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# 血管内皮功能和颈动脉内膜中膜厚度变化在糖尿病肢体动脉闭塞症中的表达意义

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**摘要 目的:**研究血管内皮功能与颈动脉内膜中膜厚度在监测和评估糖尿病肢体动脉闭塞症病情变化中的作用及临床意义。**方法:**将2012年10月至2013年10月入院的75例糖尿病肢体动脉闭塞症患者为研究对象,按照病程分为一、二和三期组,各25例,并纳入25例健康者为对照组。测定其体内一氧化氮、内皮素1、6-酮-前列腺素F1a和血栓素B2水平变化,并运用高分辨率超声对患者及对照组颈动脉内膜中膜厚度(IMT)、内皮依赖性舒张功能(EDD)及非内皮依赖性舒张功能(EID)进行检测,分析比较各组间差异性。**结果:**随着病程变化,健康对照组与三期糖尿病肢体动脉闭塞症患者相比较,一、二和三期患者的EDD逐渐降低,且差异有统计学意义( $P<0.01$ )。三期患者的EID值较健康组、一期及二期患者低,差异有统计学意义( $P<0.01$ )。二期与三期患者IMT与对照组相比逐渐升高,差异有统计学意义( $P<0.01$ )。各病程糖尿病肢体动脉闭塞症患者的总胆固醇水平、空腹血糖水平、收缩压及舒张压均高于健康对照组( $P<0.05$ ),而各组间差异无统计学意义。**结论:**血管内皮功能及颈动脉内膜中膜厚度的变化可反映糖尿病肢体动脉闭塞症的病程发展,可作为这临床诊断与监测的参考指标。

**关键词:**糖尿病肢体动脉闭塞症;颈动脉内膜中膜厚度;血管内皮功能

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## The Significance of the Changes of Vascular Endothelial Function and Carotid Artery Intima-Media Thickness in Patients with Diabetic Arterial Occlusion of Lower Extremities

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**ABSTRACT Objective:** To investigate the changes of vascular endothelial function and carotid artery intima-media thickness and their relationship with the course of diabetic limb arterial obliteration (DLAO). **Methods:** 75 patients with Diabetic Arterial Occlusion of Lower Extremities who were treated in our hospital from October 2012 to October 2013 were chosen and divided into three groups on the basis of different disease stages. 25 healthy people were observed as the control group. The changes of vascular tension factors such as nitric oxide, endothelin-1, 6-keto-prostaglandin and thromboxane B2 were observed. Endothelium-dependent dilation (EDD), endothelium-independent dilation (EID) and IMT were measured with high resolution ultrasound. **Results:** In different stages, EDD has significantly characteristic changes, and it was reduced significantly in patients with DAO compared with those healthy control. EID of the branchial artery in patients of 3rd stage was also lower than that of the 1st, 2nd stage and the control group ( $P<0.01$ ). IMT of healthy control group were significantly lower than that of the 2nd and 3rd stage. The levels of total cholesterol, fasting blood glucose, systolic and diastolic blood pressure were significantly higher than those of healthy control group ( $P<0.05$ ). **Conclusions:** The changes of vascular endothelial function and carotid artery intima-media thickness can indicate the different stages of disease and can be used to monitor the condition of the patients.

**Key words:** Diabetic limb artery occlusion; Carotid artery intima of film thickness; Endothelial function

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### 前言

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随着饮食结构的改变及老龄化进程的加剧,糖尿病已成为危害国民健康的主要病症。糖尿病有诸多并发症,肢体动脉闭塞症便是其常见之一<sup>[1,2]</sup>。患者除了发生视网膜血管、心脑血管和肾血管的相关病变,肢体会发生动脉粥样硬化及微血管病变,造成动脉血管狭窄阻塞引起肢体缺血缺氧,以至坏疽感染致残<sup>[3-7]</sup>。本研究以2012年10月至2013年10月入院的75例

糖尿病肢体动脉闭塞症患者为研究对象,对患者的 EDD、EID、IMT 和血管张力因素等进行了分析研究,探讨血管内皮功能与颈动脉内膜中膜厚度在监测和评估糖尿病肢体动脉闭塞症病情变化中的作用,初步讨论其临床意义。

## 1 资料和方法

### 1.1 一般资料

参照中国糖尿病肢体动脉症的诊断标准,将 2012 年 10 月至 2013 年 10 月入院的 75 例糖尿病肢体动脉闭塞症患者列为

研究对象。参考 2002 年 12 月周围血管疾病专业委员会制定的糖尿病肢体动脉闭塞症诊断与分期标准,排除严重视网膜、肝、肾和心脑血管等并发症及坏疽、严重感染和脓毒血症。将患者分为三期,即局部缺血期(一),营养障碍期(二)与坏死期(三),每期 25 例,健康对照组 25 例,肝肾功能正常。均无高血压、糖尿病及冠心病等病史,体检无异常。对照组与三组患者在病程、年龄、体质质量指数(BMI)及性别方面无统计学差异( $P>0.05$ ),具有可比性,见表 1。

表 1 临床资料比较( $\bar{x} \pm s$ ,  $n=25$ )  
Table 1 Comparison of clinical data( $\bar{x} \pm s$ ,  $n=25$ )

| 组别<br>Groups                                  | 健康对照组<br>Healthy control group | 一期组<br>First stage group | 二期组<br>Second stage group | 三期组<br>Third stage group |
|-----------------------------------------------|--------------------------------|--------------------------|---------------------------|--------------------------|
| 例数(n)<br>Cases(n)                             | 25                             | 25                       | 25                        | 25                       |
| 性别(男/女)<br>Gender (male / female)             | 15/10                          | 17/8                     | 16/9                      | 15/10                    |
| 年龄(岁)<br>Age(years)                           | 65.7 $\pm$ 5.83                | 64.4 $\pm$ 7.92          | 67.3 $\pm$ 3.40           | 65.1 $\pm$ 5.51          |
| 病程(年)<br>Duration (years)                     | -                              | 5.56 $\pm$ 3.36          | 5.48 $\pm$ 4.41           | 5.98 $\pm$ 4.12          |
| BMI<br>(kg/m <sup>2</sup> )                   | 19.7 $\pm$ 2.42                | 21.8 $\pm$ 1.20          | 20.5 $\pm$ 1.77           | 21.5 $\pm$ 2.29          |
| 空腹血糖(mmol/L)<br>Fasting blood-glucose(mmol/L) | 4.38 $\pm$ 0.81                | 8.64 $\pm$ 1.79**        | 7.52 $\pm$ 2.26**         | 8.54 $\pm$ 4.76**        |

注:与健康对照组相比较,\*\* $P<0.01$ 。

Note :Compared with healthy control group,\*\* $P<0.01$ .

### 1.2 血管内皮功能检测

采用美国 GELOGIQ700 超声诊断仪,线阵探头频率设定为 7 MHz。测试过程中探头处于同一位置,取同一部位测量内径。受试者仰卧位,右臂 15 度轻度外展,心电图进行同步记录。取处于肘关节上 2~15 cm 内的肱动脉纵切面,测定其内后内膜间的距离,取三个心动周期测量值的平均值。调节超声束,使平行于血流方向,校正角度小于 60 度,于管腔中心取 1 mm 样框,观察多普勒频谱,待其清晰显示时,测定血流量及流速。受试者静卧,用血压计测定其血流量 F1 与肱动脉内径 D1,压力加至 280 mmHg,持续 5 min,放气,于 15s 左右测定血流量 F2,1min 后测定肱动脉内径 D2。患者休息 20min 至肱动脉内径恢复,含服硝酸甘油 0.6 mg,5 min 后测定血流量 F3 及肱动脉内径 D3。内皮依赖性舒张功能 EDD 和非内皮依赖性舒张功能 EID 的计算依照公式  $EDD = [(D2-D1)/AD1] \times 100\%$  和  $EID = [(D3-D1)/AD1] \times 100\%$ 。

### 1.3 颈动脉内膜中膜厚度检测

测定颈总动脉段及颈内动脉段后壁内膜中膜厚度,受试者去枕仰卧,使头部偏转使受检血管充分暴露,观察动脉后壁超声显像,内膜中膜厚度即为回声相对较低分隔的两条平行亮线的间距。取三次测量结果均值,并记录。

### 1.4 血管张力因素指标检测

采用硝酸还原酶法测定一氧化氮浓度水平,固相平衡饱和竞争放射免疫法测定血栓素 B2 和 6-酮-前列腺素 F1a,平衡放射免疫法测定内皮素 1。

### 1.5 统计学处理

采用 SPSS13.0 统计学软件对数据进行统计学分析,运用方差分析对多组间进行比较,运用 q 检验对组间进行比较, $P<0.01$  为有显著性统计学差异, $P<0.05$  为差异有统计学意义。

## 2 结果

### 2.1 临床资料

与健康对照组相比较,三组糖尿病肢体动脉闭塞症患者的空腹血糖水平、收缩压及舒张压明显较高,有显著性差异( $P<0.01$ ),总胆固醇水平也明显较高,有显著性差异( $P<0.05$ ),而三组糖尿病肢体动脉闭塞症患者间无显著性差异,数据见表 2。

### 2.2 血管张力因素指标变化

与健康对照组相比较,三组糖尿病肢体动脉闭塞症患者的内皮素水平及组 6-酮-前列腺素 F1a 显著降低( $P<0.01$ ),相对于一期患者,二期与三期患者均较低,且组间差异有统计学意义( $P<0.01$ );三组患者的血栓素 B2 水平及内皮素 1 显著升高( $P<0.01$ ),且三组患者相比较差异有统计学意义( $P<0.05$ ),结果见表 3。

表 2 各组间血糖、血脂与血压水平比较( $\bar{x} \pm s$ , n=25)Table 2 Comparison of blood glucose, blood fat and blood pressure between groups ( $\bar{x} \pm s$ , n=25)

| 组别<br>Groups                                   | 健康对照组<br>Healthy control group | 一期组<br>First stage group | 二期组<br>Second stage group | 三期组<br>Third stage group |
|------------------------------------------------|--------------------------------|--------------------------|---------------------------|--------------------------|
| 总胆固醇( mmol/L)<br>Cholesterol total             | 4.38± 0.73                     | 5.44± 0.66*              | 5.61± 1.12*               | 5.72± 0.99*              |
| 空腹血糖( mmol/L)<br>Fasting blood-glucose(mmol/L) | 4.89± 0.91                     | 7.43± 2.21**             | 8.49± 3.76**              | 8.94± 3.21**             |
| 收缩压(mmHg)<br>Systolic pressure(mmHg)           | 124.18± 10.83                  | 144.90± 12.46**          | 147.11± 11.72**           | 154.95± 8.81**           |
| 舒张压( mmHg)<br>Ddiastolic pressure( mmHg)       | 73.26± 6.13                    | 94.68± 7.38**            | 98.31± 5.63**             | 99.14± 7.73**            |
| 甘油三酯(mmol/L)<br>Triglycerides(mmol/L)          | 1.28± 0.41                     | 1.38± 0.93               | 1.49± 0.50                | 1.52± 0.81               |

注:与健康对照组比较,\*P&lt;0.05,\*\*P&lt;0.01。

Note :Compared with healthy control group,\*P&lt;0.05,\*\*P&lt;0.01.

表 3 血管张力因素指标比较( $\bar{x} \pm s$ , n=25)Table 3 Comparison of vascular tension factors( $\bar{x} \pm s$ , n=25)

| 组别<br>Groups                                             | 健康对照组<br>Healthy control group | 一期组<br>First stage group | 二期组<br>Second stage group | 三期组<br>Third stage group |
|----------------------------------------------------------|--------------------------------|--------------------------|---------------------------|--------------------------|
| 一氧化氮(Lmol/L)<br>Nitric oxide (Lmol/L)                    | 75.62± 5.24                    | 65.44± 6.61*             | 60.21± 4.12*◆             | 59.32± 9.81*■            |
| 6- 酮 - 前列腺素 F1a(ng/L)<br>6- keto prostaglandin F1a(ng/L) | 78.93± 6.71                    | 70.47± 7.24*             | 62.19± 4.86*■             | 58.92± 6.23*■            |
| 血栓素 -B2 (ng/L)<br>Thromboxane -B2(ng/L)                  | 77.68± 10.21                   | 84.93± 10.56*            | 97.19± 9.12*■             | 104.61± 11.82*■▲         |
| 内皮素 1(ngPL)<br>Endothelin-1(ngPL)                        | 54.29± 7.93                    | 64.65± 9.31*             | 78.31± 9.64*◆             | 89.24± 11.53* ■▲         |

注:与健康对照组比较,\*P&lt;0.01;与一期组比较,◆P&lt;0.05,■P&lt;0.01;与二期组比较,▲P&lt;0.01。

Note :Compared with healthy control group,\*P&lt;0.01;Compared with first stage group ,◆P&lt;0.05,■P&lt;0.01;Compared with second stage group ,▲P&lt;0.01.

## 2.3 EDD、EID 及 IMT 变化

研究结果发现,健康对照组及三组患者肱动脉基础内径无显著性差异。与对照组相比较,患者组 EDD 明显降低(P<0.01),组间比较显示三组不同病期患者 EDD 值有显著性差异(P<0.01)。三期患者与对照组、一期组和二期组相比明显较低,

且差异有统计学意义(P<0.01)。颈动脉内膜中膜厚度的变化研究结果发现,一期患者与对照组 IMT 值无显著性差异,而二期与三期组则明显高于一期组与对照组,且二期与三期组间比较显示三期患者 IMT 值高于二期,差异有统计学意义(P<0.01),结果见表 4。

表 4 各组间 EDD、EID 及 IMT 变化比较( $\bar{x} \pm s$ , n=25)Table 4 Comparison of EDD, EID and IMT between groups ( $\bar{x} \pm s$ , n=25)

| 组别<br>Groups                   | 健康对照组<br>Healthy control group | 一期组<br>First stage group | 二期组<br>Second stage group | 三期组<br>Third stage group |
|--------------------------------|--------------------------------|--------------------------|---------------------------|--------------------------|
| IMT(mm)                        | 0.72± 0.03                     | 0.88± 0.07               | 1.11± 0.02*■              | 1.32± 0.04*■▲            |
| EDD                            | 11.67%± 2.71%                  | 9.07%± 1.22%*            | 6.19%± 1.81%*■            | 4.91%± 1.23%*■▲          |
| EID                            | 17.08%± 1.24%                  | 14.53%± 1.36%            | 11.99%± 1.67%             | 8.91%± 4.71%*■▲          |
| 基础内径( mm)<br>Base diameter(mm) | 4.49± 0.43                     | 4.20± 0.31               | 4.61± 0.61                | 4.24± 0.53               |

注:与健康组相比较,\*P&lt;0.01;与一期组相比较,■P&lt;0.01;与二期组相比较,▲P&lt;0.01。

Note :Compared with healthy control group,\*P&lt;0.01;Compared with first stage group ,■P&lt;0.01;Compared with second stage group ,▲P&lt;0.01.

### 3 讨论

近年来,随着糖尿病发病率的升高,其严重并发症之一的糖尿病肢体动脉闭塞症发病率也随之增高<sup>[8-10]</sup>。相关文献显示,在我国 60 岁以上的糖尿病患者中糖尿病肢体动脉闭塞症的发病率高达 15.91%,在美国 70 岁以上的高龄患者中,糖尿病肢体动脉闭塞症的发病率由 3%~10%上升至 15%~20%。据报道,约有 15%的糖尿病患者最终会发展成足溃疡,发生截肢的风险是非糖尿病患者群的 5 倍。糖尿病肢体动脉闭塞症已成为糖尿病患者致残的重要原因<sup>[11,12]</sup>。患者的主要病理特征是肢体动脉中膜钙化或变性、内膜有粥样斑块出现且腔内形成继发性血栓,造成官腔狭窄甚至闭塞,最终导致患者肢体发生缺血缺氧,甚至感染坏疽<sup>[13-17]</sup>。

本研究采用高分辨率超声监测了健康者与不同病程糖尿病肢体动脉闭塞症患者的血管张力指标,并观察其变化特征,结果发现三组患者有明显的血栓素 B2 与内皮素 1 水平增高、6-酮-前列腺素 F1a 及一氧化氮水平下降,血管内皮依赖性舒张功能随着病情的加重逐渐下降,表明糖尿病肢体动脉闭塞症可破坏患者的血管张力平衡,造成内皮细胞损伤。研究数据显示一、二期患者的 EDD 与健康对照组相比较无显著性差异,说明前两期患者的血管平滑肌功能未受损,内皮细胞损伤、舒张因子灭活增加或生成减少是血管舒张功能障碍的重要原因<sup>[18]</sup>。三期患者 EID 功能明显下降说明病程发展不仅使血管内皮受损,也会损伤血管平滑肌。三组糖尿病肢体动脉闭塞症患者的 EID 值均低于健康对照组且随着病情发展逐渐降低,推测患者血管由于长期高糖刺激及缺血缺氧状态,使血管壁增厚、血管平滑肌细胞增殖及功能异常,从而使其对舒血管物质的反映性。

血管内皮是管壁与血液间的分隔,也是重要的功能器官之一。它可以释放多种收缩和舒张因子,从而调节血流和血管张力。研究表明血管内皮功能障碍可加速病程,在在糖尿病肢体血管疾病的发病中占据重要地位<sup>[19,20]</sup>。颈动脉内膜中膜厚度变化可反映大动脉形态学变化,其与糖尿病肢体动脉闭塞症患者的病情变化相一致,可随着病程的发展逐渐增厚。血管舒张功能障碍是糖尿病功能损害的表现,颈动脉内膜中膜厚度变化是病患形态异常的体现。在临床应用过程中,同时进行血管内皮功能检查和颈动脉超声检查,观测两者变化,可作为评估监测病程进展的重要指标。

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