

doi: 10.13241/j.cnki.pmb.2018.17.012

2 型糖尿病患者尿微量白蛋白水平与动脉粥样硬化的相关性研究

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摘要 目的:研究 2 型糖尿病患者尿微量白蛋白(MAU)水平与动脉粥样硬化的相关性。**方法:**抽样选取 2015 年 2 月至 2017 年 2 月我体检中心检测的 2 型糖尿病患者 500 例,根据临床数据中 MAU 水平的不同分为异常组 188 例和正常组 312 例。分别对比两组患者的临床资料以及生化指标水平,并采用多因素 Logistic 回归分析法分析患者 MAU 异常的危险因素。**结果:**异常组患者的病程、BMI、空腹血糖、甘油三酯、腰臀比均高于正常组,而高密度脂蛋白水平低于正常组($P<0.05$)。多因素 Logistic 回归分析显示影响 2 型糖尿病患者 MAU 异常的危险因素包括病程(较长)、BMI(较大)、收缩压(较高)、糖化血红蛋白(较高)、高密度脂蛋白(较低)($P<0.05$)。**结论:**2 型糖尿病患者的病程、BMI、收缩压、糖化血红蛋白、高密度脂蛋白均与 MAU 的发生密切相关,临床上可通过检查以上指标预测评估患者的病情变化以及预后情况。

关键词:2 型糖尿病;尿微量白蛋白;动脉粥样硬化;相关性;生化指标

中图分类号:R587.2 **文献标识码:**A **文章编号:**1673-6273(2018)17-3260-04

Correlation Between Microalbuminuria and Atherosclerosis in Patients with Type 2 Diabetes Mellitus

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ABSTRACT Objective: To investigate the relationship between microalbuminuria (MAU) and atherosclerosis in patients with type 2 diabetes mellitus. **Methods:** A total of 500 patients with type 2 diabetes mellitus, who were examined in the Sixth People's Hospital Affiliated to Shanghai Jiao Tong University during February 2015 to February 2017, were selected and were divided into abnormal group ($n=188$) and normal group ($n=312$) according to the different levels of MAU in clinical data. The clinical data and biochemical indexes of the two groups were compared, and the risk factors of MAU abnormalities were analyzed by multivariate Logistic regression analysis. **Results:** The course of disease, BMI, duration, fasting blood glucose, triglyceride and waist-to-hip ratio in the abnormal group were higher than those in the normal group, while the levels of high density lipoprotein was lower than that in the normal group ($P<0.05$). Logistic regression analysis showed that the risk factors of MAU abnormalities in the patients with type 2 diabetes mellitus were the longer course of disease, larger BMI, higher systolic pressure, higher glycosylated hemoglobin, lower high density lipoprotein ($P<0.05$). **Conclusion:** The course of disease, BMI, systolic pressure, glycosylated hemoglobin and high density lipoprotein in the patients with type 2 diabetes mellitus are closely correlated with the occurrence of MAU. In the clinical work, the condition and prognosis of patients with type 2 diabetes mellitus can be predicted by examining the above indexes.

Key words: Type 2 diabetes mellitus; Microalbuminuria; Atherosclerosis; Correlation; Biochemical indexes

Chinese Library Classification(CLC): R587.2 **Document code:** A

Article ID: 1673-6273(2018)17-3260-04

前言

糖尿病在临床上的发病率相对较高,对社会及患者家属都造成了不同程度的压力^[1,2]。其中 2 型糖尿病患者主要表现为糖代谢紊乱、血压升高等引起的血流动力学变化,随着病程的不断延长,患者的病情也会越发严重^[3-5]。而临床上有研究报道显

示:尿微量白蛋白(microalbuminuria, MAU)是临床上早期监测肾损伤的主要生化指标之一,且由于 MAU 的发生和内皮功能受损存在密切相关,因此 MAU 不但是糖尿病肾病的预测指标,同时与糖尿病大血管病变可能也存在一定相关性^[6-8]。鉴于此,本文通过研究 2 型糖尿病患者 MAU 水平与动脉粥样硬化的关系,目的在于明确 MAU 在 2 型糖尿病患者心血管病变中

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(收稿日期:2017-11-23 接受日期:2017-12-18)

所发挥的作用,从而为临床糖尿病血管并发症的预防以及治疗提供参考依据。现作如下报道。

1 资料与方法

1.1 临床资料

1.1.1 样本来源 2015年2月至2017年2月期间,我体检中心共检测并纪录在案的2型糖尿病患者就诊资料共13595例/套。在全部数据中,共有563例MAU阳性(MAU水平在20 $\mu\text{g}/\text{min}$ ~200 $\mu\text{g}/\text{min}$)的资料。从中按1/3抽样,即188个样本,作为MAU异常组。再从MAU阴性(MAU水平低于20 $\mu\text{g}/\text{min}$)的资料中抽取312个样本,作为MAU正常组。即共500个样本纳入本研究。抽样方法为完全随机,即给每个样本分配一个0-1间的随机数,按随机数大小顺序排列后,抽取前188或312个样本。

1.1.2 纳排标准 纳入标准:(1)所有患者均符合1999年世界卫生组织(WHO)所制定的2型糖尿病诊断标准;(2)均有完整的临床资料。排除标准:(1)伴有急慢性感染、创伤或手术者;(2)由多种原因导致的心、肝等脏器功能障碍者;(3)合并血液系统疾病、免疫系统疾病以及恶性肿瘤患者;(4)常规尿蛋白水平高于200 $\mu\text{g}/\text{min}$ 者;(5)入院前6个月内接受过血管紧张素II受体拮抗剂以及血管紧张素转化酶抑制剂治疗者。所有患者均知情并签署了同意书,且本研究经医院伦理委员会批准^[9,10]。

1.1.3 一般资料比较 异常组男性患者83例,女性患者105例,年龄38-65岁,平均年龄(51.99 $\pm$ 11.72)岁。正常组男性患者144例,女性患者168例,年龄37-66岁,平均年龄(51.79 $\pm$ 12.06)岁。两组患者在性别、年龄等方面比较无显著性差异($P>0.05$),存在可比性(参见表1)。

1.2 研究方法

分别对所有患者的基本资料进行详细的记录分析,主要包括病程、BMI、病程、腰围、臀围、收缩压、舒张压、糖化血红蛋白、空腹血糖、总胆固醇、甘油三酯以及高、低密度脂蛋白等。其中腰臀比=腰围/臀围。其中尿微量白蛋白检测方式如下:分别于清晨取患者第1次晨尿中段5 mL,采用免疫比浊法测量MAU水平,具体操作严格按照试剂盒(和光纯药工业株式会社)说明书进行。之后让所有患者进行10 h禁食,并于次日清晨采集空腹肘正中静脉血5 mL,采用自动生化仪分别检测患者空腹血糖、总胆固醇、甘油三酯以及高、低密度脂蛋白水平。同时,采用高压液相色谱离子交换法检测糖化血红蛋白水平。

1.3 观察指标

分别对比两组患者病程、BMI、腰臀比、收缩压、舒张压、糖化血红蛋白、空腹血糖、胆固醇、甘油三酯以及高、低密度脂蛋白水平。

1.4 统计学方法

使用SPSS20.0软件进行数据分析。对于计数资料,以例数和率表示,组间差异予以 χ^2 检验;对于计量资料,以($\bar{x}\pm s$)表示,组间差异实施t检验。2型糖尿病患者MAU发生及相关因素采用多因素Logistic回归分析,相关性采用Pearson相关性分析。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者的基本资料以及各项生化指标水平对比

异常组患者的病程、BMI、空腹血糖、甘油三酯、腰臀比均高于正常组,而高密度脂蛋白水平显著低于正常组($P<0.05$)。异常组患者的收缩压、糖化血红蛋白均高于正常组($P<0.01$)。详见表1。

表1 两组患者的基本资料以及各项生化指标水平对比($n, \bar{x}\pm s$)

Table 1 Comparison of basic data and biochemical indexes between the two groups($n, \bar{x}\pm s$)

Indexes	Abnormal group($n=188$)	Normal group($n=312$)	t/χ^2	P
Gender(male/female)	83/105	144/168	0.190	0.663
Average age(years old)	51.99 $\pm$ 11.72	51.79 $\pm$ 12.06	0.182	0.856
Course of disease(year)	8.06 $\pm$ 2.52	7.54 $\pm$ 2.32	2.350	0.019
BMI (Kg/m^2)	35.42 $\pm$ 19.77	29.21 $\pm$ 14.59	3.737	0.000
Systolic pressure (mmHg)	134.25 $\pm$ 18.54	131.02 $\pm$ 19.51	1.827	0.068
Diastolic pressure (mmHg)	74.83 $\pm$ 23.80	76.55 $\pm$ 16.85	0.868	0.386
Fasting blood glucose (mmol/L)	6.00 $\pm$ 1.95	5.67 $\pm$ 1.62	2.041	0.042
Glycosylated hemoglobin (%)	6.04 $\pm$ 1.05	5.88 $\pm$ 1.05	1.650	0.099
Triglyceride (mmol/L)	2.24 $\pm$ 1.75	1.86 $\pm$ 1.90	2.231	0.026
Cholesterol (mmol/L)	5.11 $\pm$ 1.01	5.15 $\pm$ 1.15	0.394	0.694
High density lipoprotein (mmol/L)	1.24 $\pm$ 0.27	1.42 $\pm$ 0.41	5.913	0.000
Low density lipoprotein (mmol/L)	3.11 $\pm$ 0.79	3.07 $\pm$ 0.86	0.519	0.604
Waist (cm)	92.90 $\pm$ 8.07	81.46 $\pm$ 10.10	13.941	0.000
Hipline (cm)	103.21 $\pm$ 3.52	93.47 $\pm$ 5.55	24.005	0.000
Waist-to-hipratio	0.90 $\pm$ 0.07	0.87 $\pm$ 0.08	4.396	0.000

2.2 2 型糖尿病患者 MAU 异常的多因素 Logistic 回归分析

以本文研究对象 500 例资料为样本,以 2 型糖尿病患者 MAU 异常状况为应变量(赋值 1= 异常,0= 正常),以单因素分析(表 1)中 $P<0.1$ 的各指标为自变量(赋值列入表 2),纳入建立非条件 Logistic 回归分析模型。回归过程采用后退法(退出

$\alpha=0.05$)进行自变量的选择和剔除。经回归得:影响 2 型糖尿病患者 MAU 异常的危险因素包括病程(较长)、BMI(较大)、收缩压(较高)、糖化血红蛋白(较高)、高密度脂蛋白(较低),均有统计学意义($P<0.05$),OR 在 1.2~2.1 之间。见表 2。

表 2 2 型糖尿病患者 MAU 异常的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis of MAU abnormalities in patients with type 2 diabetes mellitus

Influence factors	Assignment specification	Regression coefficient	Standard error	χ^2	P	OR	OR 95% confidence interval
BMI (Kg/m ²)	1:≥ 29,0:<29	0.743	0.258	8.283	0.004	2.103	1.268~3.489
Course of disease(year)	1:≥ 8,0:<8	0.326	0.141	5.327	0.021	1.385	1.050~1.826
Systolic pressure (mmHg)	1:≥ 130,0:<130	0.177	0.085	4.350	0.037	1.194	1.011~1.410
Glycosylated hemoglobin (%)	1:≥ 6,0:<6	0.416	0.126	10.826	0.001	1.516	1.183~1.942
High density lipoprotein (mmol/L)	1:≤ 1.3,0:>6	0.664	0.246	7.273	0.007	1.942	1.199~3.146

Note: The dimension of assignment refers to table 1. Each range level is the average value of 500 samples, and take appropriate reference to the normal range of the clinical value.

3 讨论

近年来随着我国人们生活方式以及饮食习惯的不断改变,2 型糖尿病的发病率呈逐年上升趋势,导致心脑血管事件的发生率日益增加,对人们的生命健康安全造成了严重威胁^[11-13]。2 型糖尿病患者常伴有不同的并发症发生,尤其是糖尿病肾病,存在相当长时间的无症状阶段,很难在早期被发现是导致患者死亡的主要原因之一^[14-16]。MAU 属于临床上影响 2 型糖尿病患者预后的主要指标之一,其能有效反映糖尿病患者肾脏病变以及心脑血管疾病发生、发展情况,是动脉粥样硬化和血管损伤的重要指标,同时也是肾小球损伤的早期评价指标^[17-19]。因此,本文通过研究 2 型糖尿病患者 MAU 与动脉粥样硬化的相关性,目的在于为临床进一步评估 2 型糖尿病患者的预后情况提供有效指标。

本研究结果显示:异常组患者的病程、BMI、空腹血糖、甘油三酯、腰臀比均高于正常组,而高密度脂蛋白水平显著低于正常组。影响 2 型糖尿病患者 MAU 异常的危险因素包括 BMI(较大)、病程(较长)、收缩压(较高)、糖化血红蛋白(较高)、高密度脂蛋白(较低),提示了 2 型糖尿病患者的病程、BMI、收缩压、糖化血红蛋白、高密度脂蛋白水平与 MAU 的发生存在密切相关,同时也提示了 MAU 可能是 2 型糖尿病患者合并动脉粥样硬化的一个新指标^[20,21]。究其原因,我们认为 2 型糖尿病患者由于长期处于糖、脂代谢紊乱状况,从而导致了血管内皮细胞遭受损害,进一步引发内皮细胞功能的紊乱,而血管内皮功能损害不但存在于肾脏的微血管,同时也存在于全身大血管,其中血浆脂蛋白可通过受损的内皮细胞渗透到内皮下,最终促进了动脉粥样硬化的发生^[22-24]。另有研究报道显示,2 型糖尿病患者由于长期处于血糖紊乱状态,从而可能导致肾小球的滤过率、灌注量以及内压增高,进一步促使肾小球的滤过膜通透性增加;与此同时,高血糖可通过增加多元醇代谢旁路活化以及激活蛋白激酶 C 等一系列机制导致尿蛋白排泄率的增多^[25-27]。另外,有研究学者认为脂代谢紊乱也会介导以及加重 2 型

糖尿病患者肾功能损害,引发 MAU,其主要机制可能如下:(1) 高密度脂蛋白经由血管内皮进入血管壁中,从而使得肾入球小动脉玻璃样变,弓状动脉以及小叶间动脉肌内膜肥厚,进一步对肾功能造成损害;(2) 增加了细胞因子释放以及细胞外基质的产生,同时可直接对肾小球足细胞造成损害;(3) 促使肾小球基底膜的磷酸酯成分发生改变,增加了通透性^[28-30]。

综上所述,2 型糖尿病患者的病程、BMI、收缩压、糖化血红蛋白、高密度脂蛋白均与 MAU 的发生存在密切相关,临床工作中可综合以上指标对患者的病情变化以及预后情况进行预测评估。

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