

Hyperglycemia Should be Accepted and Safe in Pediatric Cardiac Surgery

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Points

- Causal association of hyperglycemia and adverse outcome is uncorroborated
- Intra-operative hyperglycemia is potentially beneficial to some organ systems
- Unintended consequences of tight glycemic control pose greater risk of injury
- We lack the skills and technology to tightly control glucose without adverse events

Recovery in out-of-hospital cardiac arrest

Group	Number of patients	Glucose (mg/dl)
Never awakening	154	341 ± 13°
Ever awakening:	276	262 ± 7
Persistent deficiencies	90	286 ± 15°°
No deficiencies	186	251 ± 7

Longstreth WT Ann Neurology 15:59-65, 1985

The NEW ENGLAND JOURNAL of MEDICINE

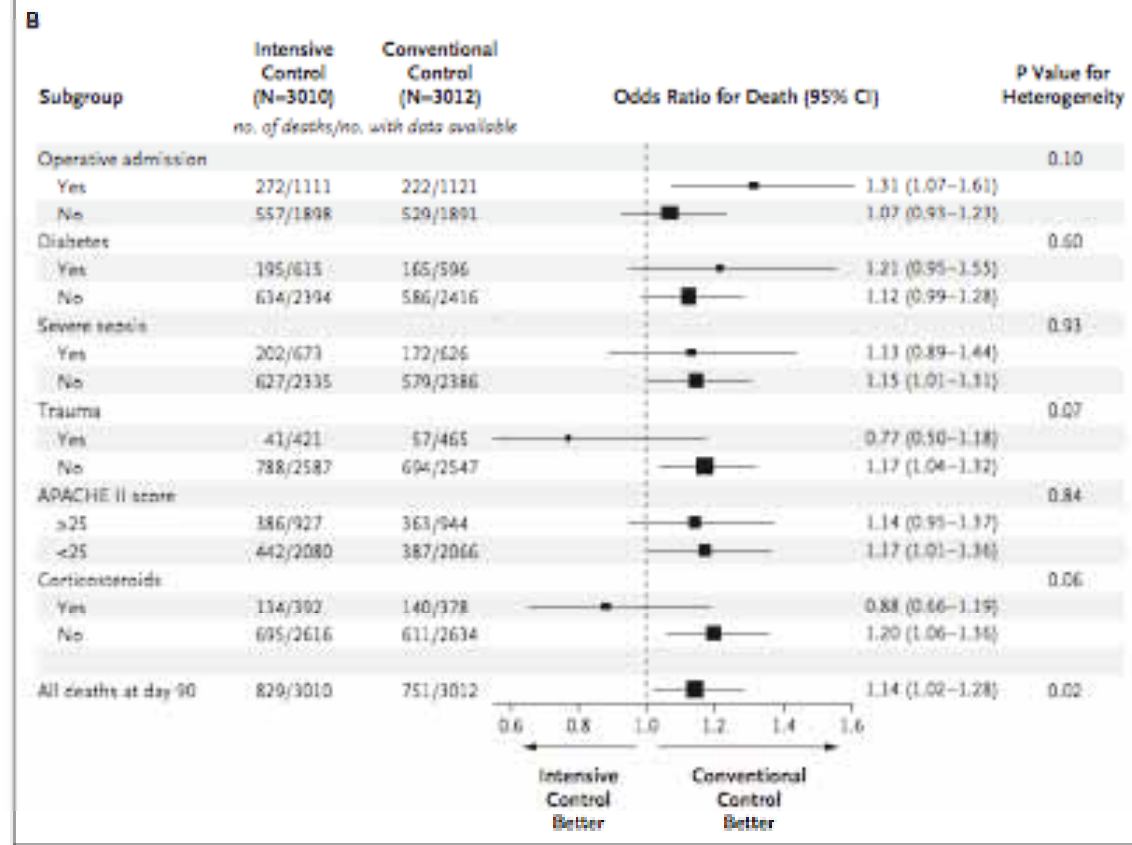
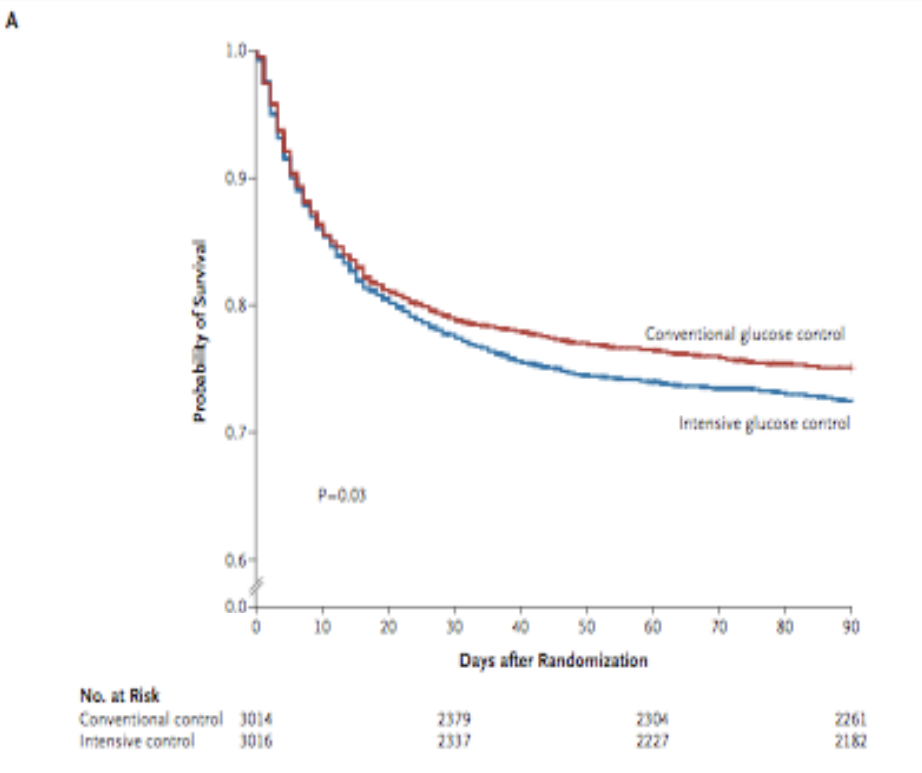
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Intensive versus Conventional Glucose Control in Critically Ill Patients

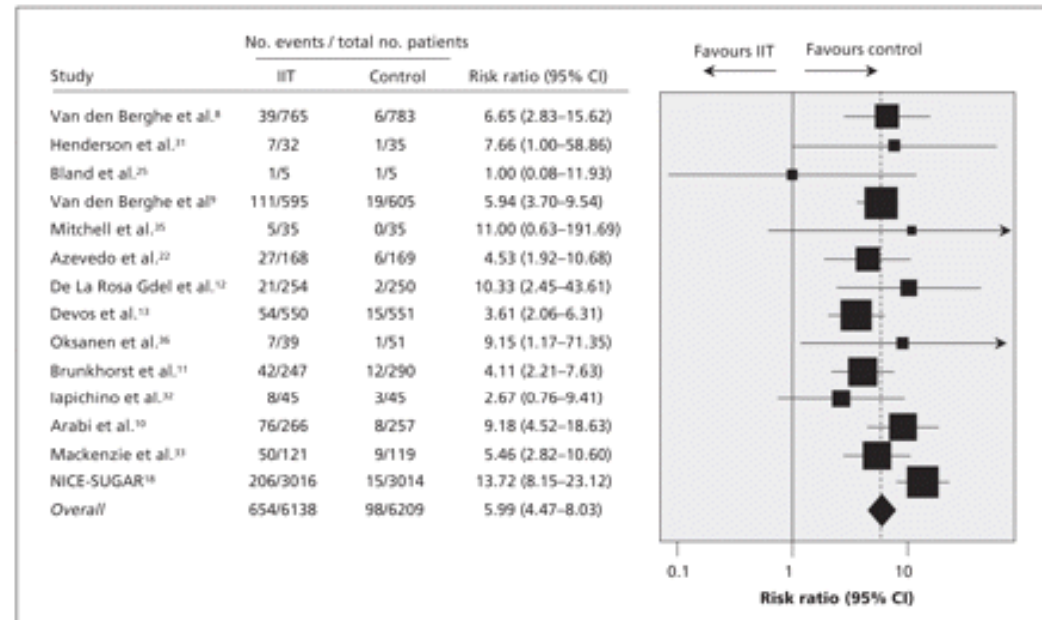
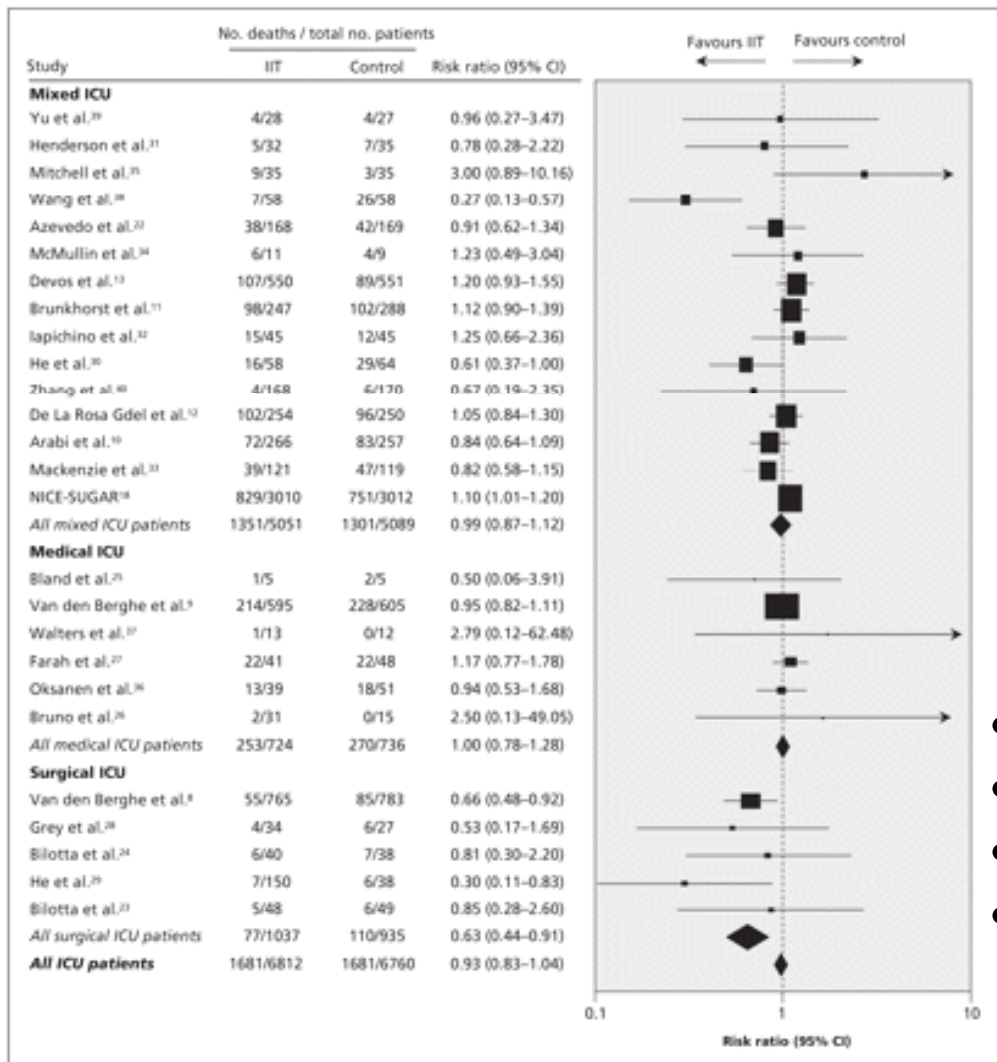
The NICE-SUGAR Study Investigators*



- 6104 adult ICU patients
- Prospective, randomized trial of glucose control

Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data

Donald E.G. Griesdale MD MPH, Russell J. de Souza RD MSc, Rob M. van Dam PhD, Daren K. Heyland MD, Deborah J. Cook MD MSc, Atul Malhotra MD, Rupinder Dhaliwal RD, William R. Henderson MD, Dean R. Chittock MD MS(Epi), Simon Finfer MBBS, Daniel Talmor MD MPH



- 26 randomized adult trials of int insulin therapy
- 13,567 patients
- No benefit on mortality
- Significant risk ratio for severe hypoglycemia

Neurologic Outcome and Hyperglycemia

CLINICAL INVESTIGATIONS

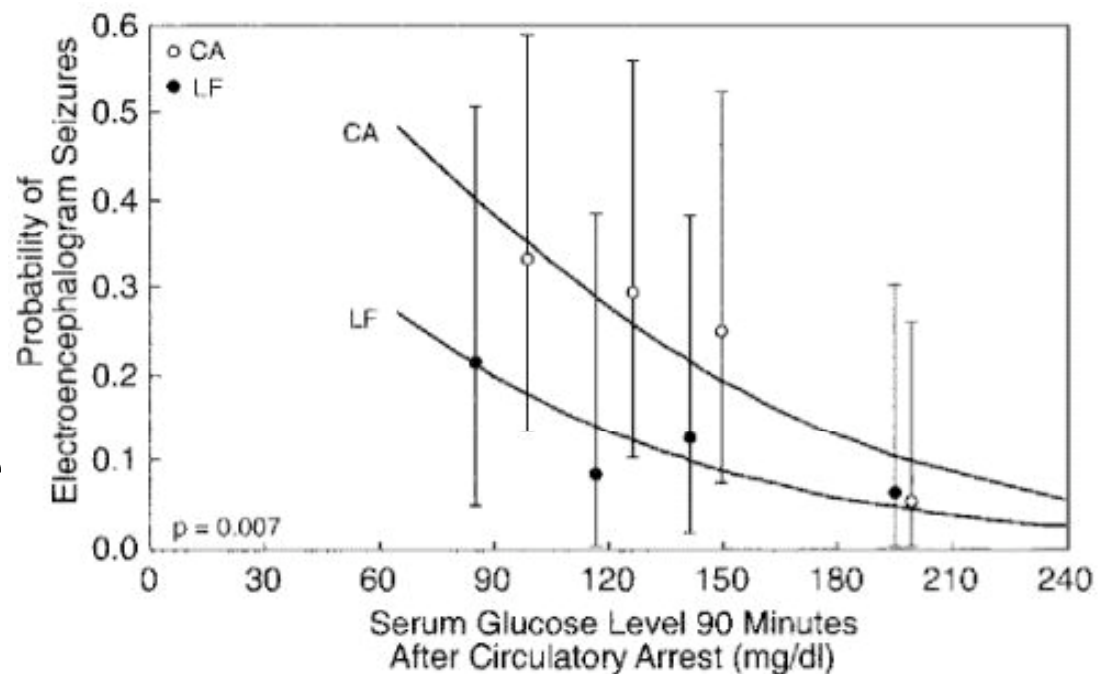
Anesthesiology 2004; 100:1345-52

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Intraoperative Hyperglycemia during Infant Cardiac Surgery Is Not Associated with Adverse Neurodevelopmental Outcomes at 1, 4, and 8 Years

Sarah de Ferranti, M.D., M.P.H.,* Kimberlee Gauvreau, Sc.D.,† Paul R. Hickey, M.D.,‡ Richard A. Jonas, M.D.,§ David Wypij, Ph.D.,|| Adre du Plessis, M.D.,# David C. Bellinger, Ph.D., M.Sc.,** Karl Kuban, M.D., S.M.Epi.,†† Jane W. Newburger, M.D., M.P.H.,‡‡ Peter C. Laussen, M.B. B.S.§§

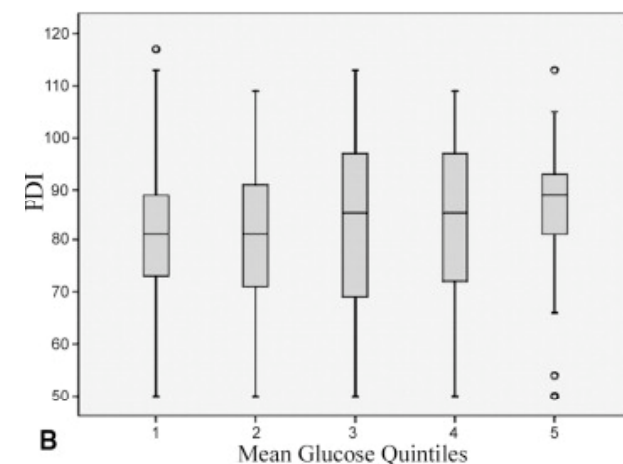
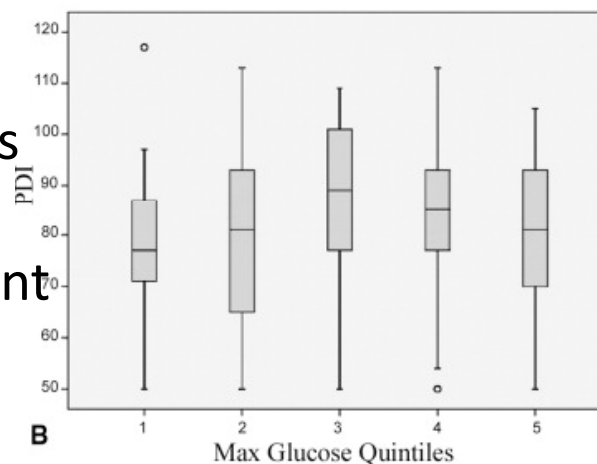
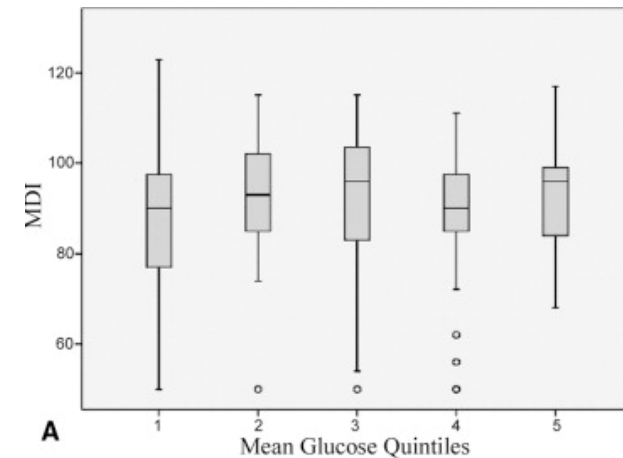
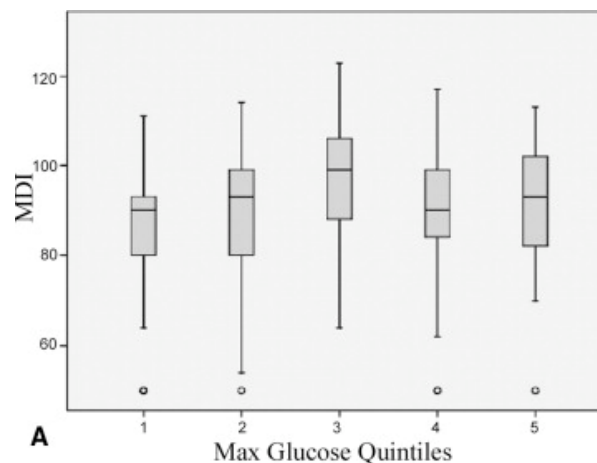
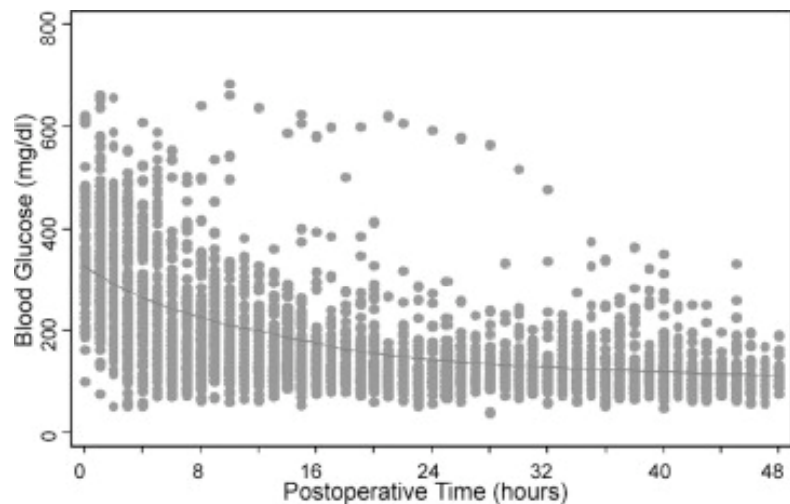
- Prospective observational study
- 171 neonates for ASO
- DHCA vs. Low-flow
- Early postop EEG seizure activity
 - trend lower with increased glu
- Late neurodevelopmental outcome
 - no difference through 8 years



Hyperglycemia After Infant Cardiac Surgery Does Not Adversely Impact Neurodevelopmental Outcome

Jean A. Ballweg, MD, Gil Wernovsky, MD, Richard F. Ittenbach, PhD,
Judy Bernbaum, MD, Marsha Gerdes, PhD, Paul R. Gallagher, MA,
Troy E. Dominguez, MD, Elaine Zackai, MD, Robert R. Clancy, MD,
Susan C. Nicolson, MD, Thomas L. Spray, MD, and J. William Gaynor, MD

Divisions of Pediatric Cardiology, General Pediatrics, Psychology, Genetics, Neurology, Cardiothoracic Anesthesiology, and Cardiothoracic Surgery, and Biostatistics and Data Management Core, The Cardiac Center at The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania



- Retrospective review 180 patients
- All under 6 months at surgery
- Return at 1 year for ND assessment
- No differences in MDI or PDI

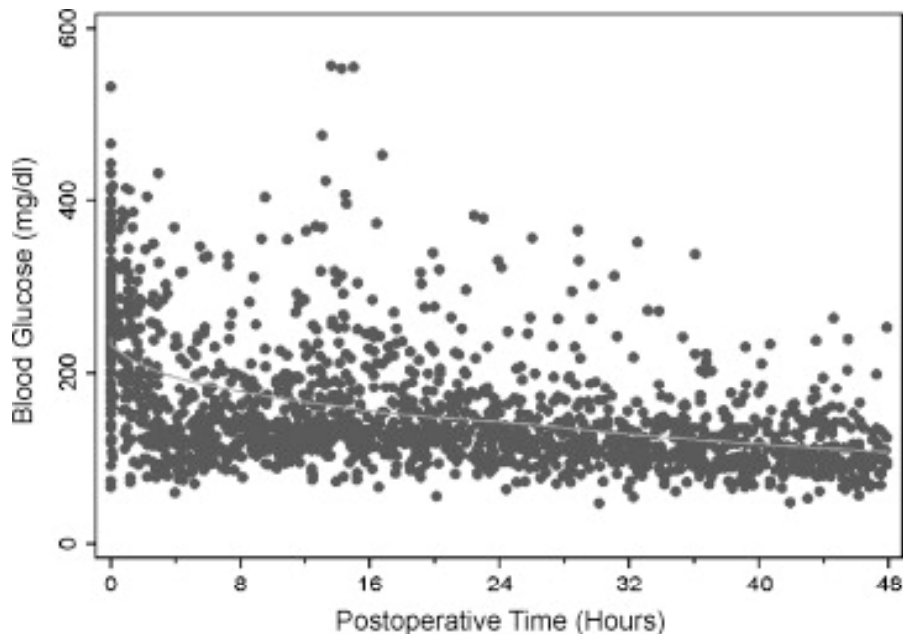
Hypoplastic Left Heart Syndrome

Hyperglycaemia after Stage I palliation does not adversely affect neurodevelopmental outcome at 1 year of age in patients with single-ventricle physiology^{☆,☆☆}

Jean A. Ballweg^{*}, Richard F. Ittenbach, Judy Bernbaum, Marsha Gerdes, Troy E. Dominguez, Elaine H. Zackai, Robert R. Clancy, James William Gaynor

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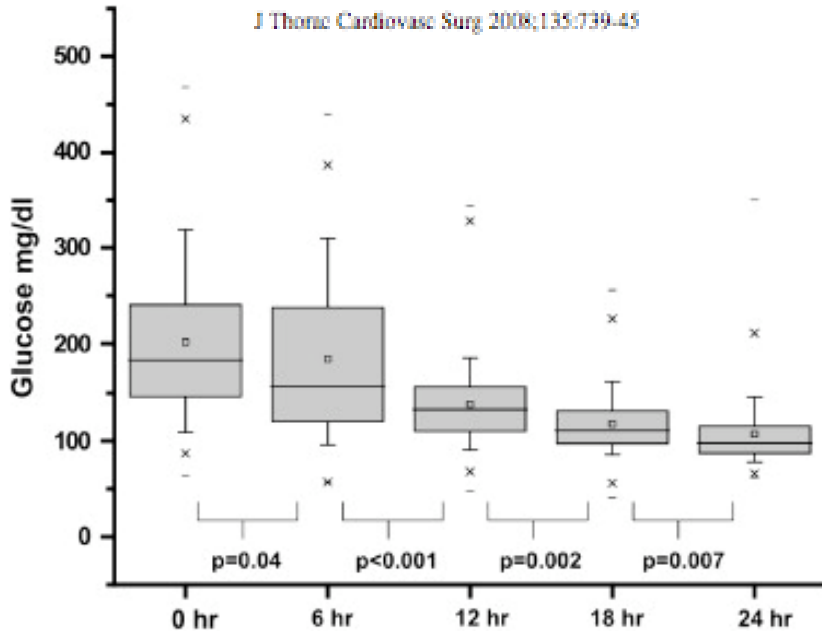
- Retrospective review of 162 HLHS cases
- Analyzed outcome in relation to glucose
- Initial, maximum, minimum, mean
- 1 year MDI, PDI no relation to any point
- Nor mortality, ECMO or LOS

Adverse events and glucose

Glycemic profile in infants who have undergone the arterial switch operation: Hyperglycemia is not associated with adverse events

Joseph W. Rossano, MD,^a Michael D. Taylor, MD, PhD,^a E. O'Brian Smith, PhD,^a Charles D. Fraser, Jr, MD,^b E. Dean McKenzie, MD,^b Jack F. Price, MD,^a Heather A. Dickerson, MD,^a David P. Nelson, MD, PhD,^a and Antonio R. Mott, MD^a

J Thorac Cardiovasc Surg 2008;135:739-45



- Retrospective review
- Group 1: >50% time glucose 80-110 mg/dl
- Group 2: >50% time glucose >200 mg/dl
- Only Group 1 had increased adverse events:
 - All Adverse Events: OR 5.7 (CI 1.9-17.3)
 - Renal dysfunction: OR 11.9 (CI 2.8-50.3)
 - Hypoglycemia: OR 3.7 (CI 1.4-9.9)

Intra-operative glucose and morbidity

Association Between Intraoperative and Early Postoperative Glucose Levels and Adverse Outcomes After Complex Congenital Heart Surgery

Angelo Polito, MD; Ravi R. Thiagarajan, MBBS, MPH; Peter C. Laussen, MBBS;
 Kimberlee Gauvreau, ScD; Michael S.D. Agus, MD; Mark A. Scheurer, MD;
 Frank A. Pigula, MD; John M. Costello, MD, MPH
Circulation. 2008;118:2235-2242

Table 5. Logistic Regression Analyses of Intraoperative Glucose Variables and the Overall Composite Morbidity-Mortality Variable

Operating Room Glucose Variables	Unadjusted		Adjusted*	
	OR (95% CI)	P	OR (95% CI)	P
TWGA				
≤113	1.58 (0.61–4.06)	0.346	1.74 (0.58–5.18)	0.322
114–129	Referent	...	Referent	...
130–153	2.31 (0.95–5.60)	0.065	2.05 (0.74–5.68)	0.166
≥154	2.70 (1.12–6.48)	0.023	1.41 (0.50–3.94)	0.514
Peak glucose ≥200 mg/dL	2.67 (1.50–4.72)	<0.001	1.57 (0.79–3.13)	0.198
SD of glucose >40 mg/dL	2.60 (1.11–6.60)	0.022	1.41 (0.60–2.90)	0.344
Minimal glucose ≤75 mg/dL	2.43 (1.35–4.36)	0.003	3.10 (1.49–6.48)	0.003
Glucose >126 mg/dL for ≥4 h	2.68 (1.48–4.86)	0.001	0.95 (0.40–2.21)	0.895
Glucose >200 mg/dL for ≥0.5 h	1.88 (1.03–3.44)	0.040	1.29 (0.62–2.71)	0.499

OR indicates odds ratio; CI, confidence interval.

*Adjusted for age, prematurity, noncardiac structural anomalies, RACHS-1 category, duration of CPB, and need for reoperation or interventional catheterization during the same hospitalization.

- Retrospective review
- Composite morbidity/mortality
- Intra-operative glucose
- Only significant finding <75 mg/dL
- OR 3.1

Tight glucose control and SSI

Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomised controlled study

Dirk Vlasselaers*, Ilse Milants*, Lars Desmet*, Pieter J Wouters, Ilse Vanhorebeek, Ingeborg van den Heuvel, Dieter Mesotten, Michael P Casaer, Geert Meyfroidt, Catherine Ingels, Jan Muller, Sophie Van Cromphaut, Miet Schetz, Greet Van den Berghe

Secondary infections	Conventional	Tight control	
Number of patients with secondary infections	129 (36.8%)	102 (29.2%)	0.034
Type of infection			
Pulmonary	90 (25.6%)	68 (19.5%)	..
Bloodstream	26 (7.4%)	20 (5.8%)	..
Wound	5 (1.4%)	6 (1.7%)	..
Urinary tract	4 (1.1%)	5 (1.4%)	..
CNS	3 (0.9%)	1 (0.3%)	..
Gastrointestinal tract	1 (0.3%)	2 (0.6%)	..

Lancet 373:547-56, 2009.

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Univariate Risk Factors for SSI

	SSI n=72	Control n=144	OR (95% CI)	p
	%	%		
Demographics:				
Age <1 year	79	58	2.56 (1.35 – 4.87)	0.004
Surgical Variables:				
Preoperative hospitalization	61	40	2.22 (1.27 – 3.91)	0.006
Single ventricle	42	28	1.90 (1.03 – 3.52)	0.04
RACHS-1 category ≥ 4	40	26	1.94 (1.04 – 3.62)	0.04
CPB >105 minutes	61	43	2.20 (1.20 – 4.02)	0.01
Postoperative severity of illness:				
Postoperative O ₂ sat ≤85%	36	19	2.16 (1.18 – 3.97)	0.01
Postoperative device utilization:				
Arterial line ≥ 5 days	53	36	1.93 (1.09 – 3.42)	0.02
Mechanical vent. ≥ 3 days	56	38	2.09 (1.16 – 3.76)	0.01
CICU course:				
≥6 days CICU days	57	41	1.88 (1.06 – 3.34)	0.03

Costello JM, personal communication

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Independent Risk Factors for SSI

	Adjusted OR (95% CI)	p
All risk factors:		
Age < 1 year	2.28 (1.18 – 4.39)	0.01
CPB > 105 minutes	1.92 (1.02 – 3.62)	0.04
Risk factors known pre-op:		
Age < 1 year	2.56 (1.35 – 4.87)	0.004

Costello JM, personal communication

Cochrane Review SSIs

Peri-operative glycaemic control regimens for preventing surgical site infections in adults (Review)

Kao LS, Meeks D, Moyer VA, Lally KP

Author's conclusions

There is insufficient evidence to support strict glycemic control versus conventional management (glucose <200 mg/dl) for the prevention of SSIs. The trials were limited by small sample size, inconsistencies in the definitions of the outcome measures and methodological quality.



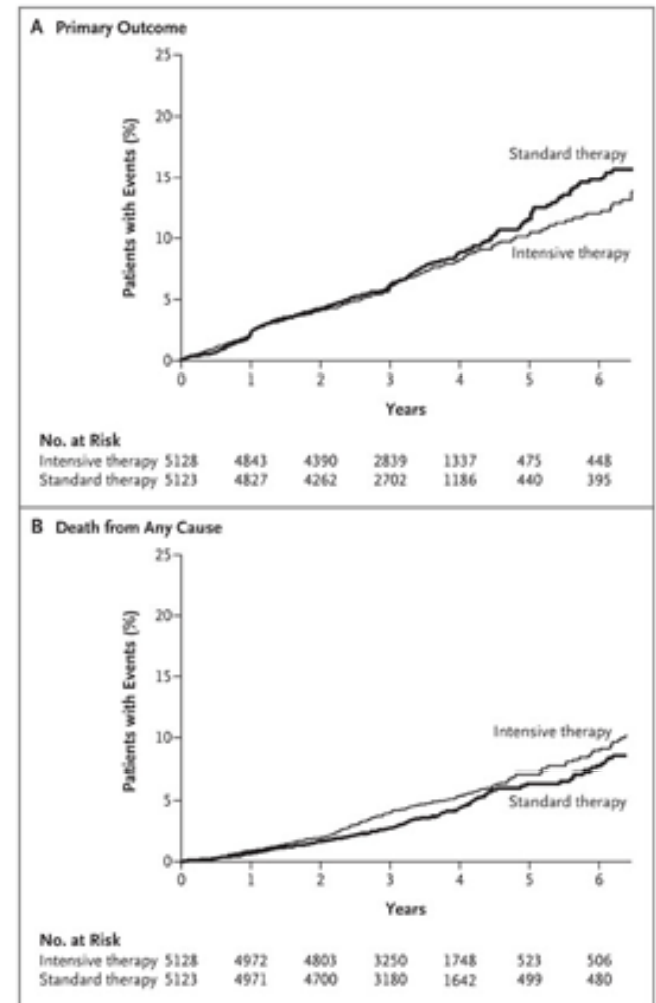
Unintended consequences

Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group*

N ENGL J MED 358:24 WWW.NEJM.ORG JUNE 12, 2008

- Adult Type 2 DM
- Intensive glucose control
- Increased mortality at 3.5 yrs
- No beneficial effect on CV events

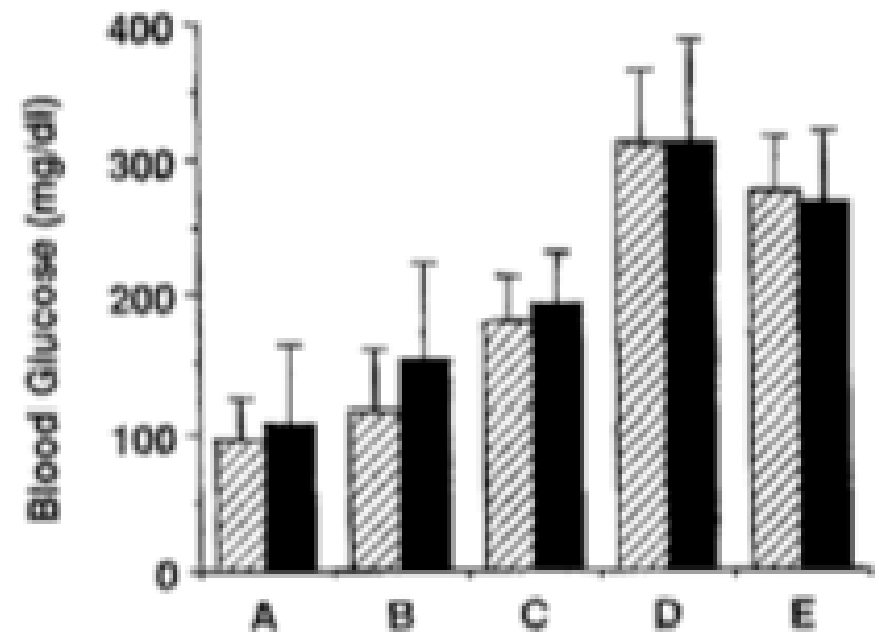


Withholding glucose solutions

The Effect of Administering or Withholding Dextrose in Pre-Bypass Intravenous Fluids on Intraoperative Blood Glucose Concentrations in Infants Undergoing Hypothermic Circulatory Arrest

Susan Craig Nicolson, MD, David R. Jobes, MD, Howard A. Zucker, MD, James M. Steven, MD, Mark S. Schreiner, MD, and Eugene K. Betts, MD

- Randomized, prospective comparison
- No difference in levels of hyperglycemia
- 5% incidence of severe hypoglycemia in LR

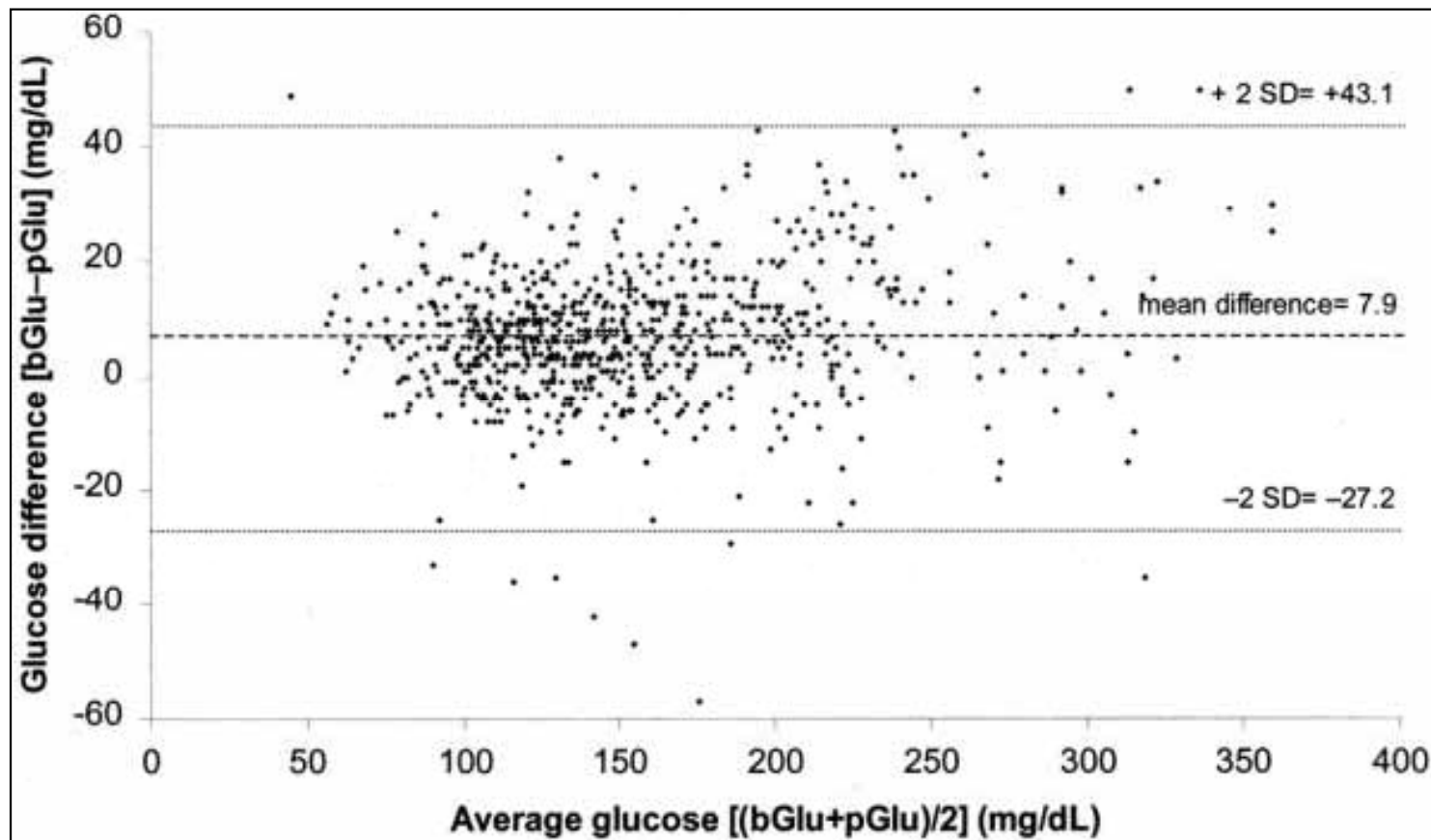


Bedside glucometer precision

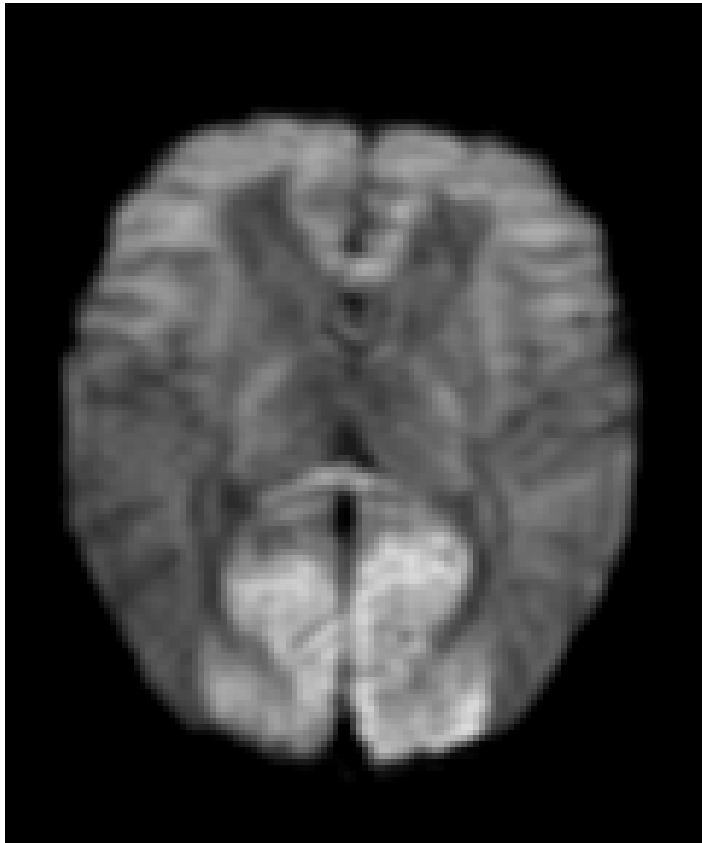
Glucose Measurement in the Operating Room: More Complicated than It Seems

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

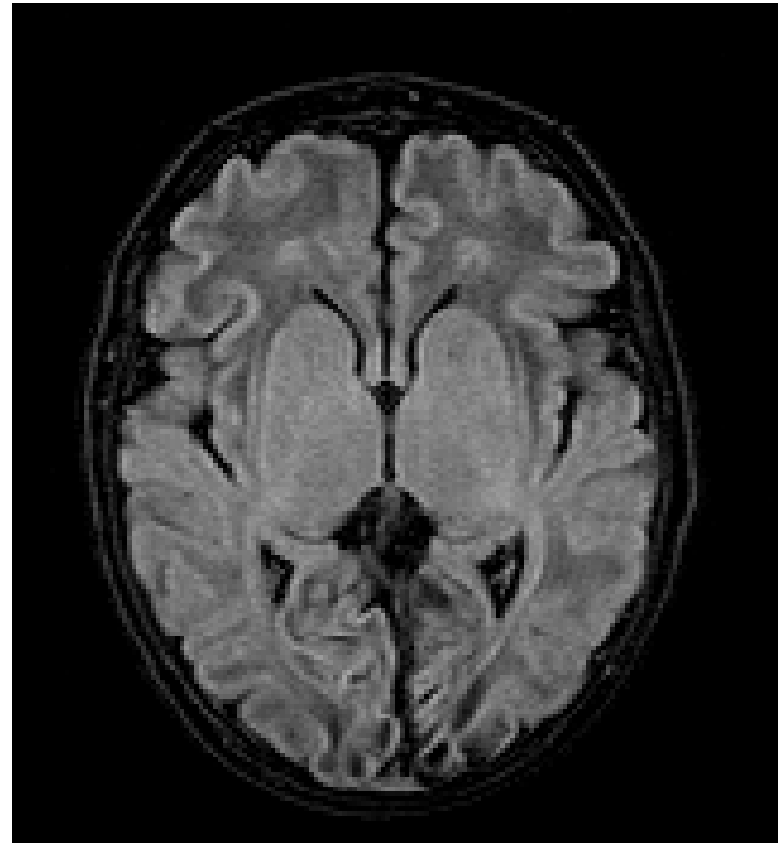
Anesth Analg 2010;110:1056-65



Hypoglycemic MRI Changes



Acute- DWI



Follow-up Flair

Conclusions

- Hyperglycemia has not been reliably demonstrated to cause adverse outcomes
- Recent large trials and meta-analyses confirm dramatic (10-25-fold) increases in hypoglycemic events with tight glucose control
- Avoidance of dextrose infusions in infant cardiac surgery will not prevent hyperglycemia and will increase incidence of hypoglycemia
- Hypoglycemia is conclusively linked to adverse outcomes
- We do not currently have the technology to provide tight glucose control safely and reliably