

· 综述 · doi:10.3969/j.issn.1671-8348.2021.16.028

网络首发 <https://kns.cnki.net/kcms/detail/50.1097.R.20210526.1536.017.html>(2021-05-26)

## 2 型糖尿病患者身体成分改变与心脑血管疾病风险关系的研究进展<sup>\*</sup>

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**[摘要]** 2型糖尿病(T2DM)患病率逐年上升,已成为影响人群身心健康第三大慢性非传染性疾病。T2DM 可增加发生冠心病、脑梗死等心脑血管疾病的风险。T2DM 患者身体成分发生改变,主要表现为内脏脂肪增多、骨密度减低等,而肥胖及内脏脂肪增多与心脑血管疾病的发生密切相关。T2DM 患者身体成分的改变可能与心脑血管疾病风险存在相关性。本文就 T2DM 患者身体成分改变与心脑血管疾病风险升高的相关性进行综述,为今后的研究提供方向。

**[关键词]** 糖尿病, 2型; 身体成分; 肥胖; 内脏脂肪; 心血管疾病; 脑血管疾病

**[中图法分类号]** R587.2      **[文献标识码]** A      **[文章编号]** 1671-8348(2021)16-2831-04

### Research progress on relationship between changes in body compositions and risk of cardio-cerebrovascular diseases in patients with type 2 diabetes mellitus<sup>\*</sup>

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**[Abstract]** The prevalence rate of type 2 diabetes mellitus (T2DM) is increasing year by year, and T2DM has become the third major chronic non-communicable disease affecting people's physical and mental health. T2DM can increase the risk of cardio-cerebrovascular diseases such as coronary heart disease and cerebral infarction. The body composition changes in T2DM patients, which are mainly manifested as visceral fat increase, bone mineral density decrease, etc. Obesity and increased visceral fat are closely related to the occurrence of cardio-cerebrovascular diseases. The changes of body compositions in patients with T2DM may be correlated with the risk of cardio-cerebrovascular diseases. This paper reviewed the correlations between the changes in body compositions and increased risk of cardio-cerebrovascular diseases in patients with T2DM to provide the directions for future researches.

**[Key words]** diabetes mellitus, type 2 ; body composition; obesity; internal fat; cardiovascular diseases; cerebrovascular disease

随着社会经济的发展、人们生活方式的改变,肥胖人口增多,加之人口老龄化加剧,糖尿病已成为影响全球人群健康的主要慢性非传染性疾病之一。我国糖尿病(diabetes mellitus, DM)患病率呈逐年上升趋势,目前已成为继心血管疾病(cardiovascular disease, CVD)和肿瘤之后第 3 位威胁居民健康和生命的疾病<sup>[1]</sup>,造成沉重的健康和经济负担,其患者以 2 型糖尿病(type 2 diabetes mellitus, T2DM)为主。目前 T2DM 的发病趋势不容乐观,是全球范围内发病率增长最快的疾病之一,已成为全球性流行性疾病,是

成年患者致死、致残的主要原因。

### 1 T2DM 患者心脑血管疾病风险增加

DM 可能引起血管病变、神经病变等多种并发症,其中血管病变是 DM 引起的最严重的并发症,包括微血管并发症和大血管并发症<sup>[2]</sup>,而冠心病、脑血管疾病及周围血管疾病等大血管并发症是导致 DM 患者死亡、残疾的主要病因<sup>[3]</sup>。研究显示, T2DM 明显增加过早死亡的风险,而 CVD 是其中最为常见的死亡原因<sup>[4]</sup>。在弗雷明汉心脏研究中显示,CVD 患者的 DM 和肥胖症患病率显著增加,由 DM 引起的

\* 基金项目:国家自然科学基金项目(81670755)。作者简介:杨丽娜(1987—),主治医师,硕士,主要从事内分泌代谢性疾病研究。

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CVD 患者比例明显增加,超过 60% 的 T2DM 患者死于 CVD,其中主要是心肌梗死(myocardial infarct, MI)或中风<sup>[5]</sup>。研究证实,T2DM 的患者较非 DM 患者具有更高的患 CVD 的风险,因此 T2DM 患者 CVD 的预防尤为重要。早期识别可能发生心血管事件的高风险人群,并针对该部分人群进行早期干预及治疗成了一种新策略。

## 2 肥胖、内脏脂肪及骨密度与 CVD 发生风险的相关性

### 2.1 体重指数(BMI)与 CVD 的相关性

动脉粥样硬化是心脑血管疾病发生的重要危险因素,研究报道 BMI 增加可明显增加动脉粥样硬化发生的风险<sup>[6]</sup>,也有研究强调了肥胖青年 CVD 发生风险的增加,以及早期干预治疗肥胖和动脉粥样硬化的必要性<sup>[7]</sup>。由此可见,BMI 的增加与心脑血管疾病风险增加具有显著相关性。同时,也有大型前瞻性研究调查了肥胖与 CVD 死亡之间的关系,根据荟萃分析结果提示在  $BMI > 25 \text{ kg/m}^2$  的人群中,BMI 每增加  $5 \text{ kg/m}^2$ ,病死率增加 40%<sup>[8-9]</sup>。另有研究显示,较高的 BMI 与 CVD 及更高的病死率有独立相关性,其中内脏脂肪组织(visceral adipose tissue, VAT)和心包脂肪组织(pericardial adipose tissue, PAT)的增加似乎带来了最大的风险<sup>[10-11]</sup>。

### 2.2 肥胖与 CVD 的相关性

已有大量文献报道,脂肪分布及全身肥胖与 DM 和 CVD 的发生风险有着重要联系,并且可能在疾病发展中起着因果作用<sup>[12-15]</sup>。一项针对成人的队列研究显示,肥胖是引起冠状动脉疾病的危险因素,且这种相关性明显独立于其他临床常见危险因素<sup>[16]</sup>。LOGUE 等<sup>[17]</sup>证实,在调整了经典的心血管风险因素、贫穷和药物等混杂因素后,肥胖明显增加致命性冠心病事件的发生风险。此外,研究证实肥胖可导致许多代谢紊乱性疾病,包括高血压、DM、血脂异常及动脉粥样硬化等,同时也增加 CVD 的患病风险,其中又以腹部脂肪的积累危害更大<sup>[18]</sup>。

### 2.3 VAT 与 CVD 的相关性

BACCHI 等<sup>[19]</sup>发现,在 T2DM 患者中,有氧运动的氧消耗能力可以由矢状腹径、骨骼肌脂肪含量和高密度脂蛋白胆固醇(HDL-C)预测,表明这些指标可能是这类人群心肺功能的影响因素。同时,心肺功能的下降与 CVD 发生风险增加有关<sup>[20]</sup>。在 DM 和非 DM 的日裔美国人研究中,内脏脂肪、血压、血浆葡萄糖都是冠心病的独立危险因素<sup>[21]</sup>。有研究表明,相较于整体肥胖,腹部脂肪分布可能是慢性心力衰竭的一个更强的风险因素<sup>[22]</sup>。可见,腹部内脏脂肪堆积在 CVD 的发展中起着重要作用,VAT 是评估 CVD 风险的重要指标。

### 2.4 骨密度与 CVD 的相关性

多项研究表明,骨密度与区域脂肪库存存在明显的

相关性<sup>[23-26]</sup>。亦有研究表明,低骨密度与冠心病的发展有关<sup>[27-30]</sup>。在韩国的一项研究中发现,在健康男性人群中,骨密度与 10 年冠心病风险有显著的相关性<sup>[31]</sup>,表明骨密度的测量有助于识别可能会增加冠心病风险的个体,特别是在骨密度低的男性患者中,探索冠心病和低骨密度的常见危险因素是很有必要的。

### 3 T2DM 患者身体成分的改变

T2DM 患者与健康人相比具有较少的总体脂肪、腿部脂肪和腿部肌肉,但有更多的躯干脂肪和肌肉,表明 DM 患者的身体成分发生改变,这些改变可能带来一定的病理、生理、代谢的改变<sup>[32]</sup>。多项研究观察到 T2DM 患者存在腹部脂肪堆积<sup>[33-34]</sup>。同时,T2DM 合并肥胖的男性患者骨密度下降,其腹部的 VAT 越高,骨密度越低<sup>[35]</sup>。T2DM 患者的体脂分布存在异常,血清瘦素水平明显升高,进而通过不同机制导致颈动脉内膜中膜复合体厚度升高,最终导致动脉粥样硬化的发生和发展<sup>[36]</sup>。

## 4 肥胖引起 CVD 发生风险升高的机制

### 4.1 脂肪组织与炎症

HOTAMISLIGIL 等<sup>[37]</sup>报道了肥胖与炎症之间的关系,并表明肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )在脂肪组织中表达增加,并具有诱发胰岛素抵抗(insulin resistance, IR)的能力。目前,脂肪组织已被确认为许多激素和细胞因子的重要来源,包括 TNF- $\alpha$ 、白细胞介素-6(IL-6)和单核细胞趋化因子蛋白-1(MCP-1)<sup>[38]</sup>。脂肪组织能释放多种促炎细胞因子<sup>[39]</sup>,因此肥胖是一种炎症状态<sup>[40]</sup>,这是肥胖另一种可能导致心血管风险升高的生物学效应。流行病学研究表明,在肥胖患者中,C 反应蛋白、IL-6 和 TNF- $\alpha$  等炎性标记物的增加与 T2DM 和 CVD 的发生风险具有较强的相关性<sup>[41]</sup>。一项针对多种族 T2DM 人群的大型研究也发现,脂肪组织分布异常是导致系统性炎症的重要决定因素<sup>[42]</sup>。

### 4.2 脂肪组织与 IR

肥胖与 IR 关系密切,而 IR 又是导致 T2DM 和 CVD 的重要因素。有学者进一步研究了脂肪分布与 IR 的相关性,发现相较于皮下脂肪,T2DM 患者的内脏脂肪才是导致 IR 的重要因素<sup>[43]</sup>。由于不同部位脂肪组织的代谢特点不同,其与 IR 的相关性也存在差异。尽管 VAT 在人体总脂肪中占比较小,但具有更强的内分泌代谢活性,能分解产生更多的游离脂肪酸,分泌更多的细胞因子(如瘦素、IL-6、TNF- $\alpha$ 、MCP-1 等),进一步增加 IR 的风险<sup>[44-45]</sup>。研究证实,VAT 与慢性低度炎症、IR、T2DM、血脂异常、高血压等导致动脉粥样硬化的重要因素密切相关,因此增加了肥胖症患者发生 CVD 的风险<sup>[46]</sup>。

综上所述,人体总脂肪与 DM、IR 等 CVD 的危险因素相关,且 VAT 与 CVD 的相关性更明确。T2DM 患者身体成分发生改变,骨密度的减少与 VAT 的增加可能使 T2DM 患者 CVD 的发生风险增加。然而,

目前国内外有关 T2DM 患者身体成分与 CVD 风险性的研究尚少,需要更多相关研究来阐明这二者之间的相关性,以对今后 T2DM 的治疗及并发症的预防提供方向。

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(收稿日期:2020-11-22 修回日期:2021-03-11)

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(收稿日期:2020-12-28 修回日期:2021-05-15)