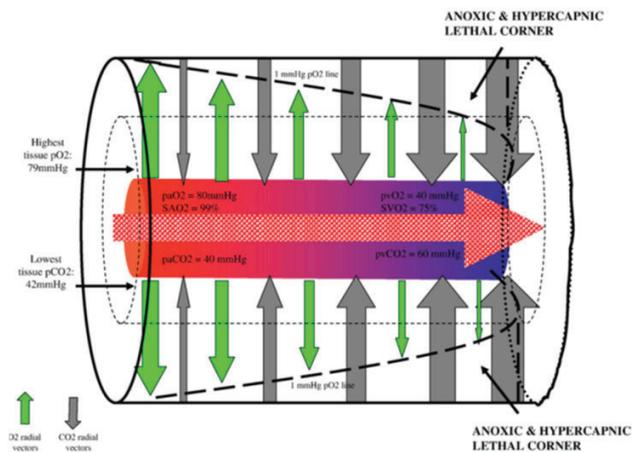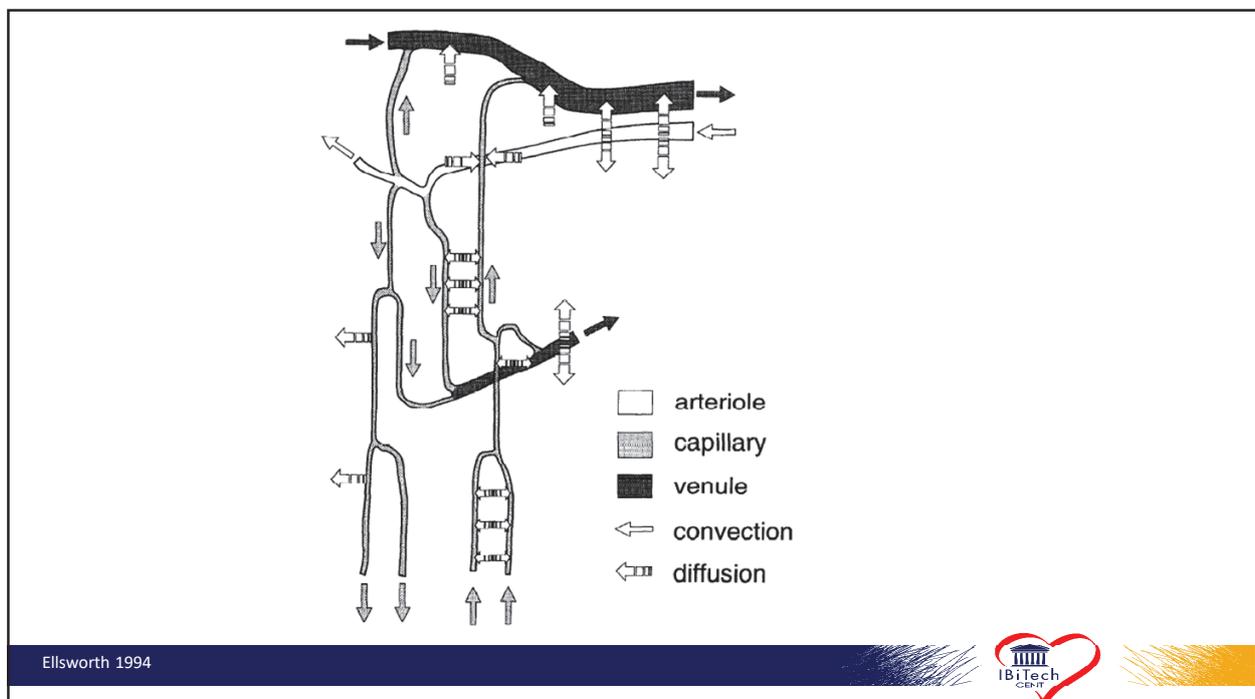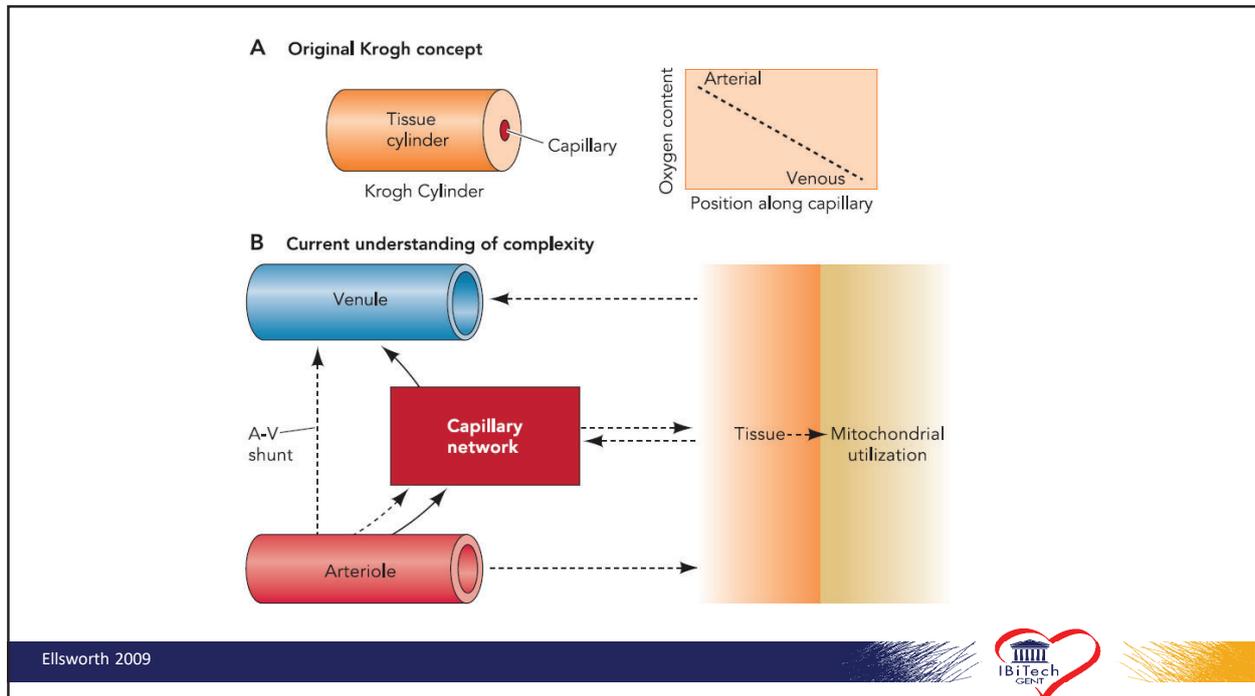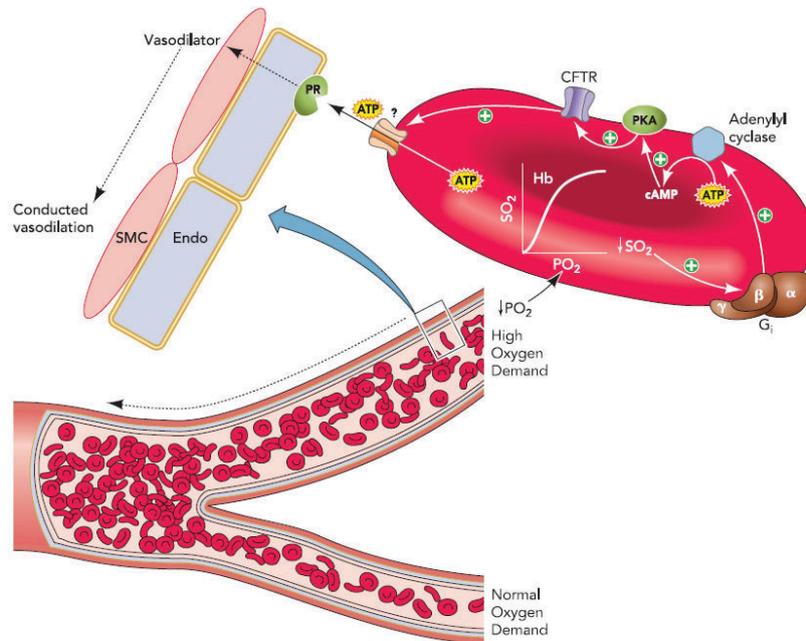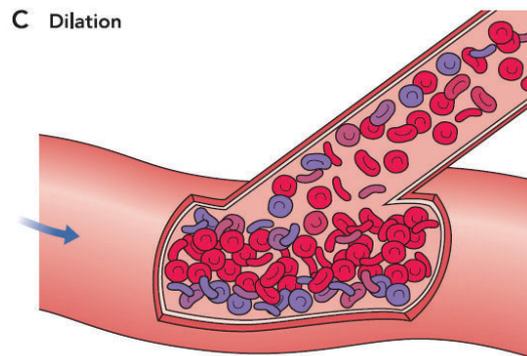
Hypoperfusion vs congestion

Mean arterial and pulmonary arterial pressures (MAP and MPAP), pulmonary artery occlusion pressure (PAOP), cardiac output (CO), mixed venous oxygen saturation (SvO_2), and arterial pH and hematocrit (Ht) in SMAO (superior mesenteric artery occlusion, $n = 7$) and SMVO (superior mesenteric vein occlusion, $n = 7$) groups

	Group	BL	II-45	R30	R60	R120
MAP, mm Hg	SMAO	122.7 ± 7.6	130.9 ± 9	122 ± 8.2	128.8 ± 7.2	128.3 ± 10.3
	SMVO	131 ± 8.1	95.7 ± 9.3[a,b]	102 ± 9.2[a,b]	106 ± 9.8[a,b]	109 ± 7.5[a,b]
MPAP, mm Hg	SMAO	14.5 ± 1.4	14.3 ± 1.8	15.8 ± 2	16.9 ± 1.6	19.1 ± 1.9[a]
	SMVO	15.2 ± 1.9	12.0 ± 2.1	13.4 ± 2.2	13.4 ± 2.3[b]	13.7 ± 2.8[b]
PAOP, mm Hg	SMAO	7.3 ± 1.4	7.7 ± 1.7	7.4 ± 1.6	7.3 ± 1.7	7.5 ± 1.7
	SMVO	7.1 ± 1.2	5.4 ± 0.9[a]	5.9 ± 1.6	4.6 ± 1.3[a,b]	5.1 ± 1.1[a,b]
CO, L/min	SMAO	2.9 ± 0.2	2.6 ± 0.2	2.3 ± 0.1	2.2 ± 0.2	2.3 ± 0.1
	SMVO	3.2 ± 0.2	2.1 ± 0.2[a]	1.9 ± 0.2[a]	1.6 ± 0.2[a,b]	1.6 ± 0.2[a,b]
Arterial lactate, mmol/l	SMAO	0.8 ± 0.1	0.8 ± 0.1	1.0 ± 0.1	0.8 ± 0.1	0.9 ± 0.3
	SMVO	1.2 ± 0.4	2.1 ± 0.4[a,b]	2.2 ± 0.4[a,b]	2.0 ± 0.3[a,b]	1.7 ± 0.1[a,b]
Arterial pH	SMAO	7.4 ± 0.02	7.42 ± 0.02	7.4 ± 0.02	7.39 ± 0.02	7.39 ± 0.01
	SMVO	7.37 ± 0.01	7.33 ± 0.01[a,b]	7.29 ± 0.02[a,b]	7.3 ± 0.01[a,b]	7.29 ± 0.02[a,b]
Arterial Ht, %	SMAO	35.3 ± 1.4	34.1 ± 0.6	36.9 ± 1.7	35.8 ± 2.1	35.5 ± 1.9
	SMVO	38.7 ± 1.1	35.8 ± 2.4	37.5 ± 2.1	38 ± 1.8	36.8 ± 2.4

Notes: Baseline (BL), 45 min after intestinal ischemia (II-45) and 30, 60, and 180 min after reperfusion (R30, R60, and R120, respectively). Data are presented as mean ± standard error of the mean.
[a]$P < 0.05$ *versus* baseline.
[b]$P < 0.05$ *versus* SMAO.

Cruz 2010

Hypoperfusion vs congestion

Intestinal oxygen delivery, consumption and extraction ratio (DO_2intest, VO_2intest and O_2ERintest), and mesenteric vein pH and hematocrit (Ht) in SMAO (superior mesenteric artery occlusion, $n = 7$) and SMVO (superior mesenteric vein occlusion, $n = 7$) groups

	Group	BL	II-45	R30	R60	R120
DO_2 intest, mL/min	SMAO	67.7 ± 9.9	-	45.4 ± 6.8^a	45.5 ± 7.5^a	38.8 ± 5.3^a
	SMVO	79.9 ± 10.5	-	$15.8 \pm 1.9^{a,b}$	$14.6 \pm 10.5^{a,b}$	$16.4 \pm 2.4^{a,b}$
VO_2 intest, mL/min	SMAO	4.9 ± 0.2	-	5.8 ± 1.3	5.1 ± 0.3	4.2 ± 1.1
	SMVO	5.8 ± 1.2	-	$2.6 \pm 0.7^{a,b}$	$3.2 \pm 0.6^{a,b}$	$3.3 \pm 0.6^{a,b}$
O_2ER intest, %	SMAO	5.0 ± 1.1	-	10.1 ± 1.9^a	10.9 ± 2.1^a	12.4 ± 2.7^a
	SMVO	5.7 ± 1.6	-	$22.7 \pm 3.8^{a,b}$	$29.0 \pm 4.8^{a,b}$	$22.9 \pm 3.8^{a,b}$
Mesenteric lactate, mmol/l	SMAO	0.9 ± 0.1	1.4 ± 0.3^a	1.7 ± 0.3^a	1.2 ± 0.2	1.3 ± 0.3
	SMVO	1.5 ± 0.4	$5.3 \pm 0.9^{a,b}$	$4.0 \pm 0.7^{a,b}$	$3.2 \pm 0.6^{a,b}$	$2.6 \pm 0.3^{a,b}$
Mesenteric vein pH	SMAO	7.38 ± 0.02	7.36 ± 0.02	7.35 ± 0.02	7.35 ± 0.02	7.35 ± 0.02
	SMVO	7.35 ± 0.02	$7.18 \pm 0.03^{a,b}$	$7.21 \pm 0.03^{a,b}$	$7.2 \pm 0.02^{a,b}$	$7.22 \pm 0.01^{a,b}$
Mesenteric vein Ht, %	SMAO	37.2 ± 1.7	34.3 ± 1.5	37.7 ± 1.3	36.7 ± 2.3	36.8 ± 1.5
	SMVO	39.2 ± 1.2	$66.4 \pm 0.9^{a,b}$	40.3 ± 2.6	39.4 ± 1.9	37.1 ± 2.0

Hypoperfusion vs congestion
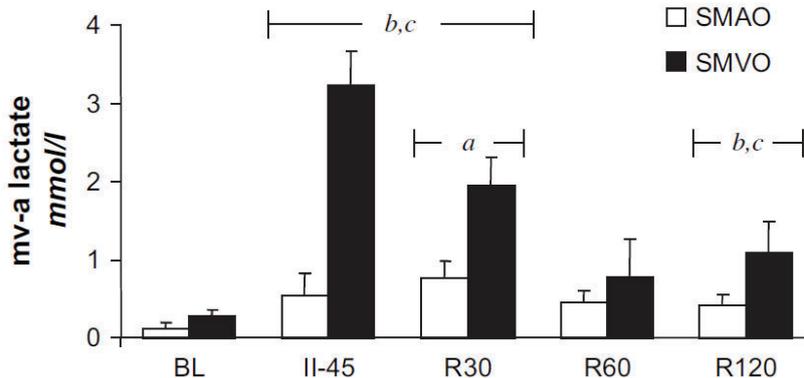
Congestion
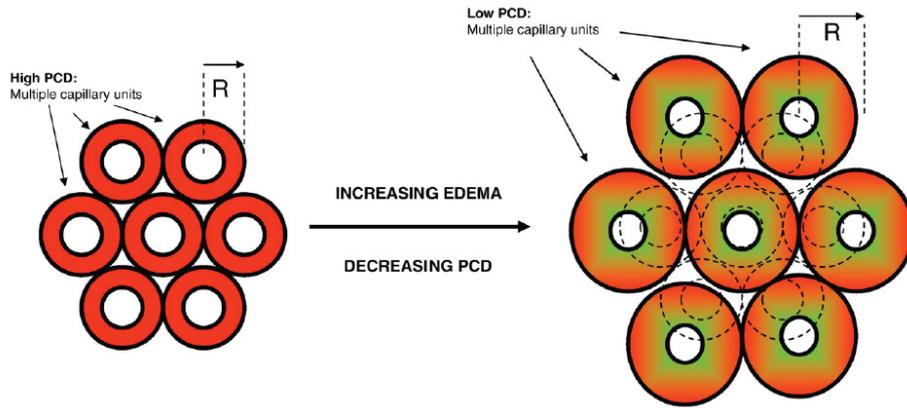
Increased RAP

Vellinga 2013

Low convective flow

Large diffusion distance

Convection limitation = **Hypovolemia**

Optimal fluid volume

Diffusion limitation = **Fluid overload**

Optimal fluid volume

Ince 2014

Perioperative oxygen debt

Shoemaker 1991

21

VO$_2$ and hemoglobin

CO = 5 L/min
SaO$_2$ = 99%
SvO$_2$ = 75%

2.5 L/min

DO$_2$ and VO$_2$

O$_2$ER=40% O$_2$ER=30% O$_2$ER=25%
SvO$_2$=60% SvO$_2$=70% SvO$_2$=75%
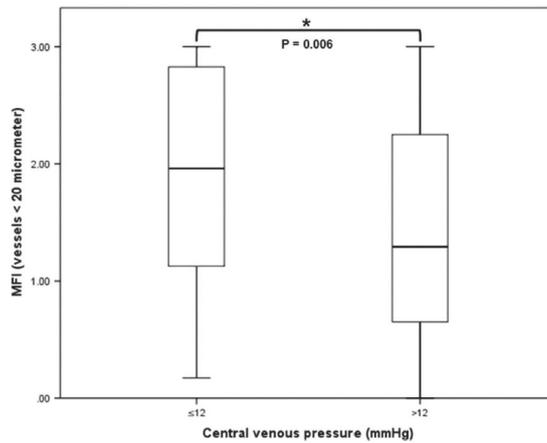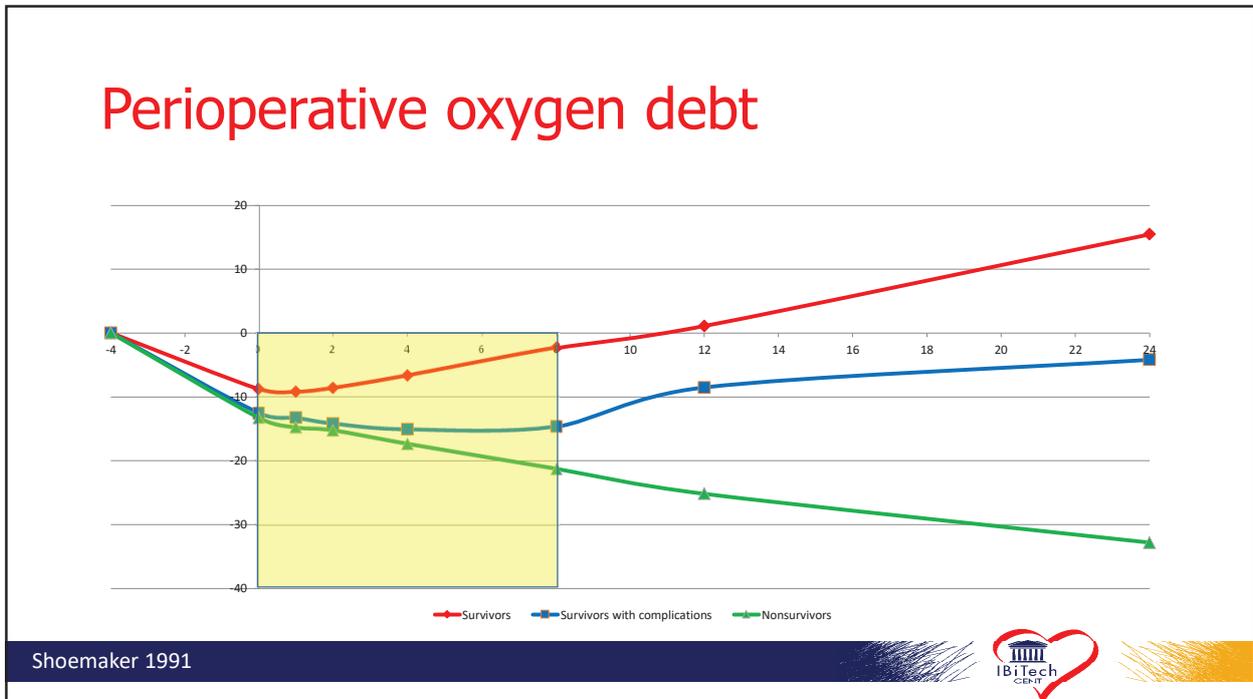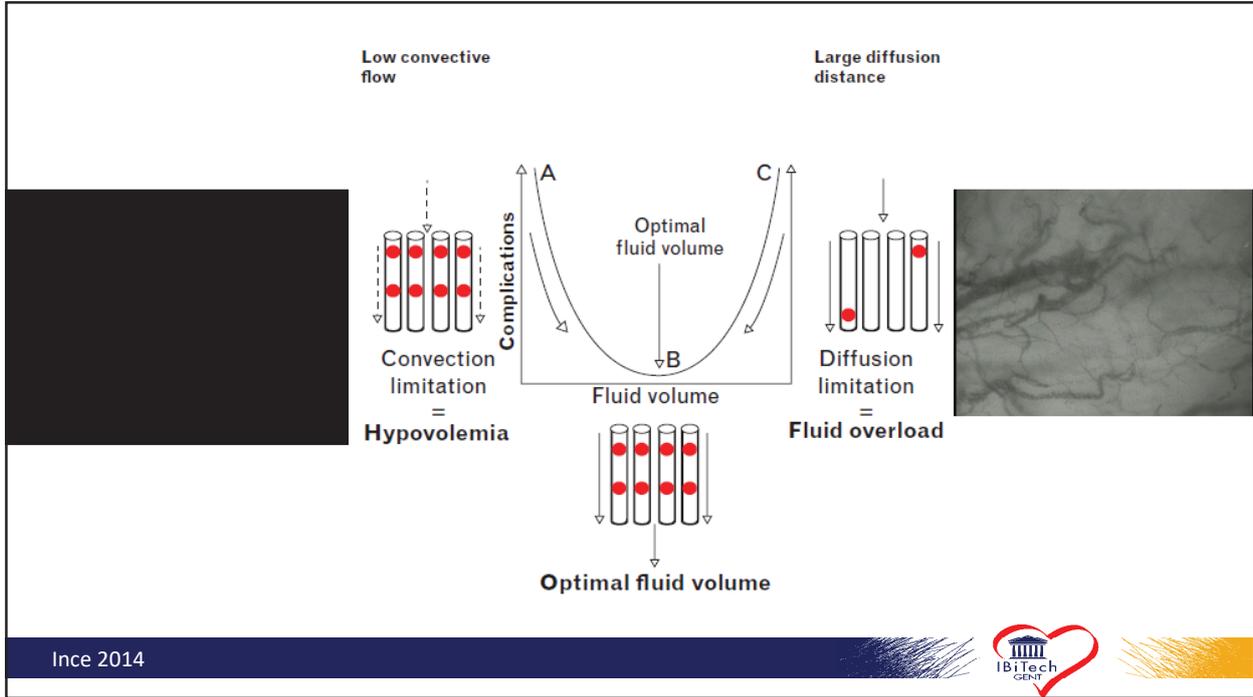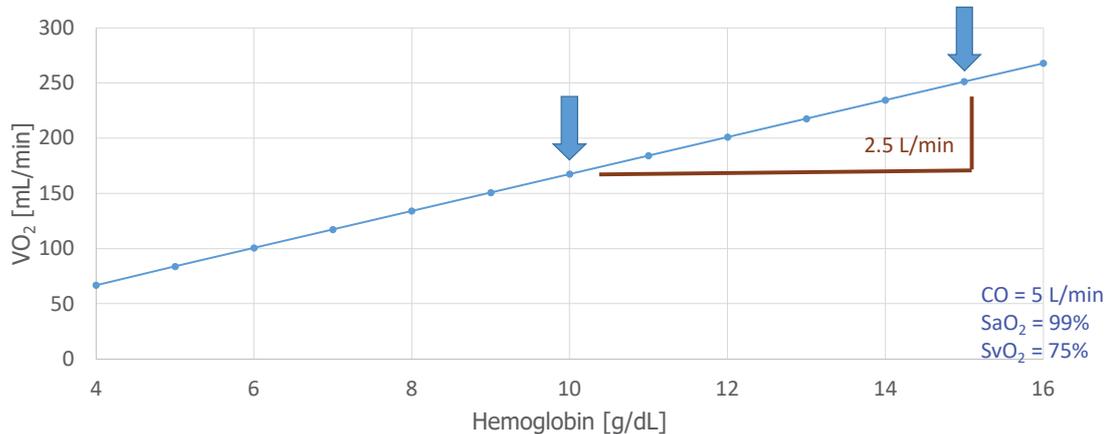
$$DO_2 = CO \cdot Hb \cdot 1.34 \cdot SaO_2$$
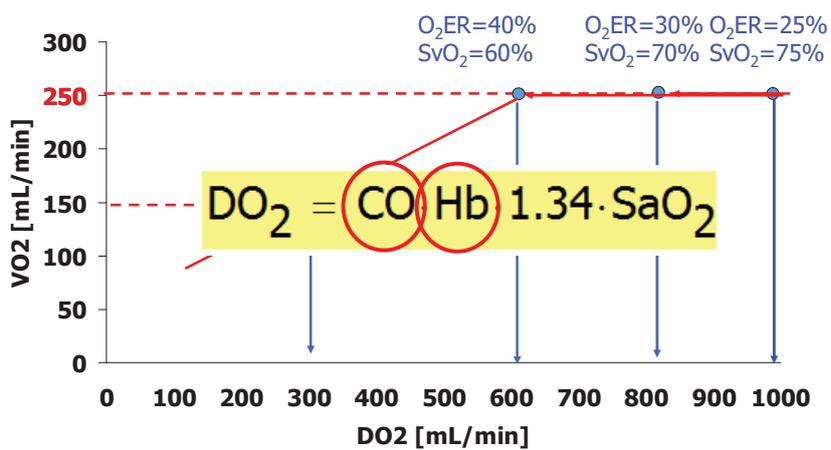
Hypothesis

• If DO_2 is a prime variable
• If most perfusionists work with a fixed CI

Must hemoglobin influence quality of Perfusion

Haematocrit during CPB

Karkouti 2005

Hematocrit during CPB

Lowest HCT on CPB is associated to:
- Reopening
- Bleeding
- Perioperative MI
- Cardiac arrest
- Stroke
- Coma
- Prolonged ventilation
- IABP
- Renal failure
- MOF

Fig 2. Receiver operating characteristic curve for the three variables being identified as independent risk factors for acute renal failure. — — = lowest hematocrit on CPB; - - - - = pump flow indexed; —— = oxygen delivery indexed. (CPB = cardiopulmonary bypass; DO₂ = two determinants of oxygen delivery; HCT = hematocrit.)

Ranucci 2005

Optimal flow and outcome

Ranucci 2005

Optimal flow and outcome

Basic patient characteristics

Characteristic	Hematocrit 25%		Hematocrit 20%		p
	Median	IQR	Median	IQR	
Age (years)	60	55–67	65	58–71	0.10
Gender (male/-female)	28/2		26/0		0.49
Height (m)	1.78	1.73–1.81	1.75	1.72–1.79	0.35
Weight (kg)	93	80–100	87	80–100	0.52
Body mass index (kg/m^2)	27.9	26.0–32.2	28.8	26.7–29.9	0.72
Preoperative hematocrit (%)	41.8	40.2–43.0	42.1	39.4–45.4	0.88
Duration of anesthesia (minutes)	300	290–320	310	290–325	0.26
Duration of surgery (minutes)	190	160–220	205	175–250	0.09
CPB time (minutes)	72	55–83	73	63–81	0.50
Aortic cross clamp time (minutes)	45	33–56	45	38–49	0.93
APACHE II score	14	9–19	16	13–27	0.09

APACHE, Acute Physiology and Chronic Health Evaluation; CPB, cardiopulmonary bypass; IQR, interquartile range.

von Heymann 2006

Outcome measures in the intensive care unit

Outcome measure	Hematocrit 25%		Hematocrit 20%		p
	Median	IQR	Median	IQR	
Number of transfused patients	1		5		0.10
Drainage loss (ml)	382	265–530	400	290–620	0.28
Patients with postoperative stroke (n)	0		0		0.99
Patients with agitated arousal reaction (n)	3		3		0.99
Patients with myocardial infarction (n)	0		0		0.99
CK/CK-MB ratio (%)	6.25	4.8–7.2	5.9	4.4–7.0	0.99
Patients with catecholamines on admission to ICU (n)	10		7		0.57
Patients with catecholamines 6 h after admission to ICU (n)	5		2		0.42
Patients with dopamine 18 h after admission to ICU (n)	2		1		0.53
Patients with respiratory failure (n)	3		3		0.99
Duration of ventilator support (hours)	10	8–12,5	10	10–12	0.36
Patients with renal failure (n)	1		1		0.99
Creatinine 18 h after admission to ICU (mg/dl)	0.92	0.82–1.19	1.06	0.90–1.14	0.30
Urine volume in ICU (ml)	2.810	2.390–3.469	2.815	2.100–3.600	0.82
Combined endpoint of organ failure (n)	8		10		0.57
Duration of ICU stay (hours)	22	21–24	23	21–28	0.24
Mortality (n)	0		1		0.48

CK, creatine kinase; CK-MB, myocardial creatine kinase; ICU, intensive care unit; IQR, interquartile range.

von Heymann 2006

IBiTech GENT

Optimal flow and outcome

Intraoperative outcome measures

Outcome measure	Hematocrit 25%		Hematocrit 20%		p
	Median	IQR	Median	IQR	
CI during CPB (l/m²/minute)	3.2	3.0–3.7	3.2	3.0–3.5	0.57
Temperature during CPB (°C)	35.6	35.0–36.0	36.8	35.4–36.0	0.12
Cumulative norepinephrine dosage during CPB (mg)	0.08	0.06–0.10	0.03	0.0–0.08	0.13
Dopamine dosage for weaning from CPB (μg/kg/minute)	1.0	0.0–3.0	1.5	0.0–3.0	0.92
Patients with catecholamines for weaning from CPB (n)	16		16		0.79
Patients with intraaortic balloon pump for weaning from CPB (n)	2		0		0.49
Patients with acute cardiac failure during weaning from CPB (n)	3		2		1.00
Urine volume during CPB (ml)	159	97–354	165	102–440	0.57

CI, cardiac index; CPB, cardiopulmonary bypass; IQR, interquartile range.

DO2 @ 25% = 356 mL/min/m²   DO2 @ 20% = 287 mL/min/m²

> 270 mL/min/m²

von Heymann 2006

IBiTech GENT

What if flow cannot augmented?
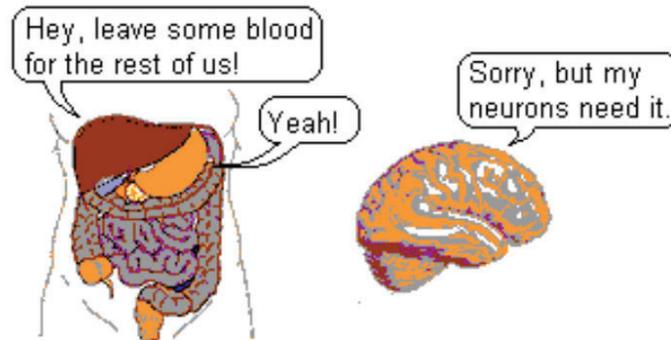
Blood transfusion: the answer?
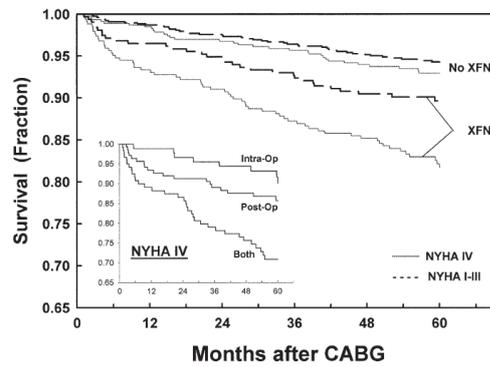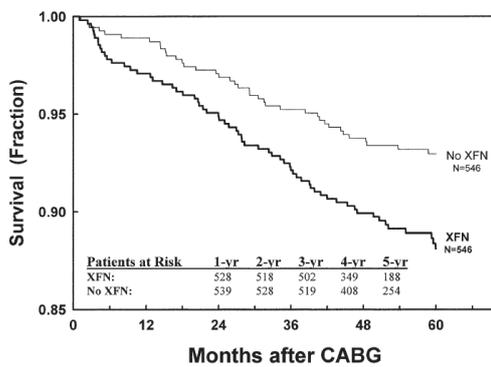
Engoren 2002

Blood transfusion the answer?
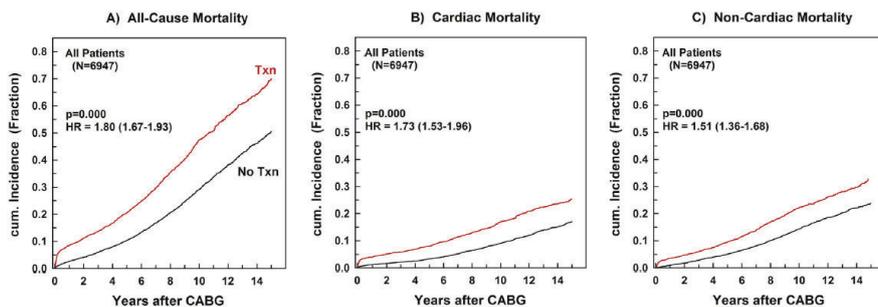
Schwann 2016

Blood transfusion: the answer?
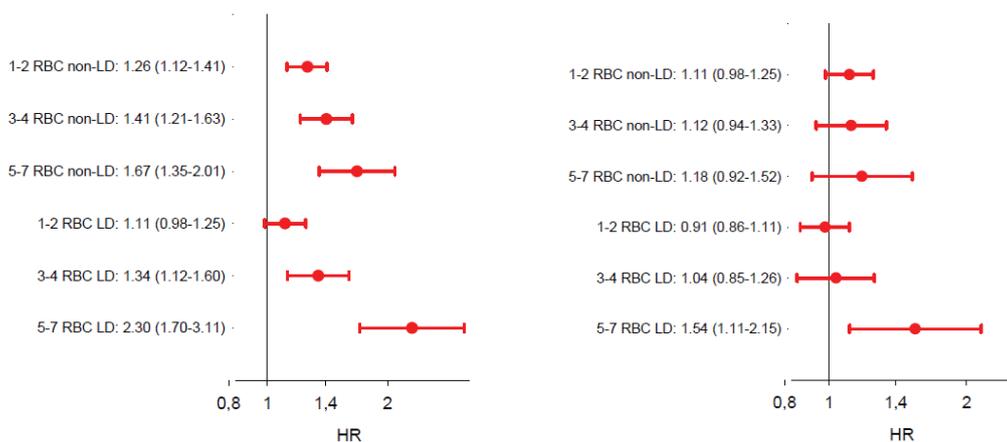
Bjursten 2016

Association Between Anemia, Bleeding, and Transfusion with Long-term Mortality Following Noncardiac Surgery

Nathaniel R. Smilowitz, MD,[a] Brandon S. Oberweis, MD,[b] Swetha Nukala, MBBS,[c] Andrew Rosenberg, MD,[d] Sibo Zhao, MS,[a] Jinfeng Xu, PhD,[a] Steven Stuchin, MD,[e] Richard Iorio, MD,[e] Thomas Errico, MD,[e] Martha J. Radford, MD,[a,f,g] Jeffrey S. Berger, MD, MS[a,h]

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Transfuse or not?

Ferraris 2015

AKI, anemia and transfusion
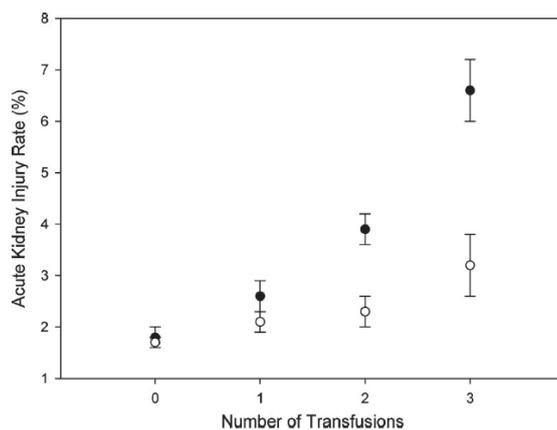
Karkouti 2011

Was transfusion efficacious?
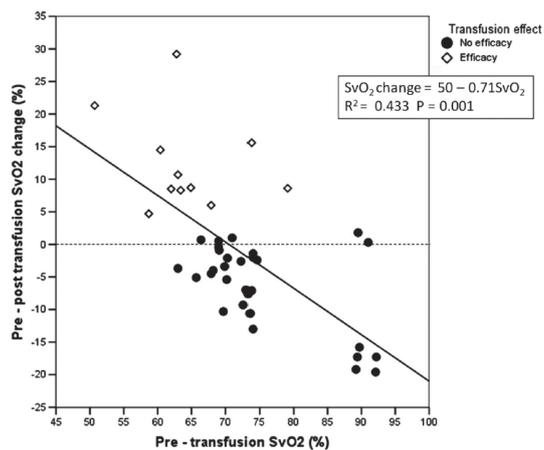
Ranucci 2011

Acute Kidney Injury and Hemodilution During Cardiopulmonary Bypass: A Changing Scenario

Marco Ranucci, MD, FESC, Tommaso Aloisio, MD, Giovanni Carboni, CCP, Andrea Ballotta, MD, FESC, Valeria Pistuddi, Lorenzo Menicanti, MD, and Alessandro Frigiola, MD, for the Surgical and Clinical Outcome REsearch (SCORE) Group

Departments of Cardiothoracic and Vascular Anesthesia and Intensive Care and Department of Cardiac Surgery, IRCCS Policlinico San Donato, Milan, Italy

Background. Severe hemodilution during cardiopulmonary bypass (CPB) is a risk factor for acute kidney injury (AKI) after heart operations. Many improvements to CPB technology have been proposed during the past decade to limit the hemodilution-related AKI risk. The present study is a retrospective analysis of the relationship between hemodilution during CPB and AKI in cardiac operations in the setting of different interventions applied over 14 years.

Methods. We retrospectively analyzed 16,790 consecutive patients undergoing heart operations from 2000 to 2013. Various risk factors for AKI were collected and analyzed, together with a number of interventions as possible modifiers of the relationship between a nadir hematocrit (HCT) value during CPB and AKI.

Results. The relationship between the nadir HCT value during CPB and AKI was confirmed in a multivariable analysis, with the relative risk of AKI increasing by 7% per percentage point of decrease of the nadir HCT value during CPB. The relative risk of AKI decreased by 8% per year of observation ($p = 0.001$) despite a significantly increased risk of AKI ($p = 0.001$). A sensitivity analysis based on differences before and after different interventions demonstrated a beneficial effect of the application of goal-directed perfusion (aimed at preserving oxygen delivery during CPB), with a reduction in the AKI rate from 5.8% to 3.1% ($p = 0.001$). A policy restricting angiographic examination on the day of operation was also useful (reduction of AKI rate from 4.8% to 3.7%; $p = 0.029$).

Conclusions. A bundle of interventions mainly aimed at limiting the renal impact of hemodilution during CPB is effective in reducing the AKI rate.

(Ann Thorac Surg 2015;100:95–100)
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Table 2. *Demographics and Renal Risk Factors of the Patient Population in the Different Periods Considered*

Period (No. of patients)	Age (y)	eGFR (mL/min)	LVEF (%)	Diabetes (%)	Redo Operations (%)	Nonelective Operations (%)	Nonisolated CABG (%)	IABP Use (%)	CPB time (min)
2000–2001 (2,714)	64.4 (10.7)	56.8 (23)	51.6 (11.8)	12.6	4.0	2.4	42.9	0.3	71.7 (37)
2002–2003 (2,694)	65.6 (11.3)	71.8 (34)	50.4 (11.6)	14.1	5.4	4.0	49.6	0.4	71.8 (36)
2004–2005 (3,006)	66.5 (11.6)	74.3 (36)	51.6 (11.9)	13.8	5.5	6.5	49.3	0.8	75.1 (38)
2006–2007 (2,313)	66.3 (11.8)	77.2 (33)	52.0 (11.1)	12.1	6.2	4.5	49.8	0.8	80.4 (39)
2008–2009 (1,829)	65.9 (12.3)	78.7 (36)	53.9 (11.8)	14.1	6.1	3.1	57.1	0.9	83.1 (37)
2010–2011 (2,157)	65.9 (13.5)	76.9 (40)	53.1 (12.0)	18.5	6.6	3.6	63.7	2.0	87.1 (44)
2012–2013 (2,077)	66.3 (13.0)	75.6 (35)	53.5 (11.5)	18.1	8.1	8.2	68.7	1.3	86.0 (42)
p value (between periods)[a]	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

[a] Analysis of variance or Pearson's χ^2 test. Data expressed as mean (standard deviation) or percentage.

CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; eGFR = estimated glomerular filtration rate; IABP = intraaortic balloon pump; LVEF = left ventricular ejection fraction.

Table 3. *Renal Risk and Renal Outcome of the Patient Population in the Different Periods Considered*

Period	No. of Patients	RRS	AKI Rate	Nadir HCT Value During CPB (%)	AKI Rate at Nadir < 24%	Odds Ratio (95% CI) for AKI As a Function of Nadir HCT Value	*p* Value for Univariate Association
2000–2001	2,714	1.49 (1.1)	124 (4.6)	25.9 (4.1)	48 (6.7)	0.92 (0.88–0.96)	0.001
2002–2003	2,694	1.36 (1.1)	118 (4.4)	27.8 (3.7)	28 (8.0)	0.89 (0.84–0.93)	0.001
2004–2005	3,006	1.36 (1.1)	229 (7.6)	26.6 (3.6)	57 (9.0)	0.95 (0.91–0.98)	0.005
2006–2007	2,313	1.25 (1.1)	133 (5.8)	26.2 (3.4)	45 (8.3)	0.93 (0.89–0.98)	0.010
2008–2009	1,829	1.34 (1.0)	47 (2.6)	26.1 (3.7)	26 (5.5)	0.85 (0.79–0.93)	0.001
2010–2011	2,157	1.51 (1.1)	84 (3.9)	26.1 (3.7)	34 (6.3)	0.85 (0.80–0.91)	0.001
2012–2013	2,077	1.70 (1.2)	58 (2.8)	28.0 (4.1)	14 (4.7)	0.91 (0.86–0.97)	0.006
Total	16,790						
p value (between periods)[a]		0.001	0.001	0.001	0.001		

[a] Analysis of variance or Pearson's χ^2 test. Data are expressed as mean (standard deviation) or number (%).

AKI = acute kidney injury; CI = confidence interval; CPB = cardiopulmonary bypass; HCT = hematocrit; RRS = renal risk score.
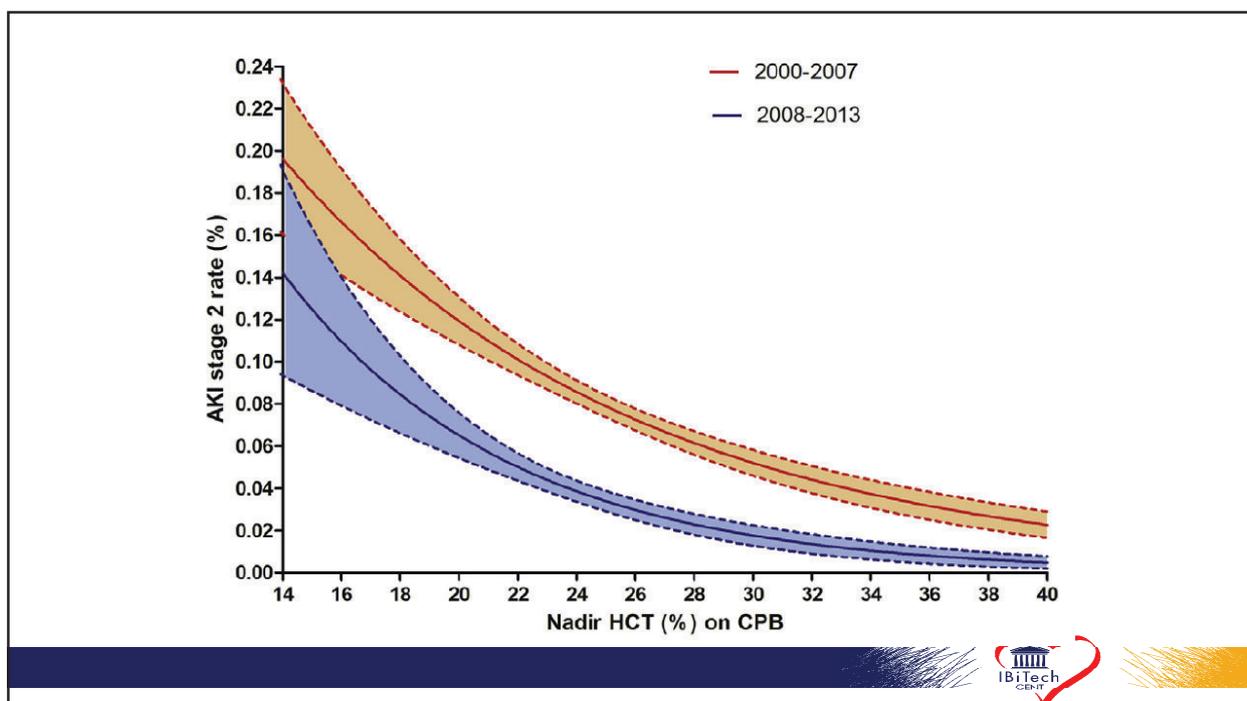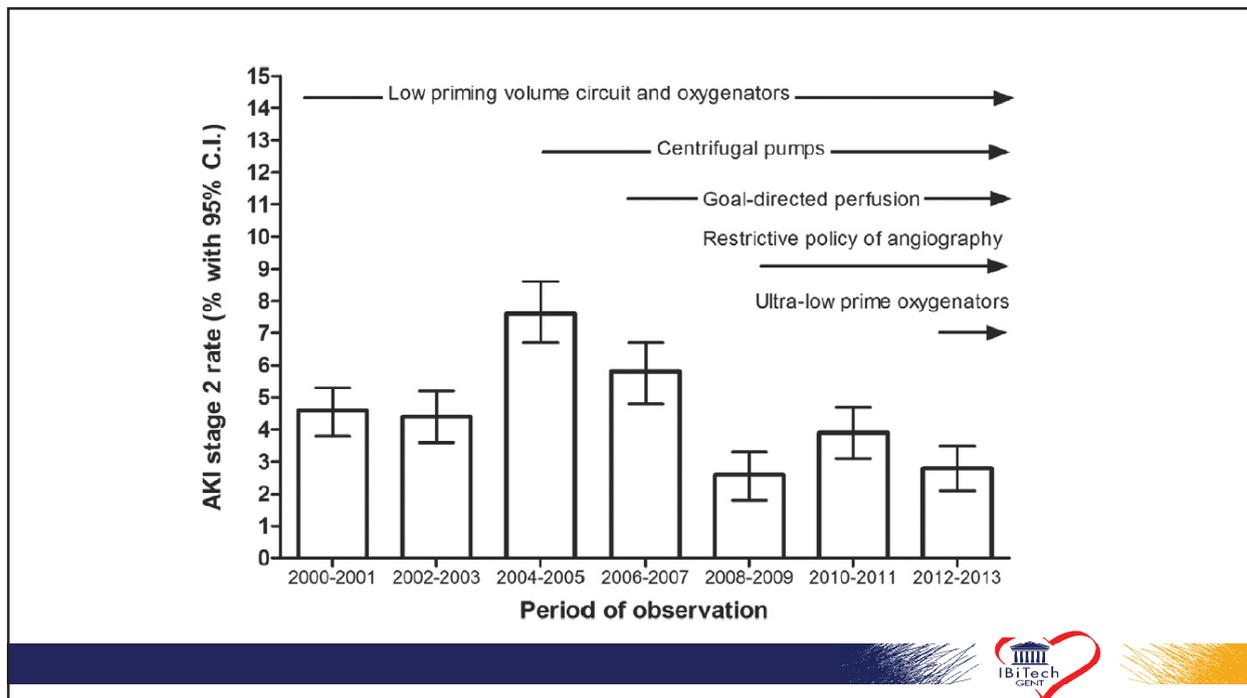
Maintain red blood cell mass

- Low priming volume
- Retrograde autologous priming
- Limit fluid delivery
- Ultrafiltration

DO_2 as a goal

- Scarce information on DO_2 during CPB
- With a constant pump flow, DO_2 is direct related to Hct
- Most CPB cases are performed at 32 - 34°C
- Pump flow = 2 - 3 L/min/m²
- => Hct = cte => DO_2 varies with 50%

Cilley 1991

Lactate as marker

Maillet 2003

ANEMIA

HYPOXIA

LOW CARDIAC OUTPUT

VO_2 (cc/kg/min)

DO_2 (cc/kg/min)

Cilley 1991

Do not measure your therapy

Lactate (mmol/L)

PRBC age (days)

PRBC<12 days
PRBC>12 days

Lactate (mmol/L)

before CPB   during CPB   end OP

Schroeder 2005
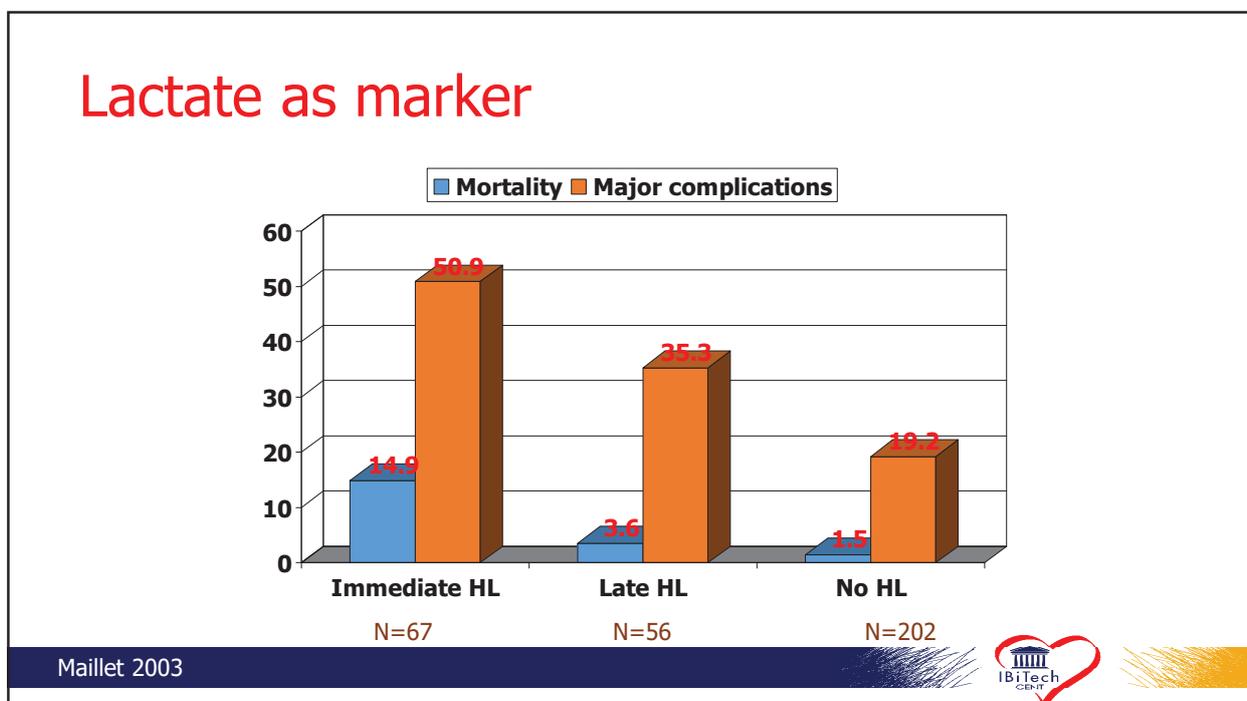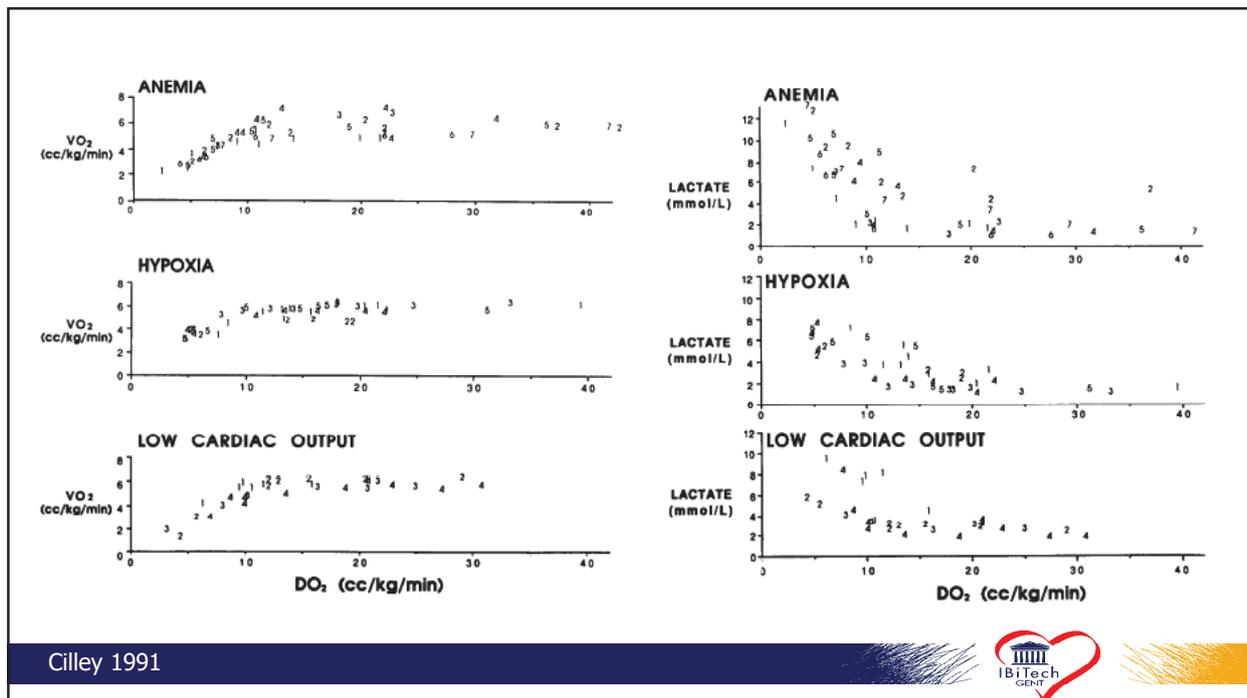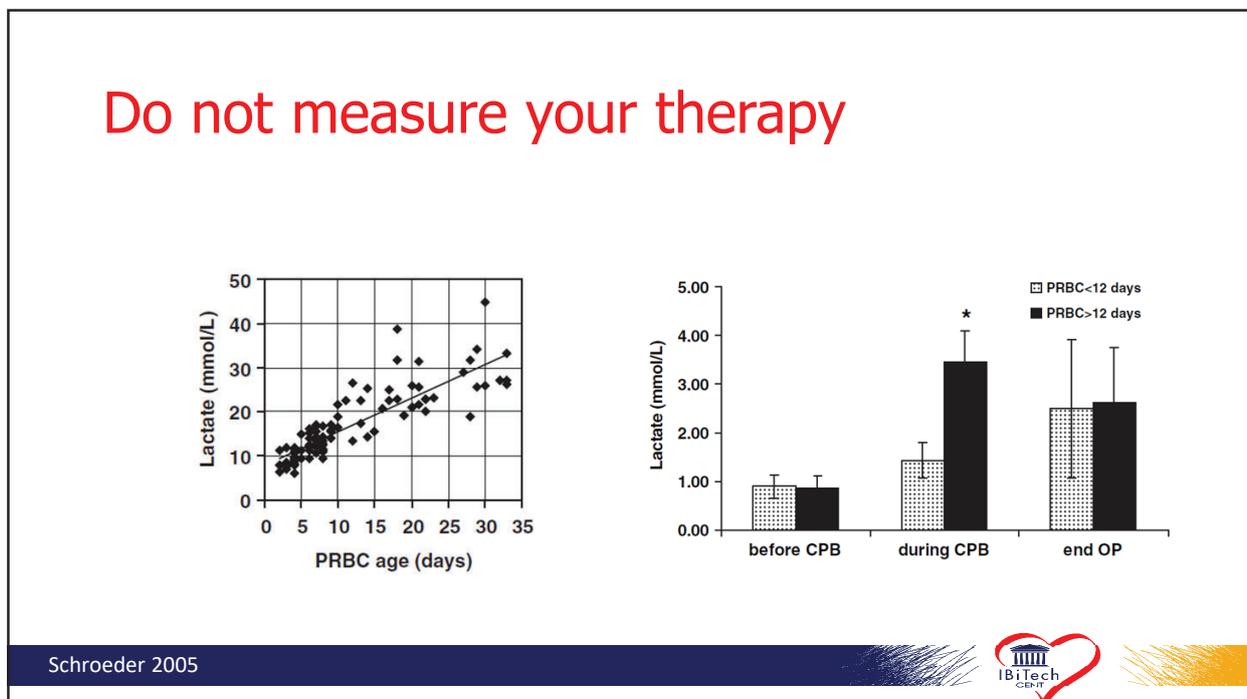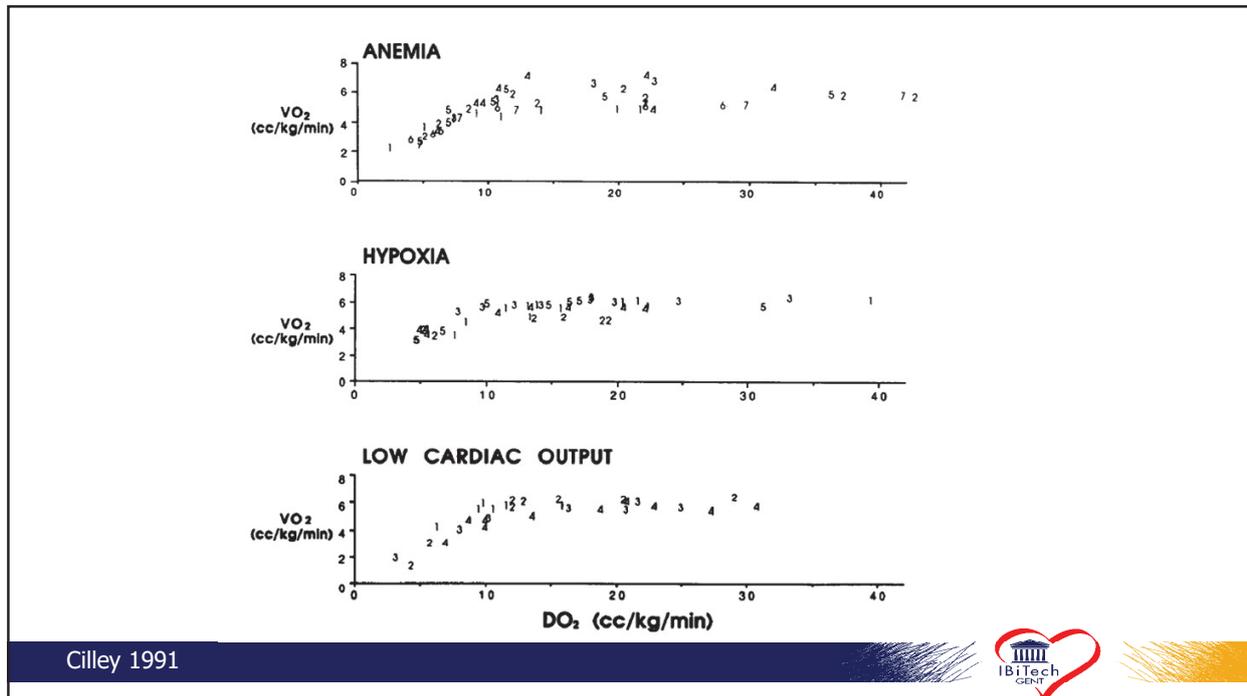
VCO$_2$ – VO$_2$
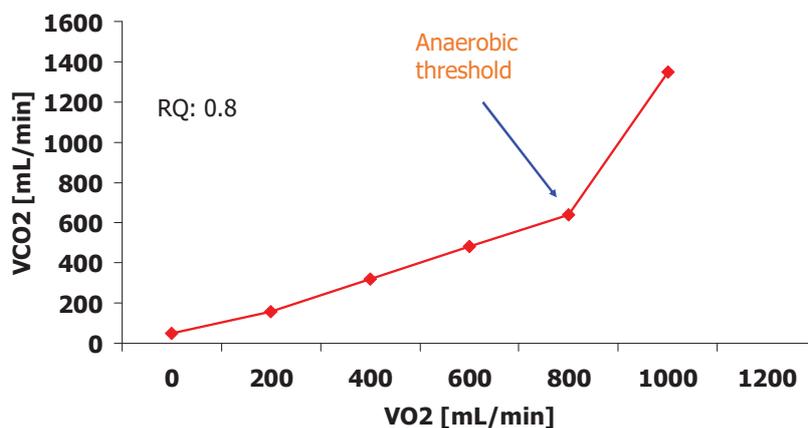
All variables
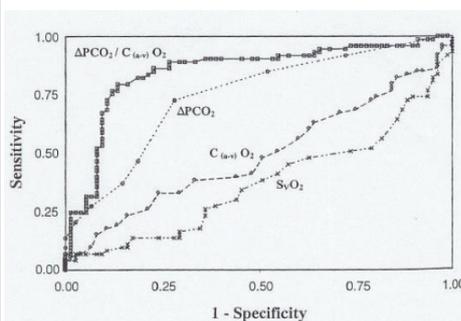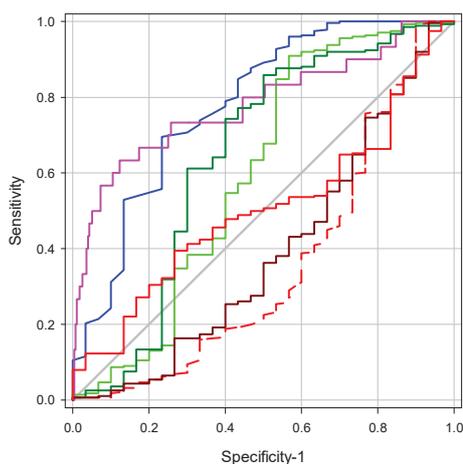
N = 42

How do we know that blood flow meet the metabolic needs of a patient?

By retrospective analysis of organ function, blood markers and morbidity

"What we need is a multivariate online analysis of risk during cardiopulmonary bypass" *Charles Wildevuur*

DO_2i => what we give to the patient

VCO_2i => what we get from the patient

Variable	Baseline	Bypass interval (min)			
		30	60	90	120
pH	7.46 ± 0.02	7.47 ± 0.1	7.45 ± 0.1	7.46 ± 0.2	7.46 ± 0.1
$Paco_2$	37.3 ± 2.4	32.4 ± 1.9	34.3 ± 1.8	33.8 ± 1.8	33.4 ± 1.9
Pao_2	310 ± 20.1	312 ± 34.1	244 ± 32.7	269 ± 42.1	284 ± 42.0
Arterial bicarbonate	27.1 ± 1.2	24.4 ± 0.8*	23.9 ± 0.8*	23.4 ± 0.6*	22.0 ± 0.7*
Hct	26.3 ± 2.2	14.6 ± 1.6*	15.9 ± 1.5*	16.4 ± 1.6*	14.4 ± 1.5*
Temperature (°C)[a]	37.3 ± 0.4	37.4 ± 0.3	37.6 ± 0.1	37.6 ± 0.2	37.6 ± 1.4

Hct = hematocrit.
[a] Temperature was measured nasopharyngeally.
* $P < 0.05$ compared with baseline value.
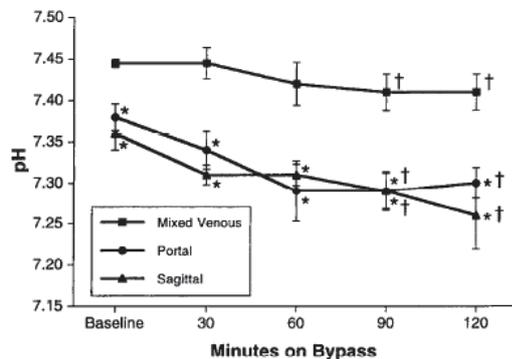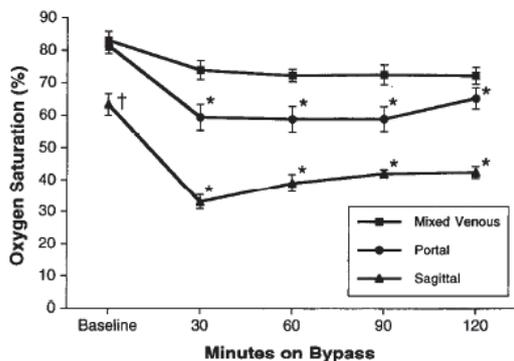
McDaniel 1995

"current guidelines for calculating pump flow during normothermic bypass may be reconciled to better match prebypass systemic oxygen delivery with oxygen delivery during CPB."

McDaniel 1995

Table 2. Univariate Analysis of Oxygen-Carbon Dioxide Derived Parameters and Other Intraoperative Variables at Arterial Lactate Determinations Below or Above the Threshold Value (3 mmol/L).

Parameter	Arterial Lactates ≤ 3 mmol/L (n = 130)	Arterial Lactates > 3 mmol/L (n = 37)	p
Pao_2 (mmHg)	225 ± 56	228 ± 44	0.7
Svo_2	0.78 ± 0.76	0.76 ± 0.8	0.15
VCO_2i (mL · min^{-1} · m^{-2})	51.4 ± 15.2	82.1 ± 38.4	< 0.001
DO_2i/VCO_2i	6.35 ± 1.7	4.14 ± 1.2	< 0.001
VCO_2i/VO_2i	0.77 ± 0.22	1.35 ± 0.68	< 0.001
Aortic cross-clamp on	72%	46%	0.003
BSA (m^2)	1.85 ± 0.2	1.62 ± 0.45	0.005
CPB time (min)	44.7 ± 36.3	68.9 ± 47.7	0.006

BSA = body surface area; CPB = cardiopulmonary bypass; Do_2i/Vco_2i = oxygen delivery indexed/carbon dioxide elimination indexed; Pao_2 = arterial oxygen tension; Svo_2 = mixed venous oxygen saturation; Vco_2i = carbon dioxide elimination indexed; Vco_2i/Vo_2i = respiratory quotient.

Table 3. Receiver Operating Characteristic Analysis and Relative Cutoff Values

Factor	AUC	p	Cutoff Value	Sensitivity	Specificity
Do_2i/Vco_2i	0.852	< 0.001	4.99	78.4%	74%
Vco_2i	0.838	< 0.001	60.7	75.7%	70.7%
Vco_2i/Vo_2i	0.803	< 0.001	0.90	75.7%	77.2%

AUC = area under the curve; Do_2i/Vco_2i = oxygen delivery indexed/ carbon dioxide elimination indexed; Vco_2i = carbon dioxide elimination indexed; Vco_2i/Vo_2i = respiratory quotient.

Ranucci 2006

Ranucci 2006
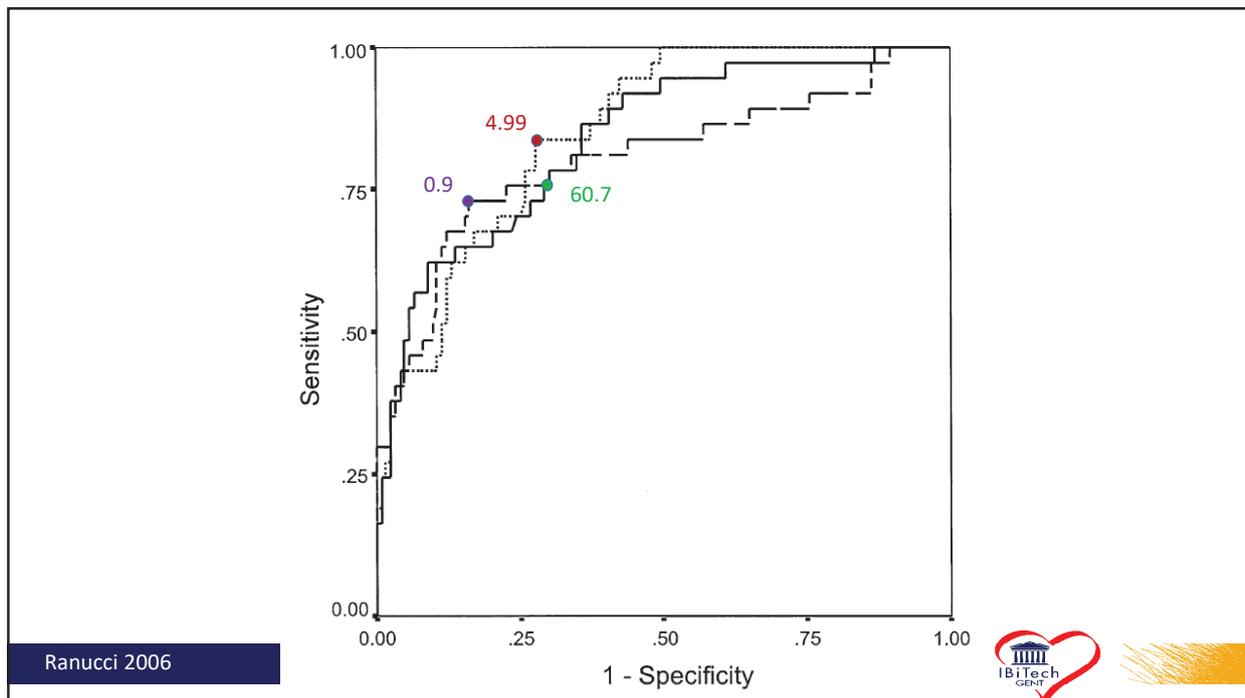
CO$_2$ can be measured in real time
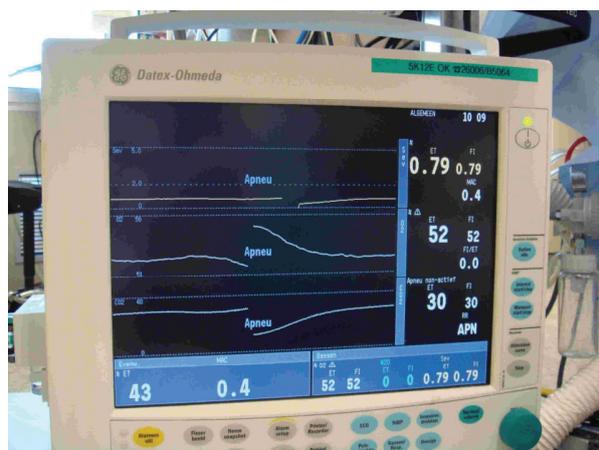
CO$_2$ production

$$VCO_2 = Q_{gas} \cdot \frac{e_{CO2}}{P_{baro}}$$

Capnography: potential problems
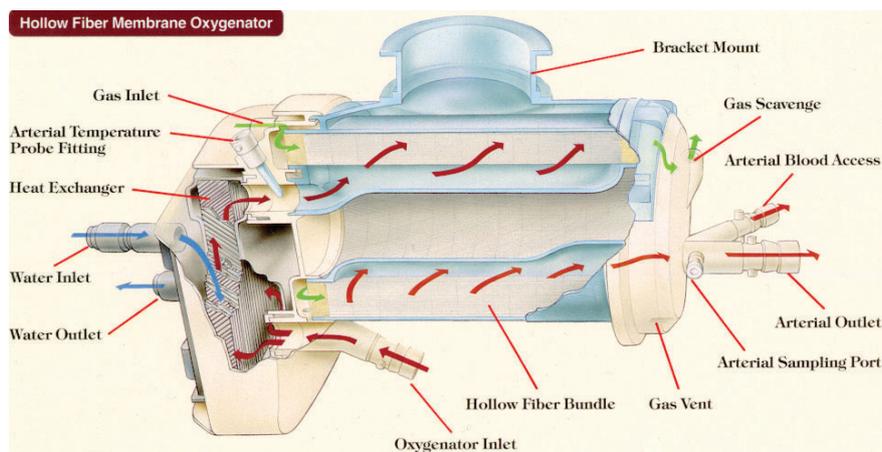
Capnography oxygenator exhaust
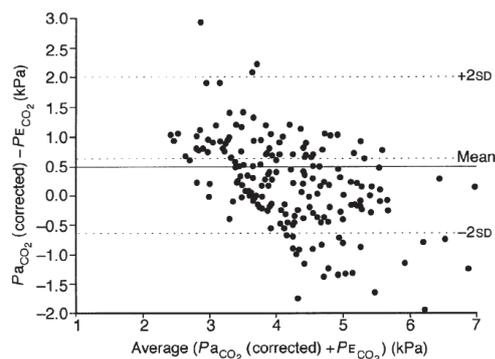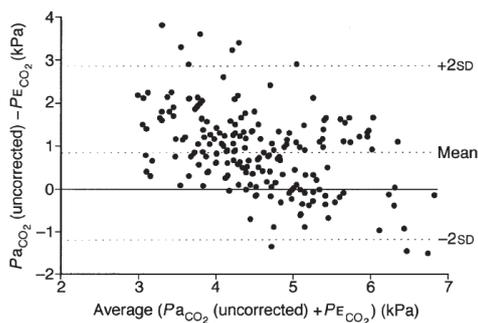
O'Leary 1999

Capnography oxygenator exhaust
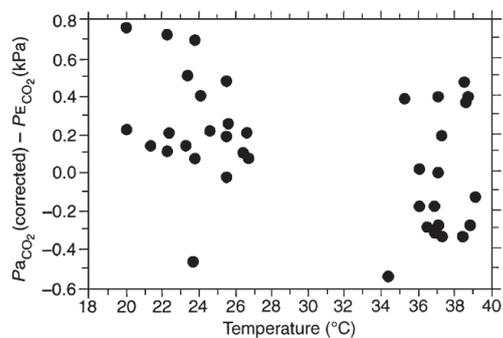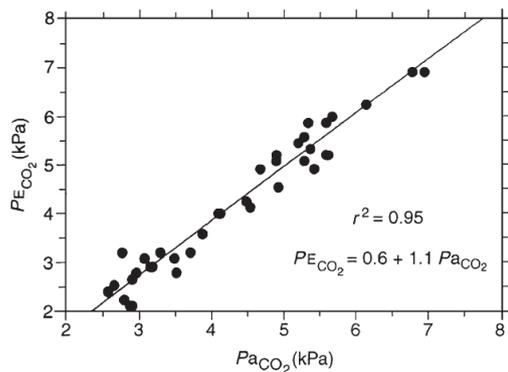
Weightman 1999

- ATP: Ambient Temperature Pressure (room air)
- ATPS: Ambient Temperature Pressure Saturated (H_2O)
- BTPS: Body Temperature Pressure Saturated (H_2O)
- STPD: Standard Temperature (0°C), Pressure (1ATM), Dry

Gas laws

$$P_1 \cdot \frac{V_1}{T_1} = P_2 \cdot \frac{V_2}{T_2} \rightarrow \frac{P_2 \cdot T_1 \cdot V_2}{T_2 \cdot V_1}$$

$$V_{STPD} := \frac{\left(P_{baro} - P_{H2O}\right) \cdot 273.15K}{P_{baro} \cdot \left(T_{art}\right)} = 0.826$$

T_{art} in K

Water vapor and temperature
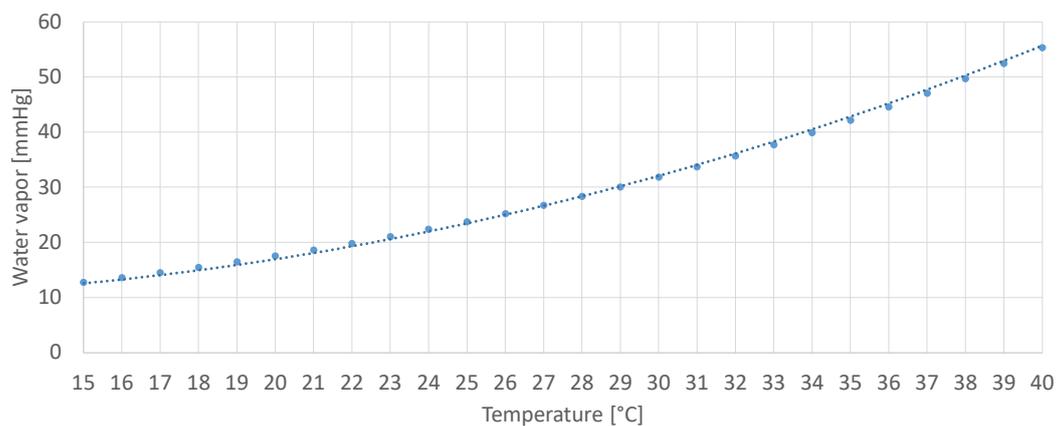
Conversion ATPS to STPD
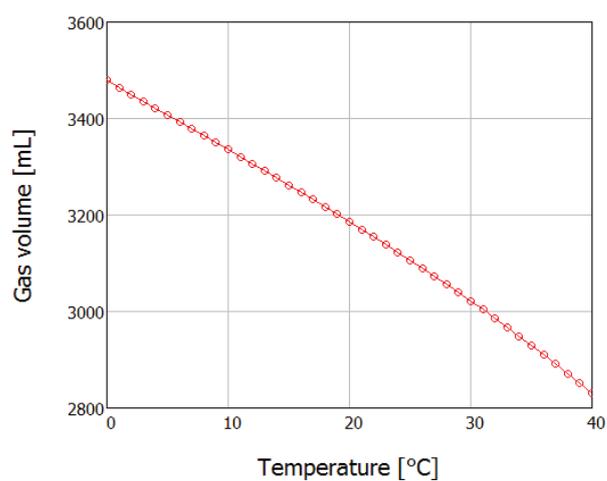
Example

- eCO_2 = 36 mmHg/760 mmHg = 4.7%
- Q_{gas} = 3000 mL/min
- $P_{barometric}$ = 760 mmHg
- T_{art} = 20°C
- BSA = 2 m²

ATPS versus STPD

Bar chart: VCO$_{2i}$ [mL/min/m²] vs temperature (20°C, 30°C, 35°C, 37°C). CO2: 71, 71, 71, 71. CO2 corrected: 65, 61, 59, 59.
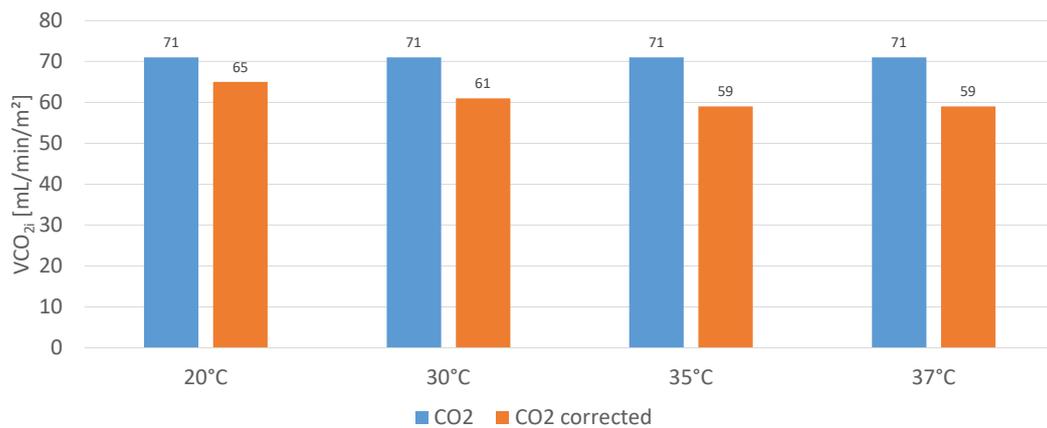
for venous return. Lowest core body temperature during CPB varied from 27°C to 37°C as requested by the surgeon. Body temperature was measured at the naso-pharingeal site and at the rectal site. This last tempera-ture was considered for correcting the values of blood gas analyses. The perfusate temperature was measured at the oxygenator site and used for correcting the values of exhaled carbon dioxide. Antegrade intermittent cold

mm Hg. The gas flow was initially settled at 50% oxygen to air ratio and a 1:2 flow ratio with the pump flow indexed, and subsequently arranged in order to maintain an arterial oxygen tension greater than 150 mm Hg and an arterial carbon dioxide tension between 33 and 38 mm Hg.

Do NOT treat PaCO$_2$
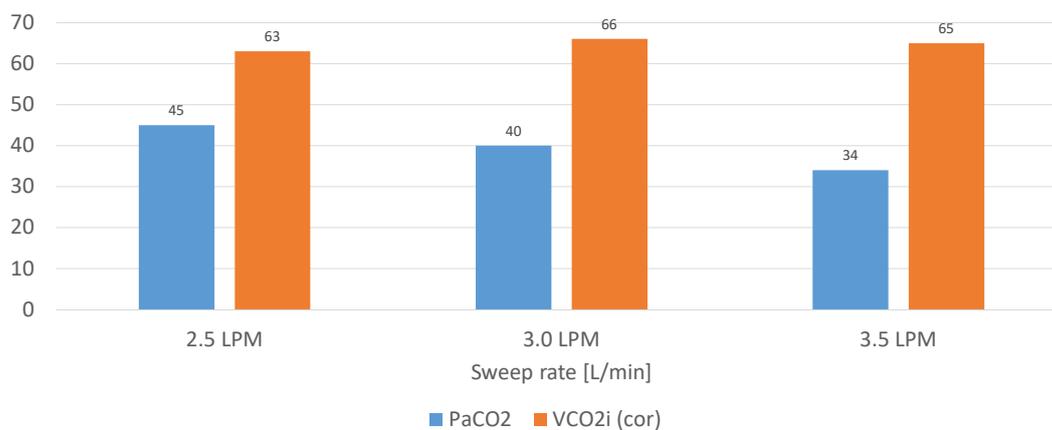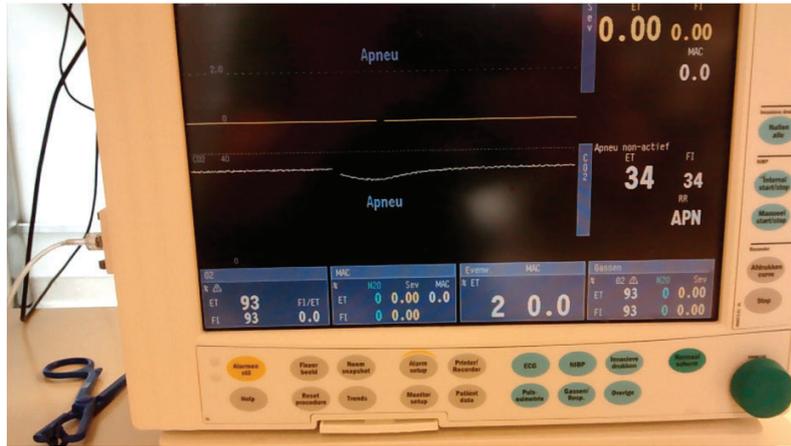
Bar chart of PaCO2 and VCO2i (cor) values by sweep rate [L/min]:
- 2.5 LPM: PaCO2 = 45, VCO2i (cor) = 63
- 3.0 LPM: PaCO2 = 40, VCO2i (cor) = 66
- 3.5 LPM: PaCO2 = 34, VCO2i (cor) = 65

Sweep rate [L/min]

Scavenging of volatile anesthetics and capnography

Scavenging of volatile anesthetics and capnography
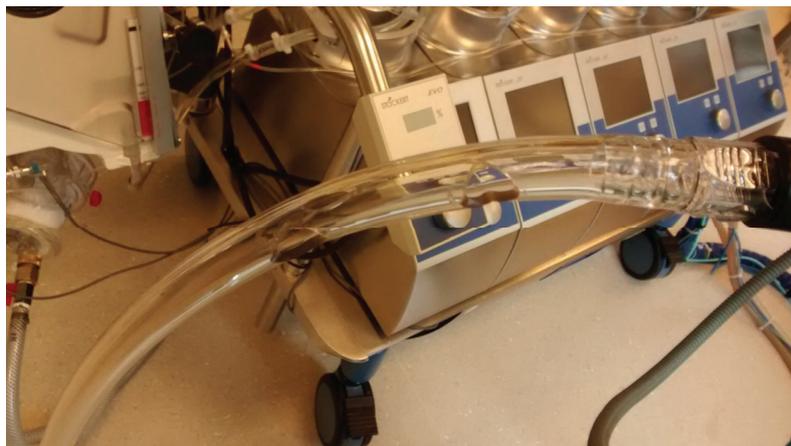
Scavenging of volatile anesthetics and capnography
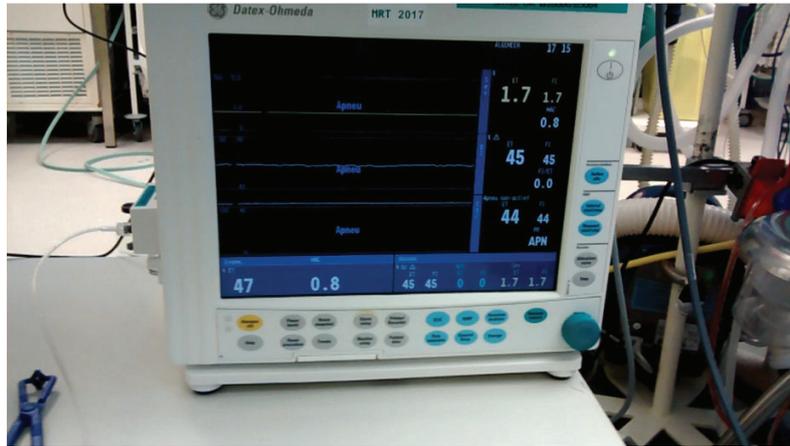
Calculation DO_2 and VCO_2

$Hb = 8 \frac{gm}{dL}$	Hemoglobin concentration
$cte = 1.34 \frac{mL}{gm}$	Maximum transport capacity hemoglobin
$SaO_2 = 99\%$	Arterial oxygen saturation
$CO = 5 \frac{L}{min}$	cardiac output or pump flow
$k_{blood} = 3.666 \cdot 10^{-5} \frac{mL}{mmHg \cdot mL}$	oxygen solubility in blood
$PaO_2 = 150 mmHg$	Partial oxygen tension

$$DO_2 = \left[\left(Hb \cdot cte \cdot SaO_2 \right) + \left(PaO_2 \cdot k_{blood} \right) \right] \cdot CO = 558 \frac{mL}{min}$$

$$V_{gas} = 2\,\frac{L}{min}$$
Gas flow

$$e_{CO2} = 40\,mmHg$$
Oxygenator exhaust CO_2

$$P_{baro} = 760\,mmHg$$
Barometric pressure

$$V_{CO2} = V_{gas} \cdot \frac{e_{CO2}}{P_{baro}} = 105\,\frac{mL}{min}$$
Uncorrected VCO_2

$$P_{H2O} = 39.9\,mmHg$$
Water vapor tension @ T_{blood}

$$T_{blood} = 34\,°C$$
Arterial blood temperature

$$V_{STPD} = \frac{(P_{baro} - P_{H2O}) \cdot 273.15K}{P_{baro} \cdot (T_{blood})} = 0.843$$
Conversion to STPD, CAVE T_{blood} is converted to K (°C + 273.15)

$$V_{CO2c} = V_{CO2} \cdot V_{STPD} = 89\,\frac{mL}{min}$$
Corrected VCO_2

$$\frac{DO_2}{V_{CO2c}} = 6.3$$

Oxygenation

$$Hb = 80\,\frac{gm}{L}$$
$$Q_{Blood} = 4.5\,\frac{L}{min}$$
$$BSA = 1.8\,m^2$$

$$SaO_2 = 99\%$$
$$PaO_2 = 150\,mmHg$$
$$k_{Blood} = 3.666 \cdot 10^{-5}\,\frac{mL}{mmHg \cdot mL}$$

CO_2

$$Q_{gas} := 2\,\frac{L}{min}$$
$$e_{CO2} := 40\,mmHg$$
$$P_{Baro} := 760\,mmHg$$

$$T_{Blood} := 34\,°C$$
$$P_{H2O} = 39.9\,mmHg$$

Spectrum

$$DO2_{M4} = \frac{\left(Hb \cdot 1.34\,\frac{mL}{gm} \cdot SaO_2\right) \cdot Q_{Blood}}{BSA} = 265 \cdot \frac{mL}{min}{m^2}$$

$$V_{CO2\_M4} = \frac{Q_{gas} \cdot \frac{e_{CO2}}{P_{Baro}}}{BSA} = 58 \cdot \frac{mL}{min}{m^2}$$

$$\frac{DO2_{M4}}{V_{CO2\_M4}} = 4.537$$

Connect

$$DO2_{Connect} = \frac{\left[\left(Hb \cdot 1.36\,\frac{mL}{gm} \cdot SaO_2\right) + (PaO_2 \cdot k_{Blood})\right] \cdot Q_{Blood}}{BSA} = 283 \cdot \frac{mL}{min}{m^2}$$

$$V_{CO2\_Connect} = \frac{\frac{(P_{Baro} - P_{H2O}) \cdot 273.15K}{P_{Baro} \cdot T_{Blood}} \cdot Q_{gas} \cdot \frac{e_{CO2}}{P_{Baro}}}{BSA} = 49.276 \cdot \frac{mL}{min}{m^2}$$

$$\frac{DO2_{Connect}}{V_{CO2\_Connect}} = 5.744$$

Develop an algorithm

DO_2/VCO_2 ratio <5

↓

Augment pump flow

Increase Hb content

Decrease T, check anesthesia level

CRITICAL CARE

RESEARCH   Open Access

O_2 delivery and CO_2 production during cardiopulmonary bypass as determinants of acute kidney injury: time for a goal-directed perfusion management?

Filip de Somer[1], John W Mulholland[2], Megan R Bryan[2], Tommaso Aloisio[3], Guido J Van Nooten[1] and Marco Ranucci[3*]

Abstract

Introduction: Acute kidney injury (AKI) is common after cardiac operations. There are different risk factors or determinants of AKI, and some are related to cardiopulmonary bypass (CPB). In this study, we explored the association between metabolic parameters (oxygen delivery (DO_2) and carbon dioxide production (VCO_2)) during CPB with postoperative AKI.

Outcome	All cases N=354	DO2 < 280 mL/min/m² N= 181	DO2 ≥ 280 mL/min/m² N= 173	P
Any AKI	75 (21.2%)	54 (29.8%)	21 (12.1%)	0.001
AKI stage 1	31 (8.8%)	23 (12.7%)	8 (4.6%)	0.007
AKI stage 2-3	44 (12.4%)	31 (17.1%)	13 (7.5%)	0.006

Goal Directed Perfusion:
What we know

- Patients who experience a nadir DO2 on CPB < 272 mL/min/m2 have a higher rate of AKI following cardiac surgery
- This information is coming from retrospective trials, and registries
- This is called «an association»

Goal Directed Perfusion:
What we don't know

- If we intentionally avoid low levels of DO2 through a GDP technique, will we be able to reduce the AKI rate?
- This is called «causative effect»
- To demonstrate that a strategy, a drug, a technique, is able to change the outcome, we need a RCT

GIFT

- Prospective, randomized, controlled trial
- Multicenter
- 10 Institutions in Europe, USA, New Zealand
- Co-ordinating Institution: IRCCS PSD
- Ethics Committee Approval at IRCCS PSD
- Registered at clinicaltrials.gov NCT02250131
- Centralized data collection at IRCCS PSD
- Statistical analysis at IRCCS PSD
- Spontaneous study with the external support of Sorin Group.
- Sorin Group shall provide resources for steering committee meetings and GDP monitor

The GDP Trial – protocol

CONTROL (N=350)	TREATMENT (N=350)
GDP monitor	GDP monitor
NO Blood prime (withdrawal)	NO Blood prime (withdrawal)
Priming volume and nature according to local standards	Priming volume and nature according to local standards
Perfusion targeted on BSA and °C	Perfusion targeted on DO2 > 280 mL/min/m2
Perfusion pressure according to local standards	Perfusion pressure according to local standards
Transfusion triggered by HCT according to local standards (<20%?)	Transfusion triggered by HCT < 21% and SVO2 < 68% and/or O2ER > 40%
Postoperative care according to local standards	Postoperative care according to local standards

GIFT
The GIFT investigators

DO2, VCO2, and DO2/VCO2 data adjudication

- NADIR DO2: maintained for at least 10 minutes (2 consecutive measures)
- Same for VCO2, and DO2/VCO2

GIFT
The GIFT investigators

PRIMARY ENDPOINT
CPB 1h-3hs

Example

- 45 y female
- 45 kg, 1.49 m²
- CI (2.4 LPM/m²) = 3.6
- Baseline Hb: 10.7 g/dL
- AVR + MVR

BSA [m²]	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49
Qblood [mL/min]	3600									
Ta [°C]	33									
PaO2 [mmHg]	128									
Hb [gm/dL]	10.7									
SaO_2 [%]	97.5									
PvO_2 [mmHg]	45.1									
SvO_2 [%]	76.1									
Qgas [mL/min]	1750									
eCO_2 [mmHg]	40									
VO2 [mL/min]	119.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_2 [mL/min]	503.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_{2i} [mL/min/m²]	338	0	0	0	0	0	0	0	0	0
VCO_2 [mL/min]	78.53	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
VCO_{2i} [mL/min]	52.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DO_{2i}/VCO_{2i}	6.4	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
Lactaat [mg/dL]	18.7									
Lactaat [mmol/L]	2.0757	0	0	0	0	0	0	0	0	0

BSA [m²]	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49
Qblood [mL/min]	3600	3600								
Ta [°C]	33	33								
PaO2 [mmHg]	128	180								
Hb [gm/dL]	10.7	8								
SaO_2 [%]	97.5	97.8								
PvO_2 [mmHg]	45.1	45								
SvO_2 [%]	76.1	76								
Qgas [mL/min]	1750	2000								
eCO_2 [mmHg]	40	40								
VO2 [mL/min]	119.71	99.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_2 [mL/min]	503.26	377.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_{2i} [mL/min/m²]	338	254	0	0	0	0	0	0	0	0
VCO_2 [mL/min]	78.53	89.74	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
VCO_{2i} [mL/min]	52.8	60.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DO_{2i}/VCO_{2i}	6.4	4.2	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
Lactaat [mg/dL]	18.7	20								
Lactaat [mmol/L]	2.0757	2.22	0	0	0	0	0	0	0	0

BSA [m²]	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	
Qblood [mL/min]	3600	3600	4200							
Ta [°C]	33	33	33							
PaO2 [mmHg]	128	180	168							
Hb [gm/dL]	10.7	8	8							
SaO_2 [%]	97.5	97.8	98							
PvO_2 [mmHg]	45.1	45	45							
SvO_2 [%]	76.1	76	80							
Qgas [mL/min]	1750	2000	2000							
eCO_2 [mmHg]	40	40	40							
VO2 [mL/min]	119.71	99.20	97.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_2 [mL/min]	503.26	377.43	441.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DO_{2i} [mL/min/m²]	338	254	296	0	0	0	0	0	0	0
VCO_2 [mL/min]	78.53	89.74	89.74	0.00	0.00	0.00	0.00	0.00	0.00	0.00
VCO_{2i} [mL/min]	52.8	60.3	60.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DO_{2i}/VCO_{2i}	6.4	4.2	4.9	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
Lactaat [mg/dL]	18.7	20	20							
Lactaat [mmol/L]	2.0757	2.22	2.22	0	0	0	0	0	0	0

BSA [m²]	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49
Qblood [mL/min]	3600	3600	4200	4300	4300	4300	4300			
Ta [°C]	33	33	33	33	33	33	34			
PaO2 [mmHg]	128	180	168	175	200	176				
Hb [gm/dL]	10.7	8	8	8.2	8.3	8.4	8.5			
SaO_2 [%]	97.5	97.8	98	98	98	97	98			
PvO_2 [mmHg]	45.1	45	45	45	43	45	40			
SvO_2 [%]	76.1	76	80	82	80	81	79			
Qgas [mL/min]	1750	2000	2000	1750	1750	1750	1750			
eCO_2 [mmHg]	40	40	40	40	38	36	47			
VO2 [mL/min]	119.71	99.20	97.06	92.93	103.81	98.10	111.19	0.00	0.00	0.00
DO_2 [mL/min]	503.26	377.43	441.24	463.03	468.68	469.49	479.97	0.00	0.00	0.00
DO_{2i} [mL/min/m²]	338	254	296	311	315	315	323	0	0	0
VCO_2 [mL/min]	78.53	89.74	89.74	78.53	74.60	70.67	91.68	0.00	0.00	0.00
VCO_{2i} [mL/min]	52.8	60.3	60.3	52.8	50.1	47.5	61.6	0.0	0.0	0.0
DO_{2i}/VCO_{2i}	6.4	4.2	4.9	5.9	6.3	6.6	5.2	#DIV/0!	#DIV/0!	#DIV/0!
Lactaat [mg/dL]	18.7	20	20	17						
Lactaat [mmol/L]	2.0757	2.22	2.22	1.887	0	0	0	0	0	0

BSA [m²]	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49
Qblood [mL/min]	3600	3600	3600	3600	3600	3600	3600			
Ta [°C]	33	33	33	33	33	33	34			
PaO2 [mmHg]	128	180	168	175	176	200	176			
Hb [gm/dL]	10.7	8	8	8.2	8.3	8.4	8.5			
SaO₂ [%]	97.5	97.8	98	98	98	97	98			
PvO₂ [mmHg]	45.1	45	45	45	43	45	40			
SvO₂ [%]	76.1	76	80	82	80	81	79			
Qgas [mL/min]	1750	2000	2000	2000	2000	2000	2000			
eCO₂ [mmHg]	40	40	40	40	38	36	47			
VO2 [mL/min]	119.71	99.20	83.19	77.80	86.91	82.13	93.09	0.00	0.00	0.00
DO₂ [mL/min]	503.26	377.43	378.20	387.66	392.38	393.06	401.84	0.00	0.00	0.00
DO₂ᵢ [mL/min/m²]	338	254	254	260	264	264	270	0	0	0
VCO₂ [mL/min]	78.53	89.74	89.74	89.74	85.26	80.77	104.78	0.00	0.00	0.00
VCO₂ᵢ [mL/min]	52.8	60.3	60.3	60.3	57.3	54.3	70.4	0.0	0.0	0.0
DO₂/VCO₂ᵢ	6.4	4.2	4.2	4.3	4.6	4.9	3.8	#DIV/0!	#DIV/0!	#DIV/0!
Lactaat [mg/dL]	18.7	20	20	17						
Lactaat [mmol/L]	2.0757	2.22	2.22	1.887	0	0	0	0	0	0

Importance of time

57

45 y.o. female, 45 Kg., 1.49 m^2
2.4 CI = 3.58 LPM, AVR MVR, Sorin Inspire™ 6
Baseline Hgb = 10.7

Time	BQ	RQ	Temp	SvO$_2$	HCT	DO$_2$i	VO$_2$	VO$_2$i/DO$_2$i	DO$_2$/VCO$_2$	VCO$_2$i
5	3.64	99	35.2	88	24	299	79.4	18.3	4.8	61.9
25	3.51	98					75.5	19	4.8	57.5
40	3.69	103					73.4	16.8	6.6	46
45	3.59	100					79.8	19	6.5	44.4
70	3.6	100					72.5	18	5.8	47.6
100 *	3.9	109					103	25.5	4.6	60.3
120	3.9	109					126.2	27	4.8	64.2
140	4	112	36.5	78	24	328	94.3	19.3	7.5	43.5

AKI Score

Pre-op creatinine = 1.07 mmol/l

Peak post creatinine = 0.77 mmol/l

* 1 unit PRBC at 110 minutes, low volume , absolute Hgb trigger reached

IBiTech GENT

---

35 y.o. male, 136 Kg., 2.55 m^2, BMI = 45
2.4 CI = 6.1 LPM, IBW = 75 Kg, IBSA = 1.9, Ideal 2.4 CI = 4.56 LPM
Redo PVR RVOT repair, Baseline Hgb = 12 g/dL

Time	BQ	RQ				VO$_2$	VO$_2$i/DO$_2$	DO$_2$/VCO$_2$	VCO$_2$i
5	4.6	0.75				5	17	6.1	43
30	5.0	0.82				1	15.4	6.9	41
60	5.0	0.82				8	13.2	6.8	44
90	5.2	0.85				2	16.3	6.4	46
125	5.0	0.82				2	18.4	5.4	52

AKI Score

Pre-op creatinine = 0.97 mmol/l

Peak post creatinine = 1.12 mmol/l

IBiTech GENT

73 y.o female, 61 Kg. critical AS, baseline HCT 27%, CBF Risk
Q_b 100% = 3.72 LPM , BSA = 1.55 M^2
MAP goal > 70 mmHg

Time	Q_b	T	Hct	DO_{2i}	VO_{2i}	VCO_{2i}	$\frac{DO_{2i}}{VCO_{2i}}$	$\frac{VCO_{2i}}{VO_{2i}}$	SVR
3	4.4	36						1.08	1572
9	4.4	34						1.20	1290
33	4.2	32						1.36	1314
63	3.77	32						1.52	1633
67	4.12	34						1.31	1430
79	4.3	35						0.99	1302
82	4.4	36	23	308	117	73	4.2	0.97	1204
93	4.62	36	24	324	113	60	5.4	0.83	1043
109	4.42	36.5	26	340	102	57	5.9	0.87	1170

AKI Score

Pre-op creatinine = 0.86 mmol/l

Peak post creatinine = 1.11 mmol/l

VO2 / VCO2i

Why does it not always work?

What we need is a multivariate online analysis of risk during cardiopulmonary bypass *Charles Wildevuur*

Which parameters?

Effect of mean arterial pressure, haemoglobin and blood transfusion during cardiopulmonary bypass on post-operative acute kidney injury

Michael Haase[1,2], Rinaldo Bellomo[3], David Story[4], Angela Letis[4], Katja Klemz[1], George Matalanis[5], Siven Seevanayagam[5], Duska Dragun[1], Erdmann Seeliger[6], Peter R. Mertens[2] and Anja Haase-Fielitz[2]
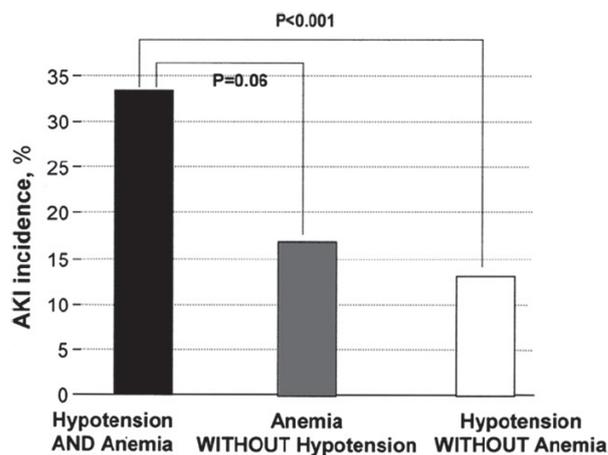
[1]Department of Nephrology and Intensive Care, Charité—University Medicine Berlin, Berlin, Germany, [2]Department of Nephrology and Hypertension & Endocrinology and Metabolic Diseases, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany, [3]Department of Intensive Care, Austin Health, Melbourne, Australia, [4]Department of Anaesthesiology, Austin Health, Melbourne, Australia, [5]Department of Cardiac Surgery, Austin Health, Melbourne, Australia and [6]Institute of Vegetative Physiology, Charité—University Medicine Berlin, Berlin, Germany

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Variable	AKI ($N = 179$)	No AKI ($N = 741$)	P univariate	Adjusted OR (95% CI)	P multivariate
Model 0					
AKICS Score, points [3][b]	5.8 (3.9–8.1)	4.3 (2.6–6.3)	<0.001	1.09 per point increase (1.04–1.15)	<0.001
Emergency[c]	25 (13.8%)	22 (3.1%)	<0.001	4.36 (2.31–8.22)	<0.001
Return to operating room, n	34 (19.0%)	52 (7.0%)	<0.001	2.74 (1.68–4.49)	<0.001
Atrial fibrillation, n	47 (26.3%)	69 (9.3%)	<0.001	2.66 (1.69–4.17)	<0.001
Intra-aortic balloon pump, n	19 (10.6%)	25 (3.4%)	<0.001	1.27 (0.61–2.66)	0.521
Intraoperative variables added to Model 0					
Haemoglobin concentration, g/dL[d]					
Median[e]	8.1 (7.4–9.3)	8.7 (7.7–9.7)	<0.001	1.18 per g/dL decrease (1.02–1.34)	0.028
Lowest[e]	7.4 (6.4–8.6)	8.2 (7.0–9.3)	<0.001	1.16 per g/dL decrease (1.03–1.31)	0.018
Variability, %[e]	1.2 (0.6–2.2)	0.9 (0.5–1.5)	<0.001	1.10 per % increase (0.94–1.28)	0.239
Arterial O_2 content, mL/dL[d]					
Median[e]	12.2 (11.2–13.9)	13.0 (11.6–14.4)	<0.001	1.13 per mL/dL decrease (1.02–1.26)	0.027
Lowest[e]	10.9 (9.6–12.5)	12.0 (10.4–13.5)	<0.001	1.11 per mL/dL decrease (1.02–1.22)	0.018
Variability, %[e]	1.7 (0.8–3.0)	1.2 (0.7–2.1)	<0.001	1.07 per % increase (0.96–1.20)	0.241
SaO_2, %	99.7 (99.6–99.8)	99.7 (99.6–99.8)	0.949	N/A	N/A
PaO_2, mmHg	324 (274–385)	319 (272–375)	0.543	N/A	N/A
Red blood cell transfusion, mL[d]	750 (500–1000)	500 (250–750)	<0.001	1.001 per mL (1.000–1.002)	0.013
Vasopressors					
Metaraminol, mg	3.5 (1.9–6.5)	3.5 (1.5–6.0)	0.852	N/A	N/A
Phenylephrine, mg	4.9 (2.2–8.5)	2.3 (1.3–4.5)	0.007	1.05 (0.95–1.16)	0.334
MAP, mmHg					
Median[e]	68.5 (64.0–73.0)	68.0 (64.0–73.0)	0.841	N/A	N/A
Lowest[e]	31.0 (25.0–36.0)	32.0 (25.5–36.5)	0.554	N/A	N/A
Variability, %[e]	16.7 (14.1–19.7)	17.0 (14.3–19.6)	0.390	N/A	N/A
AUC MAP, min × mmHg					
<50 mmHg[e]	0.32 (0.13–0.66)	0.37 (0.17–0.69)	0.304	N/A	N/A
<60 mmHg[e]	1.49 (0.86–2.68)	1.51 (0.93–2.58)	0.673	N/A	N/A
<70 mmHg[e]	5.27 (3.55–7.46)	5.17 (3.51–7.38)	0.986	N/A	N/A

Bar chart: AKI incidence, % vs three groups (Hypotension AND Anemia ~33%, Anemia WITHOUT Hypotension ~17%, Hypotension WITHOUT Anemia ~13%). P<0.001 (overall), P=0.06.

Circulation

ORIGINAL RESEARCH ARTICLE

High-Target Versus Low-Target Blood Pressure Management During Cardiopulmonary Bypass to Prevent Cerebral Injury in Cardiac Surgery Patients
A Randomized Controlled Trial

Editorial, see p 1781

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BACKGROUND: Cerebral injury is an important complication after cardiac surgery with the use of cardiopulmonary bypass. The rate of overt stroke after cardiac surgery is 1% to 2%, whereas silent strokes, detected by diffusion-weighted magnetic resonance imaging, are found in up to 50% of patients. It is unclear whether a higher versus a lower blood pressure during cardiopulmonary bypass reduces cerebral infarction in these patients.

METHODS: In a patient- and assessor-blinded randomized trial, we allocated patients to a higher (70–80 mm Hg) or lower (40–50 mm Hg) target for mean arterial pressure by the titration of norepinephrine during cardiopulmonary bypass. Pump flow was fixed at 2.4 L·min⁻¹·m⁻². The primary outcome was the total volume of new ischemic cerebral lesions (summed in millimeters cubed), expressed as the difference between diffusion-weighted imaging conducted preoperatively and again postoperatively between days 3 and 6. Secondary outcomes included diffusion-weighted imaging–evaluated total number of new ischemic lesions.

	Low-Target Group (n=99)	High-Target Group (n=98)
Age, y	65.0±10.7	69.4±8.9
Male sex, n (%)	93 (93.9)	84 (85.7)
Nonwhite race, n (%)	2 (2.0)	0 (0)
Previous myocardial infarction, n (%)*	37 (37.4)	37 (37.8)
Recent myocardial infarction (past 2 wk), n (%)	30 (30.3)	25 (25.5)
Aortic valvular disease, n (%)	34 (34.3)	34 (34.7)
Angina, CCS score >1, n (%)†	64 (64.6)	47 (48.0)
Current or previous atrial fibrillation, n (%)	14 (14.1)	13 (13.3)
Hypertension, n (%)	83 (84.8)	87 (88.8)
Diabetes mellitus, type 1 or 2 (insulin treated), n (%)	10 (10.1)	10 (10.2)
Diabetes mellitus, type 2 (non–insulin treated), n (%)	14 (14.1)	14 (14.3)
Chronic lung disease, n (%)	9 (9.1)	12 (12.2)
Current smoker, n (%)	18 (18.2)	15 (15.3)
Current alcohol abuse, n (%)	7 (7.1)	7 (7.1)
BMI, kg/m^2‡	27.0 (3.8)	27.6 (4.0)
Left ventricular ejection fraction, n (%)		
>50%	54 (54.5)	50 (51.5)
35%–50%	32 (32.3)	40 (41.2)
20%–34%	12 (12.1)	7 (7.2)
<20%	1 (1.0)	0 (0)

	Low-Target Group (n=98)	High-Target Group (n=97)
Hematocrit, before start of surgery, %	40.3±5.9	40.6±4.7
MAP before anesthesia induction, mmHg	92.3±15.7	96.9±13.4
MAP during bypass, mmHg	44.7±4.7	66.8±4.9
MAP below target during bypass, n (%)*	2 (2.0)	18 (18.5)
MAP above target during bypass, n (%)†	5 (5.1)	0 (0)
Blood flow rate during bypass, L·min^{-1}·m^{-2}	2.69±0.1	2.69±0.1
Hematocrit, mean level during bypass, %	31.5±3.8	33.1±4.2
Nadir hematocrit sampling value during bypass, %	28.7±3.7	29.2±4.0
Surgery time, min	184.9±50.8	194.3±66.6
Bypass time, min	94.0±33.0	105.6±77.4
Cross-clamp time, min‡	63.3±26.9	64.8±32.6
Peak lactate level during surgery, mmol	2.25±0.83	2.16±0.82
Norepinephrine infused in the OR, µg/kg	2.65±6.01	17.43±20.14
Patients receiving norepinephrine in the OR, n (%)	35 (35.7)	90 (92.7)

MAP: high vs low

	Low-Target Group, n		High-Target Group, n		Difference (95% CI)	OR (95% CI)	P Value
Primary outcome							
Total volume of new cerebral lesions, mm^3							
Complete cases, median (IQR)	89	25 (0 to 118)	80	29 (0 to 143)	0 (−25 to 0.028)*		0.41
Excluding 3 outliers, median (IQR)	88	24 (0 to 118)	78	28 (0 to 134)			
Complete cases, mean (SD)	89	415 (2682)	80	488 (2539)	8 (−978 to 994)†		0.99‡
Excluding 3 outliers, mean (SD)	88	133 (313)	78	144 (265)			
Secondary outcome							
Total number of new cerebral lesions							
Complete cases, median (IQR)	89	1 (0 to 2)	80	1 (0 to 2)	0 (0 to 0)*		0.54
Complete cases, mean (SD)	99	1.82 (3.62)	98	2.25 (4.41)	0.23 (−0.99 to 1.46)†		0.71‡
Patients with new infarcts in watershed border zones, n (%)§	89	32 (36.0)	80	33 (41.3)			0.49
Stroke, n (%)		1 (1.1)		6 (7.0)		6.64 (0.78 to 310.75)	0.06
Symptoms on awakening	97	0	92	4			
Symptom onset between days 2 and 30	97	1	92	2			
POCD, n (%)							
At 7 d	91	21 (23.1)	78	27 (34.6)		1.76 (0.90 to 3.47)	0.12
At 90 d	89	8 (9.0)	75	5 (6.7)		0.72 (0.23 to 2.31)	0.77

MAP: high vs low

	Low-Target Group	High-Target Group	OR (95% CI)	P Value
Length of stay in ICU, h, median (IQR)	21 (20–26)	21 (19–22)		0.82
ICU stays >36 h, n (%)	11 (11.5)	12 (12.6)	1.12 (0.42–2.97)	0.82
Lactate, peak value at POD 1, mmol	2.61±1.17	2.90±1.70		0.16
Inotropes >24 h, n (%)	4 (4.1)	10 (10.4)	2.72 (0.75–12.32)	0.10
Vasopressors >24 h, n (%)	3 (3.1)	10 (10.4)	3.66 (0.90–21.37)	0.05
Time to extubation, h, median (IQR)	4.6 (2.9–6.7)	4.6 (3.2–7.9)		0.43
Atrial fibrillation, n (%)	49 (49.5)	52(53.1)	1.18 (0.65–2.16)	0.57
Creatinine, peak value, mmol/L	118.0±47.4	121.9±48.6		0.57
Creatinine, doubling of baseline value, n (%)	2 (2.0)	9 (9.4)	4.93 (1.02–48.12)	0.03
Hallucinations or delirium, n (%)*	7 (7.1)	10 (10.5)	1.53 (0.50–4.95)	0.45
Length of stay in cardiac surgery ward, d	6 (5–8)	6 (5–7.75)		0.92

MAP as an absolute goal

A: After initiation of CPB without haemodynamic

B: during pressure increase with phenylephrine 20 mm Hg

C: after discontinuation of phenylephrine

Maier 2009

Kanji *et al. Journal of Cardiothoracic Surgery* 2010, **5**:71
http://www.cardiothoracicsurgery.org/content/5/1/71

JCTS JOURNAL OF CARDIOTHORACIC SURGERY

RESEARCH ARTICLE   **Open Access**

Difference between pre-operative and cardiopulmonary bypass mean arterial pressure is independently associated with early cardiac surgery-associated acute kidney injury

Hussein D Kanji[1], Costas J Schulze[1,2], Marilou Hervas-Malo[3], Peter Wang[1], David B Ross[1,2], Mohamad Zibdawi[1,2,4], Sean M Bagshaw[2,3,4*]

Table 2 Summary of intra-operative variables stratified by post-operative CSA-AKI

Variable	No AKI (n = 92)	AKI (n = 65)	p-value
Valve only surgery (%)	26 (28.3)	12 (18.5)	0.16
Combined (valve + CABG) (%)	43 (46.7)	21 (32.3)	0.07
Re-operation (%)	8 (8.7)	6 (9.2)	0.91
# Grafts (mean [± SD])	3.4 ± 1.1	3.5 ± 1.1	0.77
Duration of CPB (min, mean [± SD])	126.6 ± 52	127.2 ± 63.2	0.69
Duration of cross clamp (min, mean [± SD])	90.9 ± 46.9	88.7 ± 57.1	0.42
Average CPB MAP (mmHg, mean [± SD])	57.8 ± 5.1	56.9 ± 4.9	0.25
Minutes <MAP 60 mmHg (median [± IQR])	59 ± 65	56 ± 45	0.49
Minutes <MAP 50 mmHg (median [± IQR])	2.5 ± 10	5.0 ± 15	0.35
Delta MAP (mmHg, mean [± SD])	28.0 ± 13.2	31.3 ± 13.8	0.10
PRBC transfusions (units, mean [± SD])	1.8 ± 1.5	2.4 ± 2.3	0.27
Patients transfused with PRBC (%)	23 (25)	19 (29.2)	0.56
Insulin dose (Units, mean [± SD])	3.3 ± 1.3	3.6 ± 3.1	0.72
Furosemide dose (mg, n = 9, n = 7, mean [± SD])	22.8 ± 10.3	27.1 ± 12.5	0.50
Ultrafiltration (mL, n = 34, n = 25, mean [± SD])	1440 ± 1049	1470 ± 1344	0.98
Received tranexamic acid (%)	83 (90.2)	58 (89.2)	0.84
Received aprotinin (%)	0 (0)	0 (0)	NS
Use of side-biting clamp (%)	16 (17.4)	21 (32.2)	0.03
Average flow (mL/kg/min, mean[± SD])	60.9 ± 7.1	55.5 ± 8.4	0.001
Average temperature (°C, mean [± SD])	35.3 ± 1.4	35.5 ± 1.1	0.75

Table 3 Univariate Factors associated with early CSA-AKI

| Predictor	Odds Ratio	95% CI	P-value
Male Sex	1.06	0.5-2.1	0.87
Age (per year)	1.01	0.99-1.04	0.25
Age ≥ 75 years (present)	1.7	0.8-3.5	0.15
BMI (kg/m^2)(per 1 point)	1.2	0.8-3.5	< 0.0001
BMI ≥25 kg/m^2 (present)	4.4	1.9-10.2	0.0007
Valve disease (present)	0.55	0.3-1.0	0.06
DM (present)	2.2	1.1-4.2	0.025
PVD (present)	1.9	0.9-3.3	0.19
HTN (present)	1.7	0.9-3.3	0.12
Delta MAP (per 1 mmHg)	1.02	0.99-1.04	0.14
Delta MAP ≥26 mmHg (present)	2.1	1.1-4.2	0.024
Flow ≥54 per mL/kg/min (present)	0.2	0.1-0.5	0.0002
pH	1.4	0.8-2.7	0.26
Pre-operative ACE inhibitor (present)	0.6	0.3-1.1	0.1
Valve Surgery (present)	0.5	0.3-1	0.07
Peak CPB-MAP	0.5	0.2-0.97	0.04
Pre-operative Systolic BP (≥111 mmHg)	2.1	0.99-4.6	0.05
Duration of CPB MAP ≤60 (per 1 min)	1.99	0.9-4.4	0.89
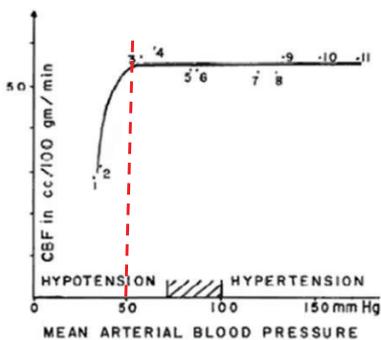
Cerebral Autoregulation

- Summarized results of 11 studies
- Plotted CBF versus MAP
- Manually drew line at 50 mmHg, lower limit of autoregulation

Quantification of autoregulation
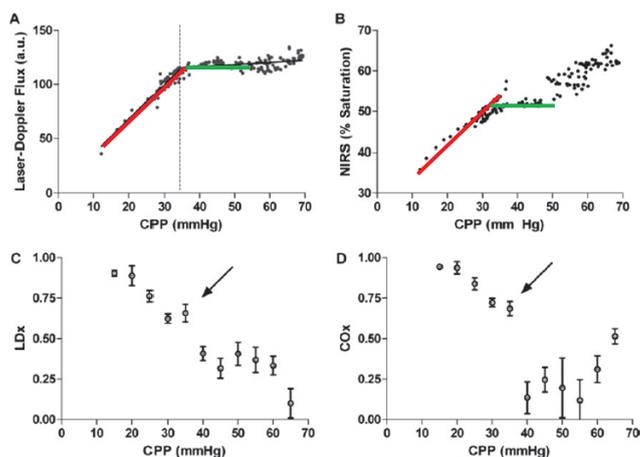
- When Cox approaches 1, autoregulation is disturbed.
  - COx > 0.30 -> no autoregulation
- When COx approaches 0, blood pressure is in the autoregulation range.
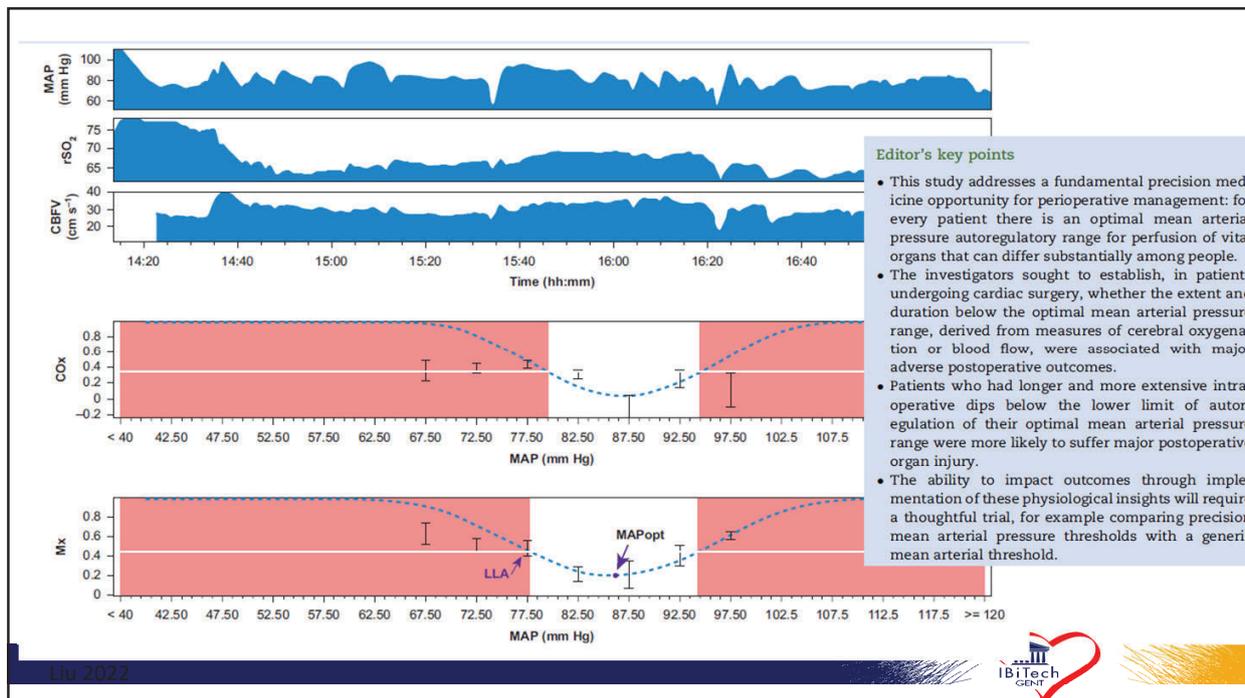 - COx < 0.30 -> cerebral autoregulation

Brady 2007

Comparison of different metrics of cerebral autoregulation in association with major morbidity and mortality after cardiac surgery

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Editor's key points

- This study addresses a fundamental precision medicine opportunity for perioperative management: for every patient there is an optimal mean arterial pressure autoregulatory range for perfusion of vital organs that can differ substantially among people.
- The investigators sought to establish, in patients undergoing cardiac surgery, whether the extent and duration below the optimal mean arterial pressure range, derived from measures of cerebral oxygenation or blood flow, were associated with major adverse postoperative outcomes.
- Patients who had longer and more extensive intraoperative dips below the lower limit of autoregulation of their optimal mean arterial pressure range were more likely to suffer major postoperative organ injury.
- The ability to impact outcomes through implementation of these physiological insights will require a thoughtful trial, for example comparing precision mean arterial pressure thresholds with a generic mean arterial threshold.
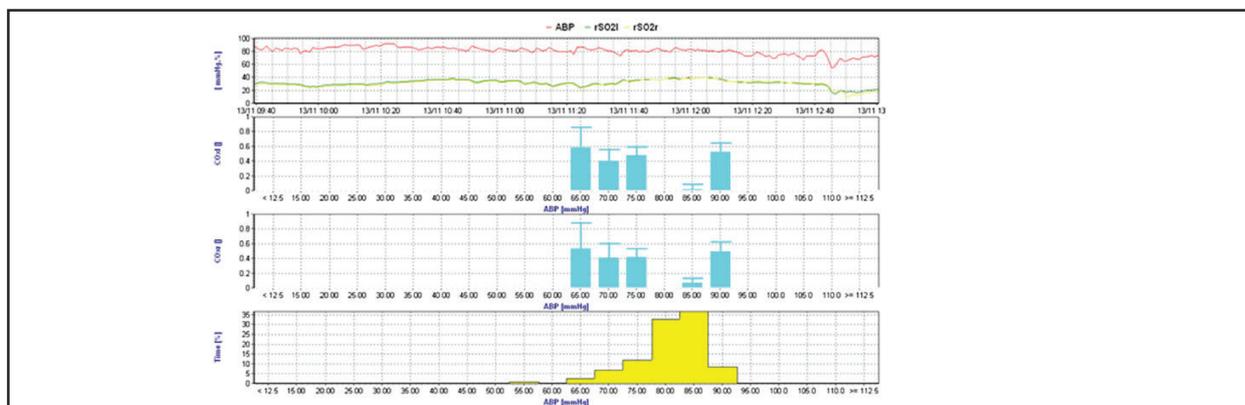
Liu 2022

TABLE 3. Specific complication rates for patients with major morbidity and mortality after surgery and relationship to duration and magnitude of mean arterial pressure below the lower limit of cerebral blood flow autoregulation measured with the cerebral oximetry index

Complication	Patients (n)	AUC$_{MAP<LLA}$ (mm Hg × min/h)		P value
		With complication	Without complication	
Stroke	18 (4.1)	20.2 ± 26.5	9.5 ± 9.3	.056
Renal failure	16 (3.6)	15.5 ± 12.7	9.7 ± 10.6	.030
Mechanical ventilation >48 h	31 (7.1)	16.5 ± 15.1	9.4 ± 10.2	<.001
Inotrope use >24 h or new IABP insertion	47 (10.8)	11.7 ± 13.1	9.7 ± 10.4	.108
Operative death	15 (3.4)	15.1 ± 19.1	9.8 ± 10.3	.081

Ono 2014

67

Autoregulation of the kidney
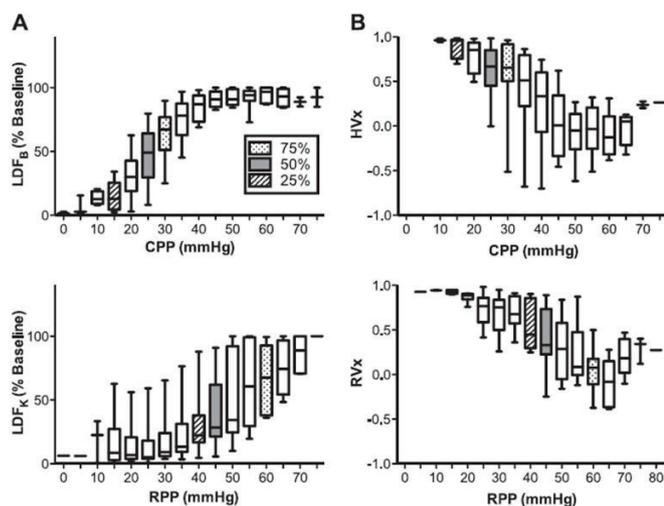
Rhee 2012

Influence of variations in systemic blood flow and pressure on cerebral and systemic oxygen saturation in cardiopulmonary bypass patients

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Editor's key points

- Maintenance of adequate tissue perfusion and oxygenation is important during anaesthesia.
- In patients undergoing cardiopulmonary bypass, the authors independently manipulated blood flow and systemic arterial pressure.
- Cerebral and systemic oxygenation were positively correlated with flow but not with pressure.

Background. Although both pressure and flow are considered important determinants of regional organ perfusion, the relative importance of each is less established. The aim of the present study was to evaluate the impact of variations in flow, pressure, or both on cerebral and whole-body oxygen saturation.

Methods. Thirty-four consenting patients undergoing elective cardiac surgery on cardiopulmonary bypass were included. Using a randomized cross-over design, four different haemodynamic states were simulated: (i) 20% flow decrease, (ii) 20% flow decrease with phenylephrine to restore baseline pressure, (iii) 20% pressure decrease with sodium nitroprusside (SNP) under baseline flow, and (iv) increased flow with baseline pressure. The effect of these changes was evaluated on cerebral (Sc_{O_2}) and systemic (Sv_{O_2}) oxygen saturation, and on systemic oxygen extraction ratio (OER). Data were assessed by within- and between-group comparisons.

Results. Decrease in flow was associated with a decrease in Sc_{O_2} [from 63.5 (7.4) to 62.0 (8.5) %, $P<0.001$]. When arterial pressure was restored with phenylephrine during low flow, Sc_{O_2} further decreased from 61.0 (9.7) to 59.2 (10.2) %, $P<0.001$. Increase in flow was associated with an increase in Sc_{O_2} from 62.6 (7.7) to 63.6 (8.9) %, $P=0.03$, while decreases in pressure with the use of SNP did not affect Sc_{O_2}. Sv_{O_2} was significantly lower ($P<0.001$) and OER was significantly higher ($P<0.001$) in the low flow arms.
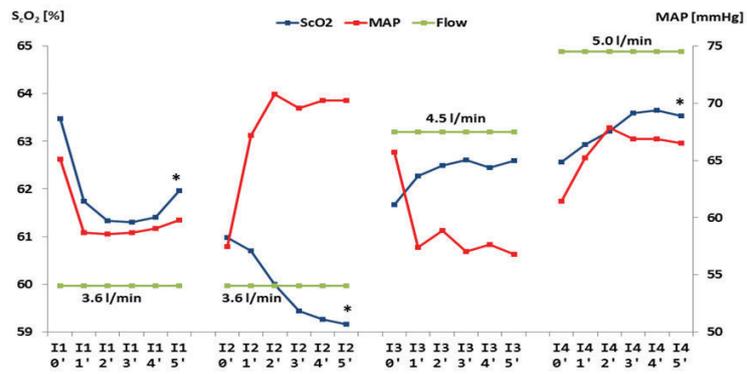
Conclusions. In the present elective cardiac surgery population, Sc_{O_2} and Sv_{O_2} were significantly lower with lower flow, regardless of systemic arterial pressure. Moreover, phenylephrine administration was associated with a reduced cerebral and systemic oxygen saturation.

Results

Analysis

Q_{blood} L/min	DO_{2i} mL/min/m²	VO_{2i} mL/min/m²	VO_{2i}/DO_{2i}
3.6 BL -20%	256	46	0.18
3.6 BL -20% + PE	256	46	0.18
4.5 BL+NSP=> -20%P	320	49	0.15
5.0 BL+20%=>MAP	356	47	0.13

Conclusion pressure vs flow

- Cerebral and venous oxygen saturations are more dependent on flow than on pressure

- Change in paradigm "pressure vs flow"
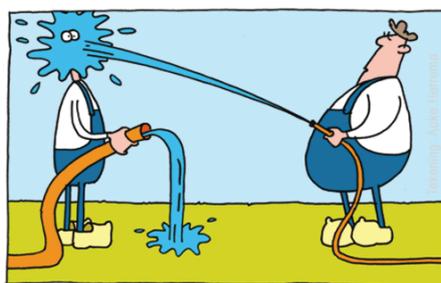
Original Manuscript

Perfusion

Perfusion
2022, Vol. 0(0) 1–9
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The multifactorial dynamic perfusion index: A predictive tool of cardiac surgery associated acute kidney injury

Marco Ranucci, Umberto Di Dedda, Mauro Cotza and Katherine Zamalloa Moreano

Abstract
Introduction: cardiac surgery associated acute kidney injury (CSA-AKI) has a number of preoperative and intraoperative risk factors. Cardiopulmonary bypass (CPB) factors have not yet been elucidated in a single multivariate model. The aim of this study is to develop a dynamic predictive model for CSA-AKI.
Methods: retrospective study on 910 consecutive adult cardiac surgery patients. Baseline data were used to settle a preoperative CSA-AKI risk model (static risk model, SRM); CPB related data were assessed for association with CSA-AKI. CPB duration, nadir oxygen delivery, time of exposure to a low oxygen delivery, nadir mean arterial pressure, peak lactates and red blood cell transfusion were included in a multivariate dynamic perfusion risk (DPR). SRM and DPR were merged into a final logistic regression model (multifactorial dynamic perfusion index, MDPI). The three risk models were assessed for discrimination and calibration.
Results: the SRM model had an AUC of 0.696 (95% CI 0.663–0.727), the DPR model of 0.723 (95% CI 0.691–0.753), and the MDPI model an AUC of 0.769 (95% CI 0.739–0.798). The difference in AUC between SRM and DPR was not significant ($p = 0.495$) whereas the AUC of MDPI was significantly larger than that of SRM ($p = 0.004$) and DPR ($p = 0.015$).
Conclusions: inclusion of dynamic indices of the quality of CPB improves the discrimination and calibration of the preoperative risk scores. The MDPI has better predictive ability than the existing static risk models and is a promising tool to integrate different factors into an advanced concept of goal-directed perfusion.

$$\text{SRM of AKI risk} = \frac{\exp(-1.079 + 0.079^*\text{CRS} + 0.035^*\text{Age} - 0.095^*\text{HCT})}{(1 + \exp[-1.079 + 0.079^*\text{CRS} + 0.035^*\text{Age} - 0.095^*\text{HCT}])}$$

Table 1. Logistic model parameter estimates, score points, and AUC for each risk factor included in the scoring model[a]

Risk Factor	Estimate (CI)	P Value	Points	AUC for Single Variable
Female gender	0.48 (0.21–0.75)	<0.001	1	55.3
Congestive heart failure	0.48 (0.20–0.76)	<0.001	1	63.9
Left ventricular ejection fraction <35%	0.39 (0.07–0.71)	0.016	1	56.4
Preoperative use of IABP	1.08 (0.49–1.67)	<0.001	2	52.6
COPD	0.70 (0.37–1.04)	<0.001	1	54.8
Insulin-requiring diabetes	0.40 (0.05–0.76)	0.026	1	54.4
Previous cardiac surgery	0.54 (0.28–0.81)	<0.001	1	57.5
Emergency surgery	1.13 (0.65–1.60)	<0.001	2	54.3
Surgery type				
valve only	0.45 (0.10–0.80)	0.013	1	63.3
CABG + Valve	0.86 (0.53–1.19)	<0.001	2	
other cardiac surgeries	1.02 (0.56–1.49)	<0.001	2	
Preoperative creatinine 1.2 to <2.1 mg/dl	0.92 (0.64–1.21)	<0.001	2	68.6
Preoperative creatinine ≥2.1 mg/dl	2.66 (2.28–3.04)	<0.001	5	

[a]CI, confidence interval; AUC, area under the receiver operating characteristic curve; IABP, intra-aortic balloon pump; COPD, chronic obstructive pulmonary disease.

**Table 2.** Cardiopulmonary bypass-related factors in AKI and non-AKI patients.

Item	AKI (N = 84)	Non-AKI (N = 746)	p
Nadir hematocrit (%)	26 (4.2)	28.6 (4.2)	0.001
Nadir oxygen delivery (ml min^{-1} m^{-2})	265 (52)	297 (46)	0.001
Time of exposure to critical oxygen delivery (min)	10.8 (12)	5.8 (10.8)	0.001
Pump flow (L/min/m^2)	2.21 (2.8)	2.29 (1.9)	0.016
Cardiopulmonary bypass duration (min)	132 (76)	95 (45)	0.001
Nadir mean arterial pressure (mmHg)	59.9 (9.3)	61.1 (8.9)	0.271
Use of norepinephrine	17 (20.2)	117 (15.7)	0.276
Peak lactates (mMol/L)	1.48 (1.42)	1.01 (0.4)	0.001
Red blood cell transfusion	22 (29.3)	53 (7.1)	0.001

Data are mean (standard deviation) or number (%). AKI: Acute kidney injury.

Thakar 2005

IBiTech GENT

$$\text{MDPI CSA} - \text{AKI risk} = \frac{\exp(-3.35 + 4.17^*\text{SRM} + 5.37^*\text{DPR})}{1 + \exp[-3.3 + 4.17^*\text{SRM} + 5.37^*\text{DPR}]}$$

Ranucci 2022

IBiTech GENT
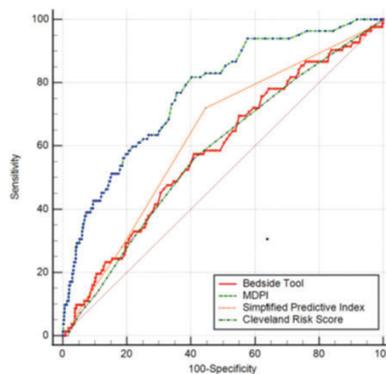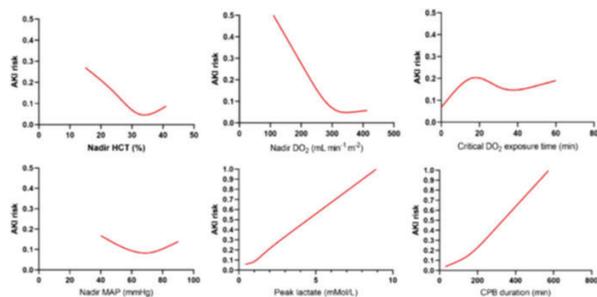
GDP and PIRO: static risk

- Male
- 60 years
- Hematocrit: 43%
- CABG

4.7%

- Female
- 60 years
- Hematocrit: 36%
- COPD
- Diabetes
- Isolate valve

11.6%

- Male
- 70 years
- Hematocrit: 40%
- EF: $< 35\%$
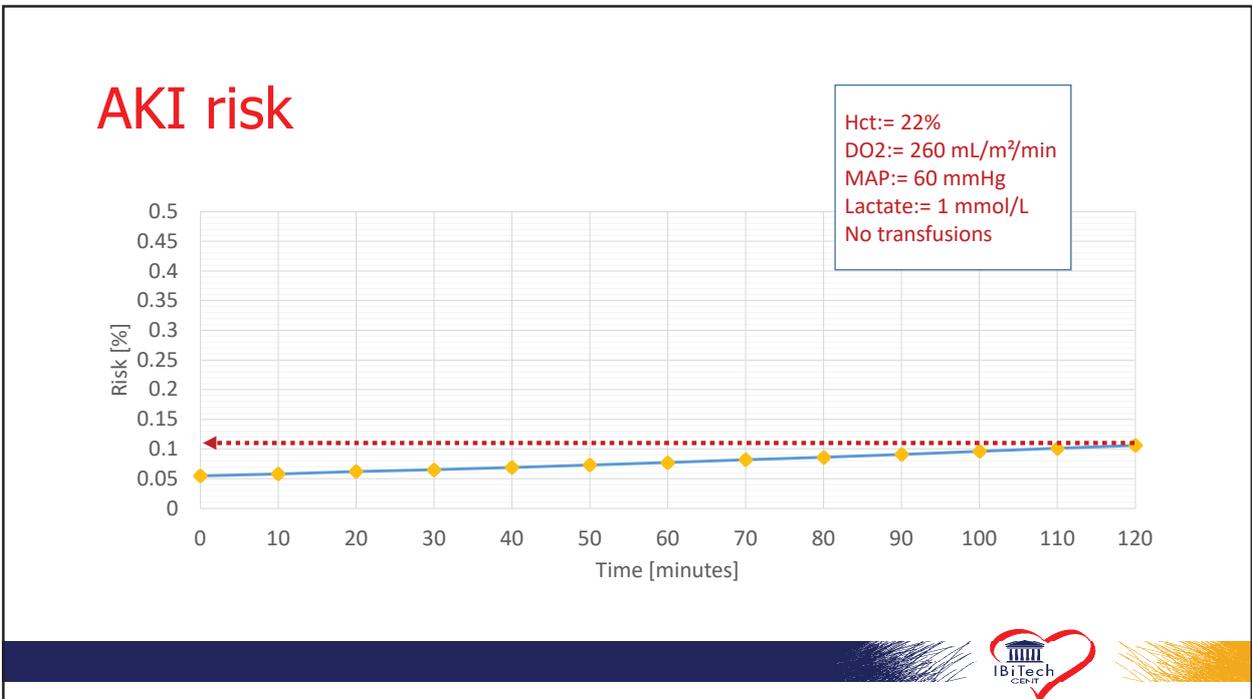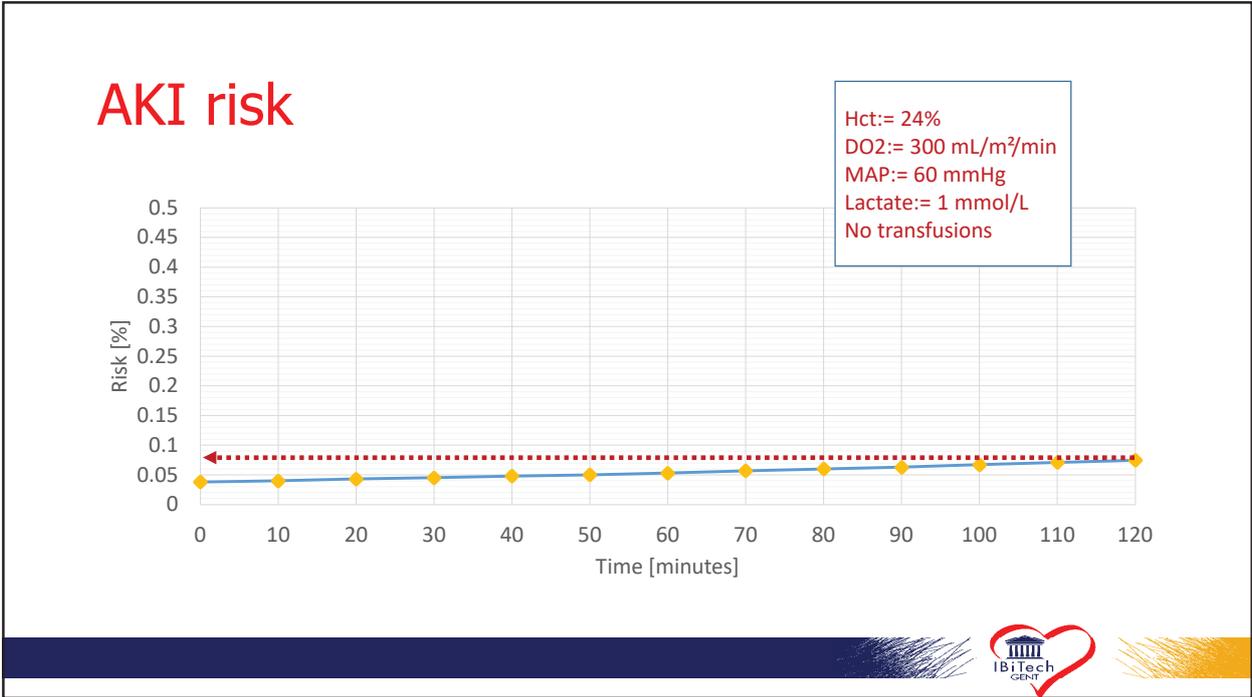- CABG + VR

10%

GDP and PIRO: perfusion related risk

- Nadir Hct:= 28%
- Nadir DO2i:= 300 mL/min
- Time below:= 0 min
- Transfusion:= 0
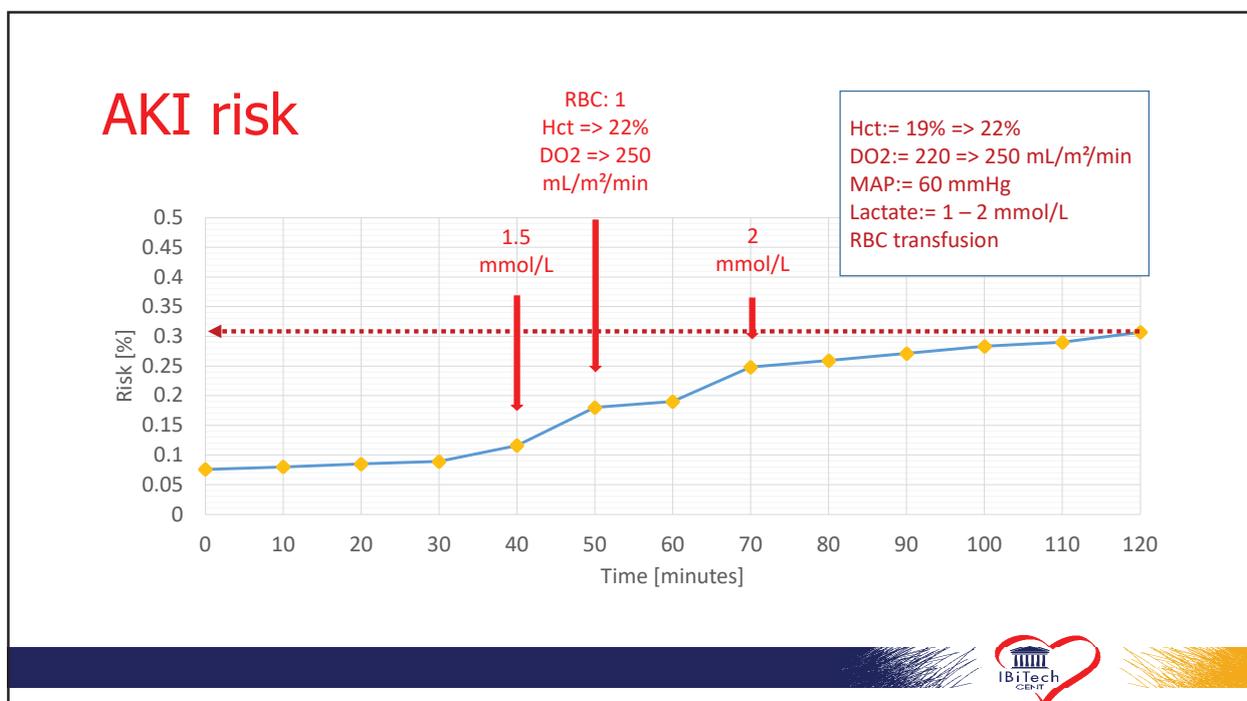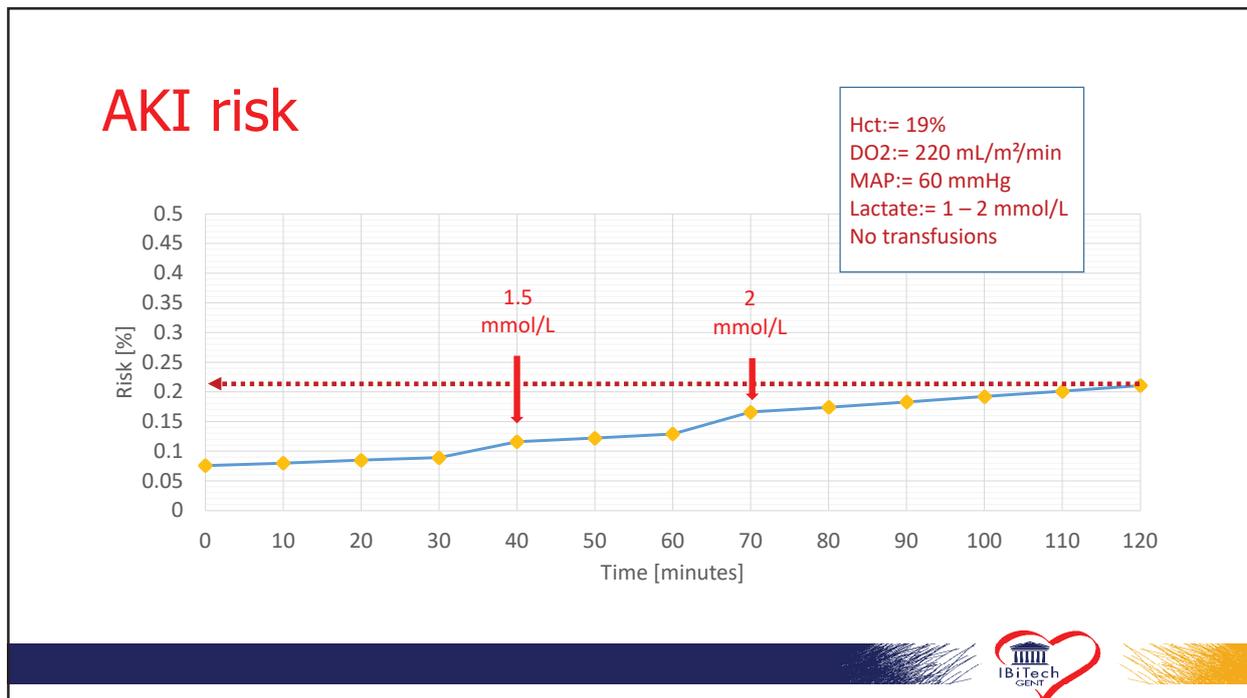- CPB:= 95 min
- Peak lactate:= 1 mmol/L
- Nadir MAP:= 60 mmHg

6.1%

- Nadir Hct:= 20%
- Nadir DO2i:= 220 mL/min
- Time below:= 15 min
- Transfusion:= 2
- CPB:= 95 min
- Peak lactate:= 4 mmol/L
- Nadir MAP:= 60 mmHg

77%

AKI risk

Hct:= 24%
DO2:= 300 mL/m²/min
MAP:= 60 mmHg
Lactate:= 1 mmol/L
No transfusions

AKI risk

Hct:= 22%
DO2:= 260 mL/m²/min
MAP:= 60 mmHg
Lactate:= 1 mmol/L
No transfusions

AKI risk

Hct:= 19%
DO2:= 220 mL/m²/min
MAP:= 60 mmHg
Lactate:= 1 – 2 mmol/L
No transfusions

AKI risk

RBC: 1
Hct => 22%
DO2 => 250
mL/m²/min

Hct:= 19% => 22%
DO2:= 220 => 250 mL/m²/min
MAP:= 60 mmHg
Lactate:= 1 – 2 mmol/L
RBC transfusion

Conclusions

- GDP should be based upon oxygen delivery and CO_2 production
- Increased RQ is indicative for a disturbed microcirculation
- MAP should stay in the autologous regulation
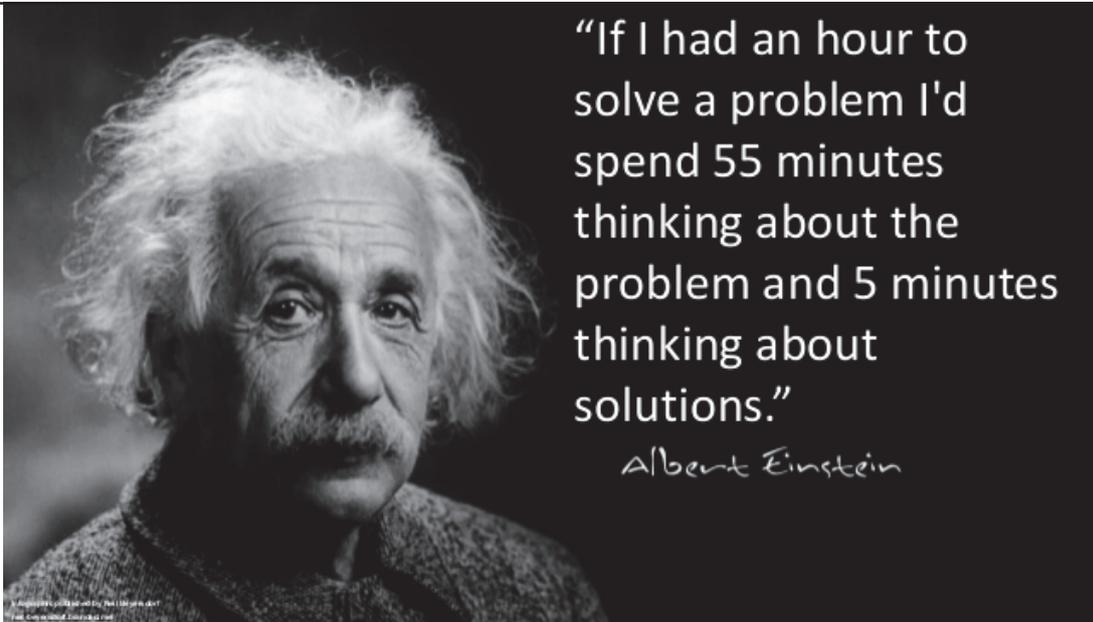- Flow is more important than pressure

Conclusions

- GDP reduces postoperative morbidity
- GDP is a multivariate online analysis of risk
- More variables are needed

Goal Directed Perfusion

Wants to preserve organ function
by influencing host response
but this asks for
continuous markers

Correct communication helps!