

· 临床研究 ·

应激性高血糖对急性ST段抬高型心肌梗死患者远期预后的影响

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【摘要】目的 探讨急性ST段抬高型心肌梗死(STEMI)患者发生应激性高血糖的相关危险因素,并评估应激性高血糖对STEMI患者远期预后的影响。**方法** 白求恩国际和平医院2009年8月至2010年4月92例初次发生STEMI的非糖尿病住院患者,根据入院后测定的空腹血糖或随机血糖分A组(应激性高血糖组)41例和B组(血糖正常组)51例。平均随访1.5年。**结果** 应激性高血糖的发生率是44.6%(41/92)。A和B组间经logistic回归分析提示女性($OR = 8.952, P = 0.013$)、心功能Killip分级越高($OR = 3.530, P = 0.048$)、肌酸激酶同工酶(CK-MB)峰值越高($OR = 9.408, P < 0.001$)均是应激性高血糖发生的相关危险因素。Cox回归对A和B组患者1~2年内发生的死亡风险进行分析,提示应激性高血糖是远期死亡($RR = 1.532, 95\%CI = 1.004 \sim 2.337, P = 0.048$)的独立预测因子。高甘油三酯血症患者远期死亡风险是正常者1.557倍($P = 0.041$)。**结论** 女性、Killip分级、CK-MB增高是应激性高血糖发生的相关危险因素。应激性高血糖可能是STEMI患者远期预后不良的独立预测因子和危险因素。高甘油三酯血症可能加重患者的死亡风险。

【关键词】 ST段抬高型急性心肌梗死; 应激性高血糖; 危险因素; 预后

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Effect of stress hyperglycemia on long-term prognosis of patients with ST segment elevation acute myocardial infarction

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【Abstract】 Objective To evaluate the predictors of stress hyperglycemia in patients with ST segment elevation acute myocardial infarction (STEMI) and the effect of stress hyperglycemia on the long-term prognosis of these patients. **Methods** A total of 92 patients who had no diabetes but suffered from STEMI for the first time admitted in our hospital from August 2009 to April 2010 were enrolled in this study. The patients were divided into stress hyperglycemia group ($n = 41$) and normal blood glucose group ($n = 51$) according to the results of fasting blood glucose or random blood glucose after admission. The patients were followed up for 1.5 years on average. **Results** The prevalence of stress hyperglycemia was 44.6% (41/92). Logistic regression analysis indicated that female ($OR = 8.952, 95\% CI = 1.579$ to $50.757, P = 0.013$), higher Killip class ($OR = 3.530, 95\% CI = 1.010$ to $12.336, P = 0.048$), and higher creatine kinase (CK)-MB ($OR = 9.408, 95\%CI = 2.782$ to $31.818, P < 0.001$) were the independent predictors of stress hyperglycemia. Cox proportional hazard regression model presented that stress hyperglycemia was an independent predictor for 1 to 2 years mortality ($RR = 1.532, 95\% CI = 1.004$ to $2.337, P = 0.048$). The long-term mortality risk of patients with hypertriglyceridemia was 1.557 times higher than those with normal triglycerides ($P = 0.041$). **Conclusion** Female, higher Killip class, and higher CK-MB are the independent predictors for stress hyperglycemia after STEMI. Stress hyperglycemia is an independent predictor and risk factor for long-term unfavorable prognosis in STEMI patients. Hypertriglyceridemia may increase the risk of death in these patients.

【Key words】 ST segment elevation acute myocardial infarction; stress hyperglycemia; risk factors; prognosis

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糖尿病增加急性心肌梗死(acute myocardial infarction, AMI)近期和远期死亡率早已被研究所证实,而既往无糖尿病患者在AMI后常常发生应激性血糖升高^[1]。AMI时血糖升高常常被认为是机体

的一种自我保护反应,研究发现血糖的升高与AMI的并发症存在相关性,并影响着AMI患者的预后^[2]。本研究入选92例首次发生ST段抬高型急性心肌梗死(ST segment elevation acute myocardial infarction,

STEMI)的住院患者,根据STEMI前、后不同的血糖水平,分析探讨应激性高血糖发生的相关危险因素及高血糖对远期预后的影响,以对临床治疗提供帮助。

1 对象与方法

1.1 研究对象

白求恩国际和平医院2009年8月至2010年4月期间初发STEMI的非糖尿病住院患者92例,其中男性79例,女性13例,年龄25~85(57.6±13.1)岁。根据入院后测定的空腹血糖或随机血糖将患者分为两组,A组(应激性高血糖组)41例:空腹血糖≥7.0mmol/L或随机血糖≥11.1mmol/L;B组(血糖正常组)51例:空腹血糖<7.0mmol/L或随机血糖<11.1mmol/L。

1.2 方法

1.2.1 诊断标准 AMI符合世界卫生组织诊断标准:持续胸痛超过30min,心电图相邻导联ST段抬高≥2mm,肌酸激酶MB同工酶(creatinine kinase isoenzyme,CK-MB)大于正常2倍以上。欧洲心脏病学协会(ESC)/美国心脏病学学会(ACC)提出新的一项诊断标准:在临床事件后第一个24h期间至少有一次肌钙蛋白T或肌钙蛋白I的最大浓度超过决定限(参考对照人群值的99%分位值)就是心肌梗死。

1.2.2 排除标准 通过口服葡萄糖耐量试验和糖化血红蛋白排除已确诊和本次住院新确诊的糖尿病患者。使用激素类药物、甲状腺功能亢进症、库欣综合征、胰腺疾病、严重肝肾功能障碍、血液病、感染、外伤、肿瘤及脑卒中均不在入选患者范围之内。

1.2.3 资料收集及随访 患者入院后立即描记18导联心电图,抽血查静脉血糖值(氧化酶法)、心肌酶谱、肌钙蛋白(参考患者外院资料)、电解质和肝肾功能。第2天早晨查空腹血糖。记录既往有否高血压、高甘油三酯血症、冠心病、脑血管病及吸烟等病史。住院1周内行超声心动图及心功能指标检查。患者出院后每6个月进行一次电话随访,随访内容包括死亡率、死亡原因及心血管事件。平均随访1.5(0.5~2.5)年,随访终点时间为2012年10月。患者住院后根据需要给予血管重建治疗[包括急诊溶栓治疗、急诊经皮冠状动脉介入治疗(percutaneous coronary intervention,PCI)及择期PCI治疗]或药物保守治疗(未行血运重建)。

1.3 统计学处理

所有数据用统计学软件SPSS13.0处理,计量资料以均数±标准差表示,计数资料以百分率表示。计量资料组间比较采用t检验,计数资料比较采用χ²

检验,如果n<40,则采用精确概率法,用logistic回归和Cox回归进行预后相关因素分析。P<0.05为差异有统计学意义。

2 结果

2.1 入院时血糖水平

A组血糖波动范围7.07~28.89(12.67±6.99)mmol/L,B组血糖波动范围4.48~6.99(5.86±0.75)mmol/L。

2.2 两组一般临床资料比较

表1结果表明,A组患者年龄偏大、Killip分级≥Ⅱ级者较多、血糖明显增高、CK-MB峰值偏大,且差异均具有统计学意义(P<0.01)。A组天冬氨酸转氨酶升高较明显,可能从一定程度上反映应激性高血糖对肝功能有损伤;两组肌酐水平虽然差异有统计学意义,但均在正常范围。

表1 两组患者基线临床资料比较
Table 1 Baseline clinical characteristics of the subjects

Item	Group A (n = 41)	Group B (n = 51)
Age(years, $\bar{x} \pm s$)	61.13 ± 11.67	54.78 ± 13.48**
Female[n(%)]	9 (22.0)	4 (7.8)
Killip classification ≥ Ⅱ [n(%)]	11 (26.8)	2 (3.9)**
Hypertension[n(%)]	17 (41.5)	21 (41.2)
Hypertriglyceridemia[n(%)]	23 (56.1)	29 (56.9)
Cerebrovascular disease[n(%)]	3 (7.3)	4 (7.8)
Coronary artery disease[n(%)]	2 (4.9)	2 (3.9)
Smoking history[n(%)]	14 (34.1)	20 (39.2)
CK(U/L, $\bar{x} \pm s$)	1617.07 ± 1211.38	1024.73 ± 1265.45
CK-MB (U/L, $\bar{x} \pm s$)	181.22 ± 188.81	83.90 ± 93.78**
Blood glucose (mmol/L, $\bar{x} \pm s$)	12.67 ± 6.99	5.86 ± 0.75**
Creatinine (μmol/L, $\bar{x} \pm s$)	88.19 ± 20.94	91.26 ± 14.74**
Aspartate aminotransferase (U/L, $\bar{x} \pm s$)	320.02 ± 147.49	254.29 ± 206.99**
LVEF (% , $\bar{x} \pm s$)	0.58 ± 0.07	0.61 ± 0.07
Anterior wall MI [n(%)]	21 (51.2)	20 (39.2)
Inferoposterior wall and right ventricle MI [n(%)]	18 (43.9)	28 (54.9)
Lateral wall MI [n(%)]	2 (4.9)	3 (5.9)
Time from onset to thrombolysis(h, $\bar{x} \pm s$)	8.04 ± 4.42	8.21 ± 3.97
Time from onset to coronary angiography(h, $\bar{x} \pm s$)	6.90 ± 3.45	7.72 ± 3.10
Emergent thrombolysis [n(%)]	8 (19.5)	6 (11.8)
Emergent primary PCI [n(%)]	25 (61.0)	25 (49.0)
Delayed PCI [n(%)]	14 (34.1)	23 (45.1)
Drug treatment [n(%)]	6 (14.6)	15 (29.4)

Group A: stress-hyperglycemia group; Group B: normal blood glucose group; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; LVEF:left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.Compared with group A, **P<0.01

2.3 应激性高血糖的危险因素分析

用logistic回归模型调整A组和B组中有统计学

差异的年龄、性别、Killip分级、LVEF、CK-MB等混杂因素后,发现女性、Killip分级、CK-MB是应激性高血糖发生的相关危险因素。女性对男性应激性高血糖发病比值比(OR值)为8.952, Killip分级每增加一个等级应激性高血糖发病OR值为3.530,表明应激性高血糖患者的心功能预后可能较差。CK-MB每增加一个等级应激性高血糖发病OR值为9.408,已有很多文献证实CK-MB峰值高低能较准确反映心肌梗死面积的大小,由此可见应激性高血糖可能引起心肌梗死面积的增加(表2)。

表2 应激性高血糖发生的危险因素分析(logistic回归分析)
Table 2 Logistic regression analysis of risk factors for stress-hyperglycemia

Factor	P	OR	95%CI
Female	0.013	8.952	1.579–50.757
Age	0.014	0.465	0.253–0.857
Killip classification	0.048	3.530	1.010–12.336
CK-MB	0.000	9.408	2.782–31.818
CK	0.045	0.543	0.299–0.986
Aspartate aminotransferase	0.803	0.879	0.321–2.412
Creatinine	0.260	0.567	0.211–1.522
LVEF	0.029	0.378	0.157–0.907
Hypertension	0.753	1.204	0.379–3.824
Hypertriglyceridemia	0.742	1.217	0.379–3.905
Cerebrovascular disease	0.678	1.603	0.173–14.838
Coronary artery disease	0.387	0.331	0.027–4.041
Smoking history	0.510	1.563	0.414–5.899

CK-MB: creatine kinase isoenzyme; CK: creatine kinase; LVEF: left ventricular ejection fraction

2.4 死亡率及危险因素分析

随访至2012年10月,共死亡23例,其中因心血管事件死亡16例,非心血管疾病死亡7例(消化道出血2例、脑出血3例、脑梗死2例),两组因心血管事件死亡原因见表3。两组各项比较差异无统计学意义($P > 0.05$)。随后纳入年龄、性别、Killip分级、LVEF、再发心绞痛、再发心肌梗死、恶性心律失常、心力衰竭等因素进行Cox回归分析(表4),结果显示STEMI后A组远期死亡风险是B组的1.532倍($P = 0.048$)。高甘油三酯血症患者远期死亡风险是正常人群1.557倍($P = 0.041$)。从而提示应激性高血糖是初发STEMI患者远期预后的独立预测因子。高甘油三酯血症对患者远期预后不利。

表4 应激性高血糖远期预后的Cox回归分析
Table 4 Cox multivariate regression analysis for long-term prognosis of stress-hyperglycemia

Factor	B	SE	Wald χ^2	P	RR	95%CI
Hypertriglyceridemia	0.443	0.217	4.179	0.041	1.557	1.018–2.382
Blood glucose	0.427	0.215	3.923	0.048	1.532	1.004–2.337

B: regression coefficient; SE: standard error; RR: relative risk; CI: confidence interval

表3 两组心血管事件死亡原因比较
Table 3 Death-caused cardiovascular events in two groups [n(%)]

Cause of death	Group A (n = 41)	Group B (n = 51)
Recurrent myocardial infarction	5 (12.20)	1 (2.00)
Recurrent angina	1 (2.40)	0 (0.00)
Heart failure	3 (7.32)	3 (5.88)
Malignant arrhythmia	1 (2.44)	2 (3.92)

Malignant arrhythmia: hemodynamics instability of auricular tachycardia, atrial fibrillation, ventricular tachycardia and ventricular fibrillation.

3 讨论

许多AMI患者早期血糖升高是应激反应所致。应激状态下交感神经兴奋,机体分解激素(高血糖素、糖皮质激素和儿茶酚胺)水平明显升高。儿茶酚胺升高血糖和促进糖原分解,高浓度肾上腺素明显抑制胰岛素合成,减少胰岛素的敏感性,进而导致血糖水平的增高^[3]。

STEMI患者出现应激性高血糖,死亡率增加^[4]。死亡率增加的主要原因是心力衰竭的发生,尤其是心室收缩障碍或心室重塑风险的不断加大^[5,6]。本研究发现STEMI伴应激性高血糖时心功能较差、心肌梗死面积较大,原因可能如下。(1)血糖升高加剧了心肌梗死时心肌耗氧,能量供应不足,导致心肌收缩力的下降,加剧心力衰竭的发生。(2)高血糖引起的渗透性利尿作用,将导致容量缺失而进一步加重心功能恶化,尤其右室梗死的患者。(3)心肌梗死区域的心肌顿抑,心内膜缺血引起部分血管闭塞以及非坏死组织血流灌注受阻^[7],同时急性血糖升高加速细胞凋亡,减少旁系血管到缺血区域的血流供应^[8–10]。最终导致无复流现象引起大面积心肌损害和左室功能削弱^[11,12]。(4)动物实验表明血糖升高通过提高白细胞黏附到微血管的能力和自由基的产生加速再灌注损伤^[13]。本研究还发现女性容易发生应激性高血糖。女性发生心肌梗死几乎是在绝经后,高血糖的发生很可能与女性激素分泌降低导致血管内皮功能减退有关,但其机制有待于进一步研究。

本研究提示STEMI后应激性高血糖远期死亡风险远远高于血糖正常人群,应激性高血糖可能为远

期预后不良的标志和独立的危险因素。我们观察到在应激性高血糖患者中,大部分在院外没有坚持监测血糖,因此是否有发展成为糖尿病的可能性不得而知,但多有心绞痛、心力衰竭并发症,经常需要服用药物,生活质量明显下降。而部分很好监测血糖的患者,血糖升高符合糖尿病特征的,在医师指导下服用降糖药或注射胰岛素,血糖控制良好,心肌梗死、心力衰竭等并发症少,生活质量好。虽然本研究随访时间短,随访样本例数少,但我们可从中受到启示,对临床上STEMI伴应激性高血糖患者进行危险分层,院外坚持监测血糖,给予适当的干预(具体因人而异),可能在一定程度上减轻冠状动脉病变及其并发症,改善远期预后。本研究还发现高甘油三酯血症患者远期预后较差,可能与血脂偏高容易形成动脉粥样斑块,通过炎症反应损伤内皮,引起心绞痛、心肌梗死等并发症导致预后不良有关。因此,控制此类患者低盐低脂饮食,强化他汀类治疗,平时加强锻炼可能对预后有利。

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