

# Early Increase in Blood Glucose in Patients Resuscitated From Out-of-Hospital Ventricular Fibrillation Predicts Poor Outcome

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**OBJECTIVE**—To describe the trend of blood glucose immediately after successful resuscitation from out-of-hospital ventricular fibrillation.

**RESEARCH DESIGN AND METHODS**—Data from cardiac arrest registry supplemented with blood glucose data were analyzed in this population-based observational study. Between 2005 and 2009, a total of 170 adult patients survived to hospital admission after resuscitation from bystander-witnessed cardiac arrest of cardiac origin and ventricular fibrillation as an initial rhythm.

**RESULTS**—Sufficient data for analysis were available in 134 (79%) patients, of whom 87 (65% [95% CI 57–73]) survived to hospital discharge in Cerebral Performance Category 1 or 2. Blood glucose did not change significantly between prehospital ( $10.5 \pm 4.1$  mmol/L) and admission ( $10.0 \pm 3.7$  mmol/L) in survivors ( $P = 0.3483$ ), whereas in nonsurvivors, blood glucose increased from  $11.8 \pm 4.6$  to  $13.8 \pm 3.3$  mmol/L ( $P = 0.0025$ ).

**CONCLUSIONS**—Patients who are resuscitated from out-of-hospital ventricular fibrillation, but whose outcome is unfavorable are characterized by significant increase of blood glucose in the ultraacute postresuscitation phase.

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Postcardiac arrest syndrome after successful cardiopulmonary resuscitation poses high mortality. Only one-third of the patients resuscitated from cardiac arrest and admitted to intensive care units survive to discharge from hospital (1). In observational studies, hyperglycemia during intensive care predicted unfavorable outcome (2,3). The aims of this study were to investigate 1) how blood glucose changes during the early postresuscitation period and 2) how changes in blood glucose affect survival in patients resuscitated from out-of-hospital ventricular fibrillation.

## RESEARCH DESIGN AND METHODS

This retrospective population-based observational study used

prospectively collected cardiac arrest registry data complemented with laboratory data. An institutional review board approved the study protocol, and consent of subjects was not required.

We included all emergency medical services personnel-confirmed out-of-hospital cardiac arrests in Helsinki during 2005–2009 fulfilling the following criteria: age  $\geq 18$  years, arrest witnessed by bystander, ventricular fibrillation as a first recorded rhythm, and survival to hospital admission. Patients with missing glucose values either in the prehospital phase or at admission were excluded. The Helsinki Cardiac Arrest Register is a prospectively collected dataset including all out-of-hospital cardiac arrests in Helsinki. Cerebral Performance Category

1–2 at the time of hospital discharge was used as a survival end point (4).

Glucose-containing fluids were not used in prehospital treatment. Blood glucose was analyzed using the Optimum Xceed glucometer (Abbott Laboratories, Alameda, CA). Blood glucose values measured in the hospital within 24 h after emergency call, as well as HbA<sub>1c</sub> (closest value measured within 1 year of cardiac arrest) values, were obtained from an electronic laboratory database.

For analysis, patients were divided into groups based on surviving status and change in blood glucose between prehospital and admission time points. Increasing blood glucose was defined as blood glucose higher measured at admission than that measured in a prehospital setting after return of spontaneous circulation (ROSC).

For proportions, 95% CIs were measured. Categorical data were analyzed using either Fisher's exact or  $\chi^2$  test. Unpaired and paired *t*, Kruskal-Wallis, and Mann-Whitney *U* tests were used to compare groups as appropriate. Normally distributed data are reported as means  $\pm$  SD and skewed variables as median (interquartile range) (IQR). Statistical analyses were carried out using GraphPad Prism 5.0 for Mac OS X (GraphPad Software, San Diego, CA).

**RESULTS**—During the study period, resuscitation was attempted in 1,075 cases. Of those, 170 patients fulfilled the study criteria and 134 (79%) had sufficient data for analysis. The number of survivors, defined as discharged in Cerebral Performance Category 1 or 2, was 87 (65% [95% CI 57–73]). Characteristics of the patients and treatment given during and after cardiac arrests are presented in Table 1.

The sample for prehospital glucose measurement was capillary blood in 106, arterial blood in 24, and venous blood in 4 cases. Time between emergency call and glucose measurement at admission was 105 min (IQR 85–132) in survivors and 114 min (91–129) in nonsurvivors, respectively ( $P = 0.3157$ ).

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Table 1—Characteristics of the patients and cardiac arrests

	Survivors	Nonsurvivors	P	Rising glucose	No rising glucose	P
N	87	47		64	70	
Patient characteristics						
Age (years), median (IQR)	61 (54–69)	69 (60–76)	0.0012	67 (58–73)	63 (55–70)	0.1528
Men	67 (77, 67–85)	38 (81, 67–90)	0.6630	50 (78, 66–89)	55 (79, 68–87)	1.000
Previously known diabetes	12 (14, 8–23)	10 (21, 12–35)	0.3293	9 (14, 7–25)	13 (19, 11.29)	0.6414
Previous use of insulin	3 (3, 1–10)	1 (2, 0–12)	1.000	2 (3, 0–11)	2 (3, 0–10)	1.000
Cardiac arrest						
First documented rhythm						
Ventricular fibrillation	85 (98, 92–100)	47 (100, 91–100)		63 (98, 91–100)	69 (99, 92–100)	
Ventricular tachycardia	2 (2, 0–8)	0 (0, 0–9)	0.5411	1 (2, 0–9)	1 (1, 0–8)	1.000
Bystander cardiopulmonary resuscitation including chest compressions						
	69 (79, 70–87)	28 (60, 45–72)	0.0250	45 (70, 58–80)	52 (74, 63–83)	0.2756
Resuscitation and postresuscitation care						
First responding unit response time (min), mean $\pm$ SD						
	7.4 $\pm$ 2.3	7.5 $\pm$ 2.5	0.8932	7.3 $\pm$ 2.5	7.7 $\pm$ 2.3	0.3968
Advanced life-support response time (min), mean $\pm$ SD						
	10.0 $\pm$ 3.5	10.3 $\pm$ 4.1	0.7089	9.4 $\pm$ 3.4	10.8 $\pm$ 3.9	0.0390
Time to ROSC, median (IQR)	15.0 (11.0–20.0)	24.0 (17.0–28.0)	<0.0001	21 (13–25)	15 (11–22)	0.0120
Adrenaline (mg), median (IQR)	0 (0–1)	2 (1–3)	<0.0001	1 (0–2)	0 (0–2)	0.0416
Prehospital thrombolysis	14 (16, 10–25)	10 (21, 12–35)	0.4846	7 (11, 5–21)	17 (24, 16–36)	0.0741
Therapeutic hypothermia	57 (66, 55–75)	25 (53, 39–67)	0.1948	38 (59, 47–71)	44 (63, 51–73)	0.8595

Data are n (%), 95% CI unless otherwise indicated.

Significant changes in blood glucose were not observed between prehospital ( $10.5 \pm 4.1$  mmol/L) and admission ( $10.0 \pm 3.7$  mmol/L) measurements in surviving patients ( $P = 0.3483$ ), whereas in nonsurvivors blood glucose increased 2.0 mmol/L from  $11.8 \pm 4.6$  mmol/L measured after ROSC to  $13.8 \pm 3.3$  mmol/L measured at admission ( $P = 0.0025$ ). No associations were observed between increasing glucose and HbA<sub>1c</sub> ( $n = 81$ ). Within 24 h after emergency call, a total of 1,275 glucose measurements were performed. Nonsurvivors had significantly higher blood glucose concentration than survivors, respectively, in 0–3 h ( $13.5 \pm 3.9$  vs.  $10.4 \pm 4.3$  mmol/L,  $P < 0.0001$ ), 3–6 h ( $10.2 \pm 4.4$  vs.  $8.2 \pm 2.7$  mmol/L,  $P < 0.001$ ), and 6–12 h ( $7.5 \pm 2.2$  vs.  $6.6 \pm 1.6$  mmol/L,  $P < 0.001$ ) but not 12–24 h ( $6.2 \pm 1.9$  vs.  $5.9 \pm 1.3$  mmol/L,  $P = 0.3509$ ) after emergency call.

**CONCLUSIONS**—The current study demonstrates that patients who are successfully resuscitated from out-of-hospital ventricular fibrillation but with unfavorable outcome are characterized by significant increase of blood glucose in the ultraacute phase before hospital admission. The increased glucose values persisted during the

early reperfusion phase, i.e., the first 12 h, in the patients with poor outcome.

Hyperglycemia at the time of hospital admission is an independent predictor of poor outcome in conditions involving ischemia and reperfusion pathology, including acute myocardial infarction (5) and ischemic stroke (6). Hyperglycemia appears to be especially detrimental during ischemia and the very early reperfusion phase. Less is known about implications of ultraacute hyperglycemia during the first hours after cardiac arrest. In animals, ventricular fibrillation with subsequent resuscitation suppresses insulin secretion and causes a more than threefold rise in blood glucose (7), peaking immediately after ROSC and declining to baseline within 2–3 h (8,9). However, in humans hyperglycemia is still commonly observed at the time of intensive care unit admission (2).

The clinical studies assessing the effects of acute glucose control in ischemia and reperfusion conditions (ischemic stroke and acute myocardial infarction) have failed to provide effective and timely glucose control. In the largest studies, the insulin has been given 4.7–13.3 h after onset of symptoms (10–12). In animal studies, the delay from onset of ischemia to insulin treatment has been shorter,

varying from immediate to 60 min (13). The optimal timing of glucose control after cardiac arrest warrants further studies, since hyperglycemia in a prehospital setting is moderately easy to treat. In our previous study (14), paramedics successfully initiated insulin infusion for stroke patients, resulting in a 1.9 mmol/L decrease in blood glucose before reaching the hospital.

The current observational study cannot account for whether treatment of acute hyperglycemia after cardiac arrest could improve outcome. The hyperglycemia after ROSC may have only indicated the patient's condition, as it was observed more commonly in patients with longer duration of resuscitation and higher cumulative adrenaline dose. Also, the glucose trends after admission need to be interpreted cautiously and not as a natural course of glucose fluctuations after cardiac arrest, since insulin is commonly given to the patients. However, hyperglycemia per se poses many detrimental effects in acutely ill patients, including upregulation of proinflammatory cytokines, endothelial dysfunction, and aggregation of thrombocytes (15).

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