

# 颈内动脉和椎动脉颅外段迂曲与急性缺血性卒中相关性分析

曹益瑞 吴波 孙家瑜

**【摘要】目的** 分析颈内动脉颅外段(EICA)和椎动脉颅外段(EVA)迂曲与急性缺血性卒中的相关性,以探讨血管迂曲原因及其诱发脑卒中的作用机制。**方法** 采用CTA测量103例急性缺血性卒中患者和103例非缺血性卒中致头晕和头痛患者EICA和EVA迂曲指数、偏离度、迂曲度和成角个数,Pearson相关分析和Spearman秩相关分析EICA和EVA迂曲指数与缺血性卒中危险因素和其他血管形态学指标的相关性,单因素和多因素逐步法Logistic回归分析筛查EICA和EVA迂曲相关危险因素。**结果** 脑卒中组患者EICA和EVA迂曲指数( $P = 0.000, 0.000$ )、偏离度( $P = 0.000, 0.000$ )、迂曲度( $P = 0.002, 0.000$ )和成角个数( $P = 0.019, 0.000$ )均高于对照组。根据梗死灶部位,进一步将脑卒中组分为前循环梗死亚组(73例)和后循环梗死亚组(30例),两亚组内(梗死侧与非梗死侧EICA,左侧与右侧EVA)和两亚组间血管形态学指标差异均无统计学意义( $P > 0.05$ );而前循环梗死亚组EICA迂曲指数( $P = 0.000$ )、偏离度( $P = 0.000$ )和迂曲度( $P = 0.045$ ),以及后循环梗死亚组EVA迂曲指数( $P = 0.000$ )、偏离度( $P = 0.000$ )、迂曲度( $P = 0.000$ )和成角个数( $P = 0.046$ )均高于对照组。选择二者迂曲指数较高的一侧,相关分析显示,缺血性卒中患者EICA迂曲指数与年龄、颈动脉粥样硬化、EICA和EVA形态学指标(除外EVA偏离度)均呈正相关( $P < 0.05$ ),而与男性呈负相关( $r_s = -0.253, P = 0.010$ );EVA迂曲指数与年龄、高血压、EICA和EVA形态学指标均呈正相关( $P < 0.05$ ),而与男性呈负相关( $r_s = -0.276, P = 0.005$ )。单因素和多因素逐步法Logistic回归分析显示,女性(EICA:  $OR = 1.458, 95\% CI: 1.111 \sim 5.166, P = 0.016$ ; EVA:  $OR = 9.092, 95\% CI: 1.294 \sim 63.872, P = 0.026$ )和年龄(EICA:  $OR = 1.050, 95\% CI: 1.013 \sim 1.088, P = 0.007$ ; EVA:  $OR = 1.084, 95\% CI: 1.003 \sim 1.138, P = 0.001$ )是EICA和EVA迂曲的独立危险因素。**结论** 缺血性卒中患者EICA和EVA迂曲无侧别、前后循环分布的差异。缺血性卒中患者EICA和EVA形态学指标显著高于非脑卒中患者。女性和高龄是EICA和EVA迂曲的独立危险因素。

**【关键词】** 颈内动脉; 椎动脉; 血管畸形; 卒中; 脑缺血; 危险因素; 回归分析

## Correlation analysis between tortuosity of extracranial internal carotid artery and extracranial vertebral artery and acute ischemic stroke

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**【Abstract】Objective** To analyze the correlation between tortuosity of extracranial internal carotid artery (EICA) and extracranial vertebral artery (EVA) and acute ischemic stroke, so as to discuss the causes of vascular tortuosity and the mechanism on inducing stroke. **Methods** This study included 103 patients with acute ischemic stroke and 103 patients without acute ischemic stroke whose manifestations were headache and dizziness. CTA was used to measure the tortuosity index (TI), deviation degree (DD), tortuosity degree (TD) and angular number (AN) of EICA and EVA. Pearson correlation analysis and Spearman rank correlation analysis were used to analyze the correlations of arterial tortuosity with risk

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factors for ischemic stroke and vascular morphology. Univariate and stepwise multivariate Logistic regression analysis were used to screen related risk factors for tortuosity of EICA and EVA. **Results** The stroke group had higher TI ( $P = 0.000, 0.000$ ), DD ( $P = 0.000, 0.000$ ), TD ( $P = 0.002, 0.000$ ) and AN ( $P = 0.019, 0.000$ ) of EICA and EVA than those in control group. According to the site of infarction, the stroke group was divided into anterior circulation infarction (ACI) subgroup ( $N = 73$ ) and posterior circulation infarction (PCI) subgroup ( $N = 30$ ), and there was no significant difference in above-mentioned vascular morphological indexes between 2 subgroups ( $P > 0.05$ , for all); in each subgroup, there was no significant difference between infarct side and non-infarct side of EICA, and between left and right EVA ( $P > 0.05$ , for all). Nevertheless, the TI ( $P = 0.000$ ), DD ( $P = 0.000$ ) and TD ( $P = 0.045$ ) of EICA in ACI subgroup were higher than those in control group; TI ( $P = 0.000$ ), DD ( $P = 0.000$ ), TD ( $P = 0.000$ ) and AN ( $P = 0.046$ ) of EVA in PCI subgroup were higher than those in control group. In stroke group, correlation analysis revealed that TI of EICA was positively correlated with age, cervical artery atherosclerosis (CAS), EICA and EVA morphological indexes (except DD of EVA;  $P < 0.05$ , for all), but was negatively correlated with male ( $r_s = -0.253, P = 0.010$ ); TI of EVA was positively correlated with age, hypertension, morphological indexes of EICA and EVA ( $P < 0.05$ , for all), but negatively correlated with male ( $r_s = -0.276, P = 0.005$ ). Univariate and stepwise multivariate Logistic regression analysis showed that female (EICA:  $OR = 1.458, 95\% CI: 1.111-5.166, P = 0.016$ ; EVA:  $OR = 9.092, 95\% CI: 1.294-63.872, P = 0.026$ ) and age (EICA:  $OR = 1.050, 95\% CI: 1.013-1.088, P = 0.007$ ; EVA:  $OR = 1.084, 95\% CI: 1.003-1.138, P = 0.001$ ) were independent risk factors for tortuosity of EICA and EVA. **Conclusions** There are no significant differences between left and right side, anterior and posterior circulation on tortuosity distribution of patients with ischemic stroke. The EICA and EVA morphological indexes of stroke patients was significantly higher than that of non-stroke patients. Female and age are independent risk factors for tortuosity of EICA and EVA.

**【Key words】** Carotid artery, internal; Vertebral artery; Vascular malformations; Stroke; Brain ischemia; Risk factors; Regression analysis

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血管迂曲作为常见的血管异常形态可以发生于全身各级动脉和静脉<sup>[1]</sup>。脑卒中患者头颈部影像学检查常发现血管迂曲,然而关于其与脑卒中关系的研究较少见诸报道。研究显示,血管迂曲与高龄、动脉粥样硬化、高血压、糖尿病和基因缺陷等均有关<sup>[2-5]</sup>,但其发生机制仍不十分清楚,是否参与缺血性卒中的发生尚待进一步研究。本研究旨在从血管形态学角度阐述颈内动脉和椎动脉颅外段迂曲及其程度与缺血性卒中之间的关系,以探讨血管迂曲原因及其可能诱发脑卒中的作用机制。

## 资料与方法

### 一、临床资料

1. 纳入标准 (1)缺血性卒中的诊断符合《中国急性缺血性脑卒中诊治指南 2014》<sup>[6]</sup>。(2)缺血性卒中首次发作。(3)发病至入院时间≤7 d。(4)发病时有明确的神经功能障碍。(5)急诊行头部MRI和颈部CTA检查证实急性缺血性卒中并测量血管参数。(6)本研究经四川大学华西医院道德伦理委员会审核批准,所有患者或其家属均知情同意并签署知情同意书。

2. 排除标准 (1)心源性栓塞,栓子源于心脏和主动脉,如心房颤动、心肌病、心脏瓣膜病和主动脉夹层等。(2)特殊的血管形态异常,如脑血管畸形、颅内动脉瘤和烟雾病(MMD)等。(3)结缔组织病致血管病变,如Loeys-Dietz综合征,Marfan综合征等。(4)导致血管变的特殊感染,如梅毒等。

3. 一般资料 缺血性卒中组(脑卒中组)选择2015年3-9月在四川大学华西医院神经内科住院治疗的103例急性缺血性卒中患者;对照组选择同期在我院神经内科住院治疗的103例非缺血性卒中致头晕和头痛患者,既往无脑卒中病史,入院后行头部CT和(或)MRI检查以排除脑卒中。

### 二、研究方法

1. 病史采集 记录患者性别、年龄、病程和既往史,实验室检查血小板计数,以及颈动脉粥样硬化(CAA)、颈动脉狭窄(CAS)和周围血管病变(PVD)比例。其中。颈动脉粥样硬化为颈部血管彩色多普勒超声(CDUS)显示管壁僵硬、中膜增厚、内膜下脂质沉积、粥样硬化斑块形成;颈动脉狭窄为颈总动脉(CCA)、颈内动脉(ICA)、颈外动脉(ECA)和椎动脉(VA)中的1支或多支病变;周围血管病变为临

床表现、体格检查或实验室检查显示四肢动脉和静脉病变。

2. 颈部CTA检查 选择颈总动脉分叉部至颈内动脉颅外段(EICA)并测量双侧颈内动脉,以及椎动脉起始部至椎动脉颅外段(EVA)。采用德国Siemens公司生产的CT扫描仪,所有患者经静脉注射碘海醇注射液欧乃派克(300 mg/ml)50~80 ml,行CTA增强扫描和血管三维重建。由同一位经过专业培训的神经内科医师采用盲法测量血管形态学指标。在三维重建图像上作出血管中轴线,以测量血管实际长度。采用荷兰Philips公司生产的Philips成像系统和工作站,以最大密度投影(MIP)旋转三维重建图像于任意方位,从不同方位确定血管起始点、最远点和角度标记无误后,测量血管实际长度、血管弯曲夹角和三维重建图像上任意两点之间的直线距离。

3. 血管形态学指标 血管形态异常以血管延长为基础<sup>[1,7]</sup>而形成弯曲、折角、缠绕、成环的形态学特征(图1)。为全面描述血管迂曲特征,测量下述4种血管形态学指标。(1)血管迂曲指数(TI):计算公式为血管迂曲指数(%)=(血管两端点实际距离/理想直线距离-1)×100%。(2)血管偏离度(DD):在血管两端点之间作一直线,血管偏离该理想直线的最远点至直线的垂直距离。(3)血管迂曲度(TD):1级,血管迂曲151°~180°;2级,血管迂曲121°~150°;3级,血管迂曲91°~120°;4级,血管迂曲31°~90°;5级,血管迂曲0°~30°;成环;缠绕。(4)血管成角个数(AN):血管并非呈理想的直线状态,而是存在生理弯曲,计数血管迂曲度≥2级(即≤150°)的折角或环(图2)。

4. 一致性检验 随机选择20例患者,于2个时间点重复测量血管形态学指标,其中,血管迂曲指数、偏离度和成角个数采用组内相关系数(ICC),迂曲度采用Kappa检验,检验值均≥0.75,表明一致性良好。

5. 统计分析方法 采用SPSS 22.0统计软件进行数据处理与分析。采用P-P图(P-P plot)和Kolmogorov-Smirnov检验行正态性检验,血管迂曲指数呈非正态分布( $P < 0.01$ ),经对数函数(ln)转换后呈正态分布,血管偏离度和成角个数呈正态分布。采用Levene检验行方差齐性检验,均方差齐性( $P > 0.05$ )。计量资料以均数±标准差( $\bar{x} \pm s$ )表示,采用配对t检验或两独立样本的t检验。血管迂曲度为

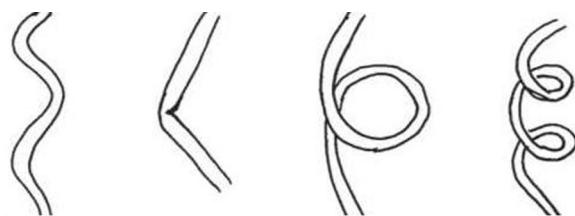


图1 血管迂曲自左至右依次为弯曲、折角和(或)扭结、成环、螺旋缠绕

**Figure 1** Various phenotypes of tortuous vessels included curving, angulation/kinking, looping and spiral twisting from left to right.

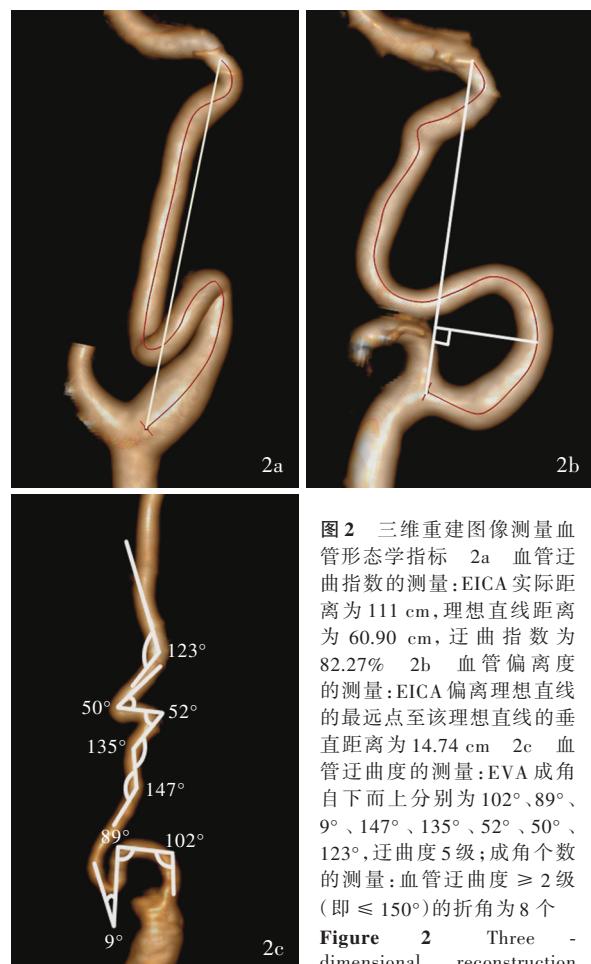


图2 三维重建图像测量血管形态学指标 2a 血管迂曲指数的测量:EICA 实际距离为 111 cm, 理想直线距离为 60.90 cm, 迂曲指数为 82.27% 2b 血管偏离度的测量:EICA 偏离理想直线的最远点至该理想直线的垂直距离为 14.74 cm 2c 血管迂曲度的测量:EVA 成角自下而上分别为 102°、89°、9°、147°、135°、52°、50°、123°, 迂曲度 5 级; 成角个数的测量: 血管迂曲度 ≥ 2 级 (即 ≤ 150°) 的折角为 8 个

**Figure 2** Three-dimensional reconstruction image was used to measure vascular morphological indexes. Measurement of TI: the actual distance of EICA was 111 cm, the linear distance was 60.90 cm, and TI was 82.27% (Panel 2a). Measurement of DD: the vertical distance from the furthest point of the ideal straight line of EICA to the ideal straight line was 14.74 cm (Panel 2b). Measurement of TD: the angles of EVA from bottom to top were 102°, 89°, 9°, 147°, 135°, 52°, 50° and 123° respectively, the TD was Level 5; measurement of AN: there were 8 angles with TD ≥ Level 2 (angle ≤ 150°, Panel 2c).

等级资料,采用Wilcoxon符号秩检验和Wilcoxon秩和检验。计数资料以相对数构成比(%)或率(%)表示,采用 $\chi^2$ 检验。EICA和EVA迂曲与急性缺血性卒

中的相关性采用 Pearson 相关分析或 Spearman 秩相关分析。血管迂曲相关危险因素筛查采用单因素和多因素逐步法 Logistic 回归分析。以  $P \leq 0.05$  为差异具有统计学意义。

## 结 果

### 一、临床资料的比较

两组患者一般资料和血管形态学指标如下。(1)脑卒中组:103例患者,男性70例,女性33例;年龄26~87岁,平均( $58.35 \pm 14.75$ )岁;既往有高血压病史57例(55.34%)、冠心病病史1例(0.97%)、糖尿病病史25例(24.27%)、高脂血症病史16例(15.53%),吸烟44例(42.72%)、饮酒26例(25.24%);血小板计数( $37 \sim 302$ ) $\times 10^9/L$ ,平均( $174.60 \pm 54.56$ ) $\times 10^9/L$ ;其中颈动脉粥样硬化19例(18.45%),颈动脉狭窄46例(44.66%),周围血管病变3例(2.91%)。EICA 迂曲指数(对数值)0.40%~4.04%,平均( $2.71 \pm 0.80$ )%;偏离度3.29~25.55 cm,平均( $12.06 \pm 4.19$ ) cm;迂曲度0~5级,中位值4(2,4)级;成角个数0~5个,平均( $2.14 \pm 0.93$ )个。EVA 迂曲指数(对数值)0.79%~3.53%,平均( $2.14 \pm 0.65$ )%;偏离度2.84~20.00 cm,平均为( $10.17 \pm 3.03$ ) cm;迂曲度0~5级,中位值为4(2,4)级;成角个数0~10个,平均为( $3.85 \pm 2.43$ )个。(2)对照组:共103例患者,男性70例,女性33例;年龄为17~85岁,平均( $58.95 \pm 15.87$ )岁;既往有高血压病史41例(39.81%)、冠心病病史6例(5.83%)、糖尿病病史16例(15.53%)、高脂血症病史17例(16.50%),吸烟30例(29.13%)、饮酒13例(12.62%);血小板计数( $10 \sim 566$ ) $\times 10^9/L$ ,平均为( $187.24 \pm 69.51$ ) $\times 10^9/L$ ;其中颈动脉粥样硬化37例(35.92%),颈动脉狭窄19例(18.45%),周围血管病变14例(13.59%)。EICA 迂曲指数(对数值)-0.22%~4.46%,平均为( $2.08 \pm 0.91$ )%;偏离度1.77~24.42 cm,平均( $7.66 \pm 3.86$ ) cm;迂曲度0~5级,中位值3(2,4)级;成角个数0~4个,平均( $1.84 \pm 0.89$ )个。EVA 迂曲指数(对数值)-0.03%~3.18%,平均( $1.41 \pm 0.75$ )%;偏离度1.60~13.66 cm,平均为( $6.34 \pm 2.76$ ) cm;迂曲度0~5级,中位值为3(2,4)级;成角个数0~8个,平均( $2.64 \pm 1.97$ )个。两组患者性别、年龄,冠心病、糖尿病、高脂血症比例,血小板计数差异无统计学意义(均  $P > 0.05$ );脑卒中组高血压( $P = 0.026$ )、吸烟( $P = 0.042$ )和饮酒( $P = 0.021$ )、颈动脉狭窄( $P =$

表1 两组患者临床资料的比较

Table 1. Comparison of clinical data between 2 groups

Item	Control (N = 103)	Stroke (N = 103)	Statistic value	P value
Sex [case (%)]			0.000	1.000
Male	70 (67.96)	70 (67.96)		
Female	33 (32.04)	33 (32.04)		
Age ( $\bar{x} \pm s$ , year)	$58.59 \pm 15.87$	$58.35 \pm 14.75$	0.114	0.910
Hypertension [case (%)]	41 (39.81)	57 (55.34)	4.983	0.026
Coronary heart disease [case (%)]	6 ( 5.83)	1 ( 0.97)	2.366	0.124
Diabetes [case (%)]	16 (15.53)	25 (24.27)	2.467	0.116
Hyperlipidemia [case (%)]	17 (16.50)	16 (15.53)	0.036	0.849
Smoking [case (%)]	30 (29.13)	44 (42.72)	4.133	0.042
Drinking [case (%)]	13 (12.62)	26 (25.24)	5.345	0.021
Platelet ( $\bar{x} \pm s$ , $\times 10^9/L$ )	$187.24 \pm 69.51$	$174.60 \pm 54.56$	0.417	0.677
CAA [case (%)]	37 (35.92)	19 (18.45)	7.946	0.005
CAS [case (%)]	19 (18.45)	46 (44.66)	16.386	0.000
PVD [case (%)]	14 (13.59)	3 ( 2.91)	7.758	0.005
EICA				
TI ( $\bar{x} \pm s$ , %)	$2.08 \pm 0.91$	$2.71 \pm 0.80$	-5.304	0.000
DD ( $\bar{x} \pm s$ , cm)	$7.66 \pm 3.86$	$12.06 \pm 4.19$	-7.838	0.000
TD [ $M(P_{25}, P_{75})$ , grade]	3.00 (2.00, 4.00)	4.00 (2.00, 4.00)	-3.089	0.002
AN ( $\bar{x} \pm s$ , number)	$1.84 \pm 0.89$	$2.14 \pm 0.93$	-2.367	0.019
EVA				
TI ( $\bar{x} \pm s$ , %)	$1.41 \pm 0.75$	$2.14 \pm 0.65$	-7.472	0.000
DD ( $\bar{x} \pm s$ , cm)	$6.34 \pm 2.76$	$10.17 \pm 3.03$	-9.464	0.000
TD [ $M(P_{25}, P_{75})$ , grade]	3.00 (2.00, 4.00)	4.00 (2.00, 4.00)	-3.815	0.000
AN ( $\bar{x} \pm s$ , number)	$2.64 \pm 1.97$	$3.85 \pm 2.43$	-3.938	0.000

Two-independent-sample  $t$  test for comparison of age, platelet, TI, DD and AN of EICA and EVA, Wilcoxon rank sum test for comparison of TD of EICA and EVA, and  $\chi^2$  test for comparison of others。CAA, cervical artery atherosclerosis, 颈动脉粥样硬化; CAS, cervical artery stenosis, 颈动脉狭窄; PVD, peripheral vascular diseases, 周围血管病变; EICA, extracranial internal carotid artery, 颈内动脉颅外段; TI, tortuosity index, 迂曲指数; DD, deviation degree, 偏离度; TD, tortuosity degree, 迂曲度; AN, angular number, 成角个数; EVA, extracranial vertebral artery, 椎动脉颅外段

0.000)比例高于对照组,颈动脉粥样硬化( $P = 0.005$ )和周围血管病变( $P = 0.005$ )比例低于对照组(表1)。两组血管形态学指标比较,脑卒中组EICA和EVA形态学指标均高于对照组( $P < 0.05$ ,表1)。

### 二、不同部位梗死灶血管形态学指标的比较

根据梗死灶部位,进一步将脑卒中组分为前循环梗死(ACI)亚组(73例)和后循环梗死(PCI)亚组(30例)。前循环梗死患者梗死侧与非梗死侧EICA形态学指标差异无统计学意义(均  $P > 0.05$ );后循环梗死患者由于双侧EVA形态异常均可引起椎-基底

**表2** 前循环梗死亚组(梗死侧与非梗死侧)和后循环梗死亚组(左侧与右侧)患者血管形态学指标的比较

**Table 2.** Comparison of vascular morphological indexes of ACI subgroup (between infarct side and non-infarct side) and PCI subgroup (between left and right)

Item	ACI (N = 73)				PCI (N = 30)			
	Infarct side of EICA	Non-infarct side of EICA	t or T value	P value	Left EVA	Right EVA	t or T value	P value
TI ( $\bar{x} \pm s$ , %)	2.69 ± 0.89	2.69 ± 0.84	- 0.420	0.967	2.11 ± 0.85	2.04 ± 0.61	0.642	0.526
DD ( $\bar{x} \pm s$ , cm)	12.29 ± 4.88	11.98 ± 4.49	0.557	0.579	9.65 ± 3.97	10.43 ± 4.00	- 1.057	0.299
TD [ $M(P_{25}, P_{75})$ , grade]	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	- 0.258	0.796	4.00 (3.00, 4.00)	3.00 (3.00, 4.00)	- 0.936	0.349
AN ( $\bar{x} \pm s$ , number)	2.13 ± 1.01	2.24 ± 1.02	- 1.239	0.219	3.73 ± 2.42	4.17 ± 2.38	- 1.257	0.219

Wilcoxon signed rank test for comparison of TD, and paired t test for comparison of others。ACI, anterior circulation infarction, 前循环梗死；PCI, posterior circulation infarction, 后循环梗死；EICA, extracranial internal carotid artery, 颈内动脉颅外段；EVA, extracranial vertebral artery, 椎动脉颅外段；TI, tortuosity index, 迂曲指数；DD, deviation degree, 偏离度；TD, tortuosity degree, 迂曲度；AN, angular number, 成角个数

**表3** 前循环梗死亚组与后循环梗死亚组患者血管形态学指标的比较\*

**Table 3.** Comparison of vascular morphological indexes between ACI subgroup and PCI subgroup\*

Item	EICA				EVA			
	ACI (N = 73)	PCI (N = 30)	t or T value	P value	ACI (N = 73)	PCI (N = 30)	t or T value	P value
TI ( $\bar{x} \pm s$ , %)	2.88 ± 0.81	2.87 ± 0.81	0.086	0.931	2.35 ± 0.64	2.29 ± 0.71	0.448	0.655
DD ( $\bar{x} \pm s$ , cm)	13.08 ± 13.08	12.95 ± 12.95	0.115	0.908	10.59 ± 3.40	10.69 ± 4.37	- 0.127	0.900
TD [ $M(P_{25}, P_{75})$ , grade]	4.00 (2.00, 4.00)	4.00 (3.00, 4.00)	- 0.061	0.952	3.00 (2.00, 4.00)	4.00 (3.00, 4.00)	- 1.043	0.297
AN ( $\bar{x} \pm s$ , number)	2.16 ± 0.93	2.07 ± 1.14	0.453	0.651	4.12 ± 2.68	4.07 ± 2.89	0.102	0.919

\*One side of EICA and EVA with higher TI, 选择EICA和EVA迂曲指数较高的一侧。Wilcoxon signed rank test for comparison of TD, and paired t test for comparison of others。EICA, extracranial internal carotid artery, 颈内动脉颅外段；EVA, extracranial vertebral artery, 椎动脉颅外段；ACI, anterior circulation infarction, 前循环梗死；PCI, posterior circulation infarction, 后循环梗死；TI, tortuosity index, 迂曲指数；DD, deviation degree, 偏离度；TD, tortuosity degree, 迂曲度；AN, angular number, 成角个数

**表4** 前循环梗死亚组和后循环梗死亚组与对照组患者血管形态学指标的比较\*

**Table 4.** Comparison of vascular morphological indexes of ACI subgroup, PCI subgroup and control group\*

Item	EICA				EVA			
	ACI (N = 73)	Control (N = 73)	t or Z value	P value	PCI (N = 30)	Control (N = 30)	t or Z value	P value
TI ( $\bar{x} \pm s$ , %)	2.88 ± 0.81	2.27 ± 0.92	4.329	0.000	2.29 ± 0.71	1.55 ± 0.67	4.130	0.000
DD ( $\bar{x} \pm s$ , cm)	13.08 ± 5.12	8.09 ± 4.05	6.534	0.000	10.69 ± 4.37	6.58 ± 3.42	4.058	0.000
TD [ $M(P_{25}, P_{75})$ , grade]	4.00 (2.00, 4.00)	3.00 (2.00, 4.00)	- 2.006	0.045	4.00 (3.00, 4.00)	2.00 (1.00, 4.00)	- 3.253	0.000
AN ( $\bar{x} \pm s$ , number)	2.16 ± 0.93	1.92 ± 0.88	1.649	0.101	4.03 ± 2.28	2.83 ± 2.28	2.040	0.046

\*One side of EICA and EVA with higher TI, 选择EICA和EVA迂曲指数较高的一侧。Wilcoxon rank sum test for comparison of TD, and two-independent-sample t test for comparison of others。EICA, extracranial internal carotid artery, 颈内动脉颅外段；EVA, extracranial vertebral artery, 椎动脉颅外段；ACI, anterior circulation infarction, 前循环梗死；PCI, posterior circulation infarction, 后循环梗死；TI, tortuosity index, 迂曲指数；DD, deviation degree, 偏离度；TD, tortuosity degree, 迂曲度；AN, angular number, 成角个数

动脉血流动力学改变而无法区分梗死侧与非梗死侧, 故仅进行左侧与右侧EVA形态学指标的比较, 差异亦无统计学意义(均P > 0.05, 表2)。两亚组患者均选择EICA和EVA迂曲指数较高的一侧进行比较, 各项血管形态学指标差异均无统计学意义(P > 0.05, 表3)。前循环梗死亚组和后循环梗死亚组分别与对照组比较, 均选择EICA和EVA迂曲指数较高的一侧, 前循环梗死亚组EICA迂曲指数( $P = 0.000$ )、偏离度( $P = 0.000$ )和迂曲度( $P = 0.045$ )均高

于对照组且差异有统计学意义, 而成角个数组间差异无统计学意义( $P > 0.05$ )；后循环梗死亚组EVA迂曲指数( $P = 0.000$ )、偏离度( $P = 0.000$ )、迂曲度( $P = 0.000$ )和成角个数( $P = 0.046$ )均高于对照组且差异有统计学意义, 提示缺血性卒中患者EICA和EVA迂曲较对照组明显(表4)。

三、血管迂曲指数与缺血性卒中危险因素和其他血管形态学指标的相关分析

脑卒中组患者选择EICA和EVA迂曲指数较高

表5 血管迂曲指数与缺血性卒中危险因素和其他血管形态学指标的相关分析(N=103)

Table 5. Correlation analysis of TI with risk factors for ischemic stroke and other vascular morphological indexes (N=103)

Item	Stroke				Control			
	EICA TI		EVA TI		EICA TI		EVA TI	
	r, or r value	P value						
Male*	-0.253	0.010	-0.276	0.005	0.190	0.054	0.224	0.023
Age#	0.443	0.000	0.547	0.000	0.492	0.000	0.465	0.000
Hypertension*	0.176	0.075	0.322	0.001	0.197	0.046	0.225	0.022
Coronary heart disease*	0.043	0.664	-0.015	0.881	0.046	0.644	0.042	0.675
Diabetes*	0.119	0.230	0.108	0.277	0.053	0.597	0.254	0.010
Hyperlipidemia*	0.039	0.697	0.079	0.426	0.048	0.627	0.107	0.281
Smoking*	-0.129	0.193	-0.096	0.333	-0.051	0.609	0.004	0.971
Drinking*	-0.070	0.485	-0.030	0.763	0.085	0.396	0.081	0.415
Platelet#	-0.040	0.687	-0.094	0.343	-0.168	0.092	-0.005	0.956
CAA*	0.195	0.048	0.056	0.577	0.103	0.302	0.130	0.191
CAS*	-0.068	0.495	0.007	0.945	0.091	0.359	0.082	0.412
PVD*	-0.054	0.585	-0.050	0.619	0.020	0.845	0.065	0.516
EICA								
TI#	—	—	0.560	0.000	—	—	0.489	0.000
DD#	0.648	0.000	0.417	0.000	0.785	0.000	0.481	0.000
TD*	0.851	0.000	0.492	0.000	0.873	0.000	0.514	0.000
AN#	0.595	0.000	0.339	0.000	0.612	0.000	0.347	0.000
EVA								
TI#	0.560	0.000	—	—	0.489	0.000	—	—
DD#	0.002	0.980	0.236	0.016	0.028	0.776	0.457	0.000
TD*	0.493	0.000	0.677	0.000	0.381	0.000	0.689	0.000
AN#	0.474	0.000	0.583	0.000	0.428	0.000	0.741	0.000

\*Spearman rank correlation, Spearman秩相关分析; #Pearson correlation, Pearson相关分析。EICA, extracranial internal carotid artery, 颈内动脉颅外段; TI, tortuosity index, 迂曲指数; EVA, extracranial vertebral artery, 椎动脉颅外段; CAA, cervical artery atherosclerosis, 颈动脉粥样硬化; CAS, cervical artery stenosis, 颈动脉狭窄; PVD, peripheral vascular diseases, 周围血管病变; DD, deviation degree, 偏离度; TD, tortuosity degree, 迂曲度; AN, angular number, 成角个数

的一侧,EICA迂曲指数与年龄、颈动脉粥样硬化、EICA和EVA形态学指标(除外EVA偏离度)均呈正相关( $P < 0.05$ ),而与男性呈负相关( $r_s = -0.253, P = 0.010$ );EVA迂曲指数与年龄、高血压、EICA和EVA形态学指标均呈正相关( $P < 0.05$ ),而与男性呈负相关( $r_s = -0.276, P = 0.005$ ;表5)。对照组患者亦选择EICA和EVA迂曲指数较高的一侧,EICA迂曲指数与年龄、高血压、EICA和EVA形态学指标(除外EVA偏离度)均呈正相关( $P < 0.05$ );EVA迂曲指数与男性、年龄、高血压、糖尿病、EICA和EVA形态学指标均呈正相关( $P < 0.05$ ,表5)。提示EICA和EVA迂曲指数与其他血管形态学指标同向变化。

#### 四、血管迂曲危险因素筛查

单因素Logistic回归分析显示,女性和年龄是

EICA迂曲相关危险因素(均 $P < 0.05$ ;表6,7);女性、年龄和高血压是EVA迂曲相关危险因素(均 $P < 0.05$ ;表6,8)。进一步行多因素逐步法Logistic回归分析显示,女性(EICA:  $OR = 1.458, 95\% CI: 1.111 \sim 5.166, P = 0.016$ ; EVA:  $OR = 9.092, 95\% CI: 1.294 \sim 63.872, P = 0.026$ )和年龄(EICA:  $OR = 1.050, 95\% CI: 1.013 \sim 1.088, P = 0.007$ ; EVA:  $OR = 1.084, 95\% CI: 1.003 \sim 1.138, P = 0.001$ )是EICA和EVA迂曲的独立危险因素(表9,10)。

## 讨 论

血管迂曲广泛存在于全身各部位,可发生于动脉、静脉和毛细血管<sup>[1]</sup>。由于研究对象、纳入标准、血管迂曲判定标准和评价方法不同,血管迂曲发生

**表6** 血管迂曲相关危险因素变量赋值表**Table 6.** Variable assignment of related risk factors for vascular tortuosity

Variable	Assignment (score)		Variable	Assignment (score)	
	0	1		0	1
Sex	Male	Female	Smoking	No	Yes
Hypertension	No	Yes	Drinking	No	Yes
Coronary heart disease	No	Yes	CAA	No	Yes
Diabetes	No	Yes	CAS	No	Yes
Hyperlipidemia	No	Yes	PVD	No	Yes

CAA, cervical artery atherosclerosis, 颈动脉粥样硬化; CAS, cervical artery stenosis, 颈动脉狭窄; PVD, peripheral vascular diseases, 周围血管病变。The same for Table 7 and 8

**表7** EICA迂曲相关危险因素的单因素Logistic回归分析**Table 7.** Univariate Logistic regression analysis of risk factors for tortuosity of EICA

Variable	b	SE	Wald $\chi^2$	P value	OR value	OR 95%CI
Sex	0.545	0.449	1.473	0.025	1.725	1.715~4.161
Age	0.048	0.015	9.838	0.002	1.049	1.018~1.081
Hypertension	0.686	0.410	2.797	0.094	1.986	0.889~4.438
Coronary heart disease	0.634	0.501	1.603	0.205	1.886	0.706~5.034
Diabetes	0.393	0.582	0.455	0.500	1.481	0.473~4.633
Hyperlipidemia	0.686	0.410	2.797	0.494	1.986	0.889~4.438
Smoking	-0.319	0.408	0.610	0.435	0.727	0.327~1.618
Drinking	-0.194	0.461	0.176	0.675	0.824	0.334~2.035
Platelet	-0.002	0.004	0.294	0.587	0.998	0.991~1.005
CAA	0.388	0.541	0.513	0.474	1.473	0.510~4.257
CAS	-0.353	0.407	0.752	0.386	0.703	0.317~1.560
PVD	-1.183	-1.242	0.907	0.341	0.306	0.027~3.496

**表9** EICA迂曲相关危险因素的多因素逐步法Logistic回归分析**Table 9.** The stepwise multivariate Logistic regression analysis of related factors for tortuosity of EICA

Variable	b	SE	Wald $\chi^2$	P value	OR value	OR 95%CI
Sex	0.377	0.646	0.341	0.016	1.458	1.111~5.166
Age	0.049	0.018	7.233	0.007	1.050	1.013~1.088
Constant	-1.371	1.352	1.027	0.311		

率也不尽相同,有文献报道,颈内动脉迂曲发生率为1.3%~40.0%<sup>[8~10]</sup>。研究显示,全身多部位动静脉迂曲与高龄、动脉粥样硬化、高血压、糖尿病和基因缺陷有关<sup>[2~5]</sup>。血管形态学方面,本研究结果显示,脑卒中组EICA和EVA迂曲指数均高于对照组,可以假设血管迂曲是脑卒中危险因素,对此我们进一步深入研究。

血管迂曲程度的评价方法至关重要,除本研究采用的迂曲指数、偏离度、迂曲度和成角个数外,还

**表8** EVA迂曲相关危险因素的单因素Logistic回归分析**Table 8.** Univariate Logistic regression analysis of risk factors for tortuosity of EVA

Variable	b	SE	Wald $\chi^2$	P value	OR value	OR 95%CI
Sex	1.455	0.588	6.124	0.013	4.284	1.353~13.562
Age	0.078	0.019	16.937	0.000	1.081	1.041~1.121
Hypertension	1.285	0.458	7.875	0.005	3.615	1.473~8.871
Coronary heart disease	2.610	10.342	1.552	0.901	23.638	7.364~71.269
Diabetes	0.342	0.529	0.418	0.518	1.407	0.499~3.967
Hyperlipidemia	-0.545	0.569	0.636	0.425	0.635	0.208~1.938
Smoking	-0.105	0.494	0.045	0.831	0.900	0.342~2.371
Drinking	-0.417	0.437	0.912	0.340	0.659	0.280~1.551
Platelet	-0.001	0.004	0.094	0.759	0.999	0.991~1.007
CAA	0.519	0.610	0.725	0.395	1.681	0.508~5.559
CAS	0.076	0.437	0.030	0.862	1.079	0.458~2.541
PVD	-1.638	1.245	1.731	0.189	0.194	0.017~2.230

**表10** EVA迂曲相关危险因素的多因素逐步法Logistic回归分析**Table 10.** The stepwise multivariate Logistic regression analysis of related factors for tortuosity of EVA

Variable	b	SE	Wald $\chi^2$	P value	OR value	OR 95%CI
Sex	2.207	0.995	4.925	0.026	9.092	1.294~63.872
Age	0.081	0.025	10.665	0.001	1.084	1.003~1.138
Hypertension	0.222	0.529	0.176	0.675	1.249	0.443~3.521
Constant	-0.930	1.772	0.275	0.600		

包括:(1)血管实际长度与理想直线距离的比值。(2)选择一个弯曲单元,以起点、终点和弧线顶点组成三角形,计算弧线顶点至底边(起点和终点连线)垂直距离与底边的比值<sup>[1]</sup>。迂曲指数是评价血管迂曲程度最客观的指标,不受血管形态的影响,本研究血管偏离度、迂曲度和成角个数均与迂曲指数保持良好一致性,仅EICA成角个数与迂曲指数不一致。血管形态受周围基质影响,Lee等<sup>[11]</sup>在猪颈动脉模型中发现血管外基质强度与血管成角个数呈

正相关。在本研究中,EICA成角个数少于EVA;而且,随着EVA迂曲指数增加,EICA和EVA偏离度均增加,而随着EICA迂曲指数增加,仅EICA偏离度增加。由此可见,相对松弛的周围结缔组织使EICA成角个数减少、偏离度增大,而固定的横突孔使EVA走行相对受限,偏离度减小,易形成更多弯曲。然而颈椎退行性变的个体差异能否使血管形态变得更加复杂并导致迂曲指数与其他血管形态学指标不一致,尚待进一步研究。

关于缺血性卒中患者动脉迂曲的分布性研究较少。Kim等<sup>[12]</sup>的研究显示,梗死侧大脑中动脉迂曲指数高于非梗死侧,但目前尚无EICA迂曲与梗死部位有关的报道。在本研究中,前循环梗死患者梗死侧与非梗死侧EICA、后循环梗死患者左侧与右侧EVA各项形态学指标均无明显差异,前循环梗死与后循环梗死患者EICA和EVA各项形态学指标亦无明显差异,而前循环梗死和后循环梗死患者EICA和EVA各项形态学指标均高于对照组,提示EICA和EVA迂曲程度与梗死部位无关,尚不能以迂曲指数预测梗死部位。

目前,血管迂曲的作用机制尚存争议,可能涉及多种因素,包括基因缺陷、高血压、血流动力学改变、血管退行性变等。首先,轴向牵拉力是维持血管形态的基础,可以防止血管迂曲,然而轴向牵拉力随血管的生长和年龄的增长而下降<sup>[13-15]</sup>,进一步导致血管迂曲<sup>[16]</sup>。其次,老龄化<sup>[1,13]</sup>和基因缺陷<sup>[17]</sup>使细胞外基质(ECM)重要成分——弹力蛋白降解或缺失,血管壁变薄<sup>[17-18]</sup>,较小的血流压力即可以引起血管弯曲<sup>[11]</sup>,形成血管迂曲。再次,血管周围结缔组织退行性变可使血管失去支撑<sup>[1]</sup>,基质金属蛋白酶-2(MMP-2)水平升高可使血管延长<sup>[19]</sup>、也可导致血管扭结缠绕。此外,Del Corso等<sup>[2]</sup>和Ghilard等<sup>[8]</sup>认为,血管迂曲更常见于女性,与本研究结果相一致。亦有研究显示,男性更易发生血管迂曲<sup>[9]</sup>。迄今尚无关于血管迂曲性别差异的机制阐述。有文献报道,老龄化、高血压、缺血性心脏病、高脂血症、吸烟、动脉粥样硬化、动脉夹层等均可导致血管迂曲等形态学异常<sup>[2,5,20-22]</sup>,其中,高血压与血管迂曲的关系尤为密切,主要是由于血流动力学改变致血管内皮损伤,从而引起动脉粥样硬化和血管形态异常<sup>[21]</sup>,然而,本研究并未显示出血管迂曲与高血压相关,可能原因是未对血压进行分层。本研究亦未发现血管迂曲与颈动脉狭窄有关。因此,尚待大样

本临床试验进一步研究。上述研究危险因素的筛查结果不一致可能系选取血管部位、纳入对象基线资料不同所致,但老龄化是较为确定的血管迂曲危险因素。Zhang等<sup>[22]</sup>研究显示,60岁以上患者更易发生血管迂曲。本研究单因素和多因素逐步法Logistic回归分析显示性别和年龄是EICA和EVA迂曲的独立危险因素,与文献报道相一致<sup>[7,12,20,23-24]</sup>。

目前尚未确定血管迂曲与缺血性卒中的关系。研究显示,颈内动脉迂曲可以引起眩晕、黑蒙、持续性耳鸣<sup>[25]</sup>,严重者甚至可以引起血管堵塞,与短暂性脑缺血发作(TIA)和缺血性卒中有关<sup>[26]</sup>。然而,Togay-Işikay等<sup>[23]</sup>和Pancera等<sup>[13]</sup>的研究并未发现动脉迂曲与脑卒中之间的关系,仅有尸检结果提示其他器官梗死可能缘于动脉迂曲<sup>[27]</sup>。在本研究中,脑卒中组患者EICA和EVA迂曲指数均高于对照组,提示缺血性卒中患者存在血管迂曲。关于血管迂曲造成的血流动力学改变,Del Corso等<sup>[2]</sup>发现,血管卷曲和高度扭曲患者发生血流动学改变的概率较高(92.04%和84.91%),低度扭曲和弯曲患者次之(80.77%和73.08%)。血管迂曲可以增加血流压降、血流阻力、次生流<sup>[28]</sup>和作用于外部的压力、剪切应力<sup>[29]</sup>;其中,血流压降随血管迂曲的增大而更加明显<sup>[30]</sup>,从而加重迂曲段以远血流灌注障碍,故推测血管卷曲和高度扭曲可能引起严重血流动力学异常。此外,血管迂曲还可以增加血液湍流<sup>[31]</sup>和剪切应力<sup>[32]</sup>,从而导致血管内皮损伤和粥样硬化斑块破裂<sup>[32]</sup>,激活血小板<sup>[31-32]</sup>和增加血小板之间的碰撞<sup>[32]</sup>,引起血小板吸附和聚集,促进血栓形成。因此,血管迂曲有可能作为脑卒中危险因素参与缺血性卒中的发生。

尽管动脉迂曲能否作为脑卒中的危险因素尚存争议,但严重的血管迂曲仍值得重视,可以通过简单、安全的手术矫正血管弯曲并固定或支架成形术,从而改善神经功能、降低美国国立卫生研究院卒中量表(NIHSS)评分,达到预期效果和降低脑卒中的风险<sup>[30,33]</sup>。因此,对于脑卒中危险因素干预或积极进行内科治疗后仍有神经功能缺损症状的患者,应谨慎外科手术治疗或介入治疗。

本研究存在的局限性和需要改进之处有以下几方面:(1)应更加细致地评价患者颈胸椎退行性变和中线状态,从而减少两点间直线距离测量和统计学的误差。(2)研究对象并发的颈动脉粥样硬化、颈动脉狭窄有可能扩大血管迂曲对缺血性卒中的

促进作用。(3)两组患者未能在基线水平上达到完全一致。改进上述不足之处的前瞻性临床试验将能够更好地研究颈部血管形态与缺血性卒中的关系。此外,本研究并未涉及颅内血管,可能影响血管迂曲与脑卒中相关性的整体判断。

## 结 论

相对于其他血管形态学指标,迂曲指数评价血管迂曲是稳定、可靠的,血管偏离度、迂曲度和成角个数均与其具有较高的一致性,有助于研究者全面了解血管形态。EICA 和 EVA 迂曲指数与女性和高龄有关,而与其他传统脑卒中危险因素无关联性。缺血性卒中患者 EICA 和 EVA 形态学指标均高于对照者,推测血管迂曲有可能促进缺血性卒中的发生,在一定程度上可能是缺血性卒中的危险因素。缺血性卒中患者 EICA 和 EVA 迂曲与梗死灶部位无关,尚不能以血管迂曲程度推测缺血性卒中可能发生的部位。在脑卒中预防方面,随着影像学技术的发展,EICA 和 EVA 迂曲指数因其易获得性、准确性和稳定性将成为有价值的预测指标。

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## • 小词典 •

## 中英文对照名词词汇(五)

无特定病原体 specific pathogen free(SPF)	迂曲度 tortuosity degree(TD)
吸入气氧浓度 fraction of inspired oxygen(FiO <sub>2</sub> )	迂曲指数 tortuosity index(TI)
系统性红斑狼疮 systemic lupus erythematosus(SLE)	原发性中枢神经系统淋巴瘤 primary central nervous system lymphoma(PCNSL)
细胞外基质 extracellular matrix(ECM)	远程康复 telerehabilitation(TR)
细胞周期蛋白依赖性激酶4 cyclin-dependent kinase 4(CDK4)	Wolf运动功能测验 Wolf Motor Function Test(WMFT)
细胞周期蛋白依赖性激酶抑制基因 2A/B cyclin-dependent kinase inhibitor 2A/B(CDKN2A/B)	Fugl-Meyer运动功能评价量表 Fugl-Meyer Assessment Scale-Motor(FMA-Motor)
下丘脑-垂体-肾上腺 hypothalamic pituitary adrenal(HPA)	运动神经元病 motor neuron disease(MND)
腺苷酸活化蛋白激酶 adenosine monophosphate-activated protein kinase(AMPK)	运动诱发电位 motor-evoked potential(MEP)
小动脉闭塞 small artery occlusion(SAO)	运动阈值 motor threshold(MT)
心源性栓塞 cardioembolism(CE)	运动再学习 motor relearning programme(MRP)
兴奋性突触后电位 excitatory postsynaptic potential(EPSP)	直接皮质电刺激 direct cortical stimulation(DCS)
虚拟现实训练在脑卒中康复中的疗效观察试验 Efficacy of Virtual Reality Exercises in STroke Rehabilitation (EVREST) trial	中国缺血性卒中亚型 Chinese Ischemic Stroke Subclassification(CISS)
选择性5-羟色胺和去甲肾上腺素再摄取抑制剂 selective serotonin and norepinephrine reuptake inhibitor (SSNRI)	中枢运动传导时间 central motor conduction time(CMCT)
选择性5-羟色胺再摄取抑制剂 selective serotonin reuptake inhibitor(SSRI)	肿瘤坏死因子-α tumor necrosis factor-α(TNF-α)
选择性去甲肾上腺素再摄取抑制剂 selective norepinephrine reuptake inhibitor(SNRI)	重症脑血管病 severe cerebral vascular disease(SCVD)
血管紧张素转换酶 angiotensin-converting enzyme(ACE)	周围血管病变 peripheral vascular diseases(PVD)
烟雾病 moyamoya disease(MMD)	周围运动传导时间 peripheral motor conduction time(PMCT)
Beck抑郁量表 Beck Depression Inventory(BDI)	椎动脉 vertebral artery(VA)
有丝分裂原激活蛋白激酶 mitogen-activated protein kinase(MAPK)	椎动脉颅外段 extracranial vertebral artery(EVA)
诱导型一氧化氮合酶 inducible nitric oxide synthase(iNOS)	Cowden综合征 Cowden's syndrome(CS)
	组内相关系数 interclass correlation coefficient(ICC)
	10 m最大步行速度 10 m Maximum Walking Speed(10 m MWS)
	最大密度投影 maximum intensity projection(MIP)
	最大输出强度 maximum stimulator output(MSO)