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老年 2 型糖尿病患者血清促甲状腺激素水平及其与冠脉病变程度的相关性分析

周熙琳¹ 顾海磊¹ 窦存芳¹ 梁 辉¹ 石 群^{2Δ}

(1 上海交通大学医学院附属新华医院崇明分院 老年科 上海 202150;

2 上海交通大学医学院附属新华医院崇明分院内分泌科 上海 202150)

摘要 目的:探讨老年 2 型糖尿病(T2DM)患者血清促甲状腺激素(TSH)水平及其与患者冠脉病变程度的相关性。**方法:**回顾性分析 2015 年 6 月~2017 年 6 月我院收治的 88 例老年 T2DM 患者(T2DM 组)、50 例健康体检者(对照组)的临床资料,根据血清 TSH 水平将 T2DM 组分为四个亚组,A 组(0.45~1.49 mIU/L,n=18)、B 组(1.50~2.49 mIU/L,n=23)、C 组(2.50~3.49 mIU/L,n=22)、D 组($\geq$ 4.5 mIU/L,n=25)。比较 T2DM 组与对照组 TSH 水平的差异,并根据计算机断层血管造影(CTA)结果计算 Gensini 评分,分析 Gensini 评分与血清 TSH 水平的关系。**结果:**T2DM 组血清 TSH 水平显著高于对照组,且随着血清 TSH 水平的升高,T2DM 患者的年龄、TC、TG、LDL-C 明显增加,而 HDL-C、T3 明显降低($P<0.05$)。C 组病变支数显著多于 A 组,重度病变的比例明显升高,而 D 组病变支数、病变程度与 A 组、B 组、C 组比较差异均有统计学意义($P<0.05$)。血清 TSH 水平与 Gensini 评分呈显著正相关($r=0.577, P<0.05$)。**结论:**老年 T2DM 患者血清 TSH 水平显著升高,且与患者冠脉病变严重程度呈显著正相关,血清 TSH 水平有助于评估老年 T2DM 患者冠脉病变的严重程度。

关键词:2 型糖尿病;老年;促甲状腺激素;冠脉病变;相关性**中图分类号:**R587.2;R541.4 **文献标识码:**A **文章编号:**1673-6273(2018)23-4482-04

Serum Thyroid Stimulating Hormone Level in Elderly Patients with Type 2 Diabetes and Its Correlation with the Severity of Coronary Artery Disease

ZHOU Xi-lin¹, GU Hai-lei¹, DOU Cun-fang¹, LIANG Hui¹, SHI Qun^{2Δ}

(1 Department of Geriatrics, Congming Branch of Xinhua Hospital Affiliated to the Medical School of Shanghai Jiaotong University, Shanghai, 202150, China; 2 Department of Endocrinology, Congming Branch of Xinhua Hospital Affiliated to the Medical School of Shanghai Jiaotong University, Shanghai, 202150, China)

ABSTRACT Objective: To explore the serum thyroid stimulating hormone level in elderly patients with type 2 diabetes(T2DM), and analyze its correlation with the severity of coronary artery disease. **Methods:** The clinical data of 88 cases of elderly patients with T2DM (T2DM group) and 50 cases of healthy control (control group) who admitted in our hospital from June 2015 to June 2017 were retrospectively analyzed. All the patients in T2DM group were assigned into 4 subgroups according to serum TSH levels: Group A (0.45-1.49 mIU/L), B (1.50-2.49 mIU/L), C (2.50-3.49 mIU/L), D (3.50-4.49 mIU/L). The change of serum level of TSH was compared between T2DM group and control group, and the Gensini score was calculated according to the results of computed tomography angiography (CTA), the correlation between Gensini score and serum TSH level was analyzed. **Results:** The serum TSH level in T2DM group was significantly higher than that of the control group, with the increase of serum TSH level, the age, TC, TG, LDL-C levels in T2DM patients were significantly increased, and HDL-C, T3 levels were obviously decreased ($P<0.05$). The number of diseased coronary vessels of group C was significantly more than that in group A, the proportion of severe lesion was significantly increased, and there was significantly difference on the number of diseased coronary vessels, lesion degree in group D compared with group A, group B and group C ($P<0.05$). The level of serum TSH was significantly positive correlated with the Gensini score ($r=0.577, P<0.05$). **Conclusions:** The serum TSH level of elderly patients with T2DM remarkably rised, and it was closely related to the severity of coronary artery lesions. Serum TSH level can contribute to assess the severity of coronary artery lesions in elderly patients with T2DM.

Key words: Type 2 diabetes mellitus; Elderly; Thyroid stimulating hormone; Coronary artery disease; Correlation**Chinese Library Classification(CLC):** R587.2; R541.4 **Document code:** A**Article ID:** 1673-6273(2018)23-4482-04

前言

作者简介:周熙琳(1972-),女,硕士,副主任医师,
E-mail: spots618@163.com

Δ 通讯作者:石群,主任医师,E-mail: shiqun10@yeah.net

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2 型糖尿病(T2DM)多见于中老年人群,大血管并发症已成为其主要的死亡原因。研究已证实年龄是其发生冠状动脉病变的独立危险因素^[1,2],且甲状腺疾病与冠脉病变等心血管疾病存在密切联系,临床或亚临床甲状腺功能异常患者可能导致心血管疾病的恶化,增加冠心病、心血管死亡等发病风险^[3-5]。老年

T2DM 患者的甲状腺功能异常的发生率约为 27.4%,占 T2DM 甲功异常患者的 60%左右^[6-8]。促甲状腺激素(TSH)广泛参与率机体的物质代谢,且对心血管系统具有一定的调节作用,但关于 TSH 与老年 T2DM 合并冠脉病变的关系尚缺乏足够证据^[9-12]。因此,本研究主要检测了老年 T2DM 患者血清 TSH 水平的变化,并分析了其与患者冠脉病变程度的相关性,旨在为老年 T2DM 患者冠脉病变的早期防治提供参考依据。

1 资料与方法

1.1 一般资料

入组标准:①符合 2007 美国糖尿病协会(ADA)制定的 T2DM 诊断标准^[13];②年龄 ≥ 60 岁,近 6 个月内未服用甲状腺激素或抗甲状腺药物;③排除甲状腺病史或手术史、吸烟史、酮症酸中毒等严重并发症,排除心肝肺等器官严重功能障碍。最终选择 2015 年 6 月~2017 年 6 月我院内分泌科收治的老年 T2DM 患者中符合上述标准的病例共 88 例(T2DM 组)。其中,男 55 例,女 33 例;年龄 $37\sim 76(54.8\pm 4.9)$ 岁;病程 $1\sim 11(5.6\pm 2.8)$ 年;体质量指数(BMI) $21.7\sim 28.5(24.1\pm 1.9)\text{kg/m}^2$ 。同时选择本院体检科的健康体检者 50 例(对照组),包括男 25 例,女 25 例;年龄 $40\sim 75(53.1\pm 4.7)$ 岁。两组性别、年龄等基本资料比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 分组

根据血清 TSH 水平^[14],由低至高将 T2DM 组分为四亚组:A 组($0.45\sim 1.49\text{ mIU/L}$, $n=18$)、B 组($1.50\sim 2.49\text{ mIU/L}$, $n=23$)、C 组($2.50\sim 3.49\text{ mIU/L}$, $n=22$)、D 组($\geq 4.5\text{ mIU/L}$, $n=25$)。

1.3 观察指标

1.3.1 生化指标及血清 TSH 测定 T2DM 患者均抽取早晨空腹静脉血 4 mL,置于含 2%乙二胺四乙酸的试管中,3 000 r/min 离心 5-10 min,保留血清并保存于 $-70\text{ }^{\circ}\text{C}$ 冰箱中备检。选择

HITACHI 7600 型全自动生化分析仪测定空腹血糖(FBG)、总胆固醇(TC)、三酰甘油(TG)、高密度脂蛋白(HDL-C)、低密度脂蛋白(LDL-C)等各项指标,同时选择 Elecsys 2010 型全自动化学发光免疫分析仪,采用电化学发光法测定血清三碘甲状腺原氨酸(T3)、甲状腺素(T4)及 TSH 水平。所有实验操作严格按说明书要求,其中血清 TSH 的正常值范围为 $0.45\sim 4.5\text{ mIU/L}$ ^[15]。

1.3.2 冠脉病变程度评估 采用 64 层螺旋 CT 进行计算机断层血管造影(CTA),并采用 Gensini 评分定量评定各冠脉血管病变狭窄程度以最严重处为标准,1 分:狭窄直径 $<25\%$,2 分: $\geq 25\%$,4 分: $\geq 50\%$,8 分: $\geq 75\%$,16 分: $\geq 90\%$,32 分: $\geq 99\%$ 。根据病变部位乘以相应系数得到最后评分,左主干 $\times 5$,左前降支近端 $\times 2.5$ 、中段 $\times 1.5$ 、远段 $\times 1$,左回旋支近端 $\times 2.5$ 、中远段 $\times 1$,后降支 $\times 1$,后侧支 $\times 0.5$ 。

1.4 统计学方法

采用 SPSS 18.0 版统计软件包进行统计分析,计量资料以($\bar{x}\pm s$)表示,多组间比较采用单因素方差分析,组间两两比较采用 LSD-t 检验,计数资料以例数表示,组间比较采用 χ^2 检验,Pearson 线性相关性分析血清 TSH 水平与 Gensini 评分的相关性,以 $P<0.05$ 视为差异有统计学意义。

2 结果

2.1 T2DM 组和对照组血清 TSH 水平的比较

T2DM 组血清 TSH 水平为(2.3 ± 0.8)mIU/L,显著高于对照组[(1.1 ± 0.3)mIU/L],差异有统计学意义($P<0.05$)。

2.2 T2DM 各亚组患者基本资料的比较

T2DM 各组性别、T2DM 病程、BMI、FBG、HbA1c 及 T4 比较差异均无统计学意义($P>0.05$)。随着血清 TSH 水平的升高,T2DM 患者的年龄、TC、TG、LDL-C 明显增加,而 HDL-C、T3 明显降低,差异均有统计学意义($P<0.05$)。见表 1。

表 1 T2DM 各组患者基本资料的比较

Table 1 Comparison of the baseline information between different groups of T2DM

Group	Group A(n=18)	Group B(n=23)	Group C (n=22)	Group D(n=25)
Age	53.1 $\pm$ 4.7	54.6 $\pm$ 5.1	56.9 $\pm$ 5.3 ^a	57.1 $\pm$ 4.9 ^{ab}
Gender(male/female)	11/7	13/10	16/6	15/10
Course of T2DM(year)	5.4 $\pm$ 2.6	5.8 $\pm$ 2.7	5.6 $\pm$ 2.7	5.7 $\pm$ 2.9
BMI(kg/m ²)	24.3 $\pm$ 1.5	24.9 $\pm$ 2.1	25.0 $\pm$ 1.8	24.4 $\pm$ 1.7
TC(mmol/L)	4.1 $\pm$ 0.5	4.2 $\pm$ 0.6	4.2 $\pm$ 0.5	4.5 $\pm$ 0.6 ^{abc}
TG(mmol/L)	1.7 $\pm$ 0.5	1.8 $\pm$ 0.6	1.8 $\pm$ 0.4	2.1 $\pm$ 0.5 ^{abc}
LDL-C(mmol/L)	3.3 $\pm$ 0.8	3.3 $\pm$ 0.7	3.7 $\pm$ 0.7 ^{ab}	3.8 $\pm$ 0.7 ^{ab}
HDL-C(mmol/L)	1.2 $\pm$ 0.4	1.2 $\pm$ 0.5	1.0 $\pm$ 0.4	0.9 $\pm$ 0.3 ^{ab}
FBG(mmol/L)	9.1 $\pm$ 1.4	9.2 $\pm$ 1.3	9.1 $\pm$ 1.7	9.2 $\pm$ 1.6
HbA1c(mmol/L)	8.9 $\pm$ 0.8	9.0 $\pm$ 0.9	9.1 $\pm$ 1.0	9.0 $\pm$ 0.8
T3(mmol/L)	2.6 $\pm$ 0.6	2.5 $\pm$ 0.5	2.3 $\pm$ 0.4 ^a	2.3 $\pm$ 0.3 ^a
T4(mmol/L)	112.9 $\pm$ 17.5	110.7 $\pm$ 17.6	108.9 $\pm$ 15.5	105.6 $\pm$ 16.4
TSH (mIU/L)	0.8 $\pm$ 0.2	1.7 $\pm$ 0.5	2.7 $\pm$ 0.9 ^{ab}	3.9 $\pm$ 1.2 ^{abc}

注:与 A 组比较,^a $P<0.05$;与 B 组比较,^b $P<0.05$;与 C 组比较,^c $P<0.05$ 。

Note: Compared with Group A ^a $P<0.05$; Compared with Group B ^b $P<0.05$; Compared with Group C ^c $P<0.05$.

2.3 T2DM 各亚组患者冠脉病变程度的比较

各组冠脉病变程度比较差异有统计学意义 ($P<0.05$), C 组病变支数显著多于 A 组, 重度病变的比例明显升高, 而 D 组病

变支数、病变程度与 A 组、B 组、C 组比较均显著升高, 差异均有统计学意义 ($P<0.05$), 见表 2。

表 2 各组 T2DM 患者冠脉病变程度的比较[例(%)]

Table 2 Comparison of the severity of coronary lesions between different groups of T2DM[n(%)]

Group	N	Number of diseased vessels		Severity of lesions	
		Single	multi	mild and moderate	Severe
Group A	18	16	2	15	3
Group B	23	17	6	18	5
Group C	22	15	7	14	8
Group D	25	8	17	6	19
P		<0.05		<0.05	

2.4 T2DM 患者血清 TSH 水平与 Gensini 评分的相关性

Pearson 相关性分析结果显示: 血清 TSH 水平与 T2DM 患者 Gensini 评分呈显著正相关 ($r=0.577, P<0.05$)。

3 讨论

近年来研究表明甲状腺功能异常也可能影响心血管疾病的发生、发展过程^[16-18]。国外研究显示在未合并 T2DM 及冠心病的人群中, 正常范围内的 TSH 水平与心血管死亡相关, 但在 T2DM 患者中是否存在该相关性仍未达成一致意见^[20-22]。老年 T2DM 患者随着病情的发展, 不仅会影响眼、血管、肾脏等器官功能, 还会对下丘脑 - 垂体甲状腺轴的调节产生影响, 进而导致胰岛素及多种相关激素分泌异常, 进而直接或间接影响甲状腺功能。T2DM 患者的甲状腺功能异常多为亚临床功能异常, 即 TSH 水平升高, 而 T₃、T₄ 水平在正常范围, 其中 TSH 作为腺垂体分泌的促进甲状腺生长与增强机能的激素, 异常升高也可加重糖、蛋白质、脂质三大代谢功能紊乱, 血流动力学异常, 并增加心血管疾病的发病风险^[23,24]。

TSH 水平升高主要通过影响血脂代谢、炎症反应、血管内皮功能、凝血及纤溶系统等多方面因素导致冠脉病变的发生和发展。本研究结果显示: T2DM 组血清 TSH 水平显著高于对照组, 且随着血清 TSH 水平的升高, T2DM 患者的 TC、TG、LDL-C 明显增加, 而 HDL-C 明显降低, 与 Onat 等^[25]研究结果一致, 说明 TSH 水平与血脂谱之间存在密切关系。有报道称胆固醇酯转移是冠脉病变的重要环节之一, 表现为 HDL-C 向 LDL-C 内源性转移, 而老年 T2DM 患者高水平的 TSH 可增强该转移过程^[26,27]。因此, 我们推测即使血清 TSH 水平在正常范围内, 随着 TSH 的升高, 也将对血脂水平造成不利影响。此外, 研究中 T2DM 患者年龄越大, 血清 TSH 水平也越高, 提示对于老年 T2DM 患者应加强对 TSH 水平监测, 预防心血管疾病的发生^[28,29]。

本研究结果显示不同 TSH 水平患者的冠脉病变程度存在明显差异, 其中 C 组病变支数显著多于 A 组, 重度病变的比例明显升高, 而 D 组无论在病变支数还是病变程度方面均显著高于 A 组、B 组、C 组, 相关性分析显示血清 TSH 水平与 Gensini 评分呈显著正相关。这些结果说明随着血清 TSH 水平

的增高, T2DM 患者冠脉的病变程度相应增加, 该指标可作为冠脉病变的一个良好预测指标。临床上对于 TSH 异常升高尤其是超过正常值范围的 T2DM 患者, 应定期复查甲状腺功能, 必要时给予抗甲减药物治疗。盍红成等^[30]研究结果显示正常范围内的 TSH 水平升高可能与 T2DM 患者的冠脉事件发生率呈正相关, 但与房颤及心源性死亡无明显相关。

综上所述, 老年 T2DM 患者血清 TSH 水平显著升高, 且与患者冠脉病变严重程度呈显著正相关, 血清 TSH 水平有助于评估老年 T2DM 患者冠脉病变的严重程度。但本研究样本量较少, 所得结果可能存在一定偏倚和局限性, TSH 对冠脉病变的影响仍有待于更大样本的多中心研究予以证实。

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