



Goal Directed Perfusion:

basic concepts and some examples

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

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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 database were used to identify patients undergoing cardiac surgery 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 ($P < .0001$), 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)

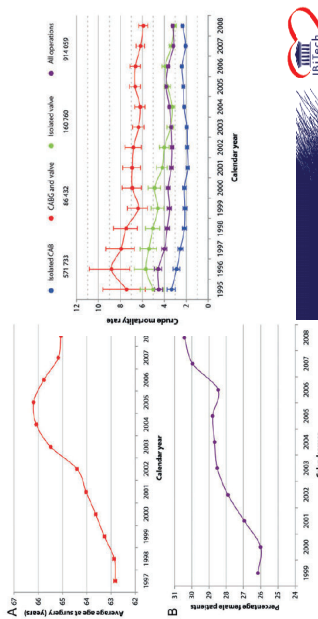


ORIGINAL ARTICLE

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

Stuart J. Head,^a Neil J. Howell,^b Ruben L.J. Ombregt,^c Ben Bridgewater,^d Bruce E. Keogh,^e Robin Krumm,^f Peter Walhovr,^g Jan E. Gummert,^h Domenico Pagano,ⁱ and A. Peter Kappeler^{a*}

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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?





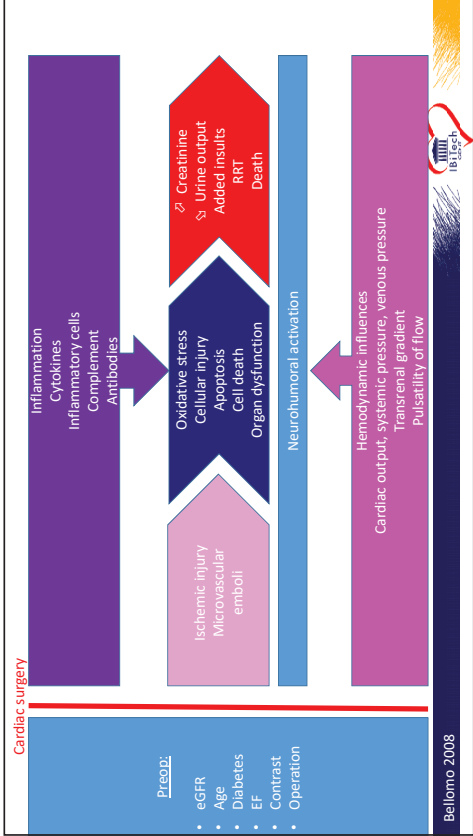
accp/sccm consensus conference

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
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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 PaCO₂ <32mmHg
- WBC: >12000 µL⁻¹ or <4000 µL⁻¹





Cardiopulmonary bypass related injury

Periopoperative:	No AKI	AKI	Ref
CABG	2,060 (70.9)	1,226 (64.7)	1,18
Valve	488 (16.6)	296 (15.1)	1,18
CABG/valve	364 (12.4)	385 (20.4)	2,31
Off-pump surgery	210 (7.2)	76 (4.0)	0,43
Number of valves, mean ± SD	1.33 ± 0.27	0.56 ± 0.56	0,43
Number of bypasses, mean ± SD	2.34 ± 0.67	2.84 ± 0.66	1,07
Pump time (minutes), mean ± SD	110 ± 54	124 ± 55	1,07
Pump time > 120 (minutes)	1,093 (37.3)	879 (46.3)	2,07
Cross-clamp time (minutes), mean ± SD	69.7 ± 40.3	77.4 ± 38.6	1,02
Cardioplegia time (minutes), mean ± SD	20.1 ± 7.6	20.7 ± 6.6	1,02
Cardioplegia	2,440 (80.2)	1,645 (86.6)	0,82
Cardioplegia hot	1,845 (61.5)	1,045 (56.2)	0,82
Cold	2,588 (87.2)	1,692 (89.1)	1,11
Cardioplegia hot short	1,722 (58.7)	1,140 (60.0)	0,85
Retrograde autologous priming (RAP)	1,925 ± 2,151	2,213 ± 2,494	1,00
Volume of fluids on bypass (mL), mean ± SD	1,150 ± 535	1,190 ± 559	1,00
Prime volume (mL), mean ± SD	0.20 ± 0.46	0.20 ± 0.65	1,00
Blood prime volume (mL), mean ± SD	0.09 ± 0.46	0.09 ± 0.46	1,00
Lowest blood temperature, mean ± SD	37.5 ± 0.41	37.5 ± 0.70	1,00
Lowest venous saturation, mean ± SD	69.82 ± 6.27	69.82 ± 6.35	1,00
Total volume of heparin > 50,000 units	1,031 (35.2)	700 (36.9)	0,97
Last potassium on bypass, mean ± SD	5.58 ± 3.32	5.58 ± 3.54	1,00
Naïve hematocrit on bypass, mean ± SD	23.28 ± 3.29	22.58 ± 3.39	0,97
Naïve hematocrit on bypass, mean ± SD	33.60 ± 3.29	33.60 ± 3.29	0,97
Ultratiltration (thermoconcentration on bypass)	136 (4.6)	139 (7.3)	1,74
Return to bypass	219 (7.5)	204 (10.7)	1,61
Acetamin use	1,157 (39.5)	936 (49.4)	2,08



Brown 2012

PIRO concept

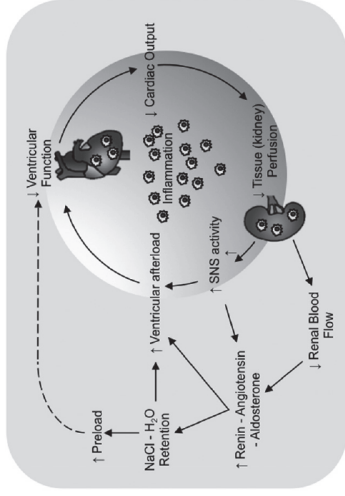
Predisposition: Premorbid illness with reduced probability of short term survival. Cultural or religious beliefs, age, gender.

Insult: Culture and sensitivity (infection) or infection pathogens; detection of disease amenable to source control.

Response: SIRS, other signs of sepsis, shock, CRP.

Organ: Organ dysfunction as number dysfunction of failing organs or composite score (e.g. MODS, SOFA, RIFLE).

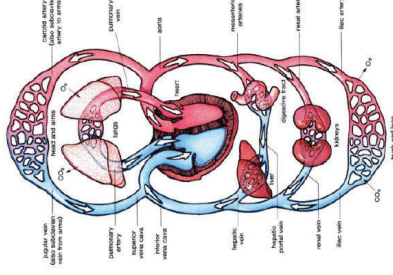
CardioRenal interrelationship in heart failure



Boudoulas 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

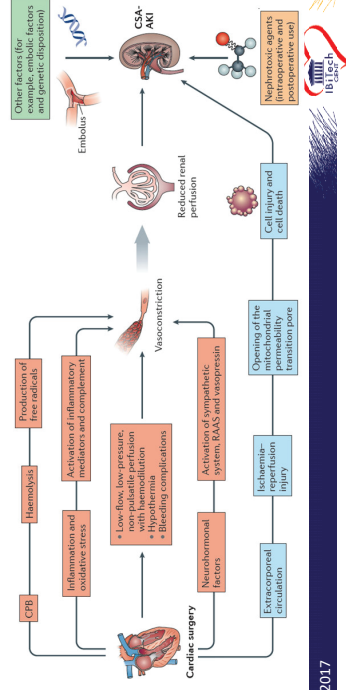


- Hematocrit: 40 – 50%
- Normal cardiac function
- Normal vascular volume

Darling 1999



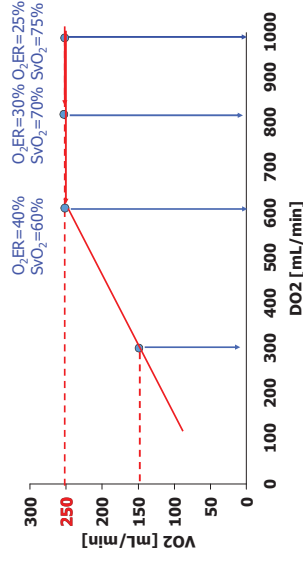
Causes



Wang 2017



DO₂ and VO₂

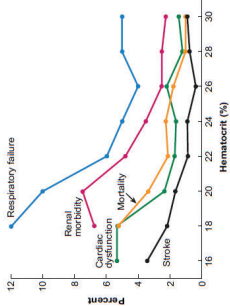


Intraoperative anemia

TABLE 2. Investigations examining effect of intraoperative anemia on postoperative outcomes

Groups	Design	n	Effects
Isakb et al. ²¹	Observational	5000	Increased morbidity and pulmonary, neurologic, renal, and cardiac morbidity
Baron et al. ²²	Observational	3000	Increased morbidity and mortality
Baron et al. ²³	Observational	3000	Major morbidity, prolonged ventilation, surgical reoperation, mediastinitis, renal dysfunction, stroke
DeGloria et al. ²⁴	Observational	6000	Increased morbidity and mortality
Jones et al. ²⁵	Randomized controlled trial	147	Decreased cardiac index and psychomotor development; increased serum lactate and total body water
Spinnola et al. ²⁶	Observational	1405	Increased morbidity
Kochman et al. ²⁷	Observational	10249	Stroke
Balentine et al. ²⁸	Observational	617	Increased risk of stroke
Balentine et al. ²⁹	Observational	617	Increased risk of stroke
Berg et al. ³⁰	Randomized controlled trial	47	Similar Q2 permeability and inflammatory response

CI, Coefficient.



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

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

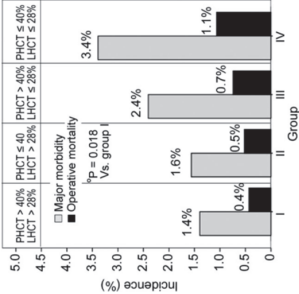
Background. Preoperative anemia and the lowest registered hematocrit value on cardiopulmonary bypass are recognized risk factors for morbidity and mortality after coronary operations. A low hematocrit often results in blood transfusions with all of the associated possible risks. However, the optimal hematocrit value for the best outcome 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 retrospective analysis 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 mortality.

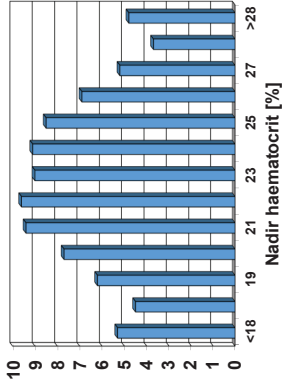
Results. After adjustment for the other explanatory variables, both the preoperative hematocrit and the lowest

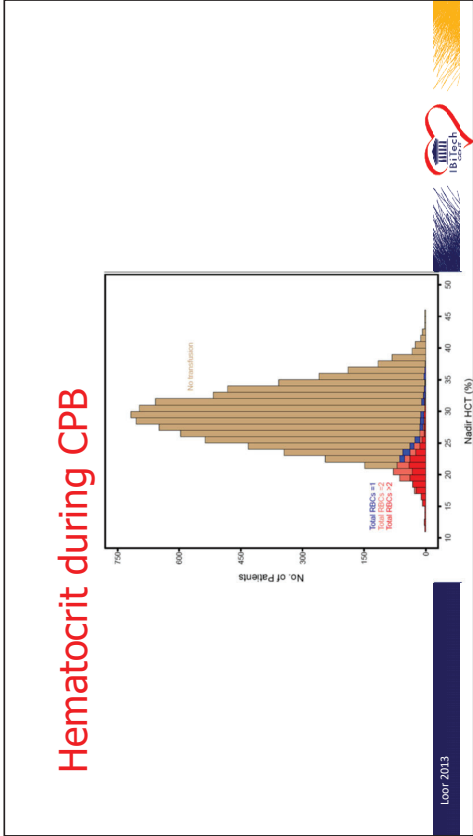
hematocrit on cardiopulmonary bypass were found to be independent risk factors for major morbidity, but not for operative mortality. However, low values of preoperative hematocrit were not associated with an increased morbidity, provided that the lowest hematocrit on cardiopulmonary bypass was above 25%. Conversely, the 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 after coronary operations. Anemia and a low hematocrit 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.

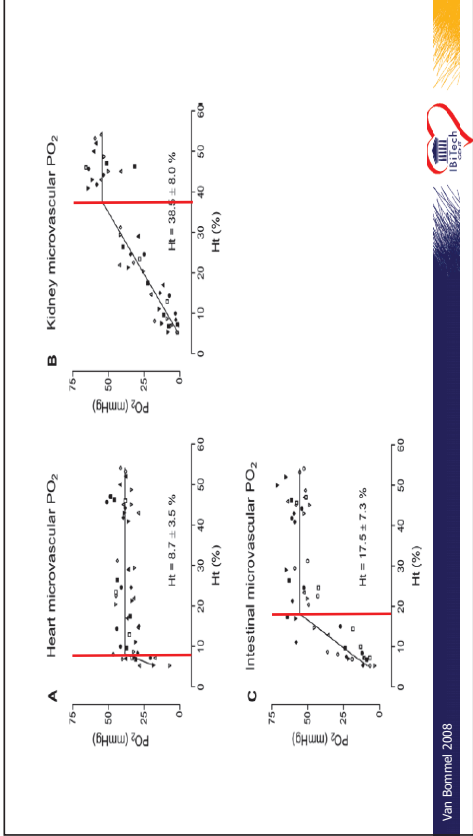


Haematocrit during CPB

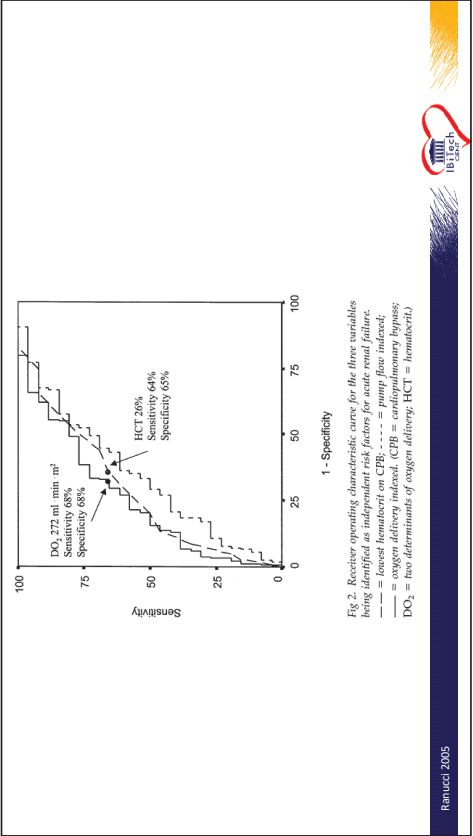




Looy 2013



Van Bommel 2008

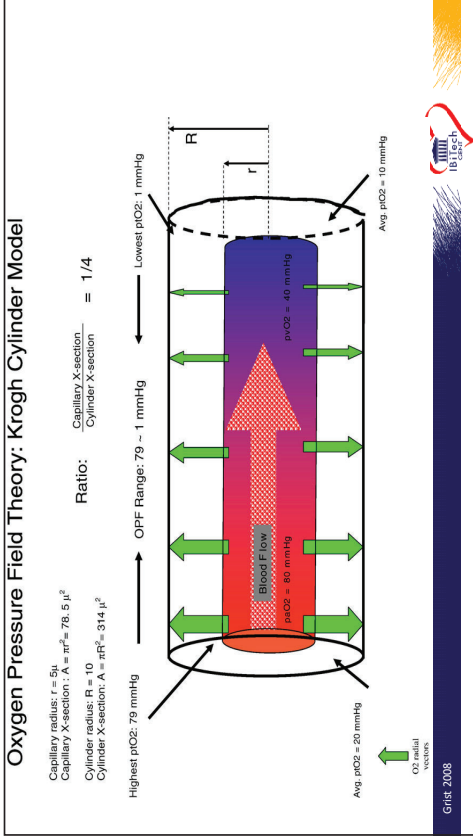
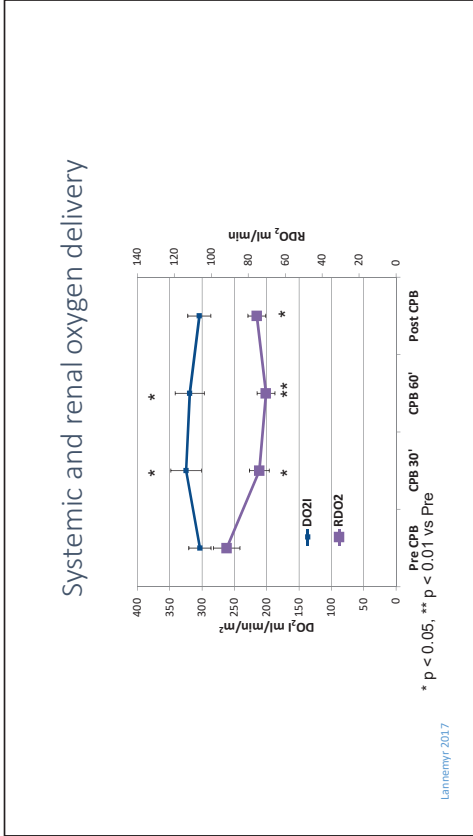
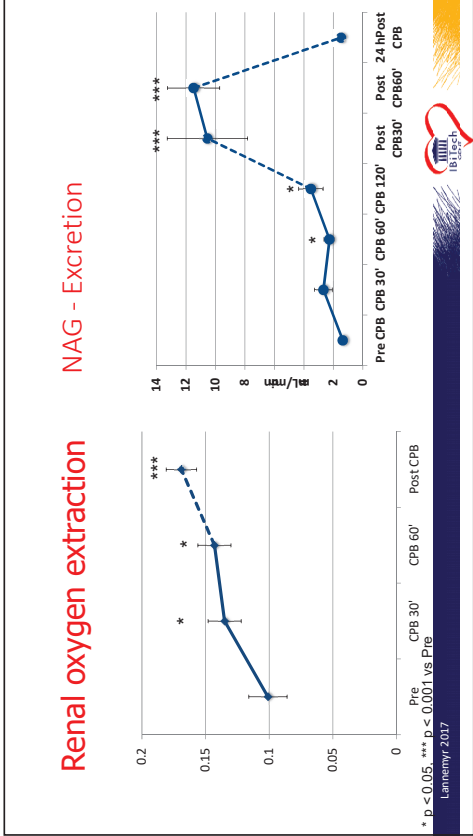
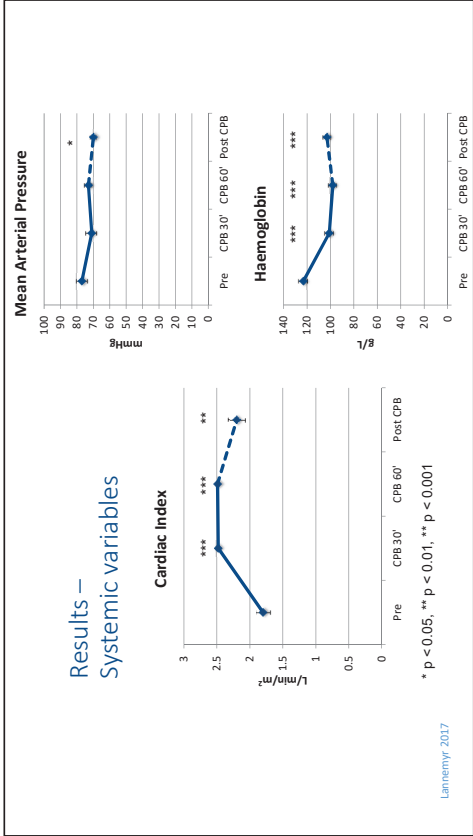


Ranucci 2005



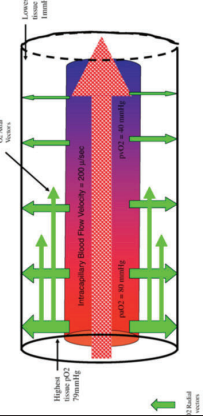
De Backer 2007





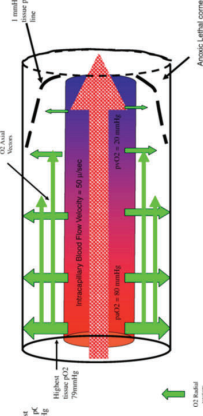
Impact of velocity

Axial Vectors & Oxygenation of the Lethal Corner:
Room Air p_{aO_2} & Normal Intracapillary Blood Flow Velocity



20% of oxygen supply venous end

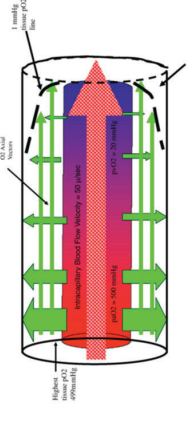
Axial Vectors & Oxygenation of the Lethal Corner:
Room Air p_{aO_2} & Slow Intracapillary Blood Flow Velocity



80% of oxygen supply venous end

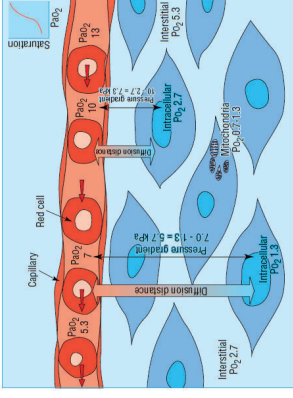
Improve diffusion component

Axial Vectors & Oxygenation of the Lethal Corner:
Hyperoxia & Slow Intracapillary Blood Flow Velocity

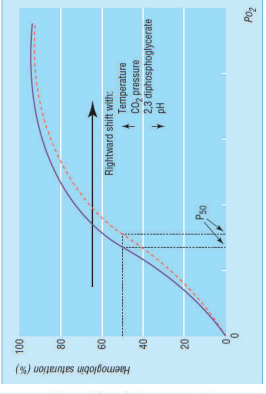


Axial kick is the use of elevated p_{aO_2} to increase the driving gradient of axial vectors in an attempt to oxygenate an anoxic lethal corner

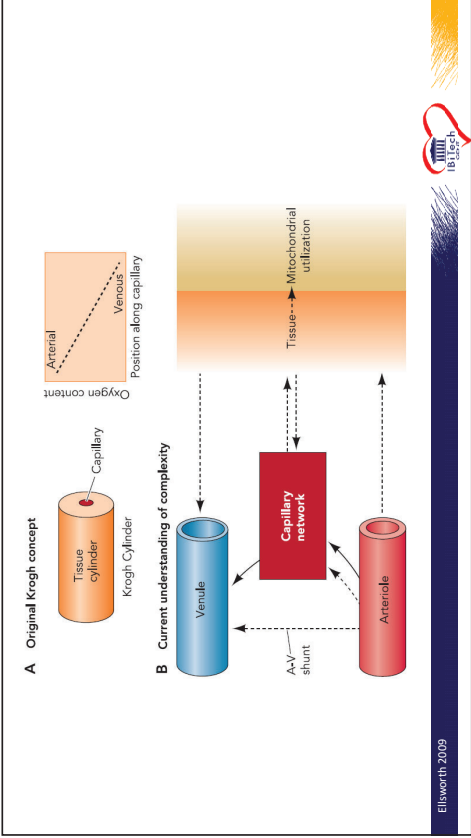
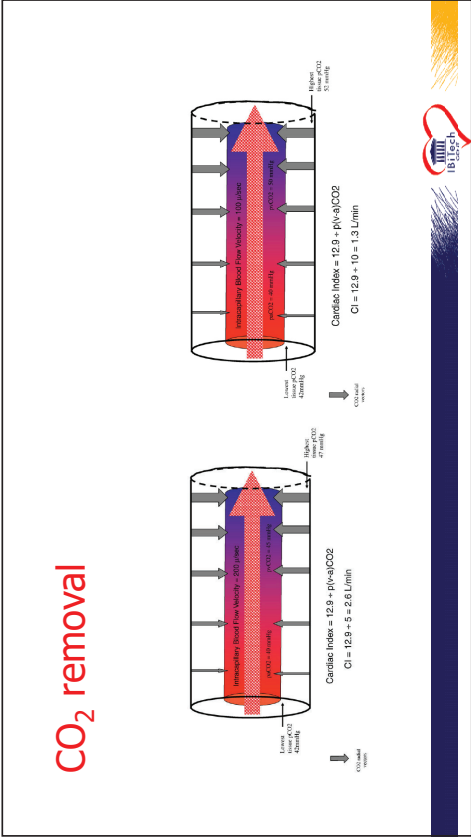
Improve diffusion component

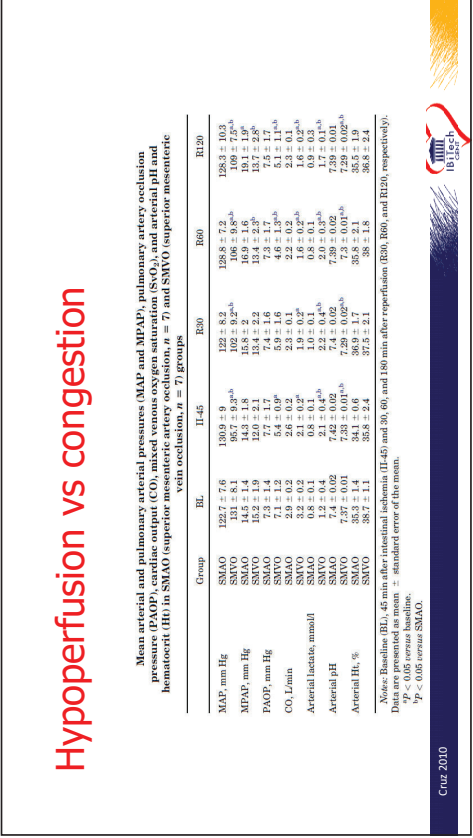
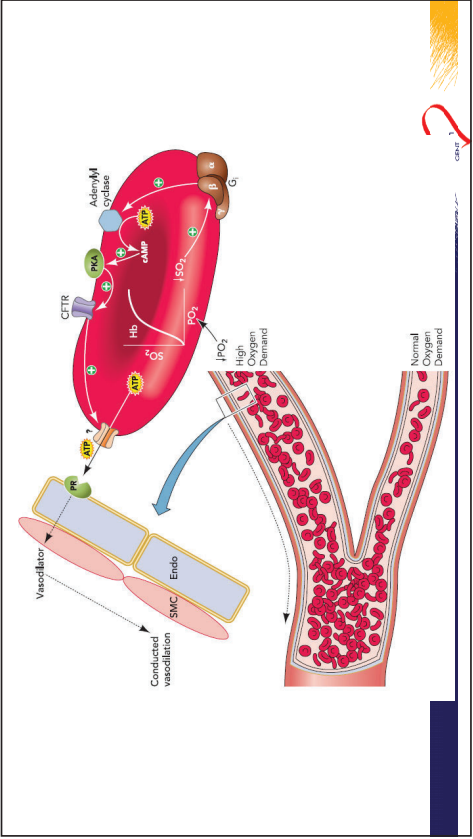
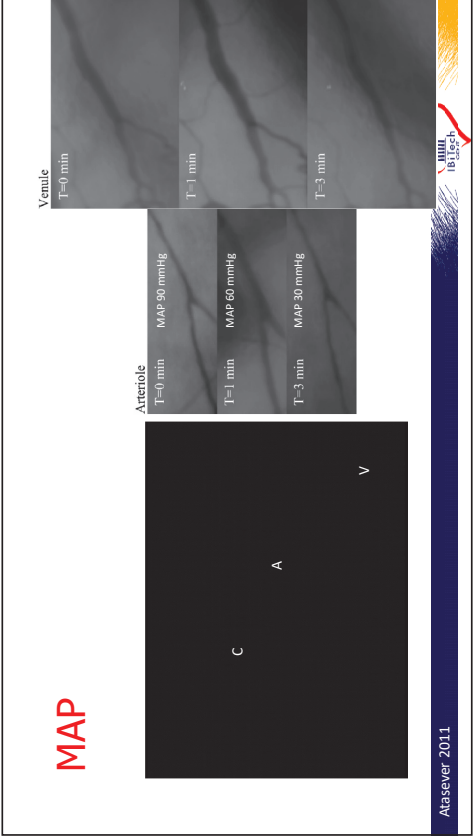
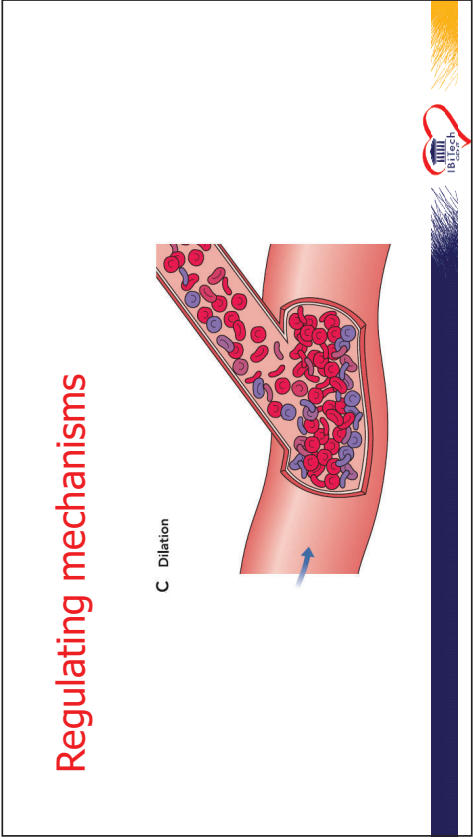


Effect of oxygen tension gradient and diffusion distance on availability of oxygen to cells



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



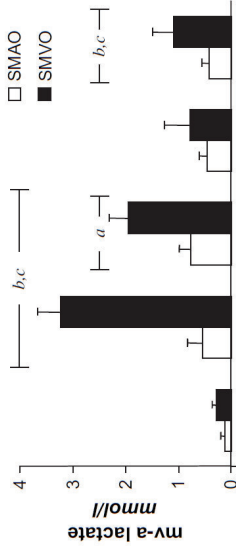


Hypoperfusion vs congestion

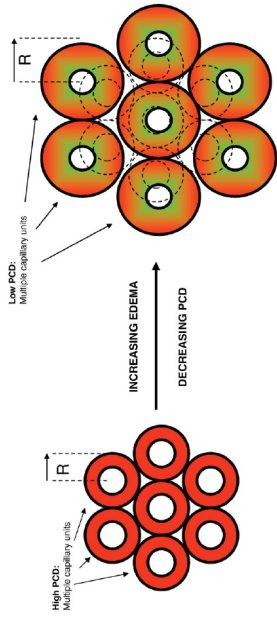
Intestinal oxygen delivery, consumption and extraction ratio (DO₂intest, VO₂intest and O₂ERintest), and mesenteric vein pH and hematocrit (Ht) in SMAO (superior mesenteric artery occlusion, n = 7) and SMVO (superior mesenteric vein occlusion, n = 7) groups

Group	BL	II-45	R30	R60	R120
DO ₂ intest, mL/min	SMAO 67.7 ± 9.9 SMVO 79.9 ± 10.5	-	45.4 ± 6.5 ^a 15.8 ± 1.9 ^{ab}	45.5 ± 7.5 ^a 14.6 ± 10.9 ^{ab}	38.8 ± 5.3 ^a 16.4 ± 2.4 ^{ab}
VO ₂ intest, mL/min	SMAO 4.9 ± 0.2 SMVO 5.0 ± 1.1	-	3.8 ± 1.3 ^a 3.9 ± 0.5 ^{ab}	5.1 ± 0.3 ^a 4.6 ± 0.5 ^{ab}	4.2 ± 1.1 ^a 3.9 ± 0.5 ^{ab}
O ₂ ER intest, %	SMAO 5.0 ± 1.1 SMVO 5.7 ± 1.6	-	10.1 ± 1.9 ^a 22.7 ± 3.5 ^{ab}	10.9 ± 2.1 ^a 29.0 ± 4.5 ^{ab}	12.4 ± 2.7 ^a 22.9 ± 3.8 ^{ab}
Mesenteric lactate, mmol/l	SMAO 0.9 ± 0.1 SMVO 1.5 ± 0.4	1.4 ± 0.3 ^a 5.3 ± 0.9 ^{ab}	1.7 ± 0.3 ^a 4.0 ± 0.7 ^{ab}	1.2 ± 0.2 ^a 3.2 ± 0.6 ^{ab}	1.3 ± 0.3 ^a 2.6 ± 0.3 ^{ab}
Mesenteric vein pH	SMAO 7.35 ± 0.02 SMVO 7.35 ± 0.02	7.18 ± 0.05 ^{ab} 7.23 ± 0.03 ^{ab}	7.21 ± 0.03 ^{ab} 7.25 ± 0.03 ^{ab}	7.22 ± 0.02 ^{ab} 7.25 ± 0.03 ^{ab}	7.22 ± 0.01 ^{ab} 7.25 ± 0.03 ^{ab}
Mesenteric vein Ht, %	SMAO 37.2 ± 1.7 SMVO 39.2 ± 1.2	34.3 ± 1.5 66.4 ± 0.9 ^{ab}	37.7 ± 1.3 40.3 ± 2.6	36.7 ± 2.3 39.4 ± 1.9	36.8 ± 1.5 37.1 ± 2.0

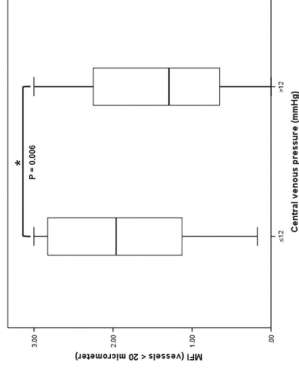
Hypoperfusion vs congestion

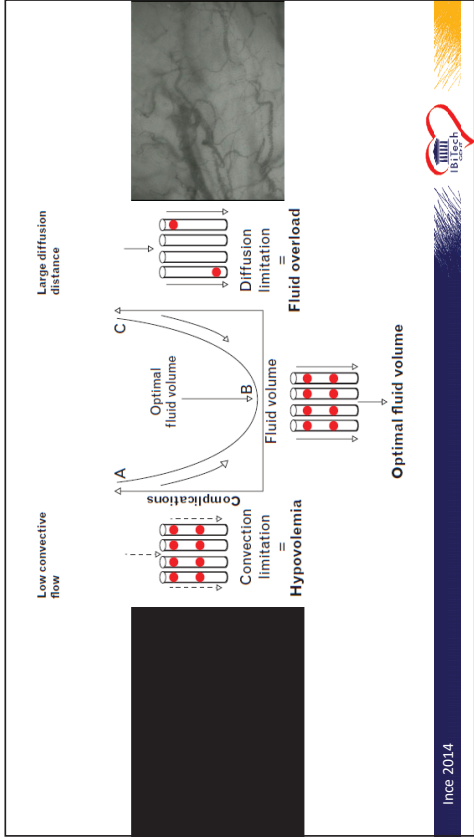


Congestion

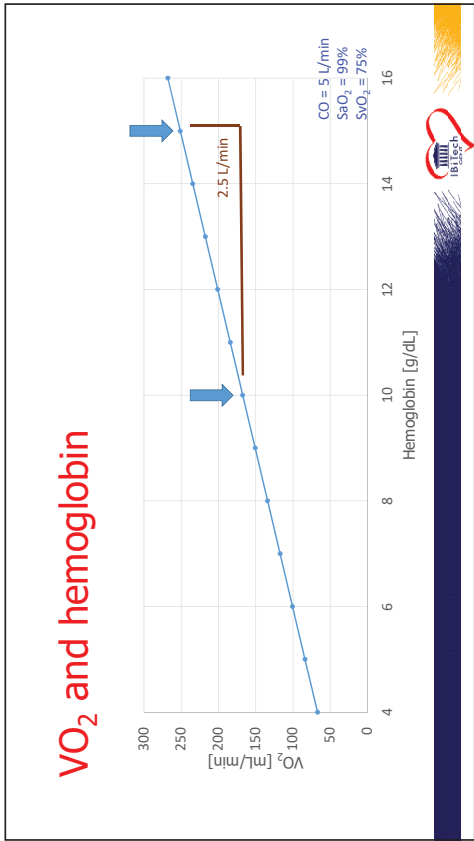


Increased RAP

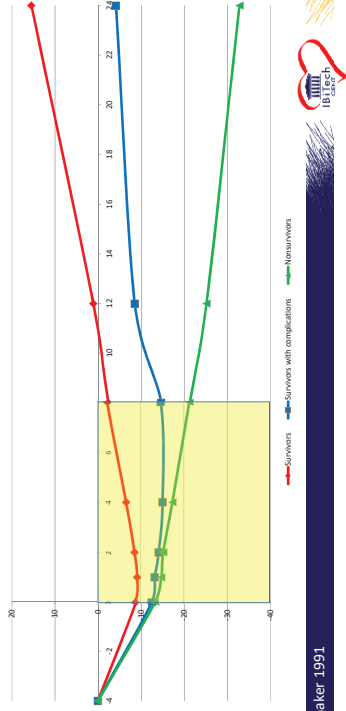




Ince 2014



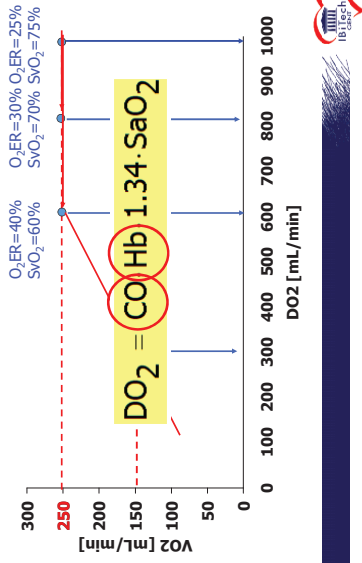
Perioperative oxygen debt



Shoemaker 1991

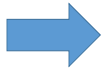


DO₂ and VO₂



Hypothesis

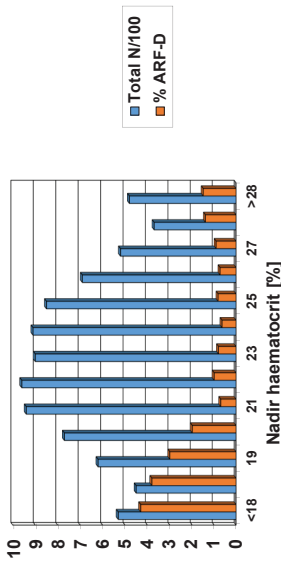
- If DO_2 is a prime variable
- If most perfusionists work with a fixed CI



Must hemoglobin influence quality of Perfusion



Haematocrit during CPB



Hematocrit during CPB

Lowest HCT on CPB is associated to:

- Reopening
- Bleeding
- Perioperative MI
- Cardiac arrest
- Stroke
- Coma
- Prolonged ventilation
- IABP
- Renal failure
- MOF

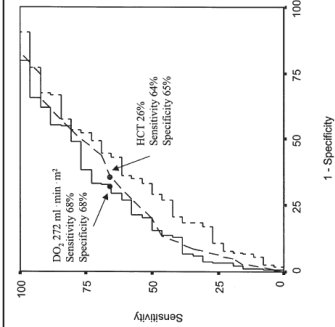
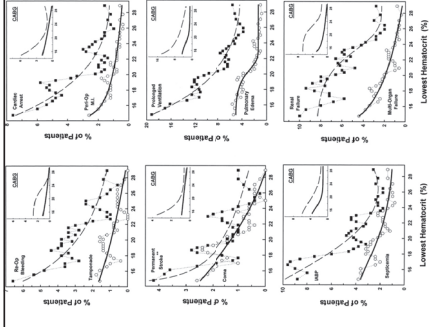
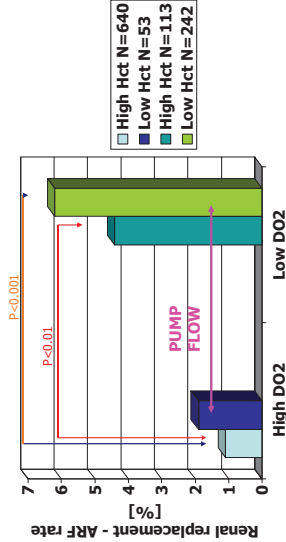


Fig 2. Receiver operating characteristic curve for the three variables being identified as independent risk factors for acute renal failure. DO_2 = oxygen delivery indexed; CPB = cardiopulmonary bypass; HCT = two determinants of oxygen delivery; HCT = hematocrit



Optimal flow and outcome



Ranucci 2005



Optimal flow and outcome

Basic patient characteristics		Hematocrit 25%			Hematocrit 20%			P
Characteristic		Median	ICQ	Median	ICQ	Median	ICQ	
Age (years)		60	55-67	65	59-71		0.10	
Gender (male/female)		28/2		28/0				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/m²)		27.9	26.0-32.2	28.6	26.7-30.9			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	290-320			0.38
Duration of surgery (minutes)		190	180-220	200	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			0.83
APACHE II score		14	9-19	16	13-27			0.09

von Heymann 2006



Outcome measures in the intensive care unit

Outcome measure	Hematocrit 25%			Hematocrit 20%			P
	Median	ICQ	Median	ICQ	Median	ICQ	
Number of transfused patients	1		5				0.10
Drainage loss (ml)	582	265-520	400	290-420			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-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			0.86
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	2,360-3,469	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; ICQ, interquartile range.

von Heymann 2006



Optimal flow and outcome

Intraoperative outcome measures

Outcome measure	Hematocrit 25%			Hematocrit 20%			P
	Median	ICQ	Median	ICQ	Median	ICQ	
GI during CPB (l/min/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	36.4-36.0			0.12
Cumulative norepinephrine dosage during CPB (mg)	0.98	0.98-2.10	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 intracardiac balloon pump for weaning from CPB (n)	2		2				0.49
Patients with acute cardiac failure during weaning from CPB (n)	3		2				1.00
Urine volume during CPB (ml)	159	97-554	165	102-440			0.57

GI, cardiac index; CPB, cardiopulmonary bypass; ICQ, interquartile range.

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

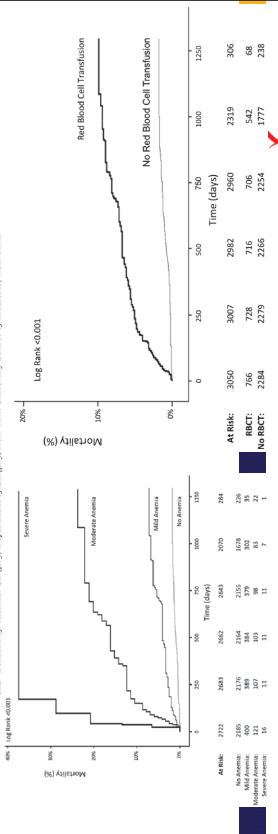
> 270 mL/min/m²

von Heymann 2006

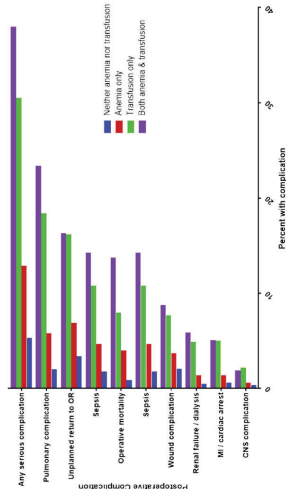


Association Between Anemia, Bleeding, and Transfusion with Long-term Mortality Following Noncardiac Surgery

Nathaniel R. Smitlowitz, MD,* Brandon S. Oberweis, MD,* Svetlana Nikala, MBBS,* Andrew Rosenberg, MD,* Sibio Zhao, MS,* Jinteng Xu, PhD,* Steven Stuchin, MD,* Richard Iorio, MD,* Thomas Ercole, MD,* Patricia J. Raftord, MD,*^{1,2,3,4}
*Division of Vascular Surgery, Department of Medicine, New York University School of Medicine, New York, NY; ¹Division of Cardiology, Department of Medicine, Columbia University Medical Center, New York, NY; ²Division of Vascular Surgery, Department of Clinical Quality and Clinical Effectiveness, Division of Vascular Surgery, Department of Anesthesiology, Division of Vascular Surgery, Department of Orthopedic Surgery, Chief Quality Officer, Division of Vascular Surgery, Division of Vascular Surgery, Department of Population Health, and, Division of Vascular Surgery, Department of Surgery, New York University School of Medicine, New York.

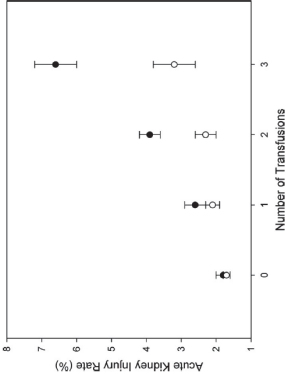


Transfuse or not?



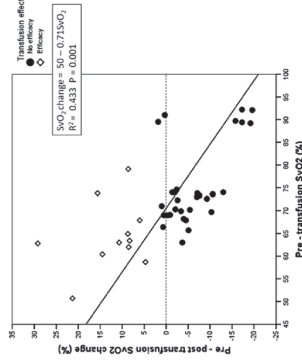
Ferraris 2015

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 in 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 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 percentage point of increase of AKI risk score. The relative risk of AKI ($p = 0.001$) 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 3.5%; $p = 0.029$). Goal-directed perfusion by means of ultra-low prime oxygenators was effective in reducing the AKI rate.

(Ann Thorac Surg 2015;100:95–100)
© 2015 by The Society of Thoracic Surgeons

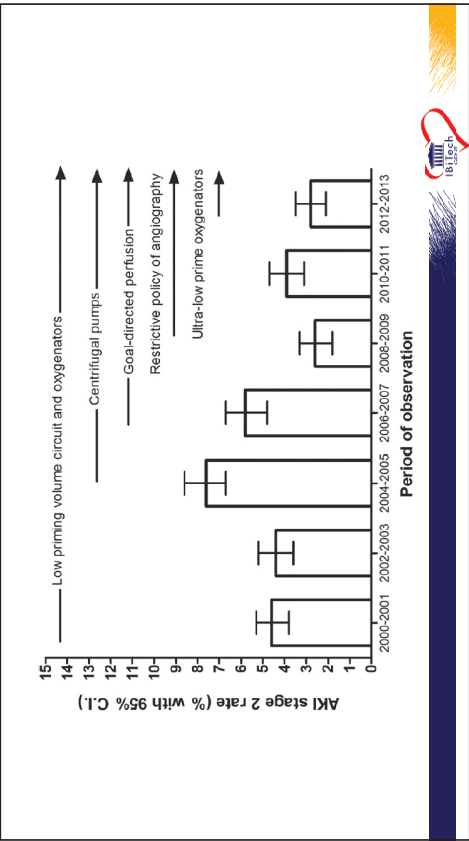


Table 2. Demographics and Renal Risk Factors of the Patient Population in the Different Periods Considered

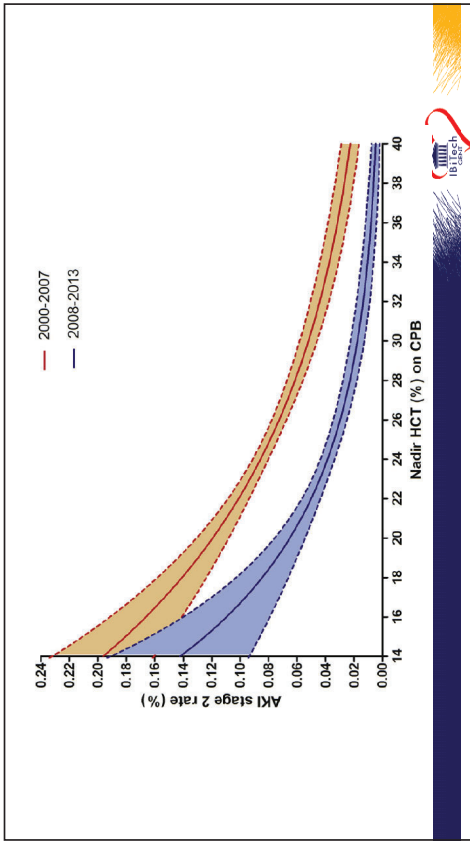
Period	No. of patients	Age (yr)	eGFR (mL/min/1.73 m ²)	LVF (%)	Diabetes (%)	Operations (%)	Reds (%)	Nonoperative Operations (%)	Nonisolated CABG (%)	IABP Use (%)	CPB time (min)
2000-2001	2,714	64.4 (10.7)	56.4 (23)	51.6 (11.8)	12.6	4.0	2.4	42.9	0.3	71.7 (37)	
2002-2003	2,694	65.6 (11.3)	57.4 (24)	52.4 (12.6)	14.1	5.4	4.0	49.6	0.4	71.8 (38)	
2004-2005	3,006	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	71.9 (37)	
2006-2009	1,829	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	80.4 (39)	
2008-2009	1,829	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	80.4 (39)	
2010-2011	2,157	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	83.1 (37)	
2012-2013	2,077	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	87.1 (44)	
Total	16,790	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5	80.0 (42)	
p value between periods		0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	

*Analysis of variance or Pearson's χ^2 test. Data are expressed as mean (standard deviation) or percentage. CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; eGFR = estimated glomerular filtration rate; IABP = intra-aortic balloon pump; LVF = left ventricular ejection fraction.

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

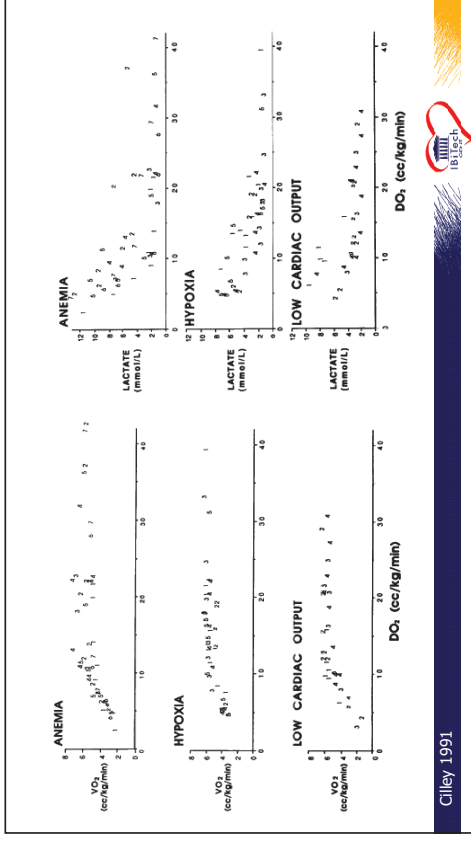
Period	No. of Patients	BRS	Age	AKI	AKI Rate	AKI Rate as a Function of AKI Rate	AKI Rate as a Function of AKI Rate	AKI Rate as a Function of AKI Rate	AKI Rate as a Function of AKI Rate
2000-2003	2,714	64.4 (10.7)	56.4 (23)	51.6 (11.8)	12.6	4.0	2.4	42.9	0.3
2002-2003	2,694	65.6 (11.3)	57.4 (24)	52.4 (12.6)	14.1	5.4	4.0	49.6	0.4
2004-2005	3,006	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
2006-2007	2,433	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
2008-2009	1,829	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
2010-2011	2,157	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
2012-2013	2,077	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
Total	16,790	65.9 (12.3)	57.2 (23)	52.0 (11.1)	12.1	6.2	3.1	45.1	0.5
p value between periods		0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

*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; IABP = intra-aortic balloon pump; LVF = left ventricular ejection fraction.



Maintain red blood cell mass

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

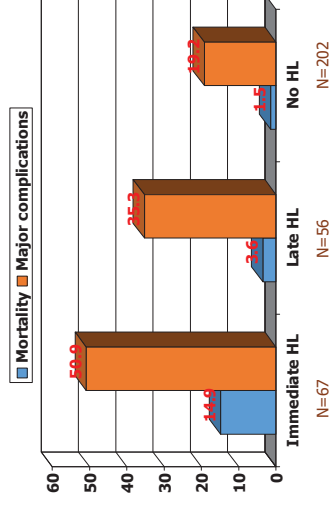


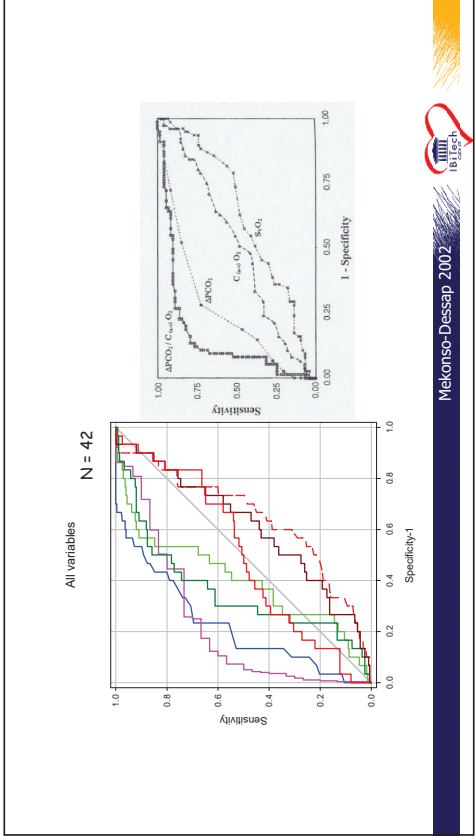
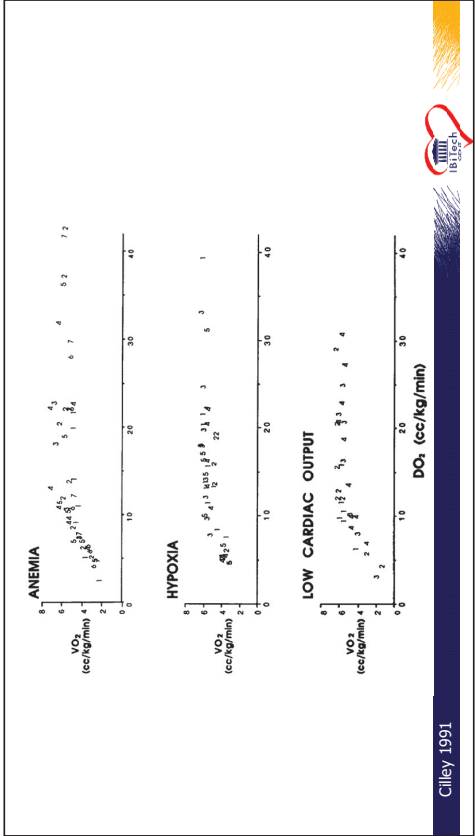
DO₂ as a goal

- Scarce information on DO₂ during CPB
- With a constant pump flow, DO₂ is direct related to Hct
- Most CPB cases are performed at 32 - 34°C
- Pump flow = 2 - 3 L/min/m²
- => Hct = cte => DO₂ varies with 50%



Lactate as marker





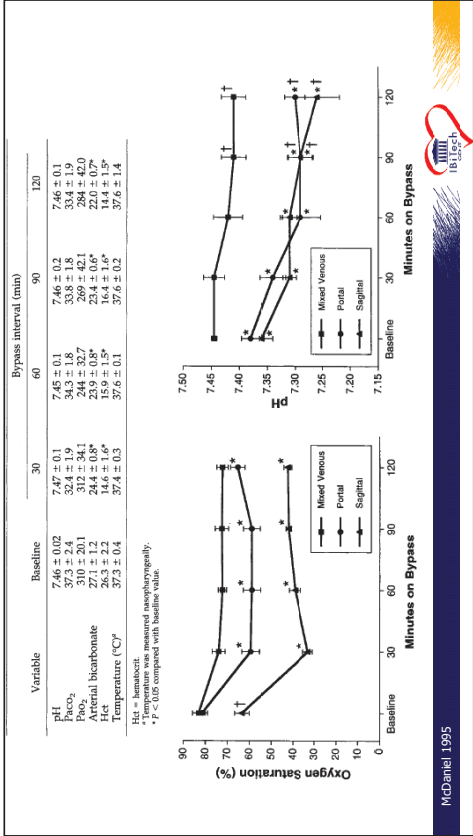
How do we know that blood flow meet the metabolic needs of a patient?

By retrospective analysis of organ function, blood markers and morbidity

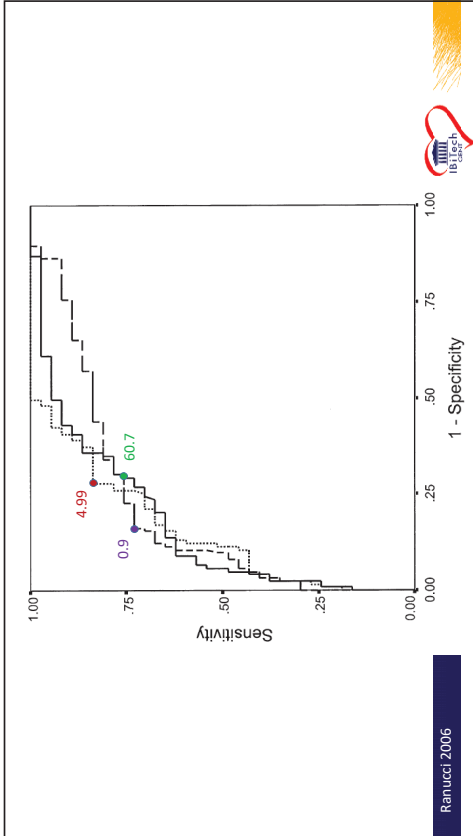
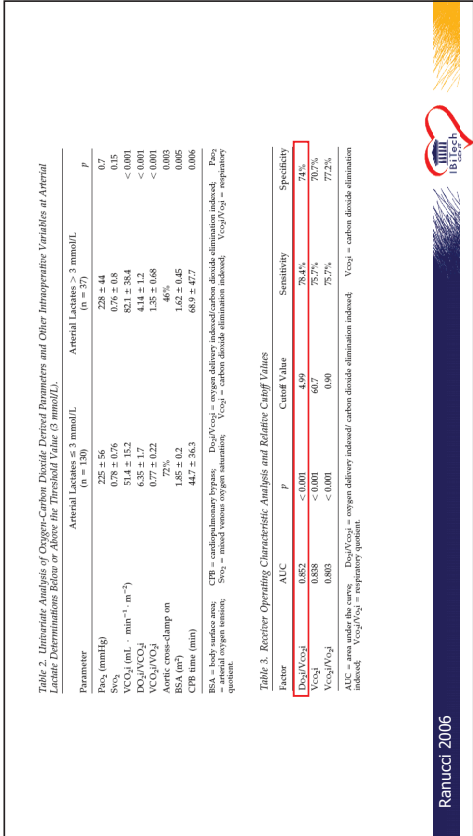
“What we need is a multivariate online analysis of risk during cardiopulmonary bypass” Charles Wildevuur

DO₂j => what we give to the patient

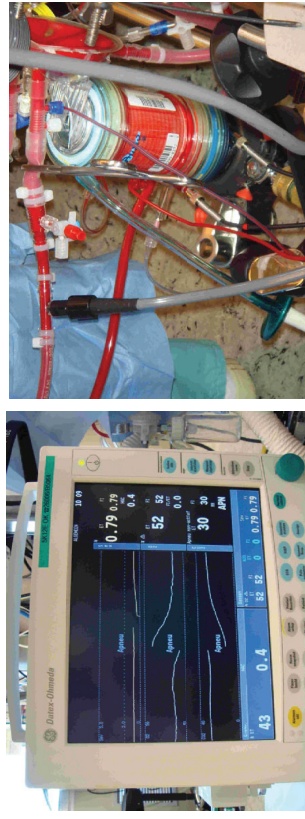
VCO₂j => what we get from the patient



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



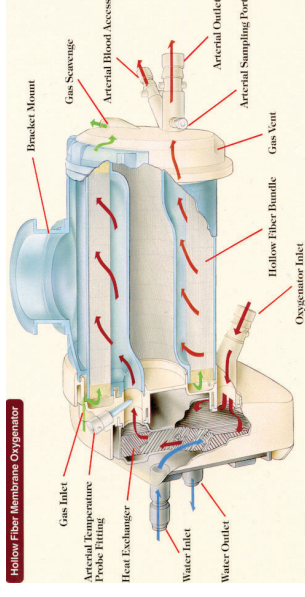
CO₂ can be measured in real time



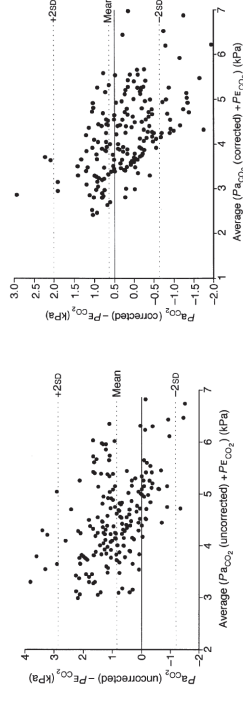
CO₂ production

$$V\dot{CO}_2 = Q_{gas} \cdot \frac{e_{CO_2}}{P_{baro}}$$

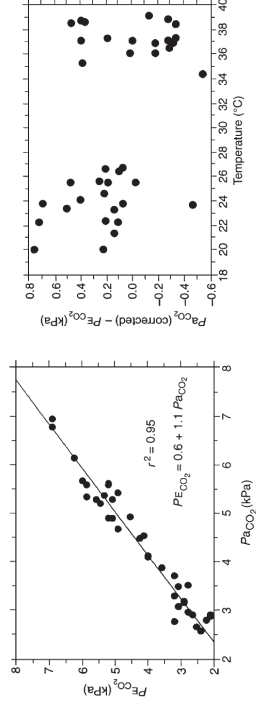
Capnography: potential problems



Capnography oxygenator exhaust



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 ($0^{\circ}C$), Pressure (1ATM), Dry

Gas laws

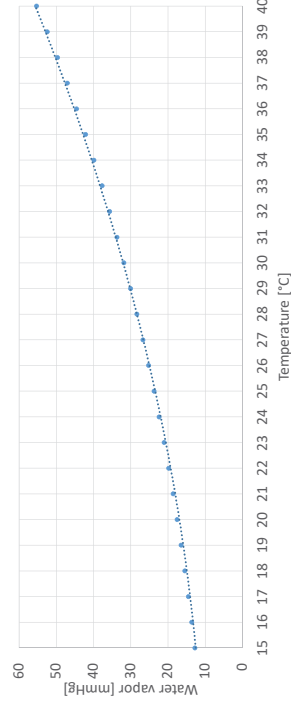
$$P_1 \cdot \frac{V_1}{T_1} = P_2 \cdot \frac{V_2}{T_2} \rightarrow \frac{P_2 \cdot T_1 \cdot V_2}{T_2 \cdot V_1}$$

$$V_{STPD} := \frac{(P_{baro} - P_{H_2O}) \cdot 273.15K}{P_{baro} \cdot (T_{at})} = 0.826$$

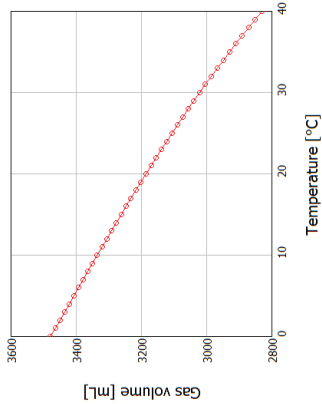
T_{at} in K



Water vapor and temperature



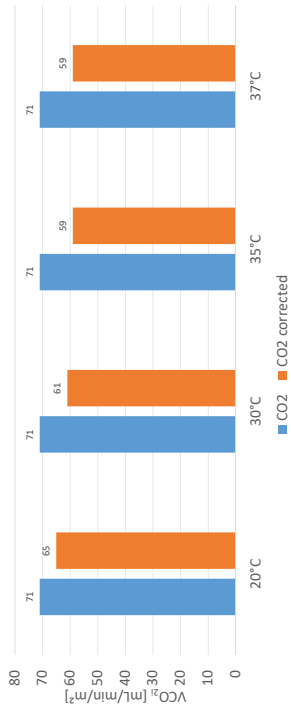
Conversion ATPS to STPD



Example

- $e\text{CO}_2 = 36 \text{ mmHg}/760 \text{ mmHg} = 4.7\%$
- $Q_{\text{gas}} = 3000 \text{ mL/min}$
- $P_{\text{barometric}} = 760 \text{ mmHg}$
- $T_{\text{art}} = 20^\circ\text{C}$
- $BSA = 2 \text{ m}^2$

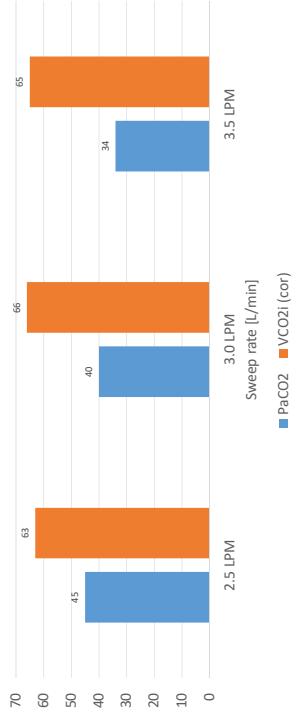
ATPS versus STPD



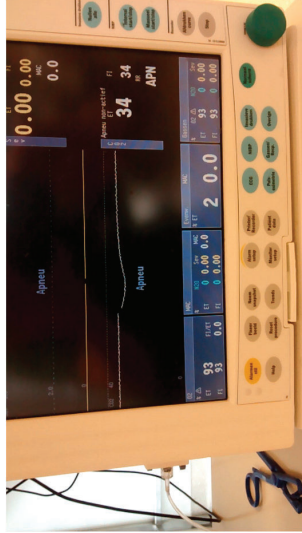
for venous return. Lowest core body temperature during CPB varied from 27°C to 37°C as requested by the surgeon. Body temperature was measured at the nasopharyngeal site and at the rectal site. This last temperature was considered for correcting the values of blood gas analyses. The perfusate temperature 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 PaCO₂



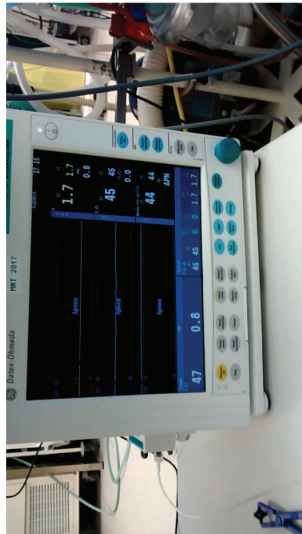
Scavenging of volatile anesthetics and capnography



Scavenging of volatile anesthetics and capnography



Scavenging of volatile anesthetics and capnography



Calculation DO₂ and VCO₂

Hb = 8 $\frac{gm}{dl}$
cte = 1.34 $\frac{mL}{gm}$
SaO₂ = 99%
CO = 5 $\frac{L}{min}$
k_{blood} = 3.666 · 10⁻⁵ $\frac{mL}{mmHg \cdot mL}$
PaO₂ = 150mmHg

Hemoglobin concentration
Maximum transport capacity hemoglobin
Arterial oxygen saturation
cardiac output or pump flow
oxygen solubility in blood
Partial oxygen tension

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



Oxygenation
Hb = 80 $\frac{gm}{L}$
SaO₂ = 99%
Q_{blood} = 4.5 $\frac{L}{min}$
BSA = 1.8m²
PaO₂ = 150mmHg
k_{blood} = 3.666 · 10⁻⁵ $\frac{mL}{mmHg \cdot mL}$

CO₂
Q_{gas} = 2 $\frac{L}{min}$
e_{CO₂} = 40mmHg
P_{Baro} = 760mmHg
T_{Blood} = 34 °C
P_{H₂O} = 39.9mmHg

Spectrum
 $DO_{2M4} = \frac{(Hb \cdot 1.34 \cdot \frac{mL}{gm} \cdot SaO_2) \cdot Q_{Blood}}{BSA} = 265 \frac{mL}{min \cdot m^2}$
 $DO_{2M4} = 4.537$
 $V_{CO2_M4} = \frac{Q_{gas} \cdot P_{Baro}}{BSA} = 58 \frac{mL}{min \cdot m^2}$
 $V_{CO2_M4} = 4.537$

Connect
 $DO_{2_Connect} = \frac{[(P_{Baro} - P_{H_2O}) \cdot \frac{mL}{gm} \cdot SaO_2] + (PaO_2 \cdot k_{blood}) \cdot Q_{Blood}}{BSA} = 283 \frac{mL}{min \cdot m^2}$
 $V_{CO2_Connect} = \frac{(P_{Baro} - P_{H_2O}) \cdot 273.15K}{BSA} \cdot \frac{Q_{gas} \cdot P_{Baro}}{P_{Baro}} = 49.276 \frac{mL}{min \cdot m^2}$
 $V_{CO2_Connect} = 5.744$



Develop an algorithm

DO₂/VCO₂ ratio <5



Augment pump flow

Increase Hb content

Decrease T, check anesthesia level



de Somer et al. Critical Care 2011, 15:R192
http://ccforum.com/content/15/R192

CRITICAL CARE

RESEARCHOpen Access

O₂ delivery and CO₂ production during cardiopulmonary bypass as determinants of acute kidney injury: time for a goal-directed perfusion management?

Filip de Somer¹, John W Mulholland², Megan R Bryan², Tommaso Aloisio³, Guido J Van Nooren¹ 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 (DO₂) and carbon dioxide production (VCO₂)) during CPB with postoperative AKI.

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»

Outcome	All cases N=354	DO ₂ < 280 mL/min/m ² N= 181	DO ₂ ≥ 280 mL/min/m ² 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 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](https://clinicaltrials.gov/ct2/show/study/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



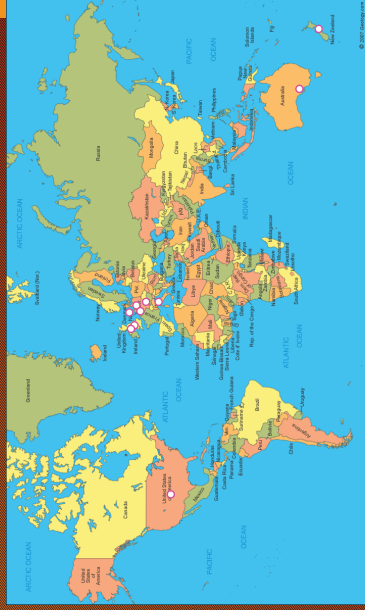
DO₂, VCO₂, and DO₂/VCO₂ data adjudication

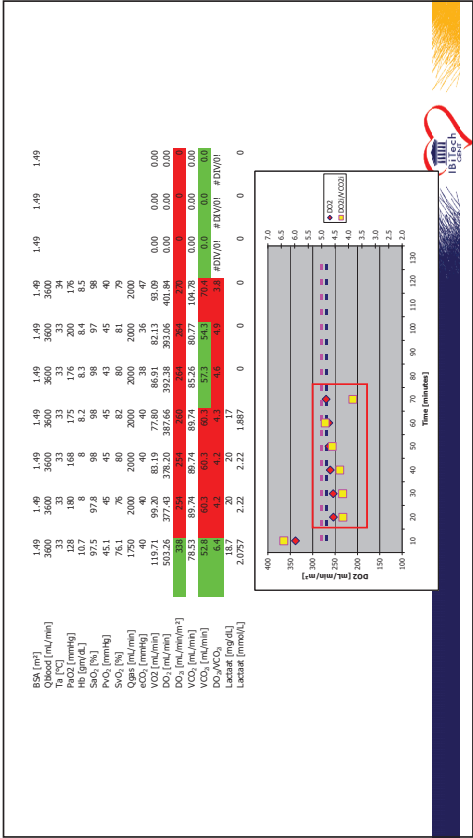
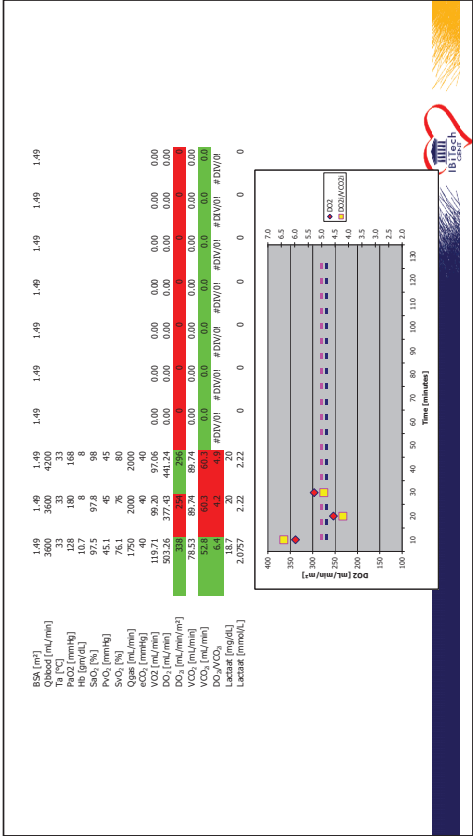
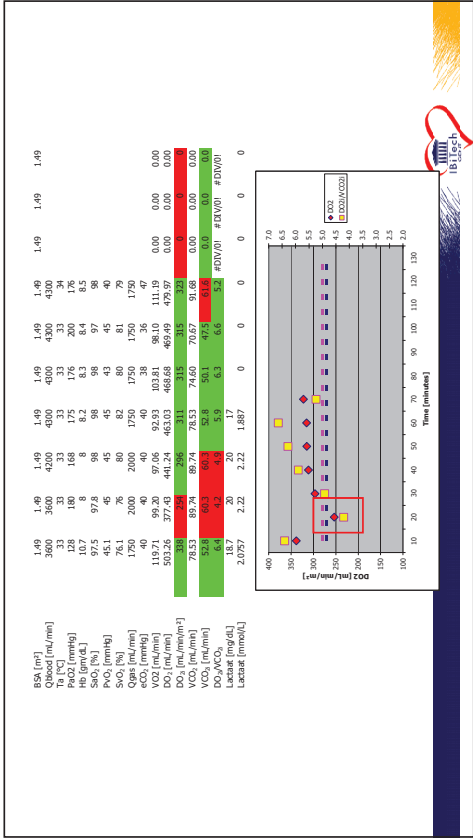
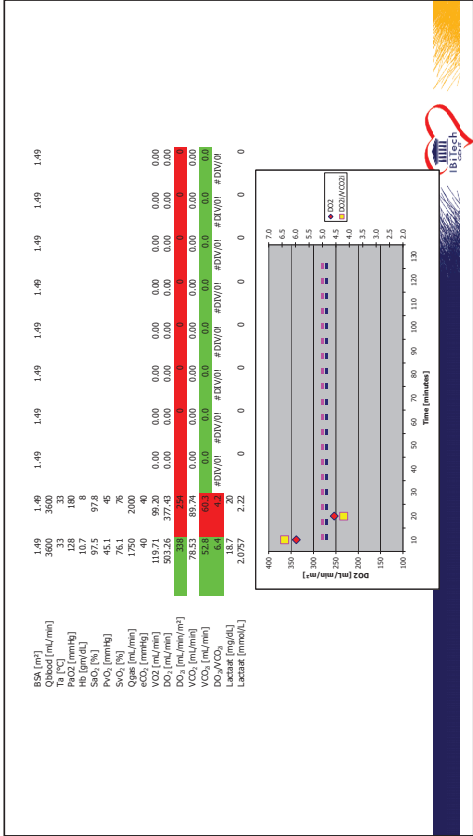
- NADIR DO₂: maintained for at least 10 minutes (2 consecutive measures)
- Same for VCO₂, and DO₂/VCO₂



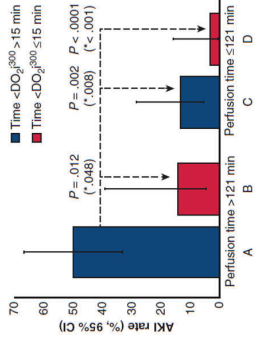
The GDP Trial - protocol

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 DO ₂ > 280 mL/min/m ²
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 SV02 < 68% and/or O ₂ ER > 40%
Postoperative care according to local standards	Postoperative care according to local standards





Importance of time



Mukaida 2019



45 y.o. female, 45 Kg., 1.49 m²
2.4 CI = 3.58 LPM, AVR MVR, Sorin Inspire™ 6
Baseline Hgb = 10.7

Time	BQ	RQ	Temp	SvO ₂	HCT	DO _{2i}	VO ₂	VO ₂ /D O ₂ i	DO ₂ /V CO 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	35.3	88	24	299	75.5	19	4.8	57.5
40	3.69	103	35.3	88	24	299	73.4	16.8	6.6	46
45	3.59	100	35.3	88	24	299	79.8	19	6.5	44.4
70	3.6	100	35.3	88	24	299	72.5	18	5.8	47.6
100 *	3.9	109	35.3	88	24	299	103	25.5	4.6	60.3
120	3.9	109	35.3	88	24	328	126.2	27	4.8	64.2
140	4	112	36.5	78	24	328	94.3	19.3	7.5	43.5

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



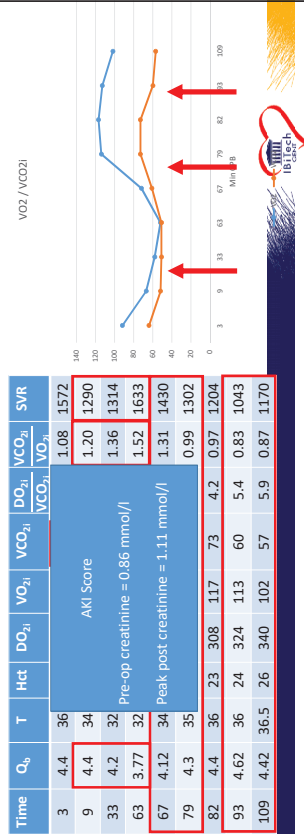
35 y.o. male, 136 Kg., 2.55 m², BMI = 45
2.4 CI = 6.1 LPM, IBW = 75 Kg, BSA = 1.9, Ideal 2.4 CI = 4.56 LPM
Redo PVR RVOT repair, Baseline Hgb = 12 g/dL

Time	BQ	RQ	AKI Score
5	4.6	0.75	
30	5.0	0.82	Pre-op creatinine = 0.97 mmol/l
60	5.0	0.82	Peak post creatinine = 1.12 mmol/l
90	5.2	0.85	
125	5.0	0.82	

$\dot{V}O_{2i}/\dot{V}O_{2i}$	$\dot{V}O_{2i}/\dot{V}O_{2i}$	$\dot{V}O_{2i}/\dot{V}O_{2i}$	$\dot{V}O_{2i}/\dot{V}O_{2i}$
5	17	6.1	43
1	15.4	6.9	41
8	13.2	6.8	44
2	16.3	6.4	46
2	18.4	5.4	52



73 y.o female, 61 Kg, critical AS, baseline HCT 27%, CBF Risk
Q_b 100% = 3.72 LPM, BSA = 1.55 M²
MAP goal > 70 mmHg



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

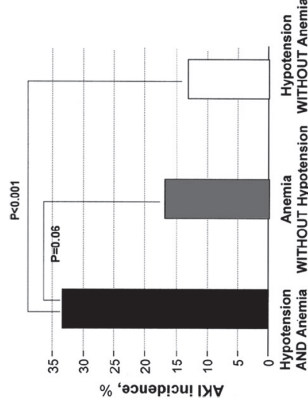
Michael Haase^{1,2}, Rinaldo Bellomo³, David Story⁴, Katja Klemp¹, George Matalanis⁵, Siven Seevanayagam⁵, Duska Dragun¹, Erdmann Seeliger⁶, Peter R. Mertens² and Anja Haase-Fielitz²

¹Department of Nephrology and Intensive Care, Charité—University Medicine Berlin, Berlin, Germany, ²Department of Nephrology and Hypertension & Endocrinology and Metabolic Diseases, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany, ³Department of Intensive Care, Austin Health, Melbourne, Australia, ⁴Department of Anaesthesiology, Austin Health, Melbourne, Australia, ⁵Department of Cardiac Surgery, Austin Health, Melbourne, Australia and ⁶Institute of Vegetative Physiology, Charité—University Medicine Berlin, Berlin, Germany

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Variable	AKI (N = 179)	No AKI (N = 741)	Adjusted OR (95% CI)	P univariate	P multivariate
Model 0					
AKICS Score, points [3] ^b	5.8 (3.9–8.1)	4.3 (2.6–6.3)	1.09 per point increase (1.04–1.15)	<0.001	<0.001
Emergency ^c	25 (13.8%)	22 (3.1%)	4.36 (2.31–8.22)	<0.001	<0.001
Return to operating room, n	34 (19.0%)	52 (7.0%)	2.74 (1.68–4.49)	<0.001	<0.001
Atrial fibrillation, n	47 (26.3%)	69 (9.3%)	2.66 (1.69–4.17)	<0.001	<0.001
Transfused blood volume, mL	19 (10.6%)	23 (3.3%)	1.27 (0.61–2.66)	0.521	0.521
Haemoglobin concentration, g/dL ^d					
Median ^e	8.1 (7.4–9.3)	8.7 (7.7–9.7)	1.18 per g/dL decrease (1.02–1.34)	0.028	0.028
Lowest ^e	7.4 (6.4–8.6)	8.2 (7.0–9.3)	1.16 per g/dL decrease (1.03–1.31)	0.018	0.018
Variability, % ^e	1.2 (0.6–2.2)	0.9 (0.5–1.5)	1.10 per % increase (0.94–1.28)	0.239	0.239
Arterial O ₂ content, mL/dL ^d					
Median ^e	12.3 (11.2–13.9)	13.0 (11.6–14.4)	1.13 per mL/dL decrease (1.02–1.26)	0.027	0.027
Lowest ^e	10.5 (9.1–12.1)	11.0 (9.6–12.5)	1.14 per mL/dL decrease (1.02–1.26)	0.018	0.018
Variability, % ^e	1.2 (0.8–3.0)	1.2 (0.7–2.1)	1.07 per % increase (0.96–1.20)	0.241	0.241
SO ₂ , %	99.7 (99.6–99.8)	99.7 (99.6–99.8)	N/A	N/A	N/A
Red blood cell transfusion, mL ^d	324 (274–385)	319 (272–375)	1.001 per mL (1.000–1.002)	0.013	0.013
Vasopressors					
Metaraminol, mg	3.5 (1.9–6.5)	3.5 (1.5–6.0)	N/A	N/A	N/A
Phenylephrine, mg	4.9 (2.2–8.5)	2.3 (1.3–4.5)	1.05 (0.95–1.16)	0.334	0.334
Meaning					
Median ^e	68.5 (64.0–73.0)	68.0 (64.0–73.0)	N/A	N/A	N/A
Lowest ^e	31.0 (25.0–36.0)	32.0 (25.5–36.5)	N/A	N/A	N/A
Variability, % ^e	16.7 (14.1–19.7)	17.0 (14.3–19.6)	N/A	N/A	N/A
AUC MAP, min × mmHg	0.32 (0.13–0.66)	0.37 (0.17–0.69)	N/A	N/A	N/A
<50 mmHg ^e	1.49 (0.86–2.68)	1.51 (0.93–2.58)	N/A	N/A	N/A
<60 mmHg ^e	5.27 (3.55–7.46)	5.17 (3.51–7.38)	N/A	N/A	N/A



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

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. The aim of this study was to evaluate the effect of high-target versus low-target blood pressure management during cardiopulmonary bypass on cerebral injury in these patients.

METHODS: In a patient- and assessor-blinded randomized trial, we allocated patients to a low-target (nontensive) or high-target (tensive) blood pressure management 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, and the number of new ischemic lesions.

Arno G. Veked, MD, PhD, MSc
Frederik Holmgren, MD, PhD, MSc
Lars S. Rasmussen, DMSc, PhD, MD
Annika Langelide, PhD, MSc
Ole B. Paulsen, DMSc, MD
Thies Lange, PhD, MSc
Carsten Thomsen, DMSc, PhD, MD
Peter Skov Olsen, DMSc, MD
Hanne Berg Ravn, DMSc, PhD, MD
Jens C. Nilsson, PhD, MD

MAP: high vs low

Primary outcome	Low-Target Group, n	High-Target Group, n	Difference (95% CI)	OR (95% CI)	P Value	
Total volume of new cerebral lesions, mm ³						
Complete cases, median (IQR)	80	29 (0 to 143)	0 (-25 to 0.026)*		0.41	
Excluding 3 outliers, median (IQR)	80	28 (0 to 138)				
Complete cases, mean (SD)	80	415 (0.662)	8 (-478 to 994)		0.991	
Excluding 3 outliers, mean (SD)	80	133 (0.13)	144 (0.05)			
Secondary outcome						
Total number of new cerebral lesions	80	1 (0 to 2)	80	1 (0 to 2)		
Complete cases, median (IQR)	80	1 (0 to 2)	80	1 (0 to 2)		
Complete cases, mean (SD)	80	1.52 (0.62)	80	2.23 (0.41)	0.114	
Pharmacological effects in watershed border zones, n (%)	80	32 (40.0)	80	25 (41.3)	0.49	
Stroke, n (%)	97	1 (1.1)	92	6 (7.0)	6.64 (0.78 to 310.75)	0.06
Symptoms on awakening	97	0	92	4		
Symptoms onset between day 2 and 30	97	1	92	2		
POCD, n (%)	91	21 (23.1)	78	27 (34.6)	1.76 (0.90 to 3.47)	0.12
AKI, d	80	8 (9.0)	75	5 (6.7)	0.72 (0.23 to 2.31)	0.77
AKI 90-d						

MAP: high vs low

Primary outcome	Low-Target Group, n	High-Target Group, n	Difference (95% CI)	OR (95% CI)	P Value	
Total volume of new cerebral lesions, mm ³						
Complete cases, median (IQR)	80	29 (0 to 143)	0 (-25 to 0.026)*		0.41	
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AKI 90-d						

Journal of
Cardiothoracic Surgery

Open Access

RESEARCH ARTICLE

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

Husein D Kanji¹, Costas J Schulze^{1,2}, Mariou Hervas-Malo³, Peter Wang¹, David B Ross^{1,2}, Mohamad Zibawi^{1,2,4}, Sean M Bagshaw^{2,3,4*}

10018136CH

1/15/2024

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	<	
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 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 CBF-MAP (ml/min)	0.5	0.2-0.97	0.04	
Pre-operative Systolic BP ≥ 111 mmHg (present)	2.1	0.9-4.6	0.05	
Duration of CBF MAP < 60 (per 1 min)	1.99	0.9-4.4	0.89	

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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 CBF 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
PfRC transfusions (units, mean ± SD)	1.8 ± 1.5	2.4 ± 2.3	0.27
Patients transfused with PfRC (%)	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

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Physiological Reviews

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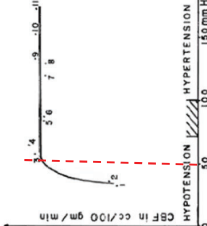
VOLUME 33

APRIL 1959

NEELSA LASEN,†

Department of Clinical Neurophysiology, University of Toronto, Toronto, Ontario, Canada

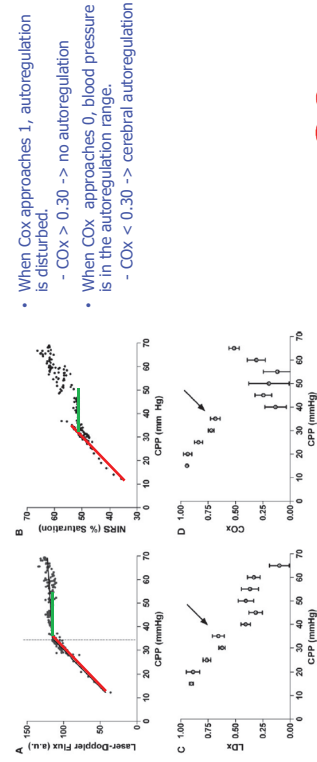
Cerebral Blood Flow and Oxygen Consumption in Man



Cerebral Autoregulation

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

Quantification of autoregulation



Brady 2007

BIA

British Journal of Anaesthesia 129 (1): 22–32 (2022)

DOI: 10.1016/j.bls.2022.03.028

Advance Access Publication Date: 18 May 2022
doi: 10.1016/j.jps.2022.03.029

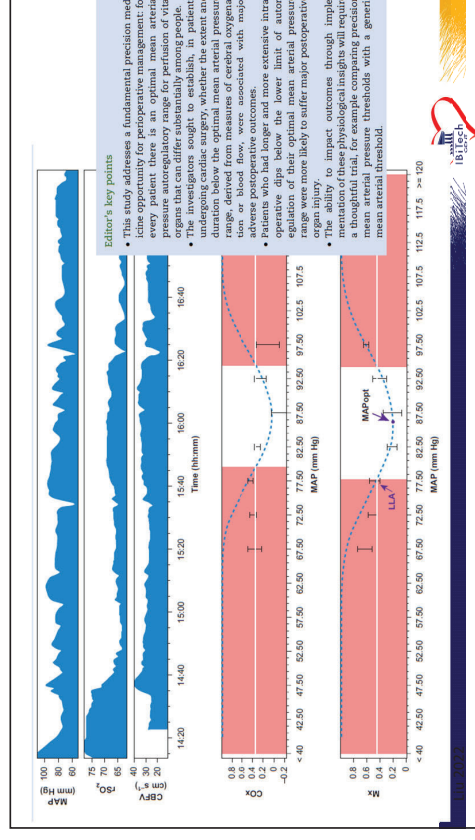
Cardiovascular

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

Xiuyun Liu^{1,2,*}, Joseph Donnelly³, Ken M. Brady⁴, Kei Akiyoshi¹, Brian Bush¹,
Raymond C. Koehler³, Jennifer K. Lee³, Charles W. Hogue⁵, Marek Czosnyka^{6,7},
Peter Smielewski¹⁶ and Charles H. Brown IV^{1,*}

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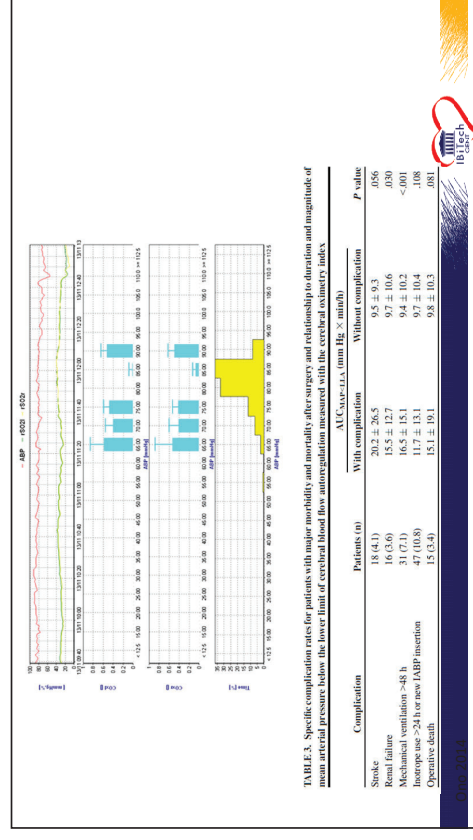
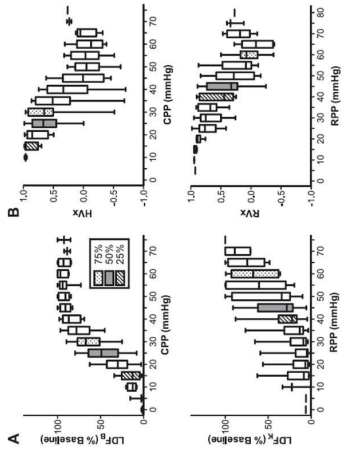


TABLE 3. Specific complication rates for patients with major morbidity and mortality after surgery and relationship to duration and magnitude of mean arterial pressure below the lower limit of cerebral blood flow autoregulation measured with the cerebral oximetry index

Complication	Patients (n)	MC _{stage-1} (n = 224) (mm Hg × min)		P value
		With complication	Without complication	
Stroke	18 (4.1)	20.2 ± 26.5	9.5 ± 9.3	.056
Renal failure	16 (3.6)	15.8 ± 12.7	9.7 ± 10.6	.030
Mechanical ventilation >48 h	31 (7.1)	16.8 ± 15.1	9.4 ± 10.2	<.001
Inotropic use >24 h or new IABP insertion	47 (10.8)	11.7 ± 13.1	11.7 ± 13.1	.108
Operative death	15 (3.4)	15.1 ± 19.1	9.8 ± 10.3	.081

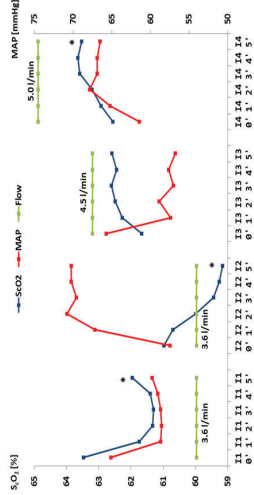
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Autoregulation of the kidney



Rhee 2012

Results



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 during cardiopulmonary bypass.
- In patients undergoing cardiopulmonary bypass, independent manipulation of blood flow and pressure.
- Cerebral and systemic oxygenation were maintained 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 systemic oxygen saturation.

Methods. In 10 patients undergoing cardiopulmonary bypass, independent manipulation of flow and pressure was achieved using a randomized crossover design, four different hemodynamic states were simulated: (i) 25% flow decrease, (ii) 25% flow increase, (iii) 25% pressure increase, and (iv) 25% pressure decrease. Cerebral and systemic oxygen saturation, cerebral and systemic oxygen extraction ratio (OER), and systemic oxygen extraction ratio (OER) were assessed by near-infrared spectroscopy.

Results. Decrease in flow was associated with a decrease in SDO₂ [from 63.5 (7.4) to 62.0 (8.5) %, $P < 0.001$]. When cerebral pressure was reduced with phenylephrine during low flow, SDO₂ further decreased from 63.0 (9.7) to 58.2 (10.2) %, $P < 0.001$. Increase in flow with phenylephrine during low flow did not affect SDO₂. SDO₂ was significantly lower ($P < 0.001$) in pressure with the use of SNP did not affect SDO₂. SDO₂ 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, SDO₂ and SDO₂ were maintained with flow but not with pressure. Cerebral and systemic oxygen saturation were maintained with flow but not with pressure. Phenylephrine administration was associated with a reduced cerebral and systemic oxygen saturation.

Keywords: cardiopulmonary bypass; cerebral oxygenation; phenylephrine; spectroscopy; near infrared

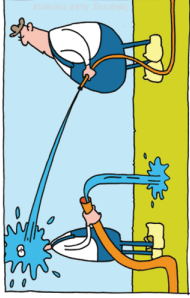
Accepted for publication: 28 March 2013

Analysis

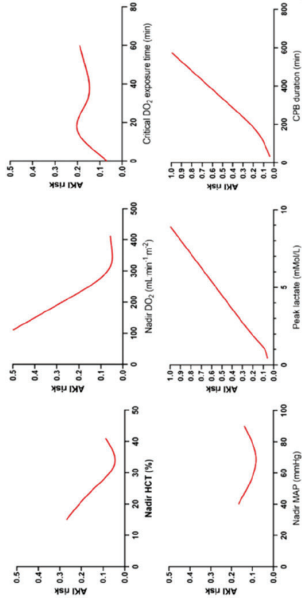
Q _{blood} L/min	DO _{2i} mL/min/m ²	VO _{2i} mL/min/m ²	VO _{2i} /DO _{2i}
3.6	256	46	0.18
BL -20%			
3.6	256	46	0.18
BL -20% + PE			
4.5	320	49	0.15
BL + NSP => -20%P			
5.0	356	47	0.13
BL +20% => MAP			

Conclusion pressure vs flow

- Cerebral and venous oxygen saturations are more dependent on flow than on pressure
- Change in paradigm “pressure vs flow”



Multivariate model



Multivariate model

Risk Factor	Points	Regression coefficient	Odds ratio
Female gender	1	0.578	1.78
Congestive heart failure	1	3.797	44.6
Left ventricular ejection fraction <35%	2	-0.264	0.77
Preoperative use of IABP	1	0.852	94.8
Intra-aortic balloon pump	1	0.498	1.65
Insulin-requiring diabetes	1	4.197	66.5
Previous cardiac surgery	2	3.652	38.5
Emergency surgery	1	-4.112	—
Vascular surgery only (reference to CABG)	2		
CABG + valve (reference to CABG)	2		
Other cardiac surgeries	2		
Preoperative creatinine 1.2 to <2.1	2		
Preoperative creatinine >2.1	2		
Preoperative creatinine >2.1 (reference to 1.2)	5		

$$\exp(-1.079 + 0.079 \cdot \text{CRS} + 0.035 \cdot \text{Age} - 0.095 \cdot \text{HCT})$$
$$(1 + \exp[-1.079 + 0.079 \cdot \text{CRS} + 0.035 \cdot \text{Age} - 0.095 \cdot \text{HCT}])$$

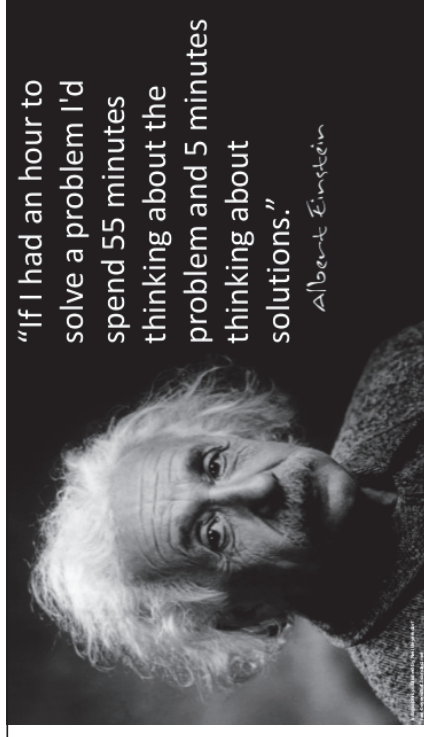
$$\text{MDPI CSA} - \text{AKI risk} = \frac{\exp(-3.35 + 4.17 \cdot \text{SRM} + 5.37 \cdot \text{DPR})}{1 + \exp[-3.3 + 4.17 \cdot \text{SRM} + 5.37 \cdot \text{DPR}]}$$

Conclusions

- GDP should be based upon oxygen delivery and CO2 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!

