

TyG指数对阿替普酶静脉溶栓治疗急性缺血性脑卒中患者预后的预测价值

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摘要 目的 探讨甘油三酯-葡萄糖(TyG)指数对阿替普酶静脉溶栓治疗的急性缺血性脑卒中(AIS)患者预后的预测价值,并联合多因素建立联合预测模型。方法 回顾性分析2019年1月至2022年10月抚顺市中心医院神经内科接受阿替普酶静脉溶栓治疗的AIS患者302例的临床资料,根据溶栓90 d时mRS评分分为预后良好组($n=193$)和预后不良组($n=109$)。采用单因素及多因素logistic回归分析影响不良预后的危险因素并建立预测模型。利用受试者操作特征(ROC)曲线分析模型的预测效能。结果 多因素logistic回归分析结果显示,溶栓前NIHSS评分高和TyG指数 ≥ 9.37 是AIS患者不良预后的独立危险因素。成功建立了AIS患者预后的预测模型: $\text{Logit}(Y) = -17.167 + 1.681 \times \text{TyG指数} + 0.147 \times \text{溶栓前NIHSS评分}$ 。TyG指数的最佳截断值为9.37。TyG指数、溶栓前NIHSS评分、联合变量(Y)预测溶栓后90 d AIS患者预后不良的ROC曲线下面积分别为0.713、0.705和0.787,联合变量(Y)的ROC曲线下面积最大。结论 TyG指数 ≥ 9.37 和溶栓前NIHSS评分高是AIS患者预后不良的独立危险因素。通过建立多因素logistic回归模型获得的联合变量(Y)的预测效能更高。

关键词 甘油三酯-葡萄糖指数; 急性缺血性脑卒中; 静脉溶栓; 预后

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Predictive value of triglyceride-glucose index on the outcome in patients with acute ischemic stroke undergoing intravenous alteplase thrombolysis

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Abstract Objective To explore the predictive role of the triglyceride-glucose (TyG) index in patients with acute ischemic stroke (AIS) treated with alteplase thrombolysis and create a comprehensive predictive model integrating multiple factors for assessing patient outcomes. **Methods** The clinical data of 302 patients with AIS undergoing alteplase intravenous thrombolysis at the Neurology Department of Fushun Central Hospital from January 2019 to October 2022 were retrospectively analyzed. The patients were categorized into a good prognosis group ($n=193$) and a poor prognosis group ($n=109$) based on their mRS scores at 90 days post-thrombolysis. Univariate and multivariate logistic regression analyses were employed to identify risk factors influencing adverse outcomes and to establish a predictive model. The predictive performance of the model was assessed using receiver operating characteristic (ROC) curve analysis. **Results** The results of the multivariate logistic regression analysis revealed that pre-thrombolysis high NIHSS score and TyG index ≥ 9.37 were independent risk factors for unfavorable prognosis in AIS patients. A predictive model for AIS patient prognosis was successfully established: $\text{Logit}(Y) = -17.167 + 1.681 \times \text{TyG index} + 0.147 \times \text{pre-thrombolysis NIHSS score}$. The optimal cutoff value for the TyG index was 9.37. The ROC areas under the curve for predicting unfavorable prognosis in AIS patients at 90 days post-thrombolysis were 0.713 for TyG index, 0.705 for pre-thrombolysis NIHSS score, and 0.787 for the combined variable (Y), with the combined variable (Y) exhibiting the largest ROC curve area. **Conclusion** TyG index ≥ 9.37 and pre-thrombolysis high NIHSS score are independent risk factors for poor prognosis. The combined variable the combined variable (Y) has higher predictive efficiency than the separate variables.

Keywords triglyceride-glucose index; acute ischemic stroke; intravenous thrombolysis; prognosis

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研究^[1]显示,急性缺血性脑卒中(acute ischemic stroke, AIS)发病率、病死率和致残率均较高。目前,阿替普酶静脉溶栓仍是AIS患者时间窗内的首选治疗方案^[2-3]。然而AIS患者溶栓治疗的有效性及其安全性存在很大的个体差异^[4]。因此,明确溶栓治疗后AIS患者预后的预测指标具有重要意义。胰岛素抵抗与AIS患者静脉溶栓后不良的结局密切相关。甘油三酯-葡萄糖(triglyceride-glucose index, TyG)指数作为评估胰岛素抵抗的新型指标,因具有高敏感性、高特异性以及操作性强等优点获得广泛关注^[5]。目前,TyG指数与静脉溶栓治疗后AIS患者预后的相关性研究未见报道。本研究回顾性分析抚顺市中心医院采用溶栓治疗的AIS患者临床资料,探讨TyG指数对AIS患者预后的预测价值,并联合多因素建立预测模型,旨在帮助医生准确评估患者的预后,为制定个性化的治疗方案,优化治疗策略提供依据。

1 材料与方法

1.1 临床资料与分组

收集2019年1月至2022年10月抚顺市中心医院神经内科接受阿替普酶静脉溶栓治疗的AIS患者的临床资料。本研究获得医院伦理委员会批准(批号:2022004),研究对象或其亲属签署知情同意书。纳入标准:(1)符合我国AIS诊治指南(2018版)^[2]的诊断标准,且经头颅CT或MR检查确诊;(2)符合阿替普酶静脉溶栓适应证并完成静脉溶栓治疗;(3)完成随访,且各项临床及实验室指标齐全。排除标准:(1)桥接血管内治疗;(2)最后确诊为非卒中;(3)合并严重的心、肝、肾等器官疾病。共纳入302例,其中男180例,女122例;年龄40~89岁,平均(64.31 ± 11.38)岁。溶栓90 d后根据改良Rankin量表(modified Rankin scale, mRS)评分^[6]进行分组:预后良好组(mRS评分≤2分, $n = 193$)和预后不良组(mRS评分>2分, $n = 109$)。

1.2 治疗方法

所有患者给予1次阿替普酶(0.9 mg/kg,德国勃林格殷格翰公司)静脉溶栓,最大剂量不超过90 mg。起始剂量为总剂量的10%,在1 min内静脉团注,其余90%药物在60 min内静脉泵入。

1.3 资料采集与预后评估

收集2组资料:(1)一般临床资料,包括性别,

年龄,卒中相关既往病史(高血压、糖尿病等),溶栓前收缩压(systolic pressure, SBP)、舒张压(diastolic pressure, DBP)、NIHSS评分,发病至静脉溶栓时间(onset to treatment time, OTT);(2)实验室指标,包括空腹血糖(fasting blood glucose, FBG)、总胆固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)、尿酸(uric acid, UA)。患者于入院24 h内空腹抽取静脉血检测各项指标。TyG指数= $\ln[\text{空腹TG}(\text{mg/dL}) \times \text{FBG}(\text{mg/dL})/2]$ ^[7]。患者溶栓90 d后进行随访,应用mRS评分对患者进行评估。mRS≤2分判定为预后良好,mRS>2分判定为预后不良。

1.4 统计学分析

采用SPSS 22.0软件进行统计分析。计量资料采用Kolmogorov-Smirnov检验进行正态分布检验,符合正态分布的计量资料以 $\bar{x} \pm s$ 表示,两组间比较采用独立样本 t 检验;不符合正态分布的计量资料以 $M(P_{25} \sim P_{75})$ 表示,2组比较采用Mann-Whitney U 检验。计数资料以率(%)表示,2组比较采用 χ^2 检验。将TyG指数作为自变量绘制受试者操作特征(receiver operating characteristic, ROC)曲线,根据约登指数标准最大化灵敏度和特异度计算最佳截断值。采用二分类logistic回归分析,将单因素分析中有统计学意义($P < 0.05$)变量进行多因素logistic回归分析并建立预测模型。利用ROC曲线评估模型性能, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 预后良好组与预后不良组患者一般临床资料比较

结果显示,预后不良组房颤、脑卒中和糖尿病病史比例高于预后良好组,FBG、TG、LDL-C、溶栓前NIHSS评分和TyG指数也高于预后良好组,差异均有统计学意义(均 $P < 0.05$),见表1。

2.2 AIS患者预后影响因素的logistic回归分析及其预测模型的建立

将单因素分析中有统计学意义($P < 0.05$)的指标纳入多因素logistic回归分析,并将TyG指数根据最佳截断值转化为二分类变量。多因素logistic回归

表1 预后良好组与预后不良组患者一般临床资料比较
Tab.1 Comparison of general clinical data between the good and poor prognosis groups

Item	Good prognosis group (n = 193)	Poor prognosis group (n = 109)	$\chi^2/t/Z$	P
Male [n (%)]	110 (56.99)	70 (64.22)	1.511	0.219
Age (year)	62 (56-70)	63 (57-76)	-0.762	0.450
Hypertension [n (%)]	87 (45.07)	45 (41.28)	0.411	0.523
Diabetes mellitus [n (%)]	80 (41.45)	59 (54.13)	4.510	0.034
CHD [n (%)]	42 (21.76)	26 (23.85)	0.142	0.707
Atrial fibrillation [n (%)]	24 (12.44)	25 (22.94)	4.357	0.037
Stroke [n (%)]	32 (16.58)	29 (26.60)	4.253	0.039
Smoking history [n (%)]	76 (39.38)	55 (50.46)	4.301	0.062
Alcohol history [n (%)]	50 (25.90)	31 (28.44)	0.773	0.380
OTT (min)	140.00 (122.00-162.00)	145.00 (120.00-198.00)	-0.222	0.824
SBP (mmHg)	153.34 ± 19.72	157.70 ± 24.66	-1.581	0.116
DBP (mmHg)	86.00 (77.00-95.00)	89.00 (80.00-98.00)	-1.667	0.096
FPG (mmol/L)	5.90 (4.99-7.48)	7.37 (5.44-10.03)	-3.962	<0.001
TC (mmol/L)	4.70 ± 0.83	4.90 ± 1.06	-1.743	0.084
TG (mmol/L)	1.78 (1.25-2.26)	2.15 (1.74-2.98)	-4.182	<0.001
HDL-C (mmol/L)	1.09 (0.94-1.28)	1.02 (0.89-1.25)	-1.621	0.106
LDL-C (mmol/L)	2.84 (2.30-3.27)	2.98 (2.38-3.68)	-2.153	0.032
UA (μmol/L)	338.00 (271.00-395.50)	330.00 (279.00-391.50)	-0.011	0.990
NIHSS pre-t	4.00 (2.00-7.00)	7.00 (4.50-11.50)	-5.940	<0.001
TyG index	9.08 ± 0.49	9.59 ± 0.54	-6.981	<0.001

CHD, coronary heart disease; OTT, onset to treatment time; NIHSS pre-t, pre-thrombolysis NIHSS score.

分析显示,溶栓前NIHSS评分高和TyG指数 ≥ 9.37是AIS患者静脉溶栓后不良预后的独立危险因素(均 $P < 0.001$,表2)。

以TyG指数最佳截断值为界值,将AIS患者分为高TyG指数组(TyG指数 ≥ 9.37, 120例)与低TyG指数组(TyG指数 < 9.37, 182例),高TyG指数组、低TyG指数组预后不良的比例分别为56.7%和 22.5%,差异有统计学意义($P < 0.01$)。建立AIS患者预后的多因素logistic回归模型^[8]: $\text{Logit}(Y) = -17.167 + 1.681 \times \text{TyG}$

指数+0.147 × 溶栓前NIHSS评分,见表3。联合变量(Y)的计算公式: $Y = \frac{e^{\text{Logit}(Y)}}{1 + e^{\text{Logit}(Y)}}$,Y为多因素logistic回

归方程计算的预测值,e为自然对数的底数。

2.3 ROC曲线分析TyG指数和溶栓前NIHSS评分对患者预后的预测价值

如表4、图1所示,TyG指数和溶栓前NIHSS评分预测AIS患者静脉溶栓后90 d不良预后的AUC分别为0.713 ($P < 0.001$)和0.705 ($P < 0.001$),联合变量(Y)

表2 AIS患者预后影响因素的logistic回归分析
Tab.2 Logistic regression analysis of risk factors affecting poor prognosis

Variable	Univariate analysis			Multivariate analysis		
	OR	95%CI	P	OR	95%CI	P
Atrial fibrillation	2.238	1.252-3.999	0.007	1.863	0.909-3.817	0.089
Stroke	2.528	1.485-4.303	0.001	1.853	0.964-3.563	0.064
Diabetes mellitus	2.312	1.334-4.303	0.006	1.874	0.937-3.674	0.079
LDL-C	1.361	1.002-1.849	0.048	1.400	0.985-1.989	0.061
NIHSS pre-t	1.155	1.095-1.217	<0.001	1.154	1.092-1.221	<0.001
TyG index (≥9.37)	4.341	2.629-7.168	<0.001	4.666	2.676-8.138	<0.001

表3 AIS患者预测预后的多因素logistic回归模型相关参数

Tab.3 Correlation parameters of multivariate logistic regression model for predicting prognosis in AIS patients

Variable	β	OR	95%CI	P
TyG index	1.681	5.372	3.041-9.489	<0.001
NIHSS pre-t	0.147	1.158	1.094-1.226	<0.001
Constant	-17.167			

NIHSS pre-t, pre-thrombolysis NIHSS score.

表4 TyG指数、溶栓前NIHSS评分及联合变量(Y) 预测效能的ROC曲线特征

Tab.4 ROC curve characteristics of prediction efficiency of single factors and combined variable (Y)

Variable	Sensibility (%)	Specificity (%)	AUC	95%CI	P
TyG index	62.4	73.1	0.713	0.651-0.774	<0.001
NIHSS pre-t	59.6	73.6	0.705	0.664-0.766	<0.001
Combined variable (Y)	68.8	75.6	0.787	0.735-0.839	<0.001

NIHSS pre-t, pre-thrombolysis NIHSS score.

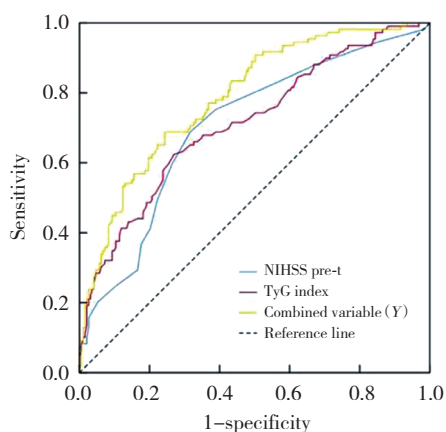


图1 TyG指数、溶栓前NIHSS评分及联合变量(Y) 预测效能的ROC曲线

Fig.1 ROC curve of prediction efficiency of single factors and combined variable (Y)

的AUC为0.787 ($P < 0.001$), 可见联合变量(Y) 诊断效能较单一指标显著升高。

3 讨论

TyG指数广泛应用于心血管疾病^[9]、高血压^[10]、糖尿病^[11]等疾病中胰岛素抵抗的评价。近年来, 国内外越来越多研究发现TyG指数与缺血性脑卒中密切相关。WANG等^[12]在一项大规模、前瞻性队列研究中发现, TyG指数升高可独立预测普通人群缺血性脑卒中的发病风险。对于高血压患者来说, TyG指数长期升高也与缺血性脑卒中发病风险增加有关,

定期监测TyG指数可能有助于识别高血压患者中脑卒中风险较高的个体^[13]。另一项研究^[14]则证实TyG指数可能是我国年轻人早发性脑卒中的主要危险因素。TyG指数还与缺血性脑卒中的危险因素(颈动脉粥样硬化斑块^[15]、颅内动脉狭窄^[16]和房颤^[17])正相关。

近年来, TyG指数对缺血性脑卒中患者临床结局的影响引起关注。一项研究^[18]发现, 老年缺血性脑卒中患者TyG指数升高与缺血性脑卒中复发相关。另外, TyG指数升高能够减弱阿司匹林的抗血小板作用, 从而影响缺血性脑卒中的治疗及预防效果^[19]。因此, 本研究选择TyG指数作为AIS患者临床结局的预测指标具有充分的依据。荣延飞等^[20]研究发现, AIS患者中TyG指数与疾病严重程度具有正向相关性, 但是此项研究排除了接受静脉溶栓的AIS患者。临床上, 静脉溶栓治疗的脑卒中患者预后不良常与脑卒中复发、严重的脑卒中后遗症(瘫痪、痴呆、尿便失禁等)以及合并脑出血、消化道出血等并发症有关^[21]。本研究针对TyG指数与静脉溶栓治疗后的AIS患者预后的相关性进行研究。结果显示, 高TyG指数组较低TyG指数组溶栓90 d后预后不良的比例更高, 并证明TyG指数是AIS患者阿替普酶静脉溶栓后预后不良的独立危险因素。NIHSS评分是全面评估脑卒中患者的可靠工具, 包括意识水平、肢体运动、感觉、语言等11项内容, 已在国际上广泛应

用。但即使由神经内科专科医生来评估NHSS评分,也不可避免存在一定的主观因素。本研究结果显示,TyG指数和NIHSS评分联合的预测价值较单一指标明显升高,同时本研究总结出了简单可行的预测公式,能够帮助临床医师快速粗略判断AIS患者的预后,从而制定个体化的治疗方案。

综上所述,TyG指数 ≥ 9.37 和溶栓前高NIHSS评分是AIS患者预后不良的独立危险因素。通过建立多因素logistic回归模型获得的联合变量(Y)的预测效能更高。本研究使用TyG指数来评估AIS静脉溶栓患者的胰岛素抵抗程度,可操作性强,具有很好的应用前景。本研究为回顾性研究,一部分患者检测前可能采取了影响FBG和TG水平的干预措施,可能会影响TyG指数,今后还需要大样本、随机对照研究来进一步论证。

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