

^{18}F -FDG PET/CT在肥胖中的应用进展

Application and progress of ^{18}F -FDG PET/CT in obesity

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引用本文:

李肖萌, 胡奕奕, 崔曹哲, 等. ^{18}F -FDG PET/CT在肥胖中的应用进展[J]. 国际放射医学核医学杂志, 2022, 46(6): 360-363. DOI: 10.3760/cma.j.cn121381-202202018-00184

Li Xiaomeng, Hu Yiyi, Cui Caozhe, et al. Application and progress of ^{18}F -FDG PET/CT in obesity[J]. *International Journal of Radiation Medicine and Nuclear Medicine*, 2022, 46(6): 360-363. DOI: 10.3760/cma.j.cn121381-202202018-00184

在线阅读 View online: <https://doi.org/10.3760/cma.j.cn121381-202202018-00184>

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国际放射医学核医学杂志. 2021, 45(5): 313-318 <https://doi.org/10.3760/cma.j.cn121381-202004037-00033>

^{18}F -FDG PET/CT 在肥胖中的应用进展

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【摘要】 肥胖已成为一种严重危害人类健康的重要问题, 其与心血管疾病、代谢性疾病和恶性肿瘤等密切相关。评估肥胖最常用的指标为体重指数、腰围和腰臀比等, 但随着对肥胖发病机制的深入研究, 不同部位及类型的脂肪组织得以区分。人体内的脂肪组织分为白色脂肪组织(WAT)和棕色脂肪组织(BAT)2种类型。WAT的过度积累是肥胖的特征, 而BAT在肥胖者中活性较低。 ^{18}F -FDG PET/CT可以同时获取不同部位及类型脂肪组织的体积和代谢情况。笔者从不同脂肪库的角度综述 ^{18}F -FDG PET/CT在肥胖中的应用进展。

【关键词】 肥胖症; 氟脱氧葡萄糖 F18; 正电子发射断层显像术; 体层摄影术, X线计算机
基金项目: 国家自然科学基金(81971655)

DOI: [10.3760/cma.j.cn121381-202202018-00184](https://doi.org/10.3760/cma.j.cn121381-202202018-00184)

Application and progress of ^{18}F -FDG PET/CT in obesity

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【Abstract】 Obesity has become an important problem that seriously endangers human health, which is closely related to cardiovascular diseases, metabolic diseases, and malignant tumors. The most commonly used indicators to assess obesity are body mass index, waist circumference, waist-to-hip ratio and so on. However, with the in-depth research on the pathogenesis of obesity, different parts and types of adipose tissue can be distinguished. There are two types of adipose tissue in the human body: white adipose tissue (WAT) and brown adipose tissue (BAT). Excessive accumulation of WAT is characteristic of obesity, while BAT is less active in obese individuals. ^{18}F -FDG PET/CT can simultaneously acquire the volume and metabolism of different parts and types of adipose tissue. The authors review the application and progress of ^{18}F -FDG PET/CT in obesity from the perspective of different adipose depots.

【Key words】 Obesity; Fluorodeoxyglucose F18; Positron-emission tomography; Tomography, X-ray computed

Fund program: National Natural Science Foundation of China (81971655)

DOI: [10.3760/cma.j.cn121381-202202018-00184](https://doi.org/10.3760/cma.j.cn121381-202202018-00184)

世界卫生组织将肥胖定义为可能损害人体健康的过度脂肪积累, 体重指数(body mass index, BMI) $\geq 30 \text{ kg/m}^2$ ^[1], 中国人的肥胖标准为 BMI $> 28 \text{ kg/m}^2$ ^[2]。肥胖增加了心血管疾病、代谢性疾病和恶性肿瘤等疾病的发生风险^[3]。Lauby-Secretan 等^[4]的研究结果显示, 肥胖与甲状腺癌、结直肠癌和绝经后乳腺癌等 13 种癌症的发生相关。

肥胖引发的临床问题主要与脂肪组织的分布和类型密切相关。人体内的脂肪组织主要分为白色脂肪组织(white adipose tissue, WAT)和棕色脂肪组织(brown adipose tissue, BAT)2种类型^[5]。肥胖的特征是 WAT 的过度积累^[6], 而诱导和激活 BAT 是治疗肥胖的有效方法^[7]。BAT 在肥胖者中含量较少、活性较低, 其与 BMI 和体脂率呈负相关^[7]。WAT

主要包括内脏脂肪组织(visceral adipose tissue, VAT)和皮下脂肪组织(subcutaneous adipose tissue, SAT)^[8]。Kuipers等^[9]的研究结果显示, VAT的积累与多种疾病及其预后相关。

大部分研究者均使用BMI等作为肥胖的评估指标,以研究肥胖与疾病的关系^[1,3-4]。脂肪组织的不同解剖分布模式对人体健康有重大影响^[10]。WAT的过度积累能反映肥胖的本质,因此,对脂肪组织分布和类型的研究至关重要。CT和MRI在定量脂肪组织方面具有良好的密度分辨率、较高的准确率和可重复性^[11]; PET/CT可同时获取脂肪组织的体积和代谢情况,且不同PET显像剂、显像方法和测量方法均为肥胖的评估提供了多种选择^[12]。

1 ¹⁸F-FDG PET/CT在肥胖者WAT中的应用

WAT中VAT的¹⁸F-FDG摄取值高于SAT,这表明VAT的代谢活性更高^[13]。VAT不仅能储存脂质,还具有活跃的内分泌和旁分泌功能,其可分泌细胞因子和生物活性介质,促进炎症进程^[14]。通过¹⁸F-FDG PET/CT显像评估组织炎症的原理是葡萄糖的代谢机制^[15],目前其已被用于研究WAT的葡萄糖代谢机制。

1.1 WAT与心血管疾病的相关性

肥胖增加了心血管疾病的发生风险,有研究者通过¹⁸F-FDG PET/CT显像获取心血管周围脂肪组织的体积和代谢信息,评估其与心血管疾病发生风险的相关性^[16-17]。Kwon等^[16]评估了SAT和VAT的体积和代谢信息与心血管疾病发生风险因素的相关性,结果显示,SAT和VAT的体积与多种心血管疾病发生的风险因素呈正相关,脂肪组织的SUV提高了心血管疾病预测模型的性能。Bucerius等^[17]发现,不同部位(颈部、胸骨前区和心包)WAT的¹⁸F-FDG摄取与颈动脉和主动脉的¹⁸F-FDG摄取呈正相关,动脉¹⁸F-FDG摄取是炎症的一种标志。

1.2 WAT与恶性肿瘤的相关性

流行病学研究结果显示,肥胖与恶性肿瘤的发生存在因果关系^[4]。Hyun等^[18]发现,在乳腺癌尤其是超重的乳腺癌女性患者中,肿瘤SUV_{max}越高,预后越差。Pahk等^[19]探讨了绝经后腔内型乳腺癌患者术前¹⁸F-FDG PET/CT评估的VAT代谢与腋窝淋巴结转移的关系,用VAT SUV_{max}与SAT SUV_{max}的比值评估VAT的代谢水平,结果显示,其与肥胖者的腋窝淋巴结转移呈正相关,并且与绝经后腔内型乳腺癌患者的全身炎症指标相关;在SUV_{max}的基础上,VAT SUV_{max}与SAT SUV_{max}的比值提高了预测腋窝淋巴结转移的准确率,其可被用作肥胖相关恶性肿瘤侵袭性的潜在指标,并有助于评估绝经后腔内型乳腺癌患者的肥胖治疗干预效果。还有研究结果显示,通过¹⁸F-FDG PET/CT显像评估的VAT代谢水平升高是甲状腺癌、多发性骨髓瘤患

者预后的相关因素,VAT代谢水平升高可能是这些恶性肿瘤早期的标志^[20-21]。

1.3 WAT与脑认知功能的相关性

有研究结果显示,依据BMI诊断的肥胖会增加患者患痴呆症的风险,而¹⁸F-FDG在阿尔茨海默病(alzheimer disease, AD)的诊断中发挥着重要作用,¹⁸F-FDG代谢水平的降低先于临床症状的出现,颞顶叶和后扣带回皮质的¹⁸F-FDG代谢水平降低可提供AD发展的时间信息^[22]。Volkow等^[23]的研究结果显示,以往多项关于肥胖会增加AD的风险及其与健康个体之间相关性的研究,揭示了高BMI和前额叶低代谢的相关性。Kim等^[24]采用¹⁸F-FDG PET/CT评估健康老年人VAT与AD发生风险的关系,未发现二者之间有相关性,但这项研究并未涉及VAT代谢与脑葡萄糖代谢的相关性。

1.4 WAT与炎症的相关性

已有研究结果显示,心血管周围WAT的¹⁸F-FDG摄取与动脉炎症呈正相关^[17]。Pahk等^[25]研究了肥胖女性VAT炎症与全身炎症指标的相关性,以评估运动对VAT炎症的改善:受试者在运动前(基线水平)和完成3个月的运动计划后均接受¹⁸F-FDG PET/CT检查,采用SUV_{max}和平均标准化摄取值(SUV_{mean})评估VAT的代谢水平;在肥胖女性中,VAT的SUV_{max}与全身炎症指标相关,运动降低了VAT的SUV_{max},并减弱了其于全身炎症指标的相关性;尽管二者同时降低,但其相关性的机制尚不明确;另外,随着运动时间的增加,VAT SUV_{max}约下降到基线水平的50%,研究者猜想这可能是正常人群VAT SUV_{max}的固有水平,但这一结果的机制有待进一步研究。

2 ¹⁸F-FDG PET/CT在肥胖者BAT中的应用

BAT通常在冷暴露或交感神经受刺激下被激活,可增加能量消耗,降低体脂率,进而降低心血管疾病的发生风险。BAT在肥胖及其继发的代谢性疾病患者中的含量较少^[7],Li等^[26]的研究结果也显示,局部热疗激活WAT棕色化可治疗肥胖。2003年,Cohade等^[27]首次在¹⁸F-FDG PET/CT显像中观察到了BAT,该研究结果显示,成年人体中存在代谢活跃的BAT,且其与低BMI、低龄、低温、女性和葡萄糖代谢水平降低相关。¹⁸F-FDG PET/CT是目前无创检测BAT的“金标准”。

¹⁸F-FDG PET/CT BAT阳性与多种疾病(包括2型糖尿病、恶性肿瘤)的治疗和预后密切相关^[28-30]。Becher等^[28]回顾性分析了52487例患者的¹⁸F-FDG PET/CT检查结果,以BAT阳性摄取与否进行分类,BAT阳性患者2型糖尿病和心血管疾病(包括冠状动脉疾病、脑血管疾病、充血性心力衰竭、高血压和血脂异常)的发病率显著降低;该研究结果还显示,BAT阳性发生率与恶性肿瘤的发生部位相关,

其与嘴唇、口咽、乳房、女性生殖器官、淋巴瘤、骨、关节及关节软骨部位的恶性肿瘤发病率呈正相关，而与消化器官、眼、神经系统和网织内皮器官部位的恶性肿瘤发病率呈负相关。

应用¹⁸F-FDG PET/CT 评估肥胖者 BAT 代谢情况的研究较少。Herz 等^[31]对严重肥胖者的 BAT 代谢情况进行了小样本量研究，40 名 II~III 级肥胖者(32 名女性、8 名男性，BMI≥35 kg/m²)经长达 150 min 的冷刺激后，35% 的患者¹⁸F-FDG PET/CT 显像呈 BAT 阳性(均为女性且体重较低者)，其 VAT 含量较 BAT 阴性的患者减少了 28.8%，这表明肥胖者中也存在代谢活跃的 BAT，¹⁸F-FDG 摄取减少与肥胖本身无关，但与 VAT 含量增加有关，代谢活跃的 BAT 与较健康的肥胖代谢表型有关。

3 肥胖者¹⁸F-FDG PET/CT 常用评估指标的建议

由于光子衰减和高散射分数导致肥胖者的 PET 图像噪声增加，其图像质量受到影响^[32]。PET 常用代谢评估指标为 SUV[SUV=组织的放射性活度/(注射剂量/患者体重)]，空腹状态下脂肪组织对¹⁸F-FDG 的摄取减少，SUV 降低，肥胖者 SUV 升高^[33]，导致高估了肥胖者的病灶代谢水平。因此，有研究者使用瘦体重校正的 SUV 评估肥胖者病灶的代谢活性^[34]。基于以上原因，实体肿瘤 PET 反应标准 1.0 (PERCIST 1.0)也推荐使用瘦体重校正的 SUV 取代 SUV 作为实体肿瘤疗效评估的代谢参数^[35]，这对治疗前后体重变化大的患者更加适用。

4 小结与展望

综上，肥胖增加了恶性肿瘤等疾病的发生风险，多伴随 WAT 分布增多，BAT 分布减少。¹⁸F-FDG PET/CT 可评估肥胖者不同类型脂肪组织的代谢活性，实现了从代谢水平研究脂肪组织与疾病的相关性，其中，WAT 尤其是 VAT 的¹⁸F-FDG 代谢与疾病的发生风险、预后呈正相关。BAT 代谢活性与女性、低体重、外界温度降低和相对低龄相关。肥胖者也存在代谢活跃的 BAT，并可能与较健康的肥胖代谢表型有关，但其目前仅为小样本量研究。肥胖者不同部位和类型脂肪组织与疾病发生的相关分子机制及其¹⁸F-FDG 代谢水平尚不明确，特别是 BAT 代谢活跃的原因还需要大样本量的临床循证证据。另外不同 PET 分子影像探针及多维代谢定量参数的应用可为肥胖相关疾病提供更有价值的参考。

利益冲突 所有作者声明无利益冲突

作者贡献声明 李肖萌负责命题的提出与设计、综述的撰写；胡奕奕、崔曹哲负责综述的修改；武志芳负责综述框架的设计、修改、审阅及最终版本的修订

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