Gruppo di ricerca geriatrica

GRG-Journal Club

25 Luglio 2008

La glicemia nell´anziano critico

Intissar Sleiman

Dipartimento di Medicina e Geriatria
Ospedale Poliambulanza-Brescia

- **Hypoglycemia**
- **Hyperglycemia**

- ✓ **Hypoglycemia**
- **Hyperglycemia**

Hypoglycemia

- **Drugs:**
  - **Insulin therapy**
  - **Sulfonylurea drugs therapy**
  - **ACE inhibitor therapy**
  - **Salicylates**
  - **Haloperidol**
  - **Trimethoprim-sulfamethoxazole and renal failure**

Hypoglycemia

- **Diseases:**
  - Shock
  - Sepsis
  - Severe liver disease
  - Chronic renal failure
  - Primary adrenal insufficiency
  - Hypopituitarism

- ✓**Hyperglycemia**

A frequent event in medicine is the "new" discovery of an old finding….

The story of hyperglycemia and acute myocardial infarction

An unusually high prevalence of glycosuria in nondiabetic patients who have acute myocardial infarction

Cruikshank BMJ, **1931**; 1: 618-619

Acute myocardial infarction. Prognostic value of white blood cell count and blood glucose level

B. Modan, S. Schor and M. Shani

Data obtained in the course of a nationwide study of patients with first acute myocardial infarction (AMI) demonstrated substantially higher hospital mortality among patients with leukocytosis or elevated blood glucose levels, or both. It is suggested that the combination of these two measurements could be used as a handy diagnostic indicator in the evaluation of some AMI patients and as a criterion for the patients' immediate disposition to a coronary care unit, rather than to a general ward.

JAMA **1975**; 233: 266-267

Stress hyperglycemia and cause of death in nondiabetic patients with myocardial infarction (Letter).
Yudkin JS, Oswald GA.
***BMJ* 294:773, 1987**

Hyperglycemia and prognosis of acute myocardial infarction in patients without diabetes mellitus.
Bellodi G, Manicardi V, Malavasi V, et al
***Am J Cardiol* 64:885– 888, 1989**

In-hospital prognosis of patients with fasting hyperglycemia after first myocardial infarction.
O'Sullivan JJ, Conroy RM, Robinson K, et al
***Diabetes Care* 14:758 –760, 1991**

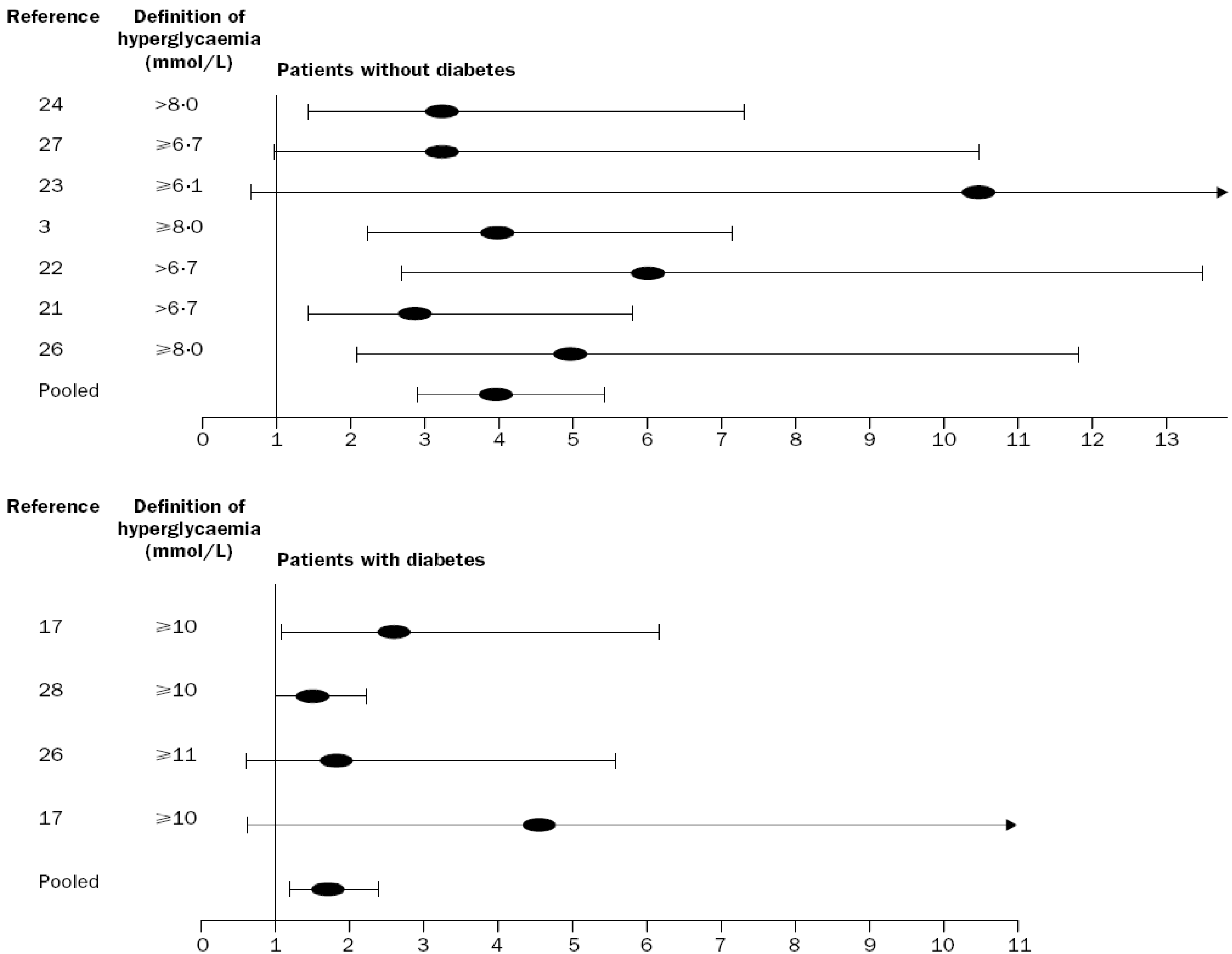
……..and extends knowledge to other similar diseases

The stroke

Reactive hyperglycaemia in patients with acute stroke.
Melamed E.
***J Neurol Sci*. 1976;29:267–275.**

Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus.
Pulsinelli WA, Levy DE, Sigsbee B, Scherer P, Plum F.
***Am J Med*. 1983;74:540 –544.**

Admission glucose level in relation to mortality and morbidity outcome in 252 stroke patients.
Woo E, Chan YW, Yu YL, Huang CY.
***Stroke*. 1988;19:185–191.**



Unadjusted relative risk of in-hospital mortality in patients with and without stress hyperglycaemia on admission

Capes S.E et al Lancet 2000; 355:773-378

Study	Outcome (CHF/Shock)	Definition of hyperglycaemia (mmol/L)	Number of events/patients at risk		Unadjusted relative risk (95% CI)
			Patients with hyperglycaemia on admission	Patients without hyperglycaemia on admission	
Patients without diabetes					
Bellodi (22)	CHF	>10	18/21	88/306	2·98 (2·33–3·82)
Leor (25)	Shock	>10	20/129	47/2673	8·82 (5·39–14·43)
Lewandowicz (27)	CHF or shock	>8	4/6	15/34	1·51 (0·77–2·98)
O'Sullivan (24)	CHF or shock	>8	13/23	181/691	2·16 (1·48–3·15)
Patients with diabetes					
Leor (25)	Shock	>10	10/306	12/357	0·97 (0·43–2·22)

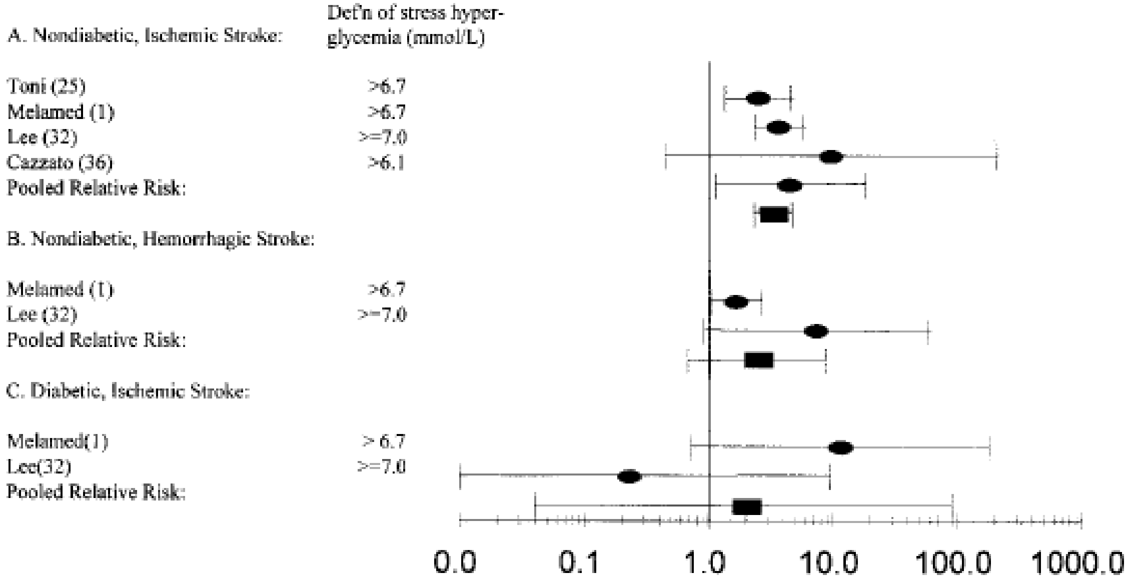
CHF=congestive heart failure; Shock=cardiogenic shock.

Table 3: **Relative risk of pump failure after myocardial infarction in patients with hyperglycaemia on admission compared with patients without hyperglycaemia**

Capes S.E et al Lancet 2000; 355:773-378

Stress hyperglycemia with myocardial infarction is associated with an increased risk of in hospital mortality in patients with and without diabetes; the risk of congestive heart failure or cardiogenic shock is also increased in patients without diabetes

Capes S.E et al Lancet 2000; 355:773-378

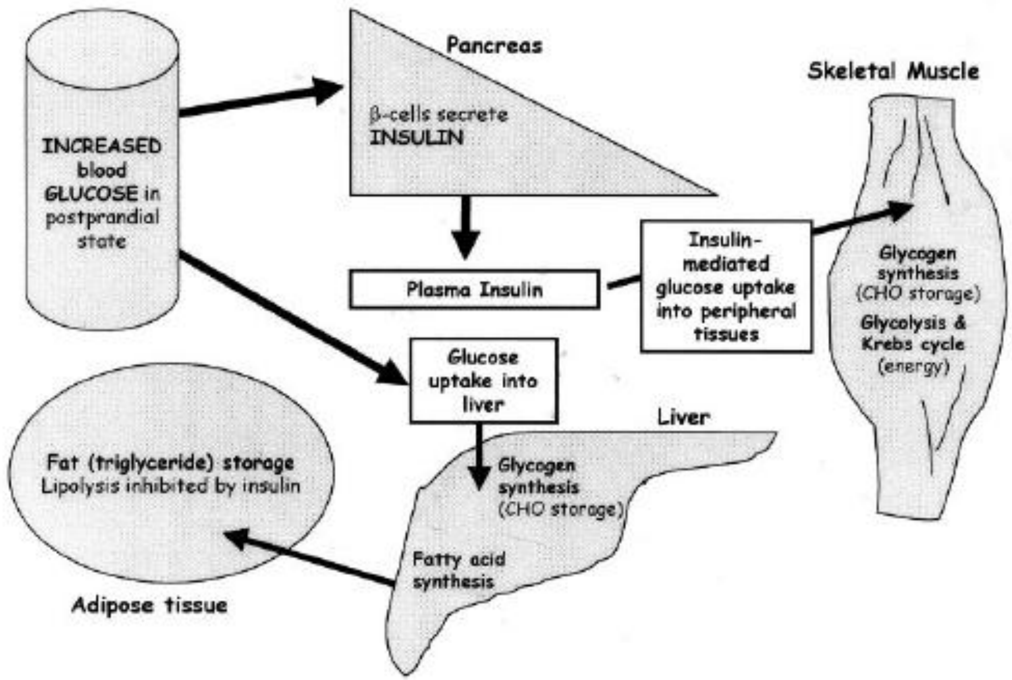


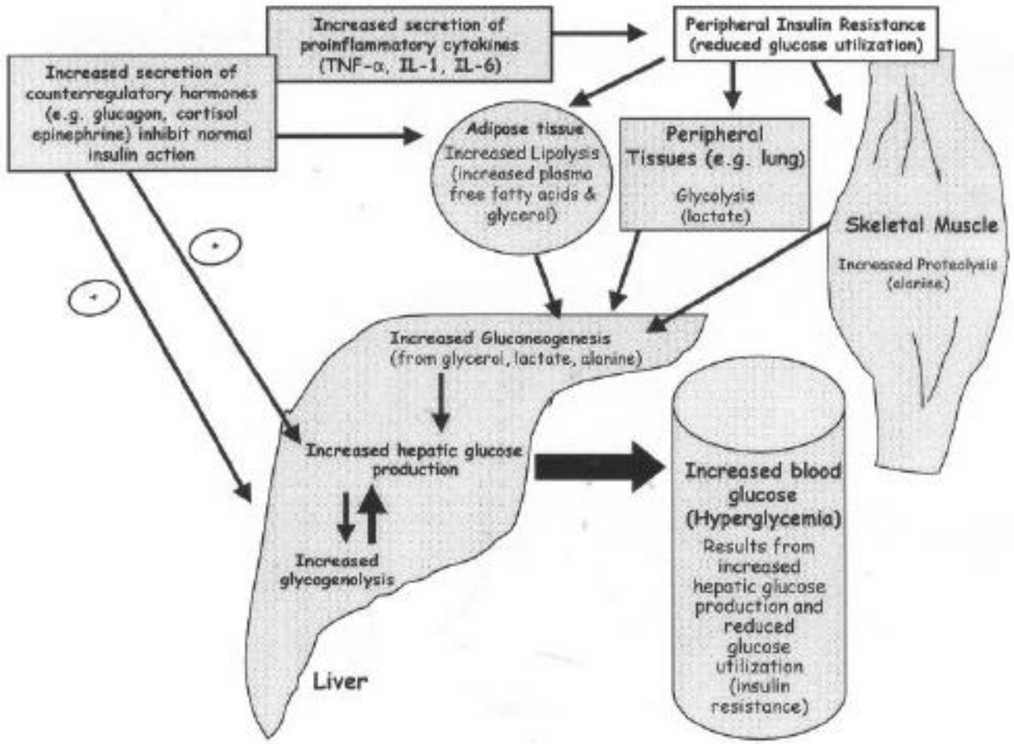
Unadjusted relative risk of in-hospital or 30-day mortality after stroke in patients with stress hyperglycemia compared with those without stress hyperglycemia. Data are shown for the 4 studies that reported separate mortality data for ischemic and hemorrhagic stroke in nondiabetic and/or diabetic patients. Ovals and bars represent relative risk and 95% CI for individual studies. Rectangles and bars represent pooled relative risk and 95% CI, derived by pooling data from the individual studies. Def'n indicates definition.

Capes S.E et al Stroke 2001; 32:2426-2432

Stress hyperglycemia predicts increased risk of in-hospital mortality after ischemic stroke in nondiabetic patients and increased risk of poor functional recovery in survivors

Capes S.E et al Stroke 2001; 32:2426-2432


Pancreas
β-cells secrete
INSULIN
Skeletal Muscle
INCREASED
blood
GLUCOSE in
postprandial
state
Plasma Insulin
Insulin-
mediated
glucose uptake
into peripheral
tissues
Glycogen
synthesis
(CHO storage)
Glycolysis &
Krebs cycle
(energy)
Glucose
uptake into
liver
Liver
Fat (triglyceride) storage
Lipolysis inhibited by insulin
Glycogen
synthesis
(CHO storage)
Fatty acid
synthesis
Adipose tissue

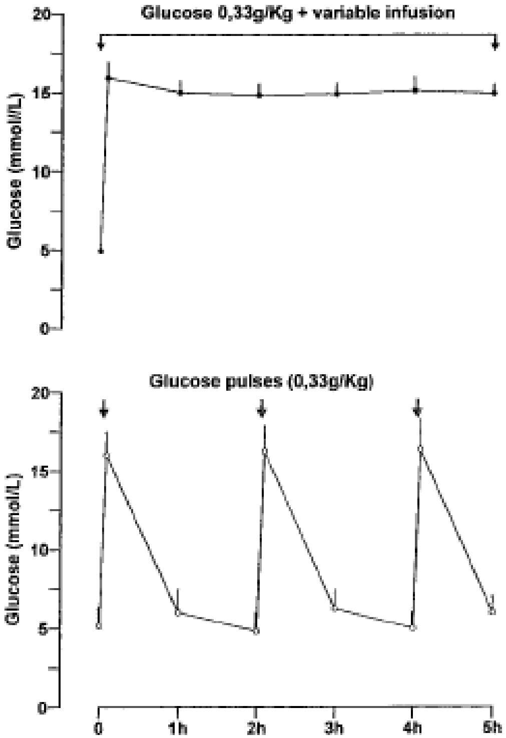

Increased secretion of proinflammatory cytokines (TNF-α, IL-1, IL-6)
Peripheral Insulin Resistance (reduced glucose utilization)
Increased secretion of counterregulatory hormones (e.g. glucagon, cortisol epinephrine) inhibit normal insulin action
Adipose tissue
Increased Lipolysis (increased plasma free fatty acids & glycerol)
Peripheral Tissues (e.g. lung)
Glycolysis (lactate)
Skeletal Muscle
Increased Proteolysis (alanine)
Increased Gluconeogenesis (from glycerol, lactate, alanine)
Increased hepatic glucose production
Increased glycogenolysis
Liver
Increased blood glucose (Hyperglycemia)
Results from increased hepatic glucose production and reduced glucose utilization (insulin resistance)

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Inflammatory Cytokine Concentrations Are Acutely Increased by Hyperglycemia in Humans: Role of Oxidative Stress

Katherine Esposito, Francesco Nappo, Raffaele Marfella, Giovanni Giugliano, Francesco Giugliano, Myriam Ciotola, Lisa Quagliaro, Antonio Ceriello and Dario Giugliano

Circulation 2002;106;2067-2072; originally published online Sep 30, 2002;



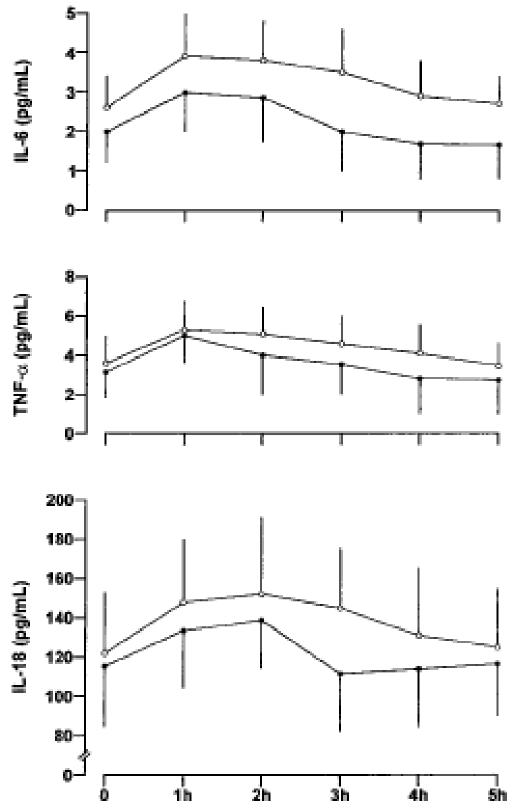


Figure 2. Circulating cytokine levels during hyperglycemic clamps in 20 control subjects (●—●) and in 12 IGT subjects (○—○).

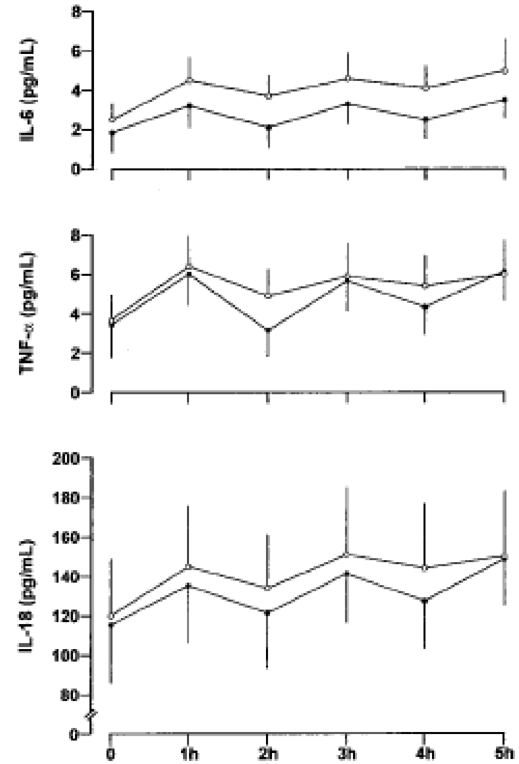


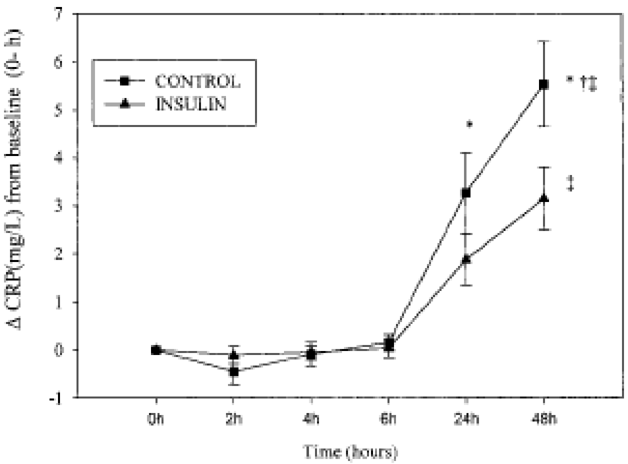
Figure 3. Circulating cytokine levels after consecutive glucose pulses in 20 control subjects (●—●) and in 12 IGT subjects (○—○).

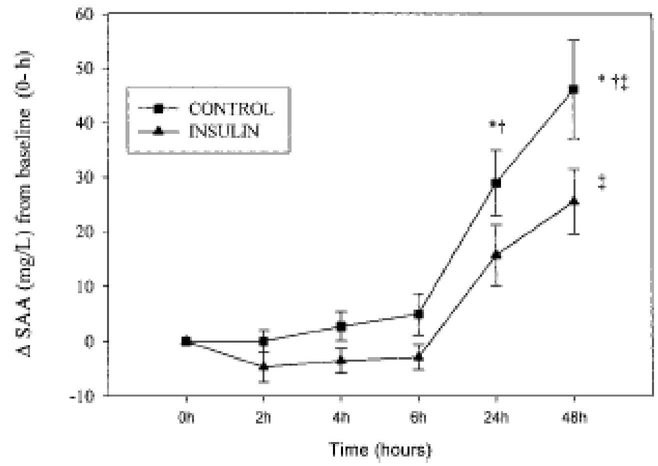
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

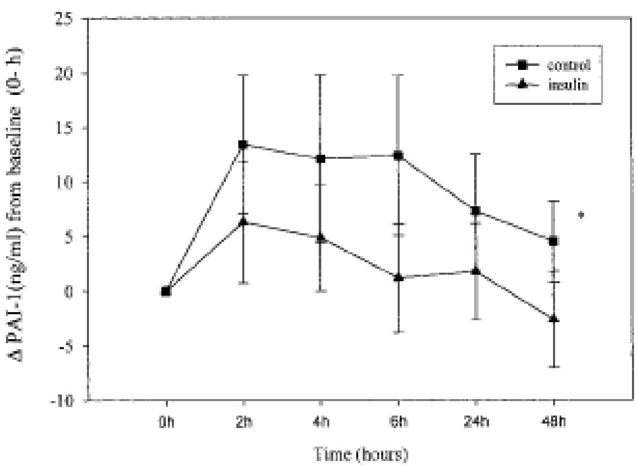
American Heart Association®
Learn and Live℠

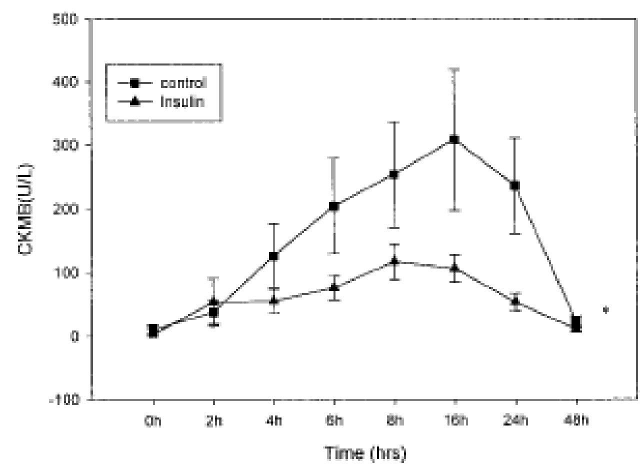
Anti-Inflammatory and Profibrinolytic Effect of Insulin in Acute ST-Segment–Elevation Myocardial Infarction

Ajay Chaudhuri, David Janicke, Michael F. Wilson, Devjit Tripathy, Rajesh Garg, Arindam Bandyopadhyay, Janeen Calieri, Debbie Hoffmeyer, Tufail Syed, Husam Ghanim, Ahmad Aljada and Paresh Dandona


Δ CRP(mg/L) from baseline (0- h)
7
6
5
4
3
2
1
0
-1
CONTROL
INSULIN
* †‡
*
‡
0h
2h
4h
6h
24h
48h
Time (hours)


Δ SAA (mg/L) from baseline (0- h)
60
50
40
30
20
10
0
-10
CONTROL
INSULIN
* †‡
*†
‡
0h
2h
4h
6h
24h
48h
Time (hours)


Δ PAI-1(ng/ml) from baseline (0- h)
25
20
15
10
5
0
-5
-10
control
insulin
*
0h
2h
4h
6h
24h
48h
Time (hours)


CKMB(U/L)
500
400
300
200
100
0
-100
control
Insulin
*
0h
2h
4h
6h
8h
16h
24h
48h
Time (hrs)

Blood glucose and prognosis of acute stroke

Power M.J et al

Age and Ageing, 1988; 17: 164-170

Summary: to study the relation of blood glucose soon after the onset of stroke and outcome in terms of fatality and functional recovery 6 months later, two prospective studies were performed.

Table IV. Study 2: HbA1 and fasting blood glucose in relation to 6-month fatality from stroke

	Outcome			*Significance*
	No. of patients	*Alive*	*Dead (%)*	
HbA1 (%)				
<6.9	34	19	15 (44)	
6.9–7.8	12	6	6 (50)	χ^2=3.38 (2 degrees of freedom)
>7.8	10	4	6 (60)	NS
Fasting blood glucose (mmol/l)				
≤7.0	37	23	14 (38)	
<7.0	21	7	16 (67)	$P<0.05$

Table III. Study 2: Means (and 95% confidence intervals) of blood glucose and HbA1 in relation to fatality

Outcome	*No. of patients*	*Blood glucose* (mmol/l)			*HbA1 (%)*
		Admission fasting	*1-month fasting*	*Mean admission*	
Alive	30	6.04 (5.37–6.71)	4.91 (4.47–5.35)	6.50 (5.89–7.11)	6.27 (5.77–6.77)
Dead	28	7.33 (6.10–8.46)	6.03 (5.01–7.05)	7.44 (6.25–8.63)	6.75 (6.15–7.35)
Significance		t=2.31; P<0.05	t=2.47; P<0.05	t=1.74; NS	t=0.47; NS

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association
Learn and Live

Admission Glucose and Mortality in Elderly Patients Hospitalized With Acute Myocardial Infarction: Implications for Patients With and Without Recognized Diabetes

Mikhail Kosiborod, Saif S. Rathore, Silvio E. Inzucchi, Frederick A. Masoudi, Yongfei Wang, Edward P. Havranek and Harlan M. Krumholz

Circulation 2005;111;3078-3086; originally published online Jun 6, 2005;
DOI: 10.1161/CIRCULATIONAHA.104.517839
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

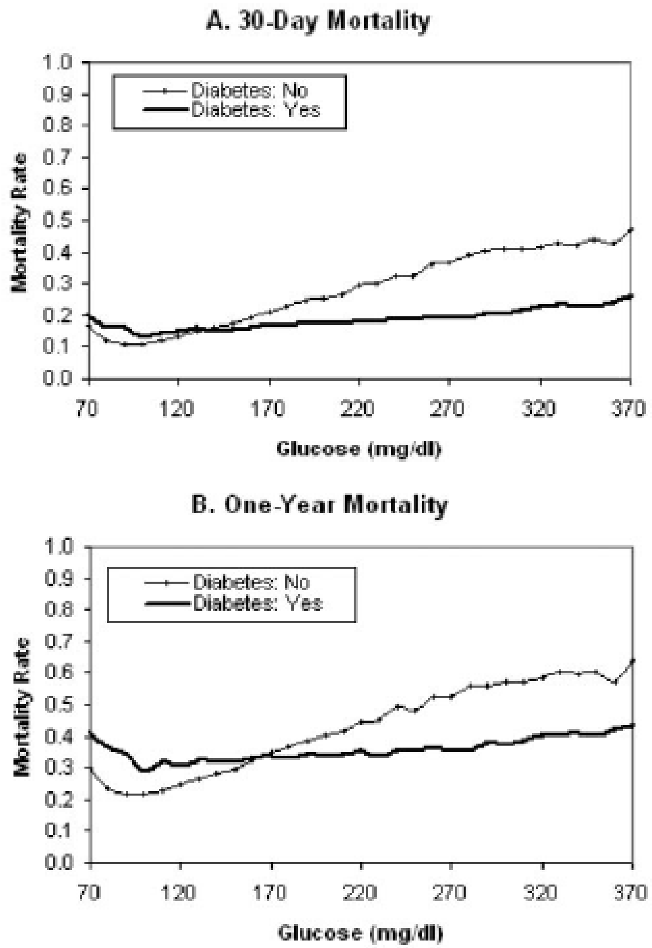

A. 30-Day Mortality
Diabetes: No
Diabetes: Yes
Mortality Rate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
70
120
170
220
270
320
370
Glucose (mg/dl)
B. One-Year Mortality
Diabetes: No
Diabetes: Yes
Mortality Rate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
70
120
170
220
270
320
370
Glucose (mg/dl)

Table 1. Characteristics of Patients with and without a History of Diabetes Mellitus (DM) Admitted to a Sub-Intensive Care Unit (ICU)

Characteristic	Total N = 1,155	With DM n = 333	Without DM: Serum Glucose Levels (mg/dL)		
			60–126 n = 516	127–180 n = 202	181–500 n = 104
Age, mean ± SD	79.2 ± 8.4	78.3 ± 8.2	79.5 ± 8.7	79.4 ± 8.1	80.4 ± 7.5
Male, n (%)	572 (49.5)	164 (49.2)	246 (47.7)	108 (53.5)	53 (51.4)
Mini-Mental State Examination score, mean ± SD (range 0–30)	20.5 ± 9.8	20.4 ± 9.4	21.2 ± 9.3	18.9 ± 11.1	19.7 ± 10.4
Geriatric Depression Scale score, mean ± SD	3.4 ± 3.0	3.7 ± 3.1	3.3 ± 3.1	3.3 ± 3.2	3.8 ± 2.8
Preadmission Barthel Index, mean ± SD (range 0–100)	69.7 ± 1.3	67.1 ± 32.4	72.4 ± 30.7	69.0 ± 31.1	76.2 ± 30.5
Main diagnosis, n (%)					
Heart failure, arrhythmias	349 (30.2)	108 (32.4)			
Respiratory failure (pneumonia, sepsis, chronic obstructive pulmonary disorder)	532 (46.0)	150 (45)			
Stroke	105 (9.1)	28 (8.4)			
Gastrointestinal bleeding	58 (5.0)	14 (4.2)			
Cancer-related diseases	45 (3.9)	7 (2.1)			
Charlson Comorbidity Index, mean ± SD (range 0–33)	6.3 ± 1.9	6.7 ± 1.8	5.9 ± 1.9	6.4 ± 1.9	6.6 ± 1.7
Acute Physiology Score, mean ± SD (range 0–33)	9.8 ± 18.7	9.3 ± 5.6	8.2 ± 5.3	13.4 ± 4.9	12.1 ± 6.2
Serum albumin, g/dL, mean ± SD	3.3 ± 1.3	3.4 ± 2.3	3.3 ± 0.6	3.3 ± 0.6	3.2 ± 0.6
Serum cholesterol, mg/dL, mean ± SD	166 ± 50	163.8 ± 53.6	167.0 ± 49.6	169.0 ± 47.8	160.0 ± 46.1
Number of drugs, mean ± SD	7.6 ± 3.1	8.3 ± 3.0	7.0 ± 2.9	7.6 ± 3.1	8.0 ± 3.0
Noninvasive ventilation, n (%)	317 (27.4)	103 (30.9)	107 (20.8)	64 (31.7)	43 (41)
Length of stay in sub-ICU, hours, mean ± SD	72 ± 60.7	71.3 ± 59	74.3 ± 64.8	69.3 ± 49.7	67.1 ± 63.3
Length of stay in hospital, days, mean ± SD	6.5 ± 5.1	6.3 ± 3.8	7.0 ± 6.0	6.2 ± 4.3	5.6 ± 4.2
45-day mortality, n (%)	257 (22.2)	71 (21.2)	90 (17.5)	52 (25.7)	44 (42)

SD = standard deviation.

JAGS 2008, 56:1106-10

Table 2. In-Hospital Mortality Rates According to Glycemic Value in 1,155 Patients with and without History of Diabetes Mellitus

Diabetes Mellitus	Serum Glucose Values, mg/dL N/Events (%) 60–126	127–180	181–500	*P*-Value
Yes	125/11 (8.8)	73/10 (13.6)	135/17 (12.6)	.51
Without history	516/58 (11.2)	202/35 (17.3)	104/36 (34.4)	.00

Table 3. Factors Associated with In-Hospital Mortality in a Group of 822 Acutely Ill Elderly Patients without History of Diabetes Mellitus Admitted to a Sub-Intensive Care Unit

Factor	n/events	Unadjusted	Adjusted
Aged ≥80	422/85	2.0 (1.3–3.0)	1.4 (0.8–2.3)
Male	408/59	0.8 (0.6–1.2)	0.9 (0.6–1.4)
Moderate to severe dementia (Mini-Mental State Examination score <18)	190/48	2.3 (1.5–3.4)	1.8 (1.1–2.9)
Serum albumin <3.5 g/dL	449/79	1.7 (1.1–2.6)	1.5 (1.0–2.5)
Acute Physiology Score ≥7	512/120	10.2 (5.1–20.4)	7.4 (3.9–14.4)
Charlson Comorbidity Index ≥6	129/75	2.4 (1.6–3.5)	1.1 (0.7–1.8)
Preadmission Barthel Index 0–95	530/117	6.5 (3.5–12.0)	3.2 (1.6–6.2)
≥9 drugs	262/71	3.2 (2.2–4.7)	2.4 (1.6–3.8)
Glycemia level, mg/dL			
60–126	515/58	1.0 ref	1.0 ref
127–180	202/35	1.6 (1.0–2.6)	1.0 (0.6–1.7)
>180	105/36	4.1 (2.5–6.7)	2.7 (1.6–4.8)

Univariate analysis and multiple logistic regression were applied to identify factors statistically associated with in-hospital mortality and to estimate adjusted odds ratio, respectively.

JAGS 2008, 56:1106-10

Glucose is a modifiable mediator of adverse event or simply a innocent marker of critical illness?

Clinical Investigation and Reports

Glycometabolic State at Admission: Important Risk Marker of Mortality in Conventionally Treated Patients With Diabetes Mellitus and Acute Myocardial Infarction

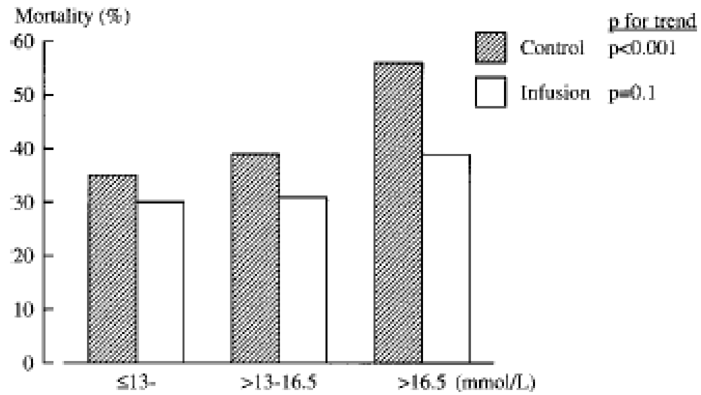
Long-Term Results From the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study

Klas Malmberg, MD, PhD; Anna Norhammar, MD; Hans Wedel, PhD; Lars Rydén, MD, PhD

Background—The Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study addressed prognostic factors and the effects of concomitant treatment and glycometabolic control in diabetic patients with myocardial infarction (AMI).

Methods and Results—Of 620 diabetic patients with AMI, 306 were randomly assigned to a ≥24-hour insulin-glucose infusion followed by multidose subcutaneous insulin. Three hundred fourteen patients were randomized as controls, receiving routine antidiabetic therapy. Thrombolysis and β-blockers were administered when possible. Univariate and multivariate statistical analyses were applied to study predictors of long-term mortality. During an average follow-up of 3.4 years (range, 1.6 to 5.6 years), 102 patients (33%) in the intensive insulin group and 138 (44%) in the control group died ($P=0.011$). Old age, previous heart failure, diabetes duration, admission blood glucose, and admission Hb A_{1c} were independent predictors of mortality in the total cohort, whereas previous AMI, hypertension, smoking, or female sex did not add independent predictive value. Metabolic control, mirrored by blood glucose and Hb A_{1c}, improved significantly more in patients on intensive insulin treatment than in the control group. β-Blockers improved survival in control subjects, whereas thrombolysis was most efficient in the intensive insulin group.

Conclusions—Mortality in diabetic patients with AMI is predicted by age, previous heart failure, and severity of the glycometabolic state at admission but not by conventional risk factors or sex. Intensive insulin treatment reduced long-term mortality despite high admission blood glucose and Hb A_{1c}. (***Circulation*. 1999;99:2626-2632.**)



Long-term (average time, 3.4 years; range, 1.6 to 5.6 years) mortality by admission blood glucose tertiles within 2 treatment groups.

TABLE 5. Independent Influence of Different Treatments on Long-Term Mortality by Multivariate Cox Regression Analysis Correcting for Age, Sex, and Congestive Heart Failure During Hospital Stay

	Patient Groups					
	All (240 of 620)		Control (138 of 314)		Intensive Insulin (102 of 306)	
Parameter	RR (95% CI)	*P*	RR (95% CI)	*P*	RR (95% CI)	*P*
Intensive insulin treatment	0.67 (0.51–0.88)	<0.01	...		...	
Thrombolysis	0.54 (0.41–0.72)	<0.001	0.63 (0.43–0.92)	<0.05	0.44 (0.28–0.72)	<0.001
β-Blockade at discharge	0.68 (0.50–0.88)	<0.01	0.55 (0.38–0.79)	<0.01	0.81 (0.52–1.27)	0.36
ACE inhibitor at discharge	1.36 (1.01–1.83)	<0.05	1.50 (1.04–2.30)	<0.05	1.20 (0.76–1.88)	0.45

See Table 2 for explanation.

The New England Journal of Medicine

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., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

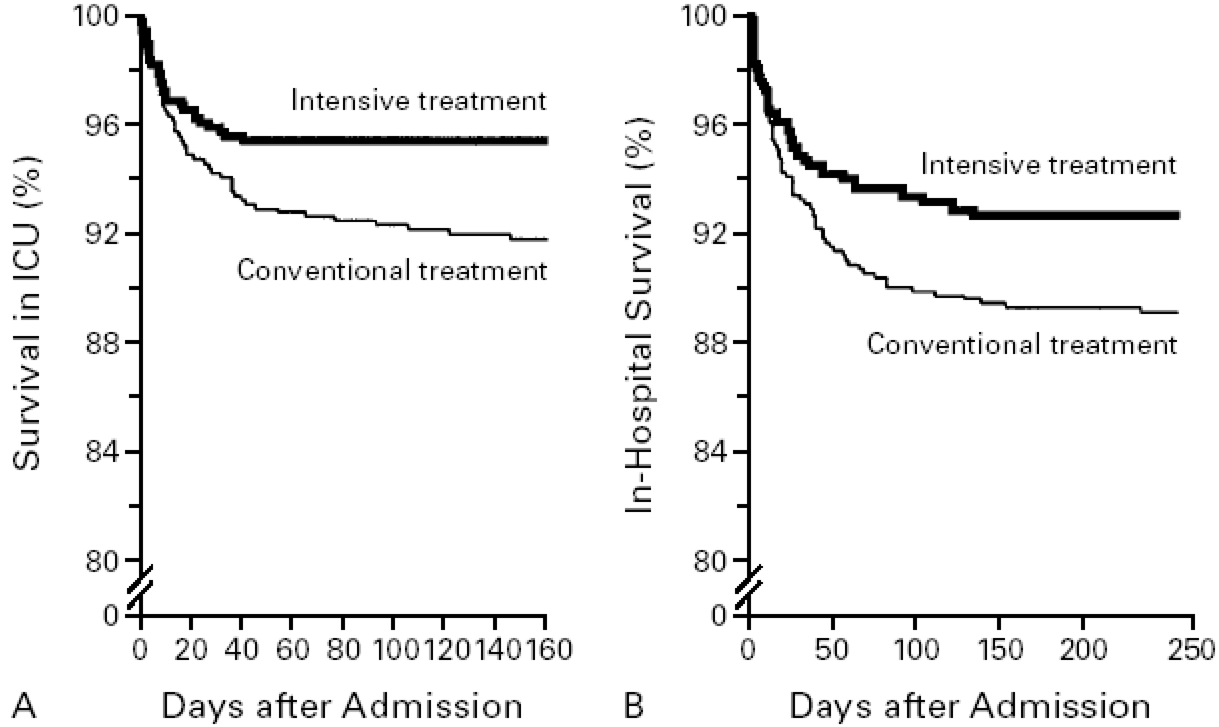


Figure 1. Kaplan–Meier Curves Showing Cumulative Survival of Patients Who Received Intensive Insulin Treatment or Conventional Treatment in the Intensive Care Unit (ICU).

Patients discharged alive from the ICU (Panel A) and from the hospital (Panel B) were considered to have survived. In both cases, the differences between the treatment groups were significant (survival in ICU, nominal $P=0.005$ and adjusted $P<0.04$; in-hospital survival, nominal $P=0.01$). P values were determined with the use of the Mantel–Cox log-rank test.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 2, 2006 VOL. 354 NO. 5

Intensive Insulin Therapy in the Medical ICU

Greet Van den Berghe, M.D., Ph.D., Alexander Wilmer, M.D., Ph.D., Greet Hermans, M.D., Wouter Meersseman, M.D., Pieter J. Wouters, M.Sc., Ilse Milants, R.N., Eric Van Wijngaerden, M.D., Ph.D., Herman Bobbaers, M.D., Ph.D., and Roger Bouillon, M.D., Ph.D.

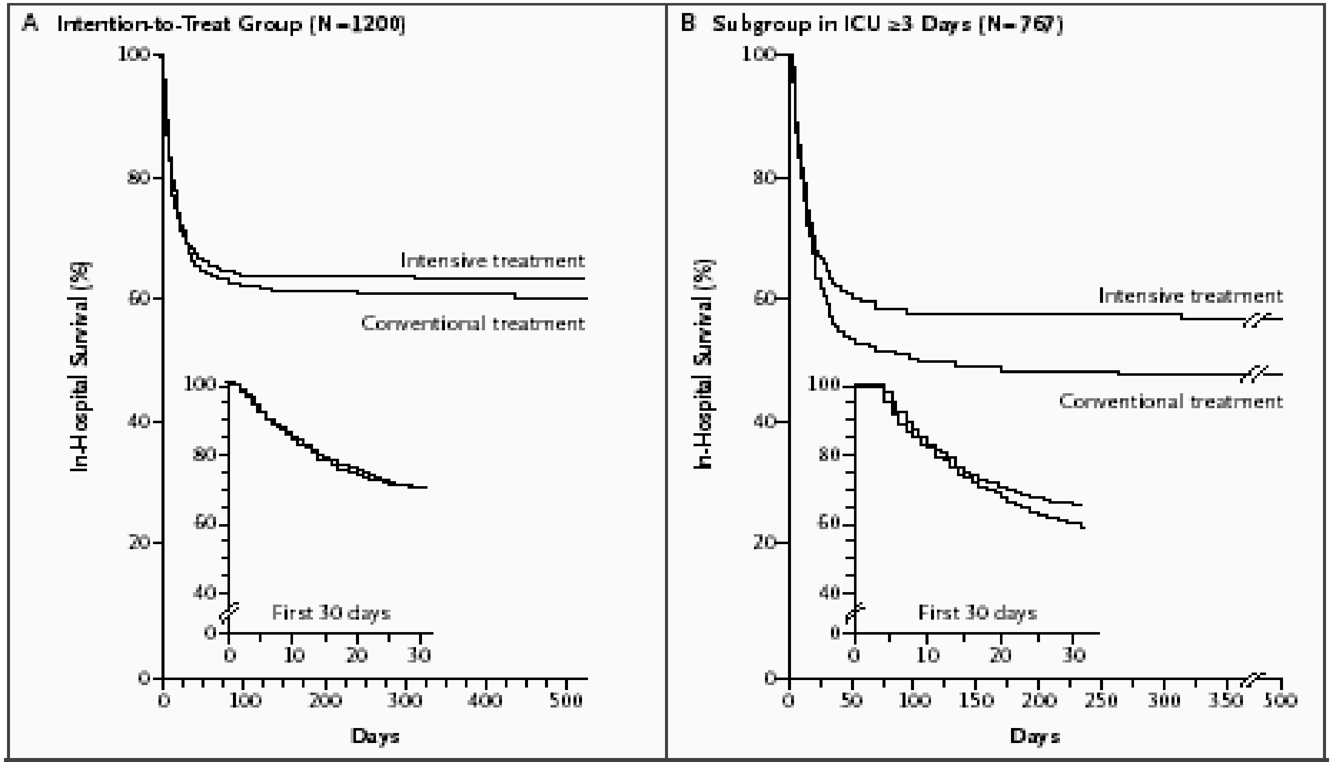


Figure 4. Kaplan–Meier Curves for In-Hospital Survival.

The effect of intensive insulin treatment on the time from admission to the intensive care unit (ICU) until death is shown for the intention-to-treat group (Panel A) and the subgroup of patients staying in the ICU for three or more days (Panel B). Patients discharged alive from the hospital were considered survivors. P values calculated by the log-rank test were 0.40 for the intention-to-treat group and 0.02 for the subgroup staying in the ICU for three or more days. P values calculated by proportional-hazards regression analysis were 0.30 and 0.02, respectively.

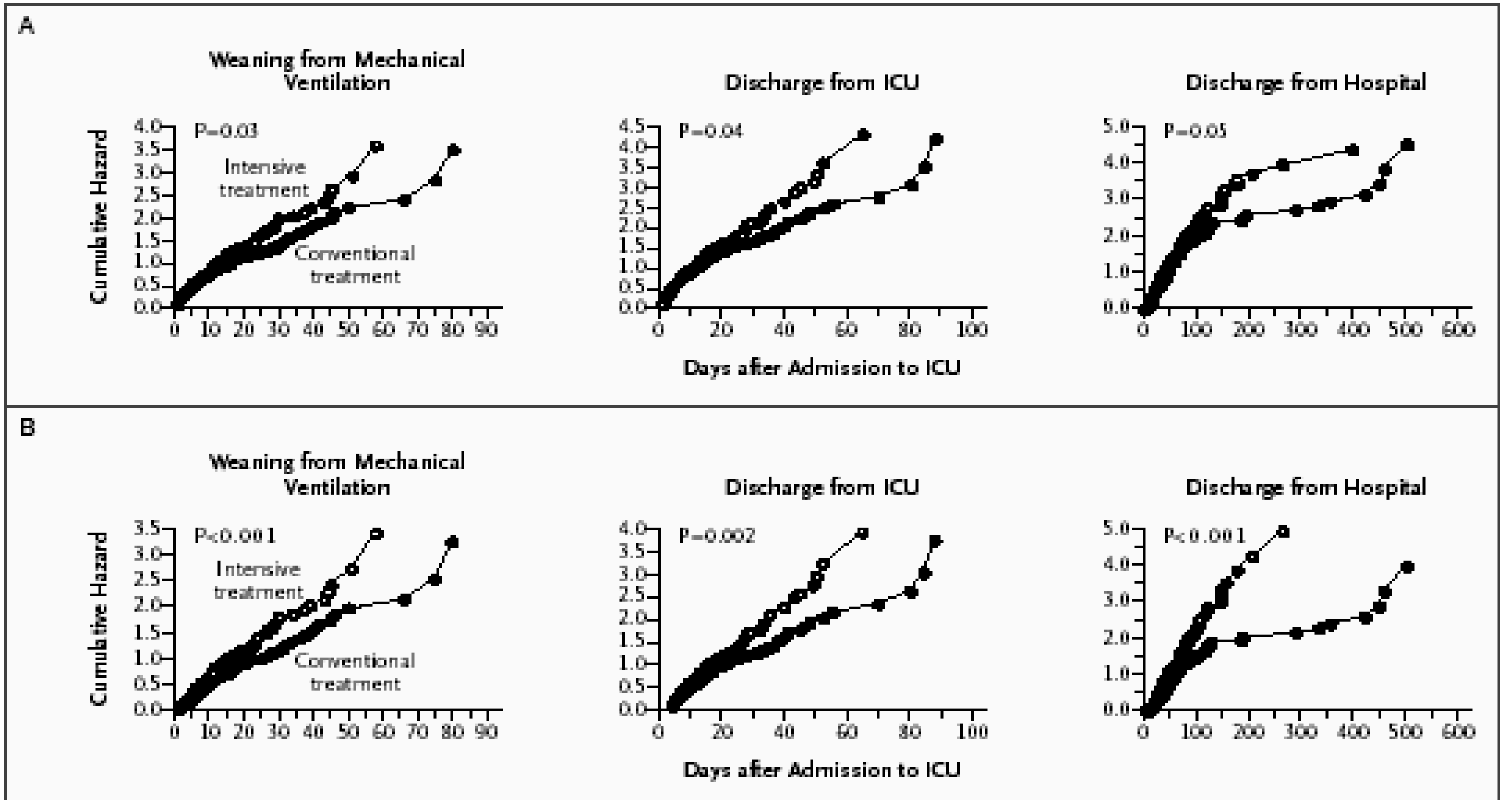


Figure 3. Effect of Intensive Insulin Therapy on Morbidity.

The effect of intensive insulin therapy on time to weaning from mechanical ventilation, time to discharge from the intensive care unit (ICU), and time to discharge from the hospital is shown for all patients (intention-to-treat analysis, Panel A) and for the subgroup of 767 patients staying in the ICU for three or more days (Panel B). P values for the comparison between the two groups were calculated by proportional-hazards regression analysis with censoring for early deaths. Circles represent patients.

Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK)

*Christopher S Gray, Anthony J Hildreth, Peter A Sandercock, Janice E O'Connell, Donna E Johnston, Niall E F Cartlidge, John M Bamford, Oliver F James, K George M M Alberti, for the GIST Trialists Collaboration**

Summary

Background Hyperglycaemia after acute stroke is a common finding that has been associated with an increased risk of death. We sought to determine whether treatment with glucose-potassium-insulin (GKI) infusions to maintain euglycaemia immediately after the acute event reduces death at 90 days.

Methods Patients presenting within 24 h of stroke onset and with admission plasma glucose concentration between 6·0–17·0 mmol/L were randomly assigned to receive variable-dose-insulin GKI (intervention) or saline (control) as a continuous intravenous infusion for 24 h. The purpose of GKI infusion was to maintain capillary glucose at 4–7 mmol/L, with no glucose intervention in the control group. The primary outcome was death at 90 days, and the secondary endpoint was avoidance of death or severe disability at 90 days. Additional planned analyses were done to determine any differences in residual disability or neurological and functional recovery. The trial was powered to detect a mortality difference of 6% (sample size 2355), with 83% power, at the 5% two-sided significance level. This study is registered as an International Standard Randomised Controlled Trial (number ISRCTN 31118803)

Findings The trial was stopped due to slow enrolment after 933 patients were recruited. For the intention-to-treat data, there was no significant reduction in mortality at 90 days (GKI *vs* control: odds ratio 1·14, 95% CI 0·86–1·51, p=0·37). There were no significant differences for secondary outcomes. In the GKI group, overall mean plasma glucose and mean systolic blood pressure were significantly lower than in the control group (mean difference in glucose 0·57 mmol/L, p<0·001; mean difference in blood pressure 9·0 mm Hg, p<0·0001).

Interpretation GKI infusions significantly reduced plasma glucose concentrations and blood pressure. Treatment within the trial protocol was not associated with significant clinical benefit, although the study was underpowered and alternative results cannot be excluded.

Lancet Neurol 2007; 6: 397–406

Published Online
March 29, 2007
DOI:10.1016/S1474-4422(07)70080-7

See Reflection and Reaction page 380

*Members listed at end of report

School of Clinical Medical Sciences, University of Newcastle, Newcastle upon Tyne, UK (C S Gray MD, A J Hildreth MPhil, J E O'Connell FRCP, D E Johnston, N E F Cartlidge FRCP, O F James FRCP, K G M M Alberti MD); University of Edinburgh, Edinburgh, UK (P A Sandercock DM); and Department of Neurology, St James Hospital, Leeds, UK (J M Bamford MD)

Correspondence to:
Prof C S Gray, City Hospitals Sunderland, Kayll Road, Sunderland SR4 7TP, UK

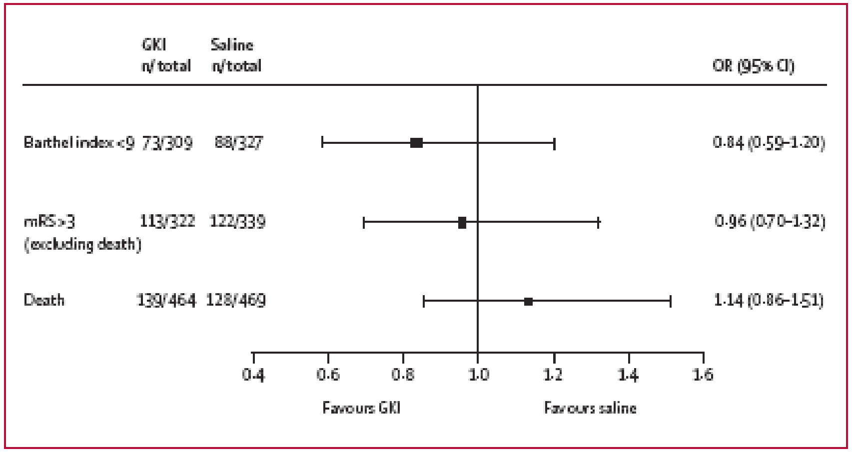


Figure 5: Common odds ratios (ORs) for primary and secondary outcomes with 95% CIs in the intention-to-treat dataset (n=933)
GKI=glucose-potassium-insulin.

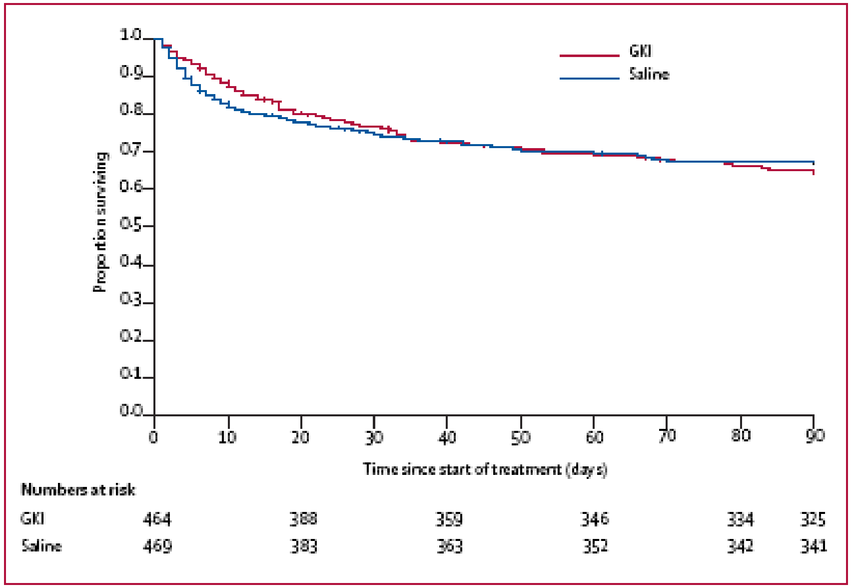


Figure 6: Kaplan-Meier survival curves to 90 days for glucose-potassium-insulin (GKI) and saline treatment groups
GKI=glucose-potassium-insulin.

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Management of Hyperglycemia in the Hospital Setting

Silvio E. Inzucchi, M.D.

N Engl J Med 2006;355:1903-11.

Table 1. Recommended Target Blood Glucose Levels for Hospitalized Patients.*

Location	American Diabetes Association[36]	American College of Endocrinology[2]
ICU	As close to 110 mg/dl as possible; generally <180 mg/dl	<110 mg/dl
General ward	As close to 90–130 mg/dl as possible; <180 mg/dl postprandial	<110 mg/dl before a meal; maximal <180 mg/dl

* The author believes these targets may be too stringent, on the basis of the available evidence. To convert values for glucose to millimoles per liter, multiply by 0.05551.

European Heart Journal (2008) **29**, 141–143
doi:10.1093/eurheartj/ehm595

EDITORIAL

Glucose-lowering therapy after myocardial infarction: more questions than answers

Peter W. Radke and Heribert Schunkert*

Universität zu Lübeck, Medizinische Klinik II, Ratzeburger Allee 160, D-23538 Lübeck, Germany

Emerging Therapies

Section Editors: Marc Fisher, MD, and Kennedy Lees, MD

Management of Hyperglycemia in Acute Stroke

How, When, and for Whom?

Michael T. McCormick, MRCP; Keith W. Muir, MD, FRCP;
Christopher S. Gray, MD, FRCP; Matthew R. Walters, MD, FRCP

Stroke. 2008;39:2177-2185

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Intensive Insulin in Intensive Care

Atul Malhotra, M.D.

……In my opinion, a reasonable approach would be to provide adequate exogenous insulin to achieve target glucose values of less than 150 mg per deciliter at least during the first three days in the ICU. If critical illness persists beyond three days……., a goal of normoglycemia (80-110 mg per deciliter) could then be considered……………..although this approach requires further study, it would seem to be a reasonable strategy that incorporates the best available evidence until more definitive data emerge.

…The balance between the potential benefits and risks (of hypoglycemia in particular) must be assessed. In very old patients with impaired mental status and consequently decreased capacity to perceive low glucose levels…

JAGS 2008, 56:1106-10

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 12, 2008 VOL. 358 NO. 24

Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group*

CONCLUSIONS

As compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels for 3.5 years increased mortality and did not significantly reduce major cardiovascular events. These findings identify a previously unrecognized harm of intensive glucose lowering in high-risk patients with type 2 diabetes. (ClinicalTrials.gov number, NCT00000620.)