

2 型糖尿病患者发生新型冠状病毒感染的危险因素分析

欧翔^{1a}, 刘丽莎^{1b}, 汤石林², 邵挥戈^{1a}

(1. 南华大学衡阳医学院附属长沙中心医院 a. 内分泌科, b. 检验科, 长沙 410004; 2. 南华大学附属第一医院重症医学科, 衡阳 421001)

摘要 目的 探讨 2 型糖尿病患者发生新型冠状病毒感染的危险因素。方法 选取未合并新型冠状病毒感染的 2 型糖尿病患者 78 例(未感染组), 合并新型冠状病毒感染的 2 型糖尿病患者 24 例(感染组), 比较两组的年龄、体质量指数、糖尿病病程、收缩压、舒张压、血脂、白细胞数、中性粒细胞数、空腹血糖、餐后 2 h 血糖、空腹 C 肽、餐后 2 h C 肽、糖化血红蛋白、 β -羟丁酸, 并分析上述因素与新型冠状病毒感染的相关性。结果 感染组的总胆固醇显著低于未感染组, 差异有统计学意义($P < 0.05$); 感染组的糖化血红蛋白和 β -羟丁酸显著高于未感染组($P < 0.05$)。Spearman 相关分析结果显示, 新型冠状病毒感染与空腹血糖、糖化血红蛋白、收缩压、 β -羟丁酸成正相关($P < 0.05$), 与总胆固醇和餐后 2 h C 肽成负相关($P < 0.05$)。Logistic 回归分析结果显示, 总胆固醇和糖化血红蛋白是 2 型糖尿病患者合并新型冠状病毒感染的重要影响因素($P < 0.05$)。结论 空腹血糖、糖化血红蛋白、收缩压、 β -羟丁酸水平升高以及总胆固醇和餐后 2 h C 肽水平降低可能是 2 型糖尿病患者发生新型冠状病毒感染的危险因素, 控制相关因素可减少 2 型糖尿病患者感染新型冠状病毒的风险。

关键词: 2 型糖尿病; 新型冠状病毒感染; 危险因素

中图分类号: R589.1

文献标志码: A

文章编号: 1008-2409(2024)03-0215-06

Analysis of risk factors of COVID-19 infection in patients with type 2 diabetes mellitus

OU Xiang^{1a}, LIU Lisha^{1b}, TANG Shilin², SHAO Huige^{1a}

(1. a. Department of Endocrinology, b. Clinical Laboratory, the Affiliated Changsha Central Hospital, Hengyang Medical School, University of South China, Changsha 410004, China; 2. Department of Intensive Care Unit, the First Affiliated Hospital of University, Hengyang Medical School, University of South China, Hengyang 421001, China)

基金项目: 湖南省自然科学基金项目(2022JJ30535); 湖南省临床医疗技术创新引导项目(2020SK53302、2021SK51820); 湖南省教育厅重点项目(23A0333); 南华大学附属长沙中心医院科研项目(YNKY202304)。

第一作者: 欧翔, 博士, 副主任医师, 研究方向为糖尿病发病机制。

通信作者: 汤石林, 286756823@qq.com; 邵挥戈, shg0568@163.com。

Abstract Objective To investigate the risk factors of corona virus disease 2019 (COVID-19) infection in patients with type 2 diabetes mellitus (T2DM). **Methods** 78 T2DM patients without COVID-19 and 24 T2DM patients with COVID-19 were selected. Age, body mass index, duration of diabetes, systolic blood pressure, diastolic blood pressure, blood lipids, white blood cell count, neutrophil count, fasting glucose, 2 h postprandial glucose, fasting C-peptide, 2 h postprandial C-peptide, glycated hemoglobin, and β -hydroxybutyrate were compared, and the correlations between the above factors and COVID-19 infection were analyzed. **Results** The level of total cholesterol in the infected group was significantly lower than that in the uninfected group. The difference was statistically significant ($P<0.05$). The levels of HbA1c and β -hydroxybutyric acid in T2DM patients with COVID-19 were significantly higher than those in T2DM patients without COVID-19 ($P<0.05$). Spearman correlation analysis showed that COVID-19 infection was positively correlated with fasting glucose, glycated hemoglobin, systolic blood pressure, and β -hydroxybutyrate ($P<0.05$) and COVID-19 infection was negatively correlated with total cholesterol and postprandial 2 h C-peptide ($P<0.05$). Logistic regression analysis revealed that total cholesterol and glycated hemoglobin were important influencing factors of T2DM patients with COVID-19 infection ($P<0.05$). **Conclusion** Elevated fasting glucose, glycated hemoglobin, systolic blood pressure, and β -hydroxybutyrate levels, as well as decreased total cholesterol and 2 h postprandial C-peptide levels, may be risk factors for the infection of COVID-19 in patients with T2DM, and control of related factors can reduce the risk of COVID-19 infection in patients with T2DM.

Keywords: type 2 diabetes mellitus; corona virus disease 2019; risk factor

2型糖尿病(type 2 diabetes mellitus, T2DM)是一种复杂的慢性代谢性疾病,包括胰岛素抵抗引起的高血糖和 β 细胞功能障碍引起的胰岛素分泌不同程度受损^[1],血糖水平持续升高可导致眼睛、血管、心脏、神经和肾脏出现严重并发症^[2-3],T2DM已成为当今最具挑战性的公共卫生问题之一。

新型冠状病毒感染(corona virus disease 2019, COVID-19)是由严重急性呼吸综合征冠状病毒2(SARS-CoV-2)感染引起的疾病^[4],已造成全球破坏性影响^[5-6]。自从出现SARS-CoV-2病毒以来,大量证据表明糖尿病患者COVID-19的发病率和死亡率特别高。糖尿病对COVID-19患者的影响巨大,早期研究^[7]结果显示,近60%的COVID-19危重病人患有糖尿病。在COVID-19相关住院监测网络中,33%的COVID-19住院患者患有糖尿病^[8]。美国关于COVID-19住院患者的大型病例研究^[9]结果表明,糖尿病是5 700例COVID-19住院患者中最常见的合并症之一。一项针对中国7 337例SARS-CoV-2患者的研究^[10]结果表明,T2DM增加了COVID-19住院患者的死亡风险。因此,糖尿病是COVID-19进展为

急性呼吸窘迫综合征(acute respiratory distress syndrome, ARDS)和出现死亡的独立危险因素^[11-13]。

然而,在COVID-19危重监护的定量评估中,糖尿病的严重程度尚未被充分考虑。COVID-19在不同血糖水平的T2DM人群中预后可能有差异^[14]。因此,本文通过对未合并COVID-19的T2DM患者与合并COVID-19的T2DM患者进行比较,探讨T2DM发生COVID-19的危险因素。

1 资料与方法

1.1 一般资料

选取2022年11月1日至2023年1月31日在南华大学衡阳医学院附属长沙中心医院住院的T2DM患者102例。T2DM的诊断主要依据《中国2型糖尿病防治指南(2020年版)》^[15]提出的诊断及分型标准。根据是否感染SARS-CoV-2病毒,将患者分为未感染组78例(男45例,女33例)和感染组24例(男7例,女17例)。本研究获得南华大学衡阳医学院附属长沙中心医院医学伦理委员会批准。

纳入标准:①年龄>18岁;②SARS-CoV-2感染

的诊断标准为所有经实时逆转录聚合酶链反应(RT-PCR)确诊的 SARS-CoV-2 感染阳性病例为感染组,阴性为未感染组。

排除标准:①妊娠妇女;②活动性癌症患者;③有精神障碍病史患者。

1.2 方法

记录两组的性别、年龄和糖尿病病程,检测体质量指数(BMI)、收缩压(SBP)、舒张压(DBP)、总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、白细胞数(WBC)、中性粒细胞数(NEUT)、空腹血糖(FBS)、餐后 2 h 血糖(2 h PG)、空腹 C 肽(FCP)、餐后 2 h C 肽(2 h-CP)、糖化血红蛋白(HbA1c)和 β-羟丁酸(β-OHB)等指标,分析这些因素与 COVID-19 的相关性。

1.3 统计学方法

采用 SPSS 22.0 统计软件进行数据分析。计量资料以($\bar{x} \pm s$)表示,用 *t* 检验。COVID-19 与各变量之间相关性采用 Spearman 相关分析和 Logistic 回归分析。*P*<0.05 表示差异具有统计学意义。

2 结果

2.1 患者基本资料

所有基本资料数据都是在 T2DM 患者入院时获取。比较两组基本资料显示,感染组的 TC 指标低于未感染组,HbA1c 和 β-OHB 指标高于未感染组,差异有统计学意义(*P*<0.05),结果如表 1 所示。

表 1 两组基本资料比较

项目	未感染组	感染组
年龄/岁	62.46±9.763	63.38±13.383
BMI/(kg/m ²)	24.077±3.010	25.196±4.095
病程/年	12.18±5.419	11.75±7.409
SBP/mmHg	138.55±16.111	145.92±15.880
DBP/mmHg	77.35±12.074	78.88±9.719
TG/(mmol/L)	1.998±1.310	1.877±0.793
LDL/(mmol/L)	2.777±0.892	2.454±0.727
HDL/(mmol/L)	1.071±0.323	0.961±0.238
TC/(mmol/L)	4.435±1.094	3.886±0.801*
WBC/(×10 ⁹ 个/L)	6.445±1.748	6.780±2.462

续表

项目	未感染组	感染组
NEUT/(×10 ⁹ 个/L)	4.097±1.625	5.137±2.468
FBS/(mmol/L)	7.196±2.582	8.280±2.944
2 h PG/(mmol/L)	12.110±4.957	12.369±4.666
FCP/(nmol/L)	0.514±0.487	0.354±0.422
2 h-CP/(nmol/L)	1.186±0.778	0.947±1.025
HbA1c/%	9.277±1.965	10.963±2.936*
β-OHB/(mmol/L)	0.136±0.174	1.217±2.528*

注:与未感染组比较,**P*<0.05。

2.2 SARS-CoV-2 病毒感染与 T2DM 各项目指标的相关性分析

Spearman 相关性分析结果显示,SARS-CoV-2 病毒感染与 TC 和 2 h-CP 成负相关(*P*<0.05),与 FBS、HbA1c、SBP、β-OHB 成正相关(*P*<0.05),结果如表 2 所示。

表 2 COVID-19 感染与 T2DM 各项目指标的 Spearman 相关性分析

项目	<i>r</i>	<i>P</i>
年龄	0.110	0.271
BMI	0.083	0.406
病程	-0.051	0.610
TG	0.030	0.766
LDL	-0.157	0.116
HDL	-0.128	0.200
TC	-0.236	0.017
WBC	0.060	0.546
NEUT	0.166	0.096
FBS	0.205	0.038
2 h PG	0.035	0.730
FCP	-0.074	0.459
2 h-CP	-0.227	0.022
HbA1c	0.250	0.011
SBP	0.205	0.038
DBP	0.083	0.407
β-OHB	0.235	0.017

注:*r*>0 表示正相关,*r*<0 表示负相关。

2.3 SARS-CoV-2 病毒感染影响因素的 logistic 回归分析

为进一步探讨 SARS-CoV-2 病毒感染的影响因素,以 T2DM 患者合并 SARS-CoV-2 病毒感染为因变量,以血脂、FBS、2 h-CP、HbA1c、SBP 和 β -OHB 等因

素为自变量,对两组数据进行 Logistic 回归分析。结果显示,TC 水平降低和 HbA1c 水平升高是 T2DM 患者发生 SARS-CoV-2 感染的重要危险因素 ($P < 0.05$),结果如表 3 所示。

表 3 T2DM 患者 COVID-19 影响因素的 Logistic 回归分析结果

影响因素	非标准化回归系数 B	标准误差	标准化回归系数 β	t	P
TC	-0.446	0.209	-1.104	-2.132	0.036
HbA1c	0.049	0.024	0.267	2.072	0.041

3 讨论

SARS-CoV-2 病毒感染是一个全球性健康问题^[16]。COVID-19 是一种由 SARS-CoV-2 及其变异体引起的新型快速变化性疾病,其相关危险因素尚不明确。大多数 COVID-19 患者无需特殊治疗即可康复,但老年人和患有心血管疾病、糖尿病、慢性呼吸道疾病和癌症等疾病的患者被归类为高危人群,他们更容易出现感染性休克、ARDS、电解质失衡和凝血障碍,甚至死亡^[17-19]。

高达 50% 的 COVID-19 死亡发生在代谢和血管疾病的个体中,这表明 SARS-CoV-2 感染与代谢内分泌系统变化有直接的联系^[20]。不仅 COVID-19 可能导致糖尿病病情或已有代谢紊乱加重,甚至出现糖尿病的严重代谢并发症^[20-21],而且糖尿病会增加发展为严重 COVID-19 的风险^[22]。然而,T2DM 与 SARS-CoV-2 病毒感染关联背后的机制尚不清楚^[23]。

T2DM 是一种慢性疾病,T2DM 患者发生 COVID-19 并发症如 ARDS、败血性休克和多器官功能障碍综合征风险增加,死亡风险也较高^[11,24]。本研究结果显示,T2DM 发生 SARS-CoV-2 感染与 FBS、HbA1c、SBP 和 β -OHB 呈正相关。

糖尿病患者易于发生感染,糖尿病是 COVID-19 死亡率和发病率的主要预测因素^[25]。糖尿病会显著增加 SARS-CoV-2 感染的严重程度和死亡风险^[26],与血糖控制良好的患者(血糖 < 180 mg/dL 或 < 10 mmol/L)相比,控制不佳的糖尿病(血糖 > 180 mg/dL 或 > 10 mmol/L)发生严重 COVID-19 的风险和死亡率更高^[27],表明血糖水平与 T2DM 患者

COVID-19 的严重程度相关。HbA1c 水平升高则表示近期糖尿病患者血糖控制不佳。T2DM 患者的 HbA1c 值 $\geq 8\%$ 与 COVID-19 的严重程度相关^[28]。8% 的 HbA1c 是 COVID-19 患者插管或死亡的严重危险因素^[29],HbA1c $\geq 9\%$ 的糖尿病患者住院风险显著增加^[30]。血糖控制不佳的糖尿病患者肺血管组织的慢性低度炎症和微血管病变,肺功能显著降低,损害肺结缔组织代谢,并导致基底膜和肺泡上皮增厚^[31],这些糖尿病患者引起 COVID-19 感染易感性增加和感染加重,其潜在机制可能与血糖升高对 SARS-CoV-2 复制、有害的免疫和炎症反应增强、高凝状态以及肾素-血管紧张素-醛固酮系统激活的直接影响有关^[19]。因此,长期血糖水平的适当管理对于降低 SARS-CoV-2 引起严重疾病的风险至关重要^[14]。

糖尿病性酮症酸中毒与 COVID-19 的严重程度密切相关,但需要进一步研究这种关系的潜在机制^[32]。SARS-CoV-2 感染在有潜在严重疾病如高血压的个体中更易发生,COVID-19 患者中有 15% 合并高血压^[33]。与糖尿病及心血管并发症相关的其他合并症也是 COVID-19 不良后果的潜在危险因素^[34]。本研究结果显示,T2DM 患者的 SBP 与 COVID-19 有主要关联,高血压与 COVID-19 患者死亡、ARDS、入住 ICU 和疾病进展的风险较高有关^[35]。SARS-CoV-2 感染与 TC 成负相关,可能与 SARS-CoV-2 感染后引起胆固醇合成减少及消耗增多有关。

4 结束语

本研究探讨了T2DM患者合并COVID-19的危险因素,为感染SARS-CoV-2的T2DM患者血糖管理提供了参考。COVID-19可能使糖尿病患者的血糖控制变得困难,T2DM和COVID-19之间的复杂相互作用使患者出现ARDS等并发症和最终死亡的风险增高,有效控制相关危险因素可减少T2DM患者感染SARS-CoV-2的风险。

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- [收稿日期:2024-04-07]
- [责任编辑:桂根浩,李佳睿 英文编辑:周寿红]