

doi: 10.13241/j.cnki.pmb.2021.18.039

超声诊断糖尿病脑血管病变及与 Hcy、CysC 及 vWF 相关性研究 *

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摘要 目的:研究超声对糖尿病合并缺血性脑血管疾病的诊断效果,并分析疾病与血清 Hcy、CysC 及 vWF 水平相关性,以期为糖尿病脑血管病的诊断提供一定的临床依据。**方法:**以糖尿病合并缺血性脑血管病患者为研究组,体检健康者为对照组,分别采用经颅多普勒超声(Transcranial Doppler, TCD)和 CT 血管造影(CT angiography, CTA)对研究组患者进行检查,分析 TCD 与 CTA 检查结果的一致性,并对两组研究对象的血清同型半胱氨酸(Homocysteine, Hcy)、胱抑素(Cystatin, CysC)以及血管性血友病因子(Von Willebrand factor, vWF)水平进行检测,对危险因素进行分析。**结果:**TCD 对血管重度狭窄的灵敏度、阳性预测值和 Kappa 值最高,阳性似然比为 $74.52 > 10$,表明 TCD 对于糖尿病合并重度脑血管狭窄的检测与 CTA 的一致性最好。Hcy、CysC 及 vWF 水平均显著升高($P < 0.05$),其中研究组 Hcy 水平为 $24.28 \pm 4.01 \mu\text{mol/L}$,显著高于对照组的 $10.31 \pm 1.45 \mu\text{mol/L}$,研究组 CysC 水平为 $1.45 \pm 0.21 \text{ mg/L}$,显著高于对照组的 $0.80 \pm 0.16 \text{ mg/L}$,研究组 vWF 水平为 $152.88 \pm 15.73 \%$,显著高于对照组的 $92.31 \pm 16.21 \%$ 。多因素回归分析显示,Hcy、CysC 及 vWF 均可作为独立预测指标,与患者疾病程度显著相关,对诊断和预后有一定的预测作用。**结论:**超声在糖尿病脑血管病的诊断中有较高的灵敏度和特异度,有重要的诊断意义,Hcy、CysC 及 vWF 均可作为糖尿病脑血管病的独立预测指标,与患者疾病程度显著相关。

关键词:糖尿病;脑血管病;超声;诊断;相关性

中图分类号:R587.2;R743;R445.1 文献标识码:A 文章编号:1673-6273(2021)18-3579-04

Ultrasound Diagnosis of Diabetic Cerebrovascular Disease and Its Correlation with Hcy, CysC and vWF*

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ABSTRACT Objective: To study the diagnostic effect of ultrasound on diabetes complicated with ischemic cerebrovascular disease, and analyze the correlation between the disease and serum Hcy, CysC and vWF levels, in order to provide a certain basis for the diagnosis of diabetic cerebrovascular disease. **Methods:** Diabetes patients with ischemic cerebrovascular disease were taken as the study group, and healthy persons were taken as the control group. TCD and CTA were used to examine the patients in the study group. The consistency of the results of TCD and CTA was analyzed, and the results of the two groups were analyzed. Serum Hcy, CysC and vWF levels were detected, and risk factors were analyzed. **Results:** TCD has the highest sensitivity, positive predictive value and Kappa-coefficient for severe vascular stenosis, and the positive likelihood ratio is $74.52 > 10$, indicating that TCD has the best consistency with CTA for the detection of diabetes with severe cerebrovascular stenosis. The levels of Hcy, CysC and vWF were significantly increased ($P < 0.05$). The level of Hcy in the study group was $24.28 \pm 4.01 \mu\text{mol/L}$, which was significantly higher than the $10.31 \pm 1.45 \mu\text{mol/L}$ of the control group. The level of CysC in the study group was $1.45 \pm 0.21 \text{ mg/L}$ was significantly higher than $0.80 \pm 0.16 \text{ mg/L}$ in the control group, and the vWF level in the study group was $152.88 \pm 15.73 \%$, which was significantly higher than $92.31 \pm 16.21 \%$ in the another group. Multivariate regression analysis manifested that Hcy, CysC and vWF can be used as independent predictors, which are significantly related to the patient's disease degree, and have a certain predictive effect on diagnosis and prognosis. **Conclusion:** Ultrasound has high sensitivity and specificity in the diagnosis of diabetic cerebrovascular disease, and has important diagnostic significance. Hcy, CysC and vWF can be used as independent predictors of diabetic cerebrovascular disease, which are significantly related to the disease degree of patients.

Key words: Diabetes; Cerebrovascular disease; Ultrasound; Diagnosis; Correlation

Chinese Library Classification(CLC): R587.2; R743; R445.1 **Document code:** A

Article ID: 1673-6273(2021)18-3579-04

* 基金项目:国家自然科学基金地区基金项目(81460696)

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(收稿日期:2021-02-26 接受日期:2021-03-22)

前言

糖尿病是最常见的代谢性疾病之一,由脂质和葡萄糖代谢紊乱所导致,常伴随多种并发症,脑血管病变是最常见的糖尿病并发症之一,病情发展迅速、严重,且经过治疗后复发率和死亡率较高^[1-3]。缺血性脑血管病是一种神经内科学的常见病,糖尿病患者的缺血性脑血管疾病已经成为致残和致死的主要因素,动脉粥样硬化是其危险因素,但是在发病早期往往没有明显的临床症状^[4-6]。因此,及早准确的诊断和治疗对糖尿病脑血管病变患者疾病的控制和预后判断至关重要。

经颅多普勒超声(Transcranial Doppler, TCD)对糖尿病合并脑血管病的诊断的灵敏度较高^[7]。有文献表明,同型半胱氨酸(Homocysteine, Hcy)、胱抑素(Cystatin, CysC)以及血管性血友病因子(Von Willebrand factor, vWF)与脑血管病的诊断和病情严重程度有密切的关系^[8-9]。Hcy水平的升高可使颈动脉内膜中层增厚,斑块形成,进而引起血管腔狭窄,导致脑血管疾病的发生^[10]。CysC是脑血管病的独立预测因子,其水平与病情程度呈正相关关系^[11]。vWF与血管损伤有关,脑血管病的发生和血管壁损伤密切相关,内皮细胞受到损伤后vWF被释放入血,能敏感的反映血管损伤和功能紊乱程度^[12]。

因此本研究采用经颅多普勒超声对糖尿病合并缺血性脑血管疾病进行诊断,且对患者血清Hcy、CysC以及vWF水平进行检测,进一步对其相关性进行分析,以期对糖尿病脑血管病的诊断提供一定的临床依据,现具体报道如下。

1 资料与方法

1.1 基本信息

以60例2017年6月-2020年6月就诊于我院的糖尿病合并缺血性脑血管病患者为研究组,其中男性35例,女性25例,平均年龄 58.53 ± 10.67 岁,平均病程 6.33 ± 2.07 年。另以60例体检健康者为对照组,男性33例,女性27例,平均年龄 57.13 ± 9.64 岁。两组患者基本资料无差异($P > 0.05$),患者及家人已了解并同意整个研究过程,本研究已向医院伦委会征得许可。

1.2 纳入与排除标准

纳入标准:符合糖尿病诊断标准^[13],符合缺血性脑血管病诊断标准^[14];对造影剂无过敏反应者;临床资料完整,签署知情同意书者。

排除标准:混合型脑卒中者;合并严重心肝肾疾病者;由于颅内感染、血液病、药物滥用等导致的脑动脉狭窄患者;有开颅术史和溶栓治疗史患者。

1.3 研究方法

仪器方法:采用GE 64层螺旋极速CT机对研究组患者进行检查,根据Heiserman狭窄程度分级对患者脑血管狭窄程度进行判断,分为轻度(50%以下)、中度(51%~75%)、重度(76%~99%)和闭塞(99%以上)。

再采用经颅多普勒超声诊断仪(南京科进公司)对研究组患者进行检查,探头频率2MHz,分别从颞、枕、眼窗进行前、后循环探测,其中前循环指标包含大脑中动脉、前动脉、颈内动脉终末端以及大脑后动脉,后循环探测指标包括基底动脉和椎动脉。

1.4 采集静脉血

研究组和对照组对象均于清晨空腹采集5 mL肘静脉血,离心后取血清待测,采用酶联免疫吸附法检测样本血清Hcy、CysC以及vWF水平。

1.5 数据处理

SPSS 19.0处理数据,计量资料以 $\bar{x} \pm s$ 表示,使用t检验,计数资料以(%)表示,使用 χ^2 检验,一致性分析采用Kappa检验,多因素分析采用Logistic回归, $P < 0.05$ 为具有统计学意义。

2 结果

2.1 TCD与CTA检查一致性分析

本研究以CTA检查结果作为诊断患者血管狭窄的标准,分析TCD对糖尿病脑血管狭窄的灵敏度、特异度等,结果见表1,TCD对血管重度狭窄的灵敏度、阳性预测值和Kappa值最高,阳性似然比为 $74.52 > 10$,表明TCD对于糖尿病合并重度脑血管狭窄的检测与CTA的一致性最好。

表1 TCD和CTA对糖尿病合并脑血管狭窄检查一致性分析(n=60)

Table 1 Analysis of consistency between TCD and CTA in examination of diabetes complicated with cerebrovascular stenosis (n=60)

Degree of stenosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio	Kappa value
Mild	54.81	98.74	60.82	98.31	41.75	0.47	0.557
Moderate	71.70	98.65	77.79	98.77	48.77	0.01	0.724
Severe	88.35	98.92	83.14	94.56	74.52	0.13	0.848
Occlude	58.24	99.64	62.54	99.64	163.51	0.44	0.599

2.2 两组血清Hcy、CysC及vWF比较

本研究对两组的血清Hcy、CysC及vWF进行检测分析,结果见表2所示。Hcy、CysC及vWF水平均显著升高($P < 0.05$),其中研究组Hcy水平为 $24.28 \pm 4.01 \mu\text{mol/L}$,显著高于对照组的 $10.31 \pm 1.45 \mu\text{mol/L}$,研究组CysC水平为 $1.45 \pm 0.21 \text{ mg/L}$,显著高于对照组的 $0.80 \pm 0.16 \text{ mg/L}$,研究组vWF水平为

$152.88 \pm 15.73 \%$,显著高于对照组的 $92.31 \pm 16.21 \%$ 。

2.3 糖尿病脑血管狭窄多因素Logistics回归分析

本研究对糖尿病脑血管狭窄超声诊断结果和Hcy、CysC及vWF进行相关性分析,结果见表3所示,多因素回归分析显示,Hcy、CysC及vWF均可作为独立预测指标,与患者疾病程度显著相关,对诊断和预后有一定的预测作用。

表 2 两组血清 Hcy、CysC 及 vWF 比较

Table 2 Comparison of serum Hcy, CysC and vWF between the two groups

Groups	Hcy($\mu\text{mol/L}$)	CysC(mg/L)	vWF (%)
Control Group (n=60)	10.31 $\pm$ 1.45	0.80 $\pm$ 0.16	92.31 $\pm$ 16.21
Study Group (n=60)	24.28 $\pm$ 4.01*	1.45 $\pm$ 0.21*	152.88 $\pm$ 15.73*

Note: * P <0.05 compared with control group.

表 3 糖尿病脑血管狭窄多因素 Logistics 回归分析

Table 3 Multivariate Logistics regression analysis of diabetic cerebrovascular stenosis

Factor	β value	SE	Wald	OR	95%CI	P
Hcy	1.815	0.527	10.862	6.148	5.841~6.456	0.001
CysC	0.809	0.342	5.603	2.234	1.143~4.431	0.012
vWF	1.757	0.668	6.954	5.783	1.570~21.385	0.008

3 讨论

TCD 为一种可实时提供脑动脉血流的检测方法,根据超声多普勒效应对颅内动脉血流动力学和各项血流生理参数进行检测,能为脑血管病的诊断、监控提供重要依据^[15,16]。TCD 对血管内的血液流动具有很高的灵敏度,能实时反馈血流频谱和声频信息^[17,18]。本研究以 CTA 检查结果作为诊断患者血管狭窄的标准,分析 TCD 对糖尿病脑血管狭窄的灵敏度、特异度等,结果显示,TCD 对血管重度狭窄的灵敏度、阳性预测值和 Kappa 值最高,阳性似然比为 $74.52 > 10$,表明 TCD 对于糖尿病合并重度脑血管狭窄的检测与 CTA 的一致性最好。与王巍^[19]的研究类似,探讨 CTA 和 TCD 对缺血性脑血管病患者颅内动脉狭窄诊断上的应用价值,TCD 与 CTA 对于颅内动脉血管狭窄检查存在良好的一致性(Kappa>0.5),特别是对于重度狭窄患者的诊断一致性最高(Kappa=0.838)。CT 血管造影准确性高、图像清晰立体,但是部分人群对 CT 对比剂存在过敏的情况,推广度受限^[20,21]。而 TCD 检查无创伤且操作简单,对颅内动脉血流情况有直观地监测,能通过血流情况反映颅内血管狭窄程度,重复性强^[22]。表明进行颅内重度狭窄的诊断结果与 CTA 的一致性很高,而对于轻、中度患者的诊断,还需要进一步优化诊断方法。

Hcy 是一种含硫氨基酸,为蛋氨酸代谢产物,具有细胞毒性,健康人群的血清 Hcy 浓度较低。Hcy 极易自身发生氧化作用,造成大量氧化物和氧自由基的生成和累积,从而伤害血管的内皮细胞致使其自身功能的丧失,导致内皮细胞无法再生^[23,24]。除此之外,Hcy 还可以使血小板变得有活力,加速血管收缩和血小板汇集,形成凝血及血栓,造成血管狭窄^[25]。CysC 为半胱氨酸蛋白酶抑制剂家族成员,CysC 会发生炎症反应,这些炎症反应会加速机体的动脉粥样硬化的发生,从而导致心脑血管疾病患者的病情加重,有研究报道,脑血管疾病的产生与患者死亡的最危险因素之一是体内血清 CysC 的浓度过高^[26,27]。vWF 多存在于内皮细胞巨核细胞和血小板中,在血小板和血管壁的结合过程中发挥重要作用^[28]。在各种因素诱导的血小板活性化时,vWF 的一段可与血管壁上的纤维蛋白和胶原结合,另一端和血小板膜蛋白结合,从而使血小板粘附于血管内皮上^[29,30]。此

外,vWF 还可通过与血小板膜糖蛋白的结合,促进血小板的聚集,若血管受到损伤,胶原纤维被暴露,除了内源性凝血途径外,内皮细胞还可表达释放 vWF,使血小板于损伤部位粘附聚集,血清 vWF 水平对反映血管损伤和功能紊乱程度有重要作用^[31]。本研究对两组的血清 Hcy、CysC 及 vWF 水平进行检测分析,结果研究组 Hcy、CysC、vWF 水平显著高于对照组,本研究对糖尿病脑血管狭窄超声诊断结果和 Hcy、CysC 及 vWF 进行相关性分析,结果显示,Hcy、CysC 及 vWF 均可作为独立预测指标,与患者疾病程度显著相关,对诊断和预后有一定的预测作用。与袁捷^[32]的研究类似,该学者探讨 2 型糖尿病患者微血管病变与血清 Hcy、Cys C 水平变化的关系,单纯糖尿病组与糖尿病合并微血管病变组 Hcy、Cys C 水平较对照组升高,糖尿病合并微血管病变组 Hcy、Cys C 水平较单纯糖尿病组升高,2 型糖尿病微血管病变的发生与血清 Hcy、Cys C 水平有关。表明在临床关注 Hcy、CysC 及 vWF 水平的变化在糖尿病脑血管疾病的诊断中有重要作用。本研究也存在一定的不足,样本量少,结果可能存在一定的偏倚。也没有对设立单纯糖尿病组,因此后续研究需要扩大样本量,对分组进一步的细化进行分析 Hcy、CysC 及 vWF 在糖尿病脑血管病的诊断价值。

综上所述,超声在糖尿病脑血管病的诊断中有较高的灵敏度和特异度,有重要的诊断意义,Hcy、CysC 及 vWF 均可作为糖尿病脑血管病的独立预测指标,与患者疾病程度显著相关。

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