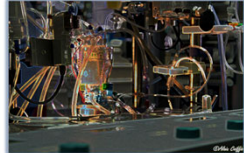


CONTRÔLE GLYCÉMIQUE PERIOPÉRAtoire EN CHIRURGIE CARDIAQUE

Prof. Alexandre OUATTARA
Service d'Anesthésie-Réanimation cardiovasculaire
Hôpital cardiologique haut-Lévêque, CHU de Bordeaux



Stress périopératoire
(cortisol, catécholamines,
interleukines 6 et 10)

Insulino-résistance périphérique
(tissus insulino-dépendants périphériques)
muscle squelettique, tissu adipeux +++
Anomalies GLUT 4

Libération AGL
(effets délétères
myocardiques)

Hyperglycémie périopératoire

Ljungqvist et al. *Surgery* 2000;28:757-60
Lipshutz et al. *Anesthesiology* 2009;110:408-21

Précoce

- Quelques heures après début de la chirurgie
- Périopératoire, postopératoire immédiat,...

Persiste plusieurs jours après chirurgie (2-3 semaines)

Facteurs aggravants

- Obésité (tissu adipeux +++)
- Chirurgie invasive (hémorragique, longue durée, hémodynamiquement intense, circulation extra-corporelle, ...)
- Jeun préopératoire prolongé (en limiter le temps ou apport glucosé...)
- Hypothermie
- Immobilisation prolongée (réhabilitation précoce)

Insulino-résistance périphérique
(tissus insulino-dépendants périphériques)
muscle squelettique, tissu adipeux

Insulin resistance after abdominal surgery

British Journal of Surgery 1994, 81, 59-63

A. THORELL, S. EFENDIC*, M. GUTNIAK*, T. HÄGGMARK and O. LJUNGQVIST

Détermination et évolution insulino-sensibilité
Cholécystectomie réglée
Clamp euglycémique hyperinsulinique

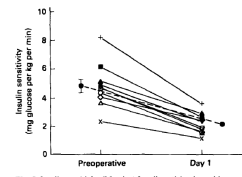


Fig. 2 Insulin sensitivity (M value) for all participating subjects before and on the first day after open cholecystectomy (n=10). —, Mean(S.E.M.)

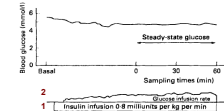
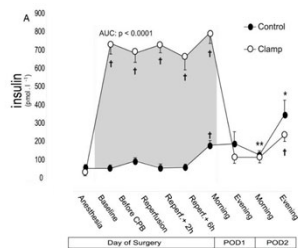
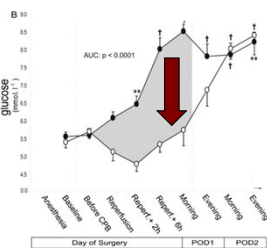


Fig. 3 Relative insulin sensitivity (calculated as postoperative M value/preoperative M value) before and on days 1, 5, 9 and 20 after open cholecystectomy. —, Mean(S.E.M.) (n=5 or 10). *P<0.05, **P<0.001 (versus preoperative values, Student's t test)

Insulino-résistance «relative»

Corrigée par un apport exogène insulinique

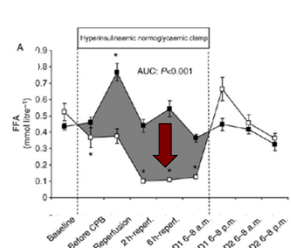
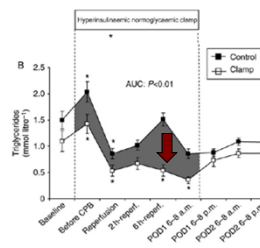


Van Wezel HB et al. *J Clin Endocrinol Metab* 2006;91:4144-53

Perioperative hyperinsulinaemic normoglycaemic clamp causes hypolipidaemia after coronary artery surgery¹

C. J. Zuurbier¹*, F. J. Hoek², J. van Dijk³, N. G. Abeling⁴, J. C. M. Meijers⁴, J. H. M. Levels⁴, E. de Jonge², B. A. de Mol² and H. B. Van Wezel¹

Br J Anaesth 2008; 100: 442-50



6

Hyperglycémie périopératoire

Les mécanismes...

- ✓ Insulino-résistance +++

Tsubo T et al. *Can J Anaesth* 1990; 37:645-9

- ✓ Stimulation production endogène de glucose

Schricker T et al. *Nutrition* 1997; 13:191-5

- ✓ Augmentation résorption rénale de glucose

Braden H et al. *Ann Thorac Surg* 1998;65:1588-93

- ✓ Diminution clairance du glucose

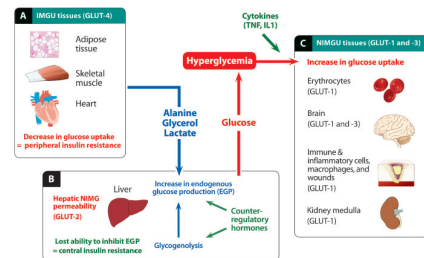
Siardil Solomon Z et al. *Acta Anaesthesiol Scand* 2006;50:848-54

CLINICAL CONCEPTS AND COMMENTARY

Glycemic Control in the Intensive Care Unit and during the Postoperative Period

Diane Lena, M.D.,* Pierre Kalfon, M.D.,† Jean-Charles Preiser, M.D., Ph.D.,‡
Carole Ichai, M.D., Ph.D.§

Anesthesiology 2011; 114:438-44



Acute hyperglycemia abolishes ischemic preconditioning in vivo

Am J Physiol 1998; 275:H721-25

JUDY R. KERSTEN, TODD J. SCHMELING, KARL G. ORTH, PAUL S. PAGEL, AND DAVID C. WARTLIER
Departments of Anesthesiology and Pharmacology and Toxicology and Division of Cardiovascular Diseases, Department of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin 53226

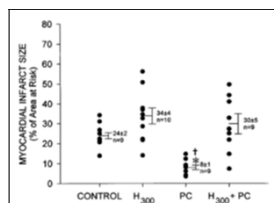
Etude expérimentale (cœurs de chien)

Ischémie (60 min) + Reperfusion (3h)

Pré-conditionnement ischémique = 4 X 5 min occlusion avant IR

Contrôle et Hyperglycémique (= 300 mg/dL) induite par perf IV

Critère de jugement = Taille de l'infarctus myocardique par rapport à la taille de la zone à risque



9

Reactive oxygen species modulate coronary wall shear stress and endothelial function during hyperglycemia

Stress oxydatif

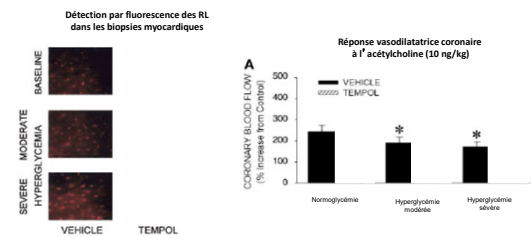
Eric B. Green,^{1,2,*} John F. LaRosa, Jr.,^{1,2,*} Dorothea Weikens,² Lars E. Olson,² Tobias T. Kren,² Douglas A. Hettrich,^{1,2} Paul S. Pagel,^{1,2} David C. Wartler,^{1,2,*} and Judy R. Kersten^{1,2}

Am J Physiol Heart Circ Physiol 284: H1552-H1558, 2003.

Modèle in vivo canin

Effets hyperglycémie 350 et 600 mg/dL (Glucose IV) sur production de RL et fonction endothéliale

Antagonisation par le tempol = analogue de la SOD (scavenger des radicaux libres)



10

Tight Glycemic Control in Diabetic Coronary Artery Bypass Graft Patients Improves Perioperative Outcomes and Decreases Recurrent Ischemic Events

Harold L. Lazar, MD; Stuart R. Chaplin, MD; Carmel A. Fitzgerald, RN; Yusheng Bao, MD; Howard Cabral, PhD; Carl S. Apstein, MD

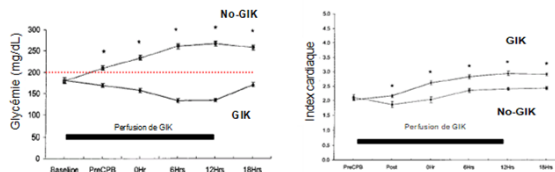
Circulation. 2004;109:1497-1502

Etude prospective randomisée

Patients diabétiques en chirurgie coronaire

- Groupe HGT 125-200 mg/dL (n=72)

- Groupe HGT <250 mg/dL (n=69)



11

Tableau: Morbi-mortalité postopératoire

	GIK (n=69)	No-GIK (n=72)
IDM postopératoire	0%	2,8%
ACFA	17%	42%*
Infections (pneumopathie ou cicatrice)	0%	13%*
Durée de ventilation (h)	6,9 ± 0,3	10,7 ± 0,6*
Score inotrope	1,2 ± 0,1	2,2 ± 0,2*
Durée de séjour en réa (h)	17,3 ± 1,0	32,8 ± 2,6*
Durée de séjour totale (j)	6,5 ± 0,1	9,2 ± 0,3*
Mortalité à 30 jours	0%	0%

Les résultats sont exprimés en % ou moyenne ± écart-type. P<0,05 versus groupe GIK

12

Moderate hyperglycemia worsens acute blood-brain barrier injury after forebrain ischemia in rats

Dietrich WD et al. *Stroke* 1993;24:111-116

Etude expérimentale *in vivo* chez rats

Effets hyperglycémie sur les lésions d'ischémie cérébrale en normothermie

Ischémie globale 20 min (occlusion 4 axes vasculaires)

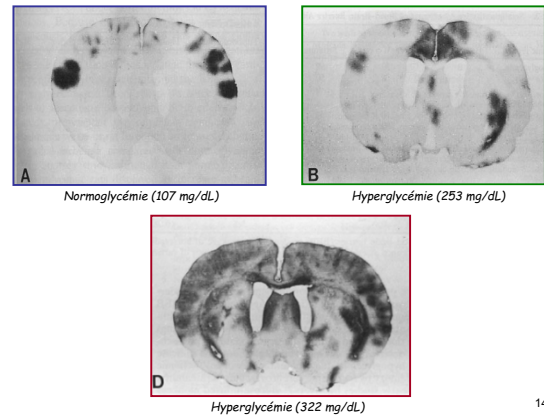
Reperfusion 30 min puis sacrifice des animaux

2 groupes - **Hyperglycémique** (n=6) Inj IP G50%, 15 min avant ischémie

- **Normoglycémique** (n=5) Inj IP solution saline avant ischémie

Quantification des lésions barrière hémato-encéphalique (BHE) par de l'extravasation du horseradish peroxidase (HRP) sur coupes histologiques

13



14

Persistent Poststroke Hyperglycemia Is Independently Associated With Infarct Expansion and Worse Clinical Outcome

Tracey A. Baird, Mark W. Parsons, Thanh Phan, Ken S. Butcher, Patricia M. Desmond, Brian M. Tress, Peter G. Colman, Brian R. Chambers and Stephen M. Davis

Stroke. 2003;34:2208-2214

TABLE 2. Correlations Between Glycemic Parameters and Outcome Measures

	<i>r</i>
Peak glucose	0.48
Mean glucose	0.42
Time in range (100-180 mg/dL)	-0.35
Time in range (180-250 mg/dL)	0.32
Time in range (>250 mg/dL)	0.45

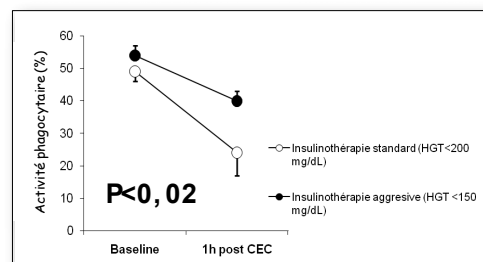
* $P < 0.05$.

*mRS= modified Rankin Score

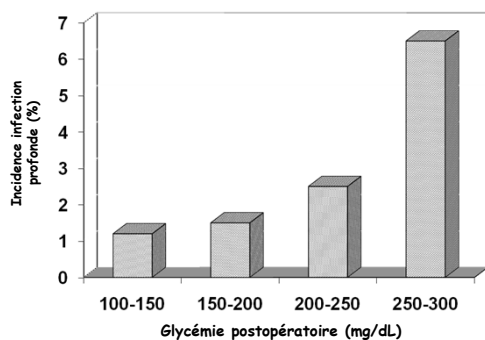
15

Insulin Infusion Improves Neutrophil Function in Diabetic Cardiac Surgery Patients

Rassias AJ et al. *Anesth Analg* 1999



16



Zerr et al *Ann Thorac Surg* 1997

17

Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting

Anthony P. Furnary, MD,^{a,d} Guangqiang Gao, MD,^a Gary L. Grunkemeier, PhD,^b YingXing Wu, MD,^b Kathryn J. Zerr, MBA,^b Stephen O. Bookin, MD,^b H. Storm Floten, MD,^{a,d} and Albert Starr, MD^{a,d}

J Thorac Cardiovasc Surg 2003

Etude prospective historique sur 15 ans

Patients diabétiques (n=3554)

Chirurgie coronaire

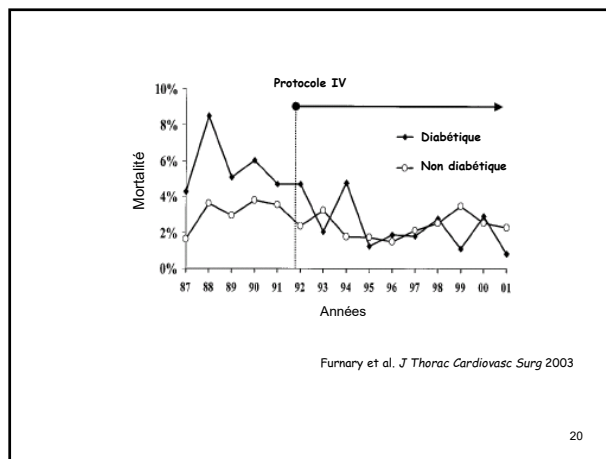
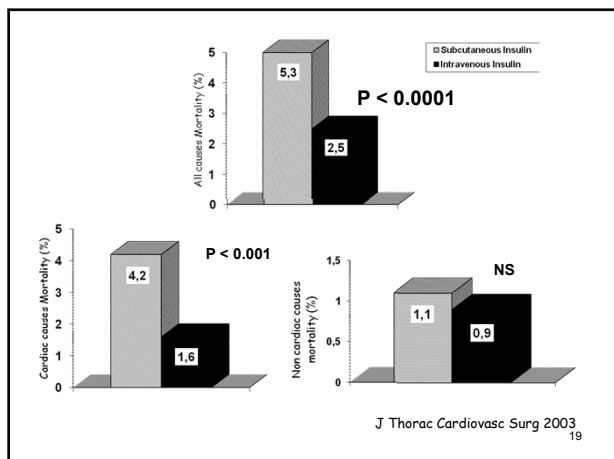
Groupe Insulinothérapie sous-cutanée 1987-1991 (n=942)

Objectif: <200 mg/dL

Groupe Insulinothérapie IVSE 1991-2001 (n=2612)

Objectifs de plus en plus audacieux (100-150 mg/dL)

18



The New England Journal of Medicine

Copyright © 2001 by the Massachusetts Medical Society

VOLUME 345 NOVEMBER 8, 2001 NUMBER 19

INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., Ph.D., PIETER WOUTERS, M.Sc., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANK BRUYNINCKX, M.D., MIET SCHETZ, M.D., Ph.D., DIRK VLAESLAERS, M.D., PATRICK FERDINAND, M.D., Ph.D., PETER LAUWERS, M.D., AND ROGER BOULLON, M.D., Ph.D.

Etude prospective randomisée unicentrique
Réanimation chirurgicale (cardiaque +++)

Insulinothérapie Intensive (80-110 mg/dL) n=765
versus
Insulinothérapie conventionnelle (180-200 mg/dL) n=783

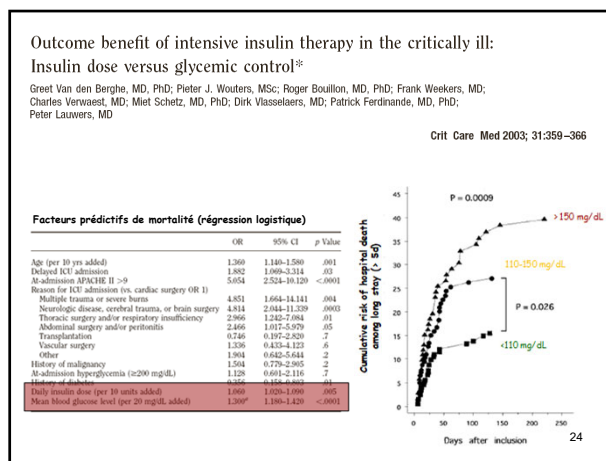
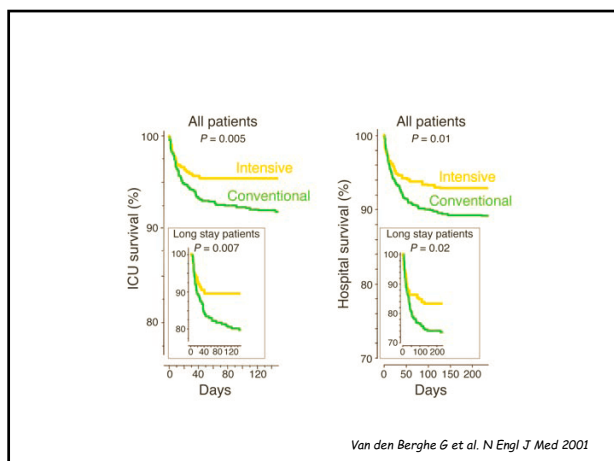
Critère de jugement principal = Mortalité durant le séjour en réanimation

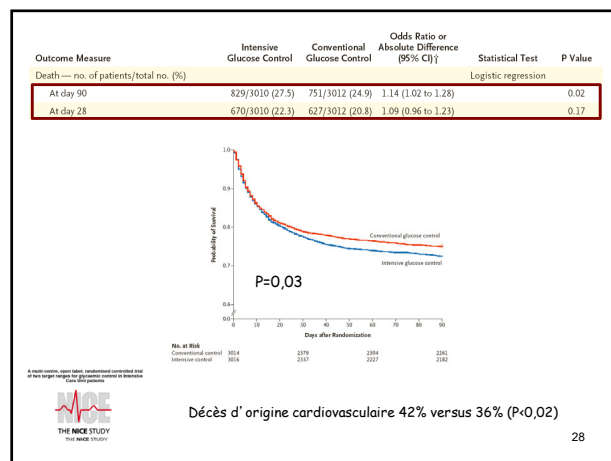
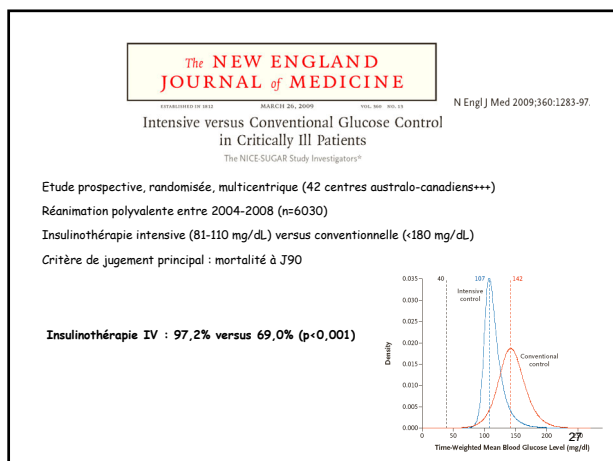
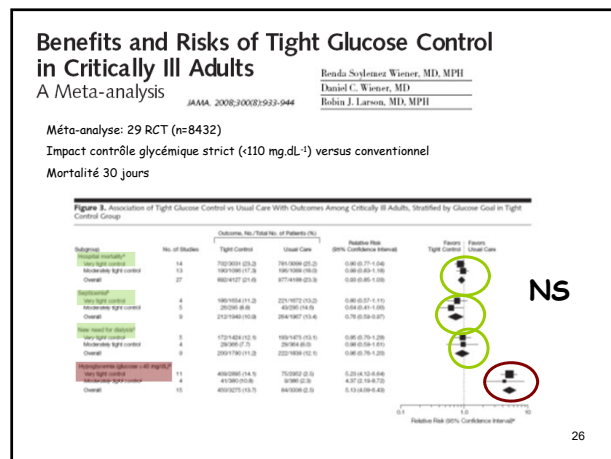
21

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	CONVENTIONAL TREATMENT (N=783)	INTENSIVE TREATMENT (N=765)
Male sex — no. (%)	557 (71)	544 (71)
Age — yr	62.2±13.9	63.4±13.6
Body-mass index†	25.8±4.7	26.2±4.4
Reason for intensive care — no. (%)		
Cardiac surgery	493 (63)	477 (62)
Noncardiac indication	290 (37)	288 (38)
Neurologic disease, cerebral trauma, or brain surgery	30 (4)	33 (4)
Thoracic surgery, respiratory insufficiency, or both	56 (7)	66 (9)
Abdominal surgery or peritonitis	58 (7)	45 (6)
Vascular surgery	32 (4)	30 (4)
Multiple trauma or severe burns	35 (4)	33 (4)
Transplantation	44 (6)	46 (6)
Other	35 (4)	35 (5)

22





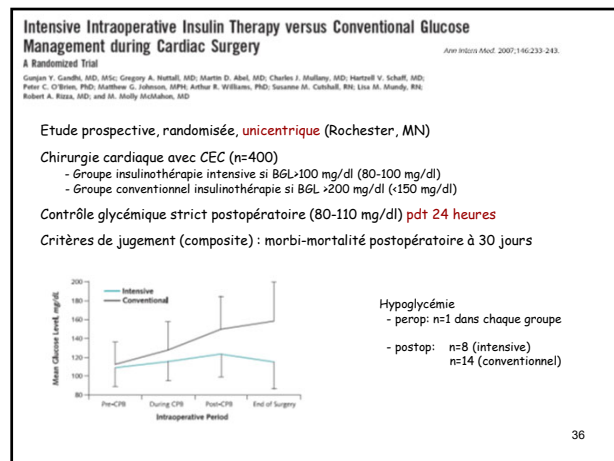
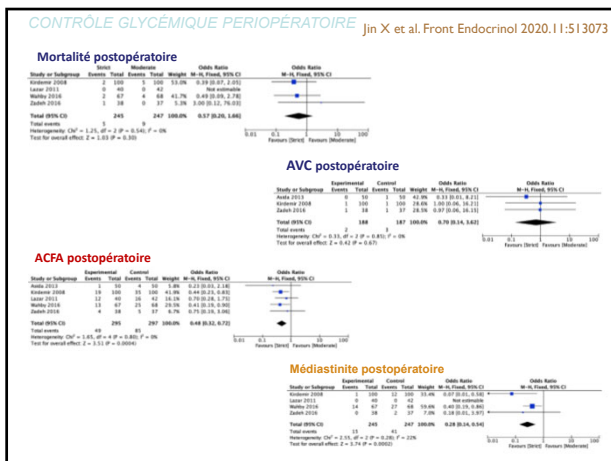
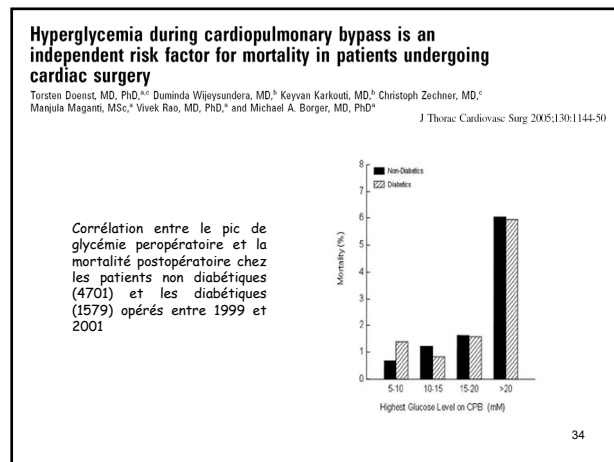
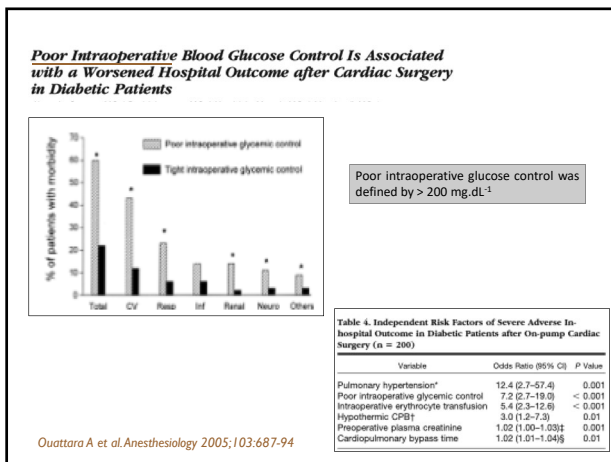
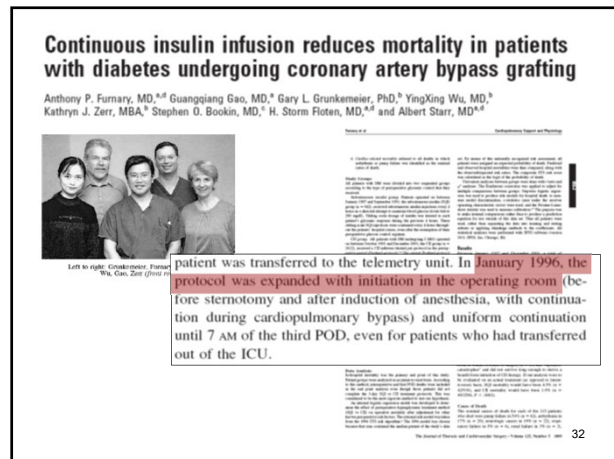
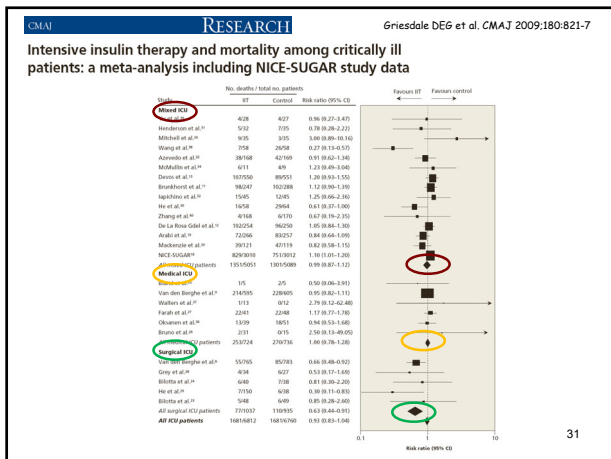


Table 4. Comparison of Primary and Secondary Outcomes*

Outcome	Intensive Treatment Group (n = 185), n (%)	Conventional Treatment Group (n = 186), n (%)	Relative Risk or Odds Ratio (95% CI)†	P Value‡
Any event§	82 (44)	86 (46)	1.0 (0.8 to 1.2)	0.71
In hospital	78 (42)	82 (44)		
Postdischarge (up to 30 days after surgery)	8 (4)	9 (5)		
Death	4 (2)	0 (0)	— (0.9 to ∞)	0.061
In hospital	4 (2)	0 (0)		
Postdischarge (up to 30 days after surgery)	0 (0)	0 (0)		
Stroke	8 (4)	1 (1)	8.0 (1.0 to 63.7)	0.020
In hospital	7 (4)	1 (1)		
Postdischarge (up to 30 days after surgery)	1 (1)	0 (0)		
Deep sternal infection	6 (3)	7 (4)	0.9 (0.3 to 2.5)	0.79
In hospital	3 (2)	1 (1)		
Postdischarge (up to 30 days after surgery)	3 (2)	6 (3)		
Cardiac arrest	1 (1)	0 (0)	— (0.1 to ∞)	0.50
In hospital	1 (1)	0 (0)		
Postdischarge (up to 30 days after surgery)	0 (0)	0 (0)		

Pas de différence significative sur la durée de séjour en réa ou à l'hôpital

37

Because of cardiopulmonary bypass (CPB)-induced alterations in insulin secretion and resistance, profound hyperglycemia occurs in patients undergoing cardiac surgery (levels may approach 1000 mg/dL). Hyperglycemia has been shown to worsen neurologic injury after focal and global cerebral ischemia, probably because of anaerobic glycolysis-induced conversion of glucose to lactate, which causes intracellular acidosis and impairment of cellular metabolism (1,2). The appropriate

intraoperative management of hyperglycemia, whether it adversely affects neurologic outcomes after cardiac surgery, remains controversial. Previous investigations have assessed intraoperative changes in a battery of neurologic examinations. However, interpretation at the time of intraoperative changes in neurologic

Attempting intraoperative tight glucose control may be difficult

Intraoperative insulin resistance (hypothermia, stress hormone, CPB...)

Postoperative requirement (insulin resistance) may decrease rapidly

Risk of postoperative hypoglycemia

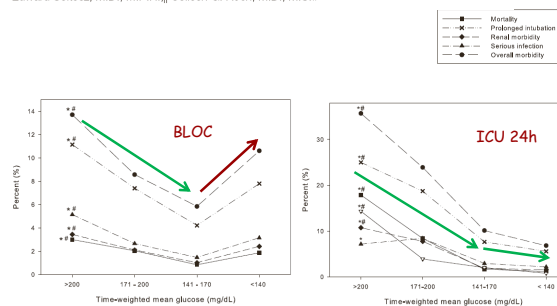
Anesth Analg 1999;89:1091-5

38

Role of Intraoperative and Postoperative Blood Glucose Concentrations in Predicting Outcomes after Cardiac Surgery

Anesthesiology 2010; 112:860-71

Andra E. Duncan, M.D.,* Alaa Abd-Elsayed, M.D.,† Ankit Maheshwari, M.D.,‡ Meng Xu, M.S.,§ Edward Soltész, M.D., M.P.H.,|| Colleen G. Koch, M.D., M.S.¶



39

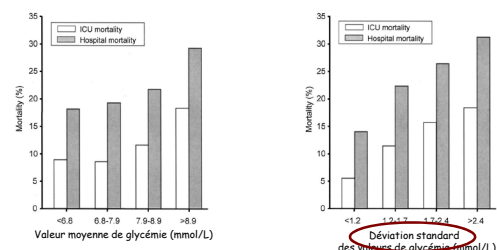
Variability of Blood Glucose Concentration and Short-term Mortality in Critically Ill Patients

Anesthesiology 2006; 105:241-52

Mortko Egi, M.D.,* Rinaldo Bellomo, M.D., F.J.F.I.C.M.,† Edward Stachowski, M.D.,‡ Craig J. French, M.D.,§ Graeme Hart, M.D.¶

Etude multicentrique rétrospective (2000-2004)

Réanimation polyvalente (n=7049)



40

Increased Glucose Variability Is Associated With Major Adverse Events After Coronary Artery Bypass

Clement KC et al. Ann Thorac Surg 2019;108:1307-13

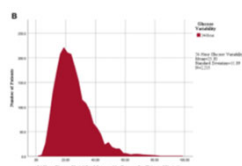


Table 2. Multivariate Logistic Regression of Postoperative Glucose Variability and Major Adverse Events*

Variable	Odds Ratio	95% CI Lower	95% CI Upper	P Value
Preoperative factors and 12-hour glucose variability				
Age	1.02	1.01	1.04	.003
Hemoglobin A _{1c}	0.97	0.98	1.07	.54
Ejection fraction	0.97	0.96	0.98	<.001
Hyperlipidemia	1.49	1.05	2.13	.027
Hypertension	0.62	0.40	0.97	.036
Square root of Cardiopulmonary bypass time (min)	1.15	1.07	1.24	<.001
Total blood products transfused in OR	1.52	1.38	1.68	<.001
12-hour glucose variability	1.06	0.87	1.29	.58
Constant	0.02			<.001

Postoperative AAE: cardiac arrest, pneumonia, renal failure, stroke, sepsis, reoperation, 30-day mortality

41

Increased Glycemic Variability in Patients with Elevated Preoperative HbA1C Predicts Adverse Outcomes Following Coronary Artery Bypass Grafting Surgery

Balachandhar Subramaniam, MD, MPH,* Adam Lerner, MD,* Victor Novack, MD, PhD,†† Kamal Khabbazi, MD,§ Maya Paryente-Wiesmann, MD,‡ Philip Hess, MD, PhD,* and Daniel Tahiror, MD, MPH*

Anesth Analg 2014;118:277-87

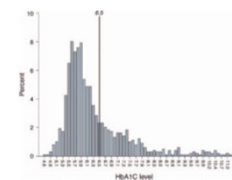


Figure 1. Hemoglobin A1C (HbA1C) distribution in our patient population. HbA1C levels (%) are seen in the axis.

Variables	All patients (n = 1465)	HbA1C <6.5% (n = 1003)	HbA1C ≥6.5% (n = 468)	P
Postoperative postoperative complications	143 (9.8%)	87 (8.7%)	56 (12.0%)	0.034
MI	5 (0.3%)	5 (0.5%)	0	0.333
Respiratory infection	32 (2.2%)	22 (2.2%)	10 (2.1%)	0.869
Deep sternal infection	15 (1%)	9 (0.9%)	6 (1.3%)	0.208
Stroke	19 (1.3%)	12 (1.2%)	7 (1.5%)	0.853
Pneumonia	36 (2.5%)	21 (2.1%)	15 (3.2%)	0.177
Renal injury	44 (3%)	27 (2.7%)	17 (3.6%)	0.280
Sepsis	1 (0.1%)	0	1 (0.2%)	0.383
Death	42 (2.9%)	30 (3%)	12 (2.6%)	0.794
All-cause mortality	122 (8.3%)	69 (6.9%)	53 (11.3%)	0.001

42

Accuracy of bedside capillary blood glucose measurements in critically ill patients

C. Dana Critchell
Vincent Savarese
Amy Callahan
Christine Aboud
Serge Jabbour
Paul Marik

Comparaison de la glycémie capillaire versus laboratoire
Réanimation polyvalente (80 patients sur 4 mois)

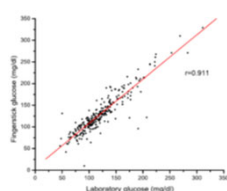
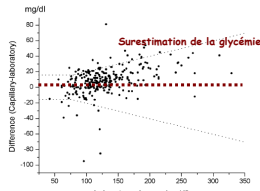


Fig. 1 Plot of laboratory glucose vs. fingerstick glucose



43

Glucose Measurement in the Operating Room: More Complicated than It Seems

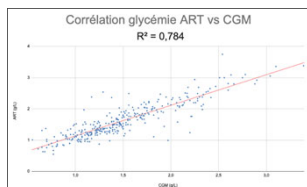
Anesth Analg 2010;110:1056-65

Mark J. Rice, MD,* Andrew D. Pitkin, MBBS, MRCP, FRCA,* and Douglas B. Coursin, MD†

Variable	Methodology affected ^a	
	GO	GD
Whole blood	↓	↓
Arterial	↑	↑
Capillary	↑	↑
Postprandial state	↑	↑
Hematocrit	↑	↑
Anemia	↑	↑
Polycythemia	↓	↓
Oxygen concentration	↑	↑
Hypoxia	↑	↑
Oxygen therapy	↑	↑
pH (6.8-7.55)	↑	↑
Low pH	—/↓	—
High pH	—/↑	—
Hypothermia	↑	↑
Hypertension	↑	↑
Drugs	↑	↑
Ascorbic acid	↓	↓
Acetaminophen	↑	↑
Dopamine	↑	↑
Iodine	↑	↑
Mannitol	↑	↑

Reprinted from Dungan et al.,²⁸ with permission.
GO = glucose oxidase; GD = glucose dehydrogenase.
^a Changes relative to venous plasma measured as central laboratory.

44

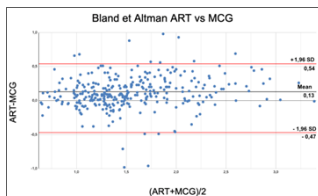


CHU BDX ANESTHÉSIE-RÉANIMATION
CARDIOVASCULAIRE



n(32)	Déviations au protocole %	Moyenne déviation d'insuline IVSE (U/kg)
43	1.14 ± 0.99	

Fiabilité discutable
Valeur de glycémie interstitielle ≠ glycémie sanguine

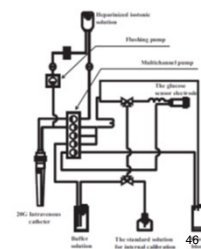
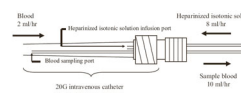


The Accuracy of a Continuous Blood Glucose Monitor During Surgery

Yamashita K et al. Anesth Analg 2008;106:160-3

Cathéter veineux à double lumière (20G)

- Rinçage en continu 8 ml/h (sérum physiologique hépariné)
- Prélèvement 10 ml/h (2 ml de sang/h +++)
- Capteur de glucose (glucose-oxydase) 95 µL
- Nouvelle valeur de glycémie toutes les 2 min
- Auto-calibration toutes les 4 heures



Accuracy and reliability of continuous blood glucose monitor in post-surgical patients

Yamashita K et al. Acta Anaesthesiol Scand 2009; 53:66-71

- Evaluation de la précision d'un capteur de monitoring glycémique en continue (STG-22)
 - KT veineux périphérique (20G) avant bras
- Etude observationnelle (n=50)
- Réanimation chirurgicale **durant 16 heures**

Etude de concordance

	Hypoglycemia (<3.89 (70) mg/dl)	Normoglycemia (3.89 (70)-10 (180) mg/dl)
n	11	161
Blood glucose measured by the ABL [®] ROFLEX (mg/dl)	0.33(0.5) ± 0.17(3)	7.39(1.33) ± 1.56(28)
Bias (mg/dl)	0.04(0.7) (-0.56) - 1.53) ~ -0.17(3)	-0.11(-2) (-0.21) - 3.7) ~ -0.02(-0.3)
Lower limits of agreement (mg/dl)	-0.33(-6) (-0.56) - 1(3) ~ -0.11(-2)	-1.33(-24) (-1.5) - 27) ~ -1.17(-21)
Upper limits of agreement (mg/dl)	0.39(7) (0.19(3) ~ 0.61(11))	1.11(20) (0.94(17) ~ 1.28(23))
Percent error for limits of agreement (%)	7	15

Data are expressed as mean ± SD and mean (95% confidence interval).

47

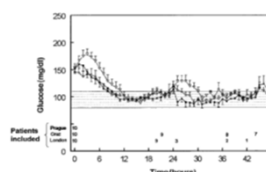
Multicentric, randomized, controlled trial to evaluate blood glucose control by the model predictive control algorithm versus routine glucose management protocols in intensive care unit patients

Plank et al. Diabetes Care 2006; 29:271-6

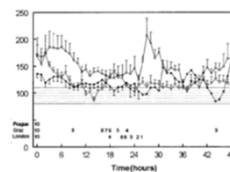
Etude multicentrique

Patients chirurgie cardiothoracique (n=60)

Variables d'entrée (glycémie, débit pompe, apport glucosé)



Avec algorithme informatisé



Sans algorithme informatisé

Moindre variabilité de la glycémie +++

48

55

PAS D'INSULINE IVSE EN SALLE

56

57

« ...suggestions that glucose solutions should be avoided in both long and short surgical procedures»

59