The Egyptian Journal of Hospital Medicine (January 2021) Vol. 82 (4), Page 641-646

Study of Hyperglycemia as a Prognostic Factor in Acute Ischemic Stroke

Samir Mohamed Attia[1], Mohamed Said Gomaa[2],
Hesham Khairy Ismaeil[3], Amr Abdel Sattar Elmetwaly*[4]
Departments of [1]Vascular Surgery, [2]Neurology, [3]Critical Care Medicine and [4]Emergency Medicine & Traumatology - Faculty of Medicine – Mansoura University
***Corresponding author:** Amr Abdel Sattar Elmetwaly, **Mobile:** (+20) 01095676360, **E-Mail:** zeroamr@ymail.com

ABSTRACT

Background: Acute ischemic stroke (AIS) is a grave threat to global healthcare system, which is accompanied by high disability and mortality. Stress hyperglycemia is common in critically ill patients and appears to be a marker of disease severity. Furthermore, both the admission as well as the mean glucose level during the hospital stay is strongly associated with patient outcomes.

Objective: To determine the impact of hyperglycemia in AIS on short-term outcome and prognosis.

Patients and methods: This was a cross-sectional study, which was carried out on 150 patients arrived to Emergency Department (ED) in Emergency Mansoura University Hospital with clinical presentation and radiological investigations of ischemic stroke over the period from June 2018 to May 2019.

Results: There were statistically significant difference as regards both onset and course of symptoms among both groups. Normoglycemic group demonstrated significant increase as regards serum creatinine, while demonstrated significant decrease as regards SBP, DBP, Glasgow coma scale (GCS) and glucose level in comparison with hyperglycemic group. Normoglycemic group demonstrated better outcomes in terms of CT brain and CBC compared to hyperglycemic group. Hyperglycemic group demonstrated abnormal outcomes in terms of ABG. Hyperglycemic group demonstrated marked increase in overall mortality rate compared to normoglycemic one. There were significant increase in ward admission cases as regards onset GCS and significant decrease as regards stay duration more than one week in comparison with ICU admission cases.

Conclusion: Stress hyperglycemia is common among acute stroke patients and was associated with less favorable outcomes especially in terms of mortality, hospital stay and functional outcome.

Keywords: Acute Ischemic Stroke, Hyperglycemia, Glasgow coma scale.

INTRODUCTION

Stroke is defined as a focal loss of brain function lasting more than 24 hours with no appearance of cause other than vascular origin resulting in acute neurologic insult that occurs as a result of one of brain ischemia or hemorrhage [(1)]. Worldwide, cerebrovascular accidents (stroke) are the second leading cause of death and the third leading cause of disability [(2)].

There are two main types of stroke, ischemic and hemorrhagic, while there is a third more minor stroke called transient ischemic attack (TIA). An ischemic stroke can be caused by a blood clot that is formed in the heart and travelled to the brain or by atherothrombosis. Hemorrhagic strokes, conversely are caused by a rupture in the blood vessels that causes bleeding within the brain. A TIA is a blood clot that temporarily interrupts blood flow in the brain and is a major risk factor for future strokes that could cause more serious damage [(3)].

Hyperglycemia is common in patients with acute stroke, occurring in up to 60% of patients overall and approximately 12–53% of acute stroke patients without a prior diagnosis of diabetes. It has been associated with increased stroke severity and mortality [(4)]. Hyperglycemia is defined as blood glucose level > 200 mg/dL. It has been observed in two thirds of all ischemic stroke subtypes on admission and in at least 50% in each subtype including lacunar strokes. Several prior studies have demonstrated that post-stroke hyperglycemia is associated with worse patient outcomes following an acute stroke, including increased post-stroke mortality [(5)].

In the absence of stroke-specific recommendations, current guidelines advice treating hyperglycemia in stroke patients as one would treat hyperglycemia in any hospitalized patient, including frequent glucose monitoring and stringent blood glucose control [(6)].

The aim of this study was to determine the impact of hyperglycemia in acute ischemic stroke on short-term outcome and prognosis.

PATIENTS AND METHODS

This was cross-sectional study conducted on 150 patients arrived to Emergency Department (ED) in Emergency Mansoura University Hospital with clinical presentation and radiological investigations of ischemic stroke within the period from June 2018 to May 2019. The patients were classified into two groups: Normoglycemic group (86) and hyperglycemic group (64).

Inclusion criteria:

1. Patients with ischemic stroke.
2. Patients aged more than 16 years old.
3. Both genders.

Exclusion criteria:

Received:17 /10 /2020
Accepted:5 /12/2020

1. Patient aged less than 16 years old.
2. Patients refuse to be included in the study.

All patients were subjected to the following:

1. **History:** Taken from the patient himself or relatives if present with altered mental status, personal history, history of the present illness and past medical history.
2. **Resuscitation:** A = Airway opening and maintenance of airway, B = Breathing and ventilation, C = Circulation and D = Disability: neurological status and Glasgow coma scale (GCS).
3. **Clinical examination:** General: level of consciousness according to GCS, blood pressure, pulse and random blood glucose. Local: neurological examination, chest and abdominal examination: (inspection, palpation, percussion and auscultation) and full clinical examination of all body.
4. **Neurological examination:** The major areas of the exam, covering the most testable components of the neurological system.
5. **Electrocardiogram (ECG):** We analyzed the first ECG made at the moment of admission and another one later during hospitalization .
6. **Computer Tomography (CT):** At the moment of admission has the possibility to show the location of lesions, size or unspecific images like diffuse cerebral edema.
7. **Other tests:** Chest X-Ray and echocardiography.

Ethical approval and written informed consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. Shapiro-Wilk test was used to check the normality of the data distribution. All tests were conducted with 95% confidence interval. P (probability) value ≤ 0.05 was considered statistically significant. Charts were generated using SPSS' chart builder and Microsoft Excel for windows 2019. Descriptive: Quantitative variables were expressed as mean and standard deviation, median, inter-quartile range, minimum and maximum as appropriate while categorical variables were expressed as frequency and percentage. Categorical group differences: Fisher exact and Chi square tests were used for inter-group comparison of nominal data using the crosstabs function. Correlations: Bivariate correlations were assessed using Pearson's or Spearman's correlation coefficient depending on the nature of data. Risk assessment: Association between risk assessment and mortality in the current study was assessed using odds ratio.

RESULTS

Table (1): Demographic characteristics and medical history of the studied patients

		Normoglycemic group (n= 86)	Hyperglycemic group (n= 64)	95% CI	p
Age (years)		61.21 ± 14.276	60.36 ± 8.445	-2.8, 4.5	0.650
Gender	**Male**	53.5% (46)	43.7% (28)		0.238
	Female	46.5% (40)	56.3% (36)		
Marital status	**Single**	5.8% (5)	0.0% (0)		0.072
	Married	94.2% (81)	100.0% (64)		
History of hypertension		60.5% (52)	92.2% (59)		**< 0.001**
History of smoking		7.0% (6)	9.4% (6)		0.592
Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when ≤ 0.05.					

The demographic characteristics and medical history of the studied patients are shown in table (1). There were no statistically significant differences among both groups in terms of age, sex, marital status and history of smoking (P > 0.05), while there was highly statistically significant difference as regards history of hypertension (P < 0.001).

Table (2): Onset and course of symptoms in the studied patients

		Normoglycemic group (n= 86)	Hyperglycemic group (n= 64)	p
Onset	**Acute**	93.0% (80)	62.5% (40)	**< 0.001**
	Old	7.0% (6)	37.5% (24)	
Course	**Stationary**	33.7% (29)	31.3% (20)	**0.013**
	Regressive	52.3% (45)	53.1% (34)	
	Progressive	2.3% (2)	15.6% (10)	
Data is expressed as percentage and frequency. P is significant when ≤ 0.05.				

Table (2) showed the onset and course of symptoms in the studied patients. There were statistically significant difference as regards both onset and course of symptoms (P < 0.05) among both groups.

Table (3): SBP, DBP, GCS, RR and creatinine and glucose levels of the studied patients

	Normoglycemic group (n= 86)	Hyperglycemic group (n= 64)	95% CI	p
SBP (mmHg)	134.07 ± 21.605	156.41 ± 23.256	-29.7, - 15.0	**< 0.001**
DBP (mmHg)	83.37 ± 10.804	90.16 ± 9.676	-10.1, -3.5	**< 0.001**
GCS	14.02 ± 1.728	14.63 ± 0.900	-1.0, -0.2	**0.007**
RR	17.63 ± 1.085	17.47 ± 1.522	-0.3, 0.6	0.478
Creatinine (mg/dl)	1.57 ± 0.035	0.98 ± 0.082	0.4, 0.8	**< 0.001**
Glucose level	103.28 ± 10.499	197.84 ± 8.288	-109.3, - 79.8	**< 0.001**

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when ≤ 0.05.

Table (3) showed vital signs, GCS and creatinine and glucose levels of the studied patients. Normoglycemic group demonstrated significant increase as regards serum creatinine, while demonstrated significant decrease as regards SBP, DBP, GCS and glucose level in comparison with hyperglycemic group (P < 0.05).

Table (4): CT brain, CBC and ABG of the studied patients

		Normoglycemic group (n= 86)	Hyperglycemic group (n= 64)	p
CT brain	**NAD**	33.7% (29)	9.4% (6)	**< 0.001**
	Infarction	33.7% (29)	43.8% (28)	
	CIC	26.7% (23)	18.8% (12)	
	MCA	5.8% (5)	9.4% (6)	
	Old infarction	0.0% (0)	18.8% (12)	
CBC	**Normal**	93.0% (80)	100.0% (64)	**0.038**
	Abnormal	7.0% (6)	0.0% (0)	
ABG	**Normal**	81.4% (70)	100.0% (64)	**< 0.001**
	Abnormal	18.6% (16)	0.0% (0)	

Data is expressed as percentage and frequency. P is significant when ≤ 0.05.

Table (4) showed the mean CT brain, CBC and ABG of the studied patients. There were highly statistically significant difference among both groups as regards Ct brain, CBC and ABG (P < 0.05), in which normoglycemic group demonstrated better outcomes in terms of CT brain and CBC, while hyperglycemic group demonstrated abnormal outcomes in terms of ABG.

Table (5): ICU stay and patients' outcome in the studied patients

	Normoglycemic group (n= 86)	Hyperglycemic group (n= 64)	P
ICU admission	19.8% (17)	18.8% (12)	0.876
Stay duration more than one week	7.0% (6)	9.4% (6)	0.592
Overall mortality	2.3% (2)	14.1% (9)	**0.009**

Data is expressed as percentage and frequency. P is significant when ≤ 0.05.

Table (5) showed the ICU stay and patients' outcome in the studied patients. There were no statistically significant differences among both groups as regards ICU admission and stay duration more than one week, while there was significant increase in overall mortality in hyperglycemic group compared to normoglycemic group (P = 0.009).

Table (6): Odds ratio of ICU admission and mortality in hyperglycemic group compared to normoglycemic group

	Odds ratio	95% CI of odds ratio
ICU admission	0.937	0.412, 2.131
Overall mortality	6.873	1.431, 33.016

Table (6) showed the Odds ratio of ICU admission and mortality rate in hyperglycemic group compared to normoglycemic group. The Odds ratio and its 95% CI were 0.937 and 0.412-2.131, respectively for ICU admission while they were 6.873 and 1.431-33.016, respectively for overall mortality.

DISCUSSION

In our study as regards demographic data there were no statistically significant differences among both studied groups in terms of age, sex, marital status and smoking habits (P > 0.05), while there was highly statistically significant differences as regards hypertension, which demonstrated higher prevalence among hyperglycemic group. Such results indicated that, entire cases were matched among all these parameters and such parameters were not interfering with the net results of the current study. Our results are in accordance with **Al-Weshahy *et al.*** [7] who conducted their study on 61 consecutive patients with acute stroke. 41 had hyperglycemia (20 diabetics and 21 non diabetics) and 20 were control. In addition, 60.7% were males with mean age of 62.9 ± 10.5 years. There were no statistically significant differences among the control and hyperglycemic cases as regards, age, sex, history of hypertension, smoking and ischemic heart diseases (IHD).

In our study, the prevalence of stress hyperglysemia among the studied cases was 42.6%, while 57.4% of which had normoglycemics. In harmony with the current study, **Al-Weshahy *et al.*** [7] conducted their study on 61 consecutive patients with acute ischemic stroke (AIS). 41 had hyperglycemia (20 diabetics and 21 non diabetics) and 20 were control. While higher levels were recorded by **Marulaiah *et al.*** [8], who demonstrated that, 56.1% of the studied subjects had capillary blood glucose >140 mg/ dL on presentation. Around 41% of the stroke patients were normoglycemic, 21.2% had stress hyperglycemia, 24.2% were known diabetics, and 13.65% were newly detected with DM. In addition, **Tziomalos *et al.*** [9] reported very low incidence as 8.6% of their AIS cases (790 consecutive patients) had stress hyperglycemia. The discrepancies between the current study and both **Marulaiah *et al.*** [8] and **Tziomalos *et al.*** [9] researches may be due to the fact that, the current study excluded the diabetic cases, while both researches were performed on diabetic and non-diabetic cases.

As regards, the onset and course of symptoms in the studied patients, acute onset was reported in 80 normoglycemic and 40 hyperglycemic patients with a statistically significant difference between both groups while old onset was reported in 6 normoglycemic and 24 hyperglycemic patients with a statistically significant difference between both groups (p < 0.001).

As regards the course, stationary course was reported in 29 normoglycemic and 20 hyperglycemic patients with a statistically significant difference between both groups. Regressive course was reported in 45 normoglycemic and 34 hyperglycemic patients with a statistically significant difference between both groups while progressive course was reported in only 2 normoglycemic cases compared to 10 hyperglycemic patients with a statistically significant difference between both groups (p < 0.013). The mechanism of such progression of stroke among hyperglycemic cases compared to normoglycemia cases may be due the effect of hyperglycemia on brain. By provoking anaerobic metabolism, lactic acidosis, and free radical production. Hyperglycemia may exert direct membrane lipid peroxidation and cell lysis in metabolically challenged tissue. Moderately and severely increased blood glucose has been found to further the metabolic state and mitochondrial function in the area of ischemic penumbra. Insulin resistance is a known risk factor for the onset of stroke acting through a number of intermediate vascular disease risk factors (i.e. thrombophilia, endothelial dysfunction, and inflammation) [10, 11].

The evolution of an acute infarction may be expedited by the same vascular factors, explaining why ischemia time seems to fly faster with patients with diabetes or grave hyperglycemia. Relative insulin deficiency liberates circulating free fatty acids, which together with hyperglycemia diminish vascular reactivity. Furthermore, lowering glucose with insulin has been reported to reduce ischemic brain damage in an animal model [12].

An important note to be considered, the majority of prior researches measured the course of AIS in terms of NIHSS. In the same line, **Al-Weshahy *et al.*** [7] demonstrated that, none of the control had any acute complications. As regards, NIHSS score, patients with hyperglycemia had higher admission (NIHSS versus control (14.9 ± 5.9 vs. 7.8 ± 3.5, p .000 respectively)). High incidence of patients with hyperglycemia are in the worse NIHSS scores (53.7% are in the moderate/severe and severe scores vs5% of the control).

As regards, vital signs, GCS, creatinine and glucose level of the studied patients, the mean SBP was statistically significant higher in hyperglycemic group compared to normoglycemic group (156.41 vs. 134.07) (p < 0.001). Similarly, the mean DBP was statistically significantly higher in hyperglycemic group compared to normoglycemic group (90.16 vs. 83.37) (p < 0.001). The mean GCS was 14.02 in normoglycemic group compared to 14.63 in hyperglycemic group with a statistically significant difference between both groups (p < 0.007). In addition, the mean RR in normoglycemic group and hyperglycemic group was 17.63 and 17.47, respectively with no statistically significant difference between both groups. The mean creatinine in normoglycemic group and hyperglycemic group was 1.57 and 0.98, respectively with a statistically significant difference between both groups (p < 0.001). The mean glucose level in normoglycemic group and hyperglycemic group was 103.28 and 197.84 respectively with a statistically significant difference between both groups (p < 0.001).

In patients with shock, plasma concentrations of epinephrine increase 50-fold and norepinephrine levels increase 10-fold. The adrenal medulla is the major source of these released catecholamines. The increased release of stress hormones results in multiple effects (metabolic, cardiovascular and immune) aimed at restoring homeostasis during stress. The HPA axis, sympathoadrenal system and proinflammatory cytokines (TNF-α, IL-1 and IL-6) act collectively and synergistically to induce stress hyperglycemia **[13].**

Despite many studies connecting hyperglycemia to worse stroke outcome, it remains in definite whether hyperglycemia is actually a marker of stroke severity or whether hyperglycemia directly contributes to brain damage **[14].** On the contrary, **Tziomalos *et al.*** **[10]** displayed that, stress hyperglycemia does not appear to be directly associated with the outcome of AIS. However, it is given that patients with stress hyperglycemia had higher prevalence of cardiovascular risk factors than patients with normoglycemia.

As regards the CT brain findings, NAD was revealed in 29 normoglycemic cases compared to 6 hyperglycemic cases. Infarction was revealed in 29 normoglycemic cases compared to 28 hyperglycemic cases. CIC was revealed in 23 normoglycemic cases compared to 12 hyperglycemic cases. MCA was revealed in 5 normoglycemic cases compared to 6 hyperglycemic cases, while Old infarction was not revealed in any of normoglycemic cases compared with 12 hyperglycemic cases. There was statistically significant difference between both groups as regards CT brain findings ($p < 0.001$).

As regards the CBC, it was normal in in 80 normoglycemic cases compared to 64 hyperglycemic cases, while it was abnormal in 6 normoglycemic cases compared to none in Hyperglycemic cases. There was statistically significant difference between both groups as regards CBC ($p= 0.038$). As regards the ABG, it was normal in in 40 normoglycemic cases compared to 64 hyperglycemic cases while it was abnormal in 16 normoglycemic cases compared to none in hyperglycemic cases. There was statistically significant difference between both groups as regards ABG ($p < 0.001$). In the same line, **Al-Weshahy *et al.*** **[7]** demonstrated that patients with hyperglycemia had higher incidence of posterior circulation affection in 19.5% (8 patients) versus 0% in control ($p = 0.03$) and a higher rate of acute complications (9.7% developed significant brain edema, 17.7% developed hemorrhagic transformation, and 2.4% has hydrocephalic changes). None of the control had any acute complications. In addition, **Marulaiah *et al.*** **[8],** displayed that stress hyperglycemia in stroke was associated with higher risk of poor functional outcome in acute ischemic stroke. Hyperglycemia at stroke onset without prior history of diabetes mellitus have particularly poor prognosis, than those with hyperglycemia in known diabetes.

As regards, ICU stay and patients' outcome in the studied patients, 17 normoglycemic patients were admitted to ICU compared to 12 hyperglycemic patients with no statistically significant difference between both groups. Also, 6 patients from each group stayed more than one week with no statistically significant difference between both groups.

As regards the overall mortality, 2 normoglycemic patients died compared to 9 hyperglycemic patients with a statistically significant difference between both groups ($p < 0.009$). This comes in agreement with **Abdelhamid *et al.*** **[14]** who demonstrated that hospital stay mean was 12.04 ± 9.61 in control group and 21.36 ± 12.49 in uncontrolled group with p-value < 0.022S. A highly statistically significant difference between controlled and uncontrolled according to increase motor power at ICU admission in controlled a highly statistically significant difference between controlled and uncontrolled according to increase motor power discharge in controlled group. A highly statistically significant difference was found between both groups as regards outcome (mortality). In addition, **Al-Weshahy *et al.*** **[7]** revealed that patients with hyperglycemia had longer hospital stay versus control [15.4 ± 7.0 vs. 9.5 ± 4.0 days, ($p = 0.008$)]. Moreover, they displayed patients with hyperglycemia had longer ICU stay versus control (12.5 ± 9.1 vs. 3.0 ± 4.2 days respectively, $P <0.001$).

Moreover, **Al-Weshahy *et al.*** **[7]** demonstrated that, patients with hyperglycemia had higher mortality rate compared to control (65.9% vs 5%, $p < 0.00$). Furthermore, **Marulaiah *et al.*** **[8],** demonstrated that patients with hyperglycemia exhibited greater functional impairment, as 96 out of 111 study subjects had mRS ≥ 3, than those with normoglycemia ($P < 0.0001$). Mortality was high in hyperglycemics when compared to normoglycemics, as out of the 20 deaths, 13 patients had hyperglycemia and seven had normoglycemia at presentation ($P < 0.015$). In addition, logistic regression analysis predicted that higher capillary blood glucose at first presentation, moderate-to-severe stroke, poor drug compliance, stress hyperglycemia, and newly detected diabetes mellitus were associated with poor functional outcome at 90 days of follow-up. Supporting to the current study, **Jørgensen *et al.*** **[15]** who displayed in their large prospective Danish study that plasma glucose level >11 mmol/L (>198 mg/dL) was associated with hospital mortality of 17% for non-diabetic patients, 24% for those with known diabetes and 32% for patients with hyperglycemia with no history of previous diabetes. Furthermore, **Capes *et al.*** **[16],** in their systematic review found that stress hyperglycemia upon hospital admission was associated with three folds higher risk of short-term

mortality compared with patients with lower glucose levels.

Conclusion:

Stress hyperglycemia is common among acute stroke patients and was associated with less favorable outcomes especially in terms of mortality, hospital stay and functional outcome. In addition, it could be used as a predictor for overall mortality and outcomes.

References

1. **Sacco R, Kasner S, Broderick J *et al.* (2013):** An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke, 44 (7): 2064-2089.
2. **World Health Organization (2016):** Stroke: a global response is needed. Available at: http://www.who.int/bulletin/volumes/94/9/16-181636
3. **Mozzafarian D, Benjamin E, Go A *et al.* (2016):** on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation, 133 (4): 38–360.
4. **Szczudlik A, Slowik A, Turaj W et *al.* (2001):** Transient hyperglycemia in ischemic stroke patients. Journal of the Neurological Sciences, 189 (1-2): 105-111.
5. **Williams L, Rotich J, Qi R *et al.* (2002):** Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. Neurology, 59 (1): 67-71.
6. **Kitabchi A, Umpierrez G, Murphy M *et al.* (2003):** Hyperglycemic crises in patients with diabetes mellitus. Diabetes Care, 26: 109-114.
7. **Al-Weshahy A, El-Sherif R, Selim K *et al.* (2017):** Short term outcome of patients with hyperglycemia and acute stroke. The Egyptian Journal of Critical Care Medicine, 5 (3): 93-98.
8. **Marulaiah S, Reddy M, Basavegowda M *et al.* (2017):** Admission hyperglycemia an independent predictor of outcome in acute ischemic stroke: A longitudinal study from a tertiary care hospital in South India. Nigerian Journal of Clinical Practice, 20 (5): 573-580.
9. **Tziomalos K, Dimitriou P, Bouziana S *et al.* (2017):** Stress hyperglycemia and acute ischemic stroke in-hospital outcome. Metabolism, 67: 99-105.
10. **Klijn C, Hankey G (2003):** Management of acute ischaemic stroke: new guidelines from the American Stroke Association and European Stroke Initiative. The Lancet Neurology, 2 (11): 698-701.
11. **Lindsberg P, Roine R (2004):** Hyperglycemia in acute stroke. Stroke, 35(2): 363-364.
12. **Marik P, Bellomo R (2013):** Stress hyperglycemia: an essential survival response! Critical Care, 17 (2): 305-309.
13. **Poppe A, Majumdar S, Jeerakathil T *et al.* (2009):** Admission hyperglycemia predicts a worse outcome in stroke patients treated with intravenous thrombolysis. Diabetes Care, 32 (4): 617-622.
14. **Abdelhamid A, El-Gendy H, Nosseir M *et al.* (2020):** Hyperglycemia as a Prognostic Factor In Acute Ischemic Stroke Patients. QJM: An International Journal of Medicine, 113 (1): 39-46.
15. **Johnston K, Hall C, Kissela B *et al.* (2009):** Glucose Regulation in Acute Stroke Patients (GRASP) trial: a randomized pilot trial. Stroke, 40 (12): 3804-3809.
16. **Capes S, Hunt D, Malmberg K *et al.* (2001):** Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke, 32 (10): 2426-2432.