·专题论坛·

身体成分测量在减重代谢手术疗效评价中的应用和价值

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【摘要】 减重代谢手术是治疗肥胖的重要措施,接受手术治疗的人数正在逐年增加,但疗效评价体系仍未完全统一。体质指数(BMI)是衡量肥胖程度的常用指标,普遍应用于代谢领域的研究,由于其存在无法权衡脂肪分布等局限对研究结果的影响,故目前争议较大。近年来,身体成分变化与代谢疾病风险的关联受到广泛关注,减重代谢手术对身体成分变化的影响逐渐成为减重代谢外科领域的研究热点,身体成分测量作为BMI的潜在替代指标,其有望改善和规范减重代谢手术的疗效评价,因此,身体成分测量的方法和标准化也迫在眉睫。本文将回顾现有研究证据,对身体成分测量在减重代谢手术疗效评估中的应用进行剖析,以提供新的见解并探索未来的研究方向。

【关键词】 肥胖; 减重代谢手术; 身体成分; 体质指数; 疗效评价
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Application and value of body composition measurement in the evaluation of efficacy of bariatric and metabolic surgery

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【Abstract】 The use of bariatric and metabolic surgery as a central treatment for obesity has been steadily increasing. BMI, as a widely used metric for assessing obesity, has considerable relevance in the field of metabolic research. However, its limitations, such as its inability to account for variations in fat distribution, remain a subject of considerable controversy. In recent years, there has been a surge of interest in the relationship between changes in body composition and the risk of metabolic disease. Consequently, the study of the effects of bariatric and metabolic surgery on changes in body composition has become a major focus of bariatric and metabolic surgery research. As a potential replacement for BMI, body composition measurements are expected to improve and standardize the assessment of the effectiveness of bariatric and metabolic surgery. This underscores the urgent need for the development of methods and standards for body composition measurement. This paper undertakes a comprehensive review of the existing evidence on the application of body composition measurement techniques for the efficacy evaluation of bariatric and metabolic surgery. The intent is to provide new insights and pave the way for the exploration of future research directions in this area.

【Key words】 Obesity; Bariatric and metabolic surgery; Body composition; Body mass index; Efficacy evaluation

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减重代谢手术已被证明是治疗肥胖和2型糖尿病(type 2 diabetes mellitus, T2DM)的最有效措施[1-4]。减重代谢手术例数随着肥胖和T2DM发病率的快速增长而逐年增加。据国际肥胖和代谢紊乱外科联合会(The International Federation for the Surgery of Obesity and Metabolic Disorders, IFSO)统计,2018年全球范围内减重代谢手术例数已达到2008年(344 221例)的两倍,共计696 191例[5]。但随着手术数量的增加,相应的疗效评价标准并不完全统一,这不利于不同术式及其个体病情差异的减重代谢手术疗效评估,将成为减重代谢外科进一步学科发展的阻力。

体质指数(body mass index, BMI)作为衡量肥胖程度的常用指标,以该指标进行的肥胖与心血管疾病死亡率关联研究却发现"肥胖悖论"[6]。这些肥胖的心血管疾病患者被发现有更好的预后,即不良健康表型反而获得了矛盾的生存益处[7]。使用潜在替代BMI的身体成分测量指标在这类研究中减少了脂肪分布、体脂百分比等混杂因素的干扰,展现了一定的研究价值[8]。随着身体成分的变化与心血管等多种代谢疾病风险的关系逐渐得到广泛研究,身体成分测量在评估非手术减肥策略方面的潜力亦得到研究证明[9-14]。近年来,身体成分测量逐渐成为减重代谢外科的研究热点,有望弥补BMI的局限[15]。本文将回顾关于身体成分测量在减重代谢手术疗效评估中的应用,以提供新的见解并探索未来的研究方向。

一、减重代谢手术疗效评价及传统评价标准研究现状

当前,因肥胖患者的体质量减轻、BMI下降以及合并症缓解情况在接受减重代谢术后可被明显观察到,故普遍应用于减重代谢手术对肥胖症治疗效果评价[16-17]。1991年,美国国立卫生研究院的共识声明发布的第一个减重代谢手术指南,将BMI作为重要手术指征衡量指标,同时亦作为主要传统疗效评价标准[18-19]。但其应用已引起争议,因为大多研究表明,存在"肥胖悖论"的研究仅使用BMI衡量肥胖程度,在内脏脂肪组织和身体成分等方面往往被低估,其没有考虑脂肪分布的个体差异[20]。许多研究支持,在确定老年人及某些人群肥胖相关的健康风险和心血管代谢风险时,内脏脂肪和无脂肪体质量等身体成分测量指标可能比BMI更可靠[21]。

近年来,亚洲代谢外科共识会议(Asian Consensus Meeting on Metabolic Surgery, ACMOMS)、亚洲糖尿病外科治疗研讨会(Asian Diabetes Surgery Summit, ADSS)等提出,减重代谢手术指标需要标准化、个体化和全面化的共识,疗效评价指标需结合BMI、代谢指标及其他身体成分测量指标如腰围、腰臀比和区域脂肪分布等,未来甚至建议还需考虑功能限制、心理或精神障碍等主观情况[22-23]。即目前传统疗效评价标准的客观评价指标部分除BMI及一些代谢指标外,其他身体成分指标的纳入尚未实现统一规范。

二、减重代谢手术对身体成分的影响

1. 整体趋势:减重代谢手术能够有效和持久地降低脂肪量和体脂百分比,但往往伴随肌肉质量的降低,后者一直是研究领域争论的焦点。Haghighat等[24]的Meta分析结果显示,在减重代谢手术后12个月,脂肪量和体脂百分比呈持续下降趋势,没有明显的平稳期。Nuijten等[25]的研究结果表明,手术后肌肉质量减少主要发生在术后3个月内,至术后12个月下降的速度逐渐减缓,无脂肪体质量和骨骼肌质量表现出相似的趋势。因此,预防肌肉质量减少的关键时间是在减重代谢手术后的3个月以内。而在减重代谢手术疗效评估方面,Sivakumar等[26]的研究表明,减重代谢手术后在相同的脂肪量降低下,肌肉质量减少较少的患者具有更好的减重效果。T2DM患者在接受袖状胃切除术治疗后无脂肪体质量及骨骼肌质量比例的增加与T2DM的缓解相关[27-28]。一些观察性研究报告发现,肌肉质量的减少甚至会增加全因死亡率[29-31]。但也有研究人员认为,减重代谢手术引起的肌肉质量减少可能不一定有害[32]。

总之,现有的研究提示,术前和术后的身体成分测量都有助于准确评估治疗肥胖及相关代谢疾病减重代谢手术的有效性,并指导术后管理。值得注意的是,肌肉纤维本身存在性别差异,而术后观察到男性的肌肉质量比女性减少更多[33-35];老年患者则常表现为肌肉减少性肥胖表型,因为年龄因素本身容易导致衰老相关的肌肉损失[36-37]。也就是

说,目前身体成分受减重代谢手术的长期影响尚未得到充分研究,且可能被性别和衰老的影响混淆,且当前身体成分的测量方法尚不完全统一,上述情况可能是造成现有研究结果存在异质性的原因。

2. 术后区域脂肪动员:不同部位脂肪组织的代谢意义存在显著的异质性[38]。与单纯的BMI或体脂率升高相比,脂肪组织的病理变化如脂肪细胞肥大、皮下脂肪组织扩张能力下降、内脏脂肪组织和其他异位脂肪沉积等,与机体代谢紊乱的发生发展关系更为密切。Stefan[39]提出,从体脂分布的角度更能全面解释心血管代谢障碍的人群异质性,以弥补基于BMI的肥胖诊断标准不能全面反映机体代谢风险的短板。与皮下脂肪组织良好的扩张能力有助于脂肪储存和代谢缓冲相反,过量的内脏脂肪组织通常会对新陈代谢产生不利影响[39-41]。其他异位脂肪沉积的负面影响更为严重,例如由肝脏脂肪沉积导致的肝细胞脂肪变性和炎性反应,进而显著增加肝硬化和肝癌的风险[42-44]。胰腺脂肪沉积则可增加胰腺炎和T2DM的风险[45]。同理,心脏脂肪堆积增加心肌梗死等心脏代谢风险[46]。故而对减肥过程中的区域脂肪动员的研究逐渐火热,区域脂肪动员的情况也逐渐成为评估减肥策略的重要指标。例如,地中海饮食可特异调动心脏、肝脏和胰腺中的异位脂肪,而运动对降低内脏脂肪组织有独立贡献[11];利拉鲁肽联合生活方式干预可显著减少内脏脂肪[12];与德谷胰岛素相比,替西帕肽更能降低肝脏脂肪含量、腹部皮下脂肪组织和内脏脂肪组织[13]。

然而,减重代谢手术对区域脂肪动员影响的研究却非常有限,现有证据表明,在整体减重效果相似的情况下,Roux-en-Y 胃旁路术显著减少了Android区(上半身,尤其是腹部)脂肪和内脏脂肪组织。Miller等[47]和Bazzocchi等[48]分析了患者在接受胃旁路术治疗1年后的身体成分变化,均发现腹部皮下脂肪组织、腹部内脏脂肪组织、躯干脂肪量和Android区域脂肪量的下降幅度均高于全身脂肪量的降低幅度,而Gynoid区域(下半身,尤其是臀部和大腿)、四肢的脂肪量降低低于全身脂肪量的降低,这表明胃旁路术不仅显著降低脂肪量,且特异性地调动腹部脂肪,能够促进代谢健康的脂肪分布。Favre等[49]则进一步发现,T2DM患者接受胃旁路术后的内脏脂肪下降高于糖代谢正常者和糖耐量受损患者。对于袖状胃切除术后对区域脂肪动员的影响则存在争议,Tałałaj等[50]发现,肥胖患者在接受袖状胃切除术治疗1年后,全身脂肪总质量的减少明显大于肌肉总质量的减少,而内脏脂肪量的减少却少于皮下脂肪量,内脏脂肪在总脂肪中的比例从术前的24.9%增加到术后的28.0%,表明袖状胃切除术不利于代谢健康体脂的分布;相反,Maïmoun等[51]却发现,袖状胃切除术与胃旁路术RYGB相似,术后也同样能够特异性地调动腹部脂肪,对身体脂肪的代谢健康型分布产生有利影响。

总的来说,应系统地看待减重代谢手术对身体成分的影响,即关注其相对变化,这似乎比身体成分质量变化的绝对值更有意义。减重代谢手术的目标应该是将增加的体脂百分比校正至正常范围。另一方面,代谢异常导致肥胖和T2DM患者肌肉质量处于相对缺乏的水平,脂肪量过度积累的负面影响掩盖了肌肉质量增加的好处,随着减重代谢手术后脂肪量的显著降低,基线肌肉质量较高的患者显现出胰岛素敏感性恢复的优势,更有利于T2DM的改善和缓解,由此凸显出加强预防术后肌肉质量减少的必要性。综合性别和年龄等因素,对高BMI、T2DM、男性和老年患者进行减重代谢手术后监测和预防肌肉质量的减少尤为重要[29,33-35]。鉴于区域脂肪代谢意义的异质性,对于其精细的动员情况,未来的研究需要对测量和计算方法进行统一和标准化,并深入进行相应的机制研究,有利于该领域研究的发展。

3. 身体成分测量方法:目前用于减重代谢手术前后身体成分测量常用方法包括磁共振成像(magnetic resonance imaging,MRI)、计算机断层扫描(computed tomography,CT)、双能X射线吸收法(dual-energy X-ray absorptiometry,DXA)和生物电阻抗分析(bioelectrical impedance analysis,BIA)[52]。

MRI是一种利用不同组织对磁场反应的特异性来测量身体成分的检查技术,具有高精度、优异的重复性、无辐射风险以及强大的软组织分辨率等优点。磁共振质子密度脂肪分数技术在检测异位脂肪方面具有高度灵敏性,几乎能量化身体任何部位的成分并实现图像的三维重建,其他测量方法难以媲美,尤其可以精确捕捉一些特殊脂肪库的动员情况,如肝脏、胰腺、肌肉和舌等[53-55],使得MRI始终是研究领域的高级别证据。然而,MRI存在高成本、检查耗时长以及对图像扫描和后处理技术的高要求,限制了其在临床实践中的应用[56-58]。

CT利用X射线通过不同组织的衰减来实现对不同组织的区分,并形成横截面图像。CT较强的组织分辨能力和三维重建技术也可以测量器官中的脂肪含量[59]。然而,辐射暴露和相对高昂的检查成本同样限制了其在临床实践中的应用。由于CT测量内脏脂肪的准确性高于MRI且扫描时间更短,因此,目前CT主要用于精确测量减重代谢手术对腹部内脏脂肪和皮下脂肪的影响[60-61]。

DXA则是利用两种能量峰值(40 keV和70~80 keV)的X射线对不同组织衰减的不同区分身体成分[62-63]。被认为测量身体成分的"金标准",具有无创、低辐射暴露、快速测量等优点而被广泛应用[50,62-64]。DXA通过预设的标记线将人体划分为研究所需的特定区域,甚至可以基于经验证的预测算法估计身体成分分布[65]。因此,DXA通常用于准确评估减重代谢手术对身体成分和分布的影响。然而,有研究表明,对于躯干脂肪厚度较大的中心性肥胖的个体,DXA的准确性会降低[66]。

BIA通过施加低电压电流测量不同组织的电阻来估计身体成分,具有成本低、移动性好、无辐射风险且对操作人员技术要求低等优点,但测量结果易受人体水合状态、BMI、种族、环境温度、湿度和电极位置的影响[67]。不同制造商的BIA在电压、电流、电极编号和算法模型上存在差异,导致BIA测量结果的可重复性较差,与DXA之间测量结果的一致性不佳,导致研究结果间存在异质性[64]。近年来,虽然一些新开发的BIA技术提高了精度,但仍未解决对某些部位的脂肪量估计存在偏差的问题[68-70]。因此,很大程度限制了其在高质量研究中的应用。

总之,MRI和CT是基于标准化特征直接对身体成分成像的准确测量方法,结果可靠,是高质量研究的优先选择;DXA和BIA是基于数学模型来计算身体成分,准确性相对欠佳。然而,鉴于检查成本、操作难易等实际因素,小样本的研究中可优先考虑使用MRI和CT确保研究的精度;而DXA和BIA仍然是大样本人群研究的优先选择,应在未来优化算法提高准度。

四、小结与展望

随着减重代谢外科的蓬勃发展及医疗研究及临床应用的模式变革,身体成分测量作为一种潜力斐然的客观评价指标,必将成为未来研究的重要方向。回顾现有研究的发现与局限,我们展望未来的研究方向,可聚焦于以下有待阐明的关键点:(1)应该对减重代谢手术相关的前瞻性队列和随机对照试验进行长期随访,以确定手术对身体成分的长期影响;(2)优化并逐渐规范身体成分测量在减重代谢手术临床实践和研究中的应用,包括测量技术、随访时间点和报告格式等方面的规范化;(3)进行随机对照试验研究进一步阐明不同手术方法对身体成分影响的差异;(4)使用MRI或CT准确评估减重代谢手术中特定区域脂肪沉积的动员情况,如心外膜脂肪组织、血管周围脂肪组织、肾周脂肪组织、胰腺脂肪沉积和肌内脂肪组织等,并进行深入的机制探究;(5)开发并验证基于身体成分测量的手术疗效预测模型,以丰富或替代传统有争议的评价指标(如BMI),探索更精准的手术适应证及疗效评价指标,最终推动减重代谢手术评价体系的进一步完善。

综上所述,通过对身体成分测量相关的前瞻性研究、测量方法优化、减重代谢手术对身体成分影响的深入研究、特定区域脂肪评估及疗效预测模型开发等方面的探索,有望实现减重代谢手术评价指标体系的规范化。

利益冲突 所有作者均声明不存在利益冲突

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·读者·作者·编者·

在本刊发表的论文中可直接使用的英文缩写名词

AEG（食管胃结合部腺癌）
AJCC（美国癌症联合委员会）
ASA（美国麻醉医师协会）
ASCO（美国临床肿瘤协会）
BMI（体质指数）
CEA（癌胚抗原）
CI（置信区间）
CSCO（中国临床肿瘤学会）
DFS（无病生存率）
DNA（脱氧核糖核酸）
EMR（内镜黏膜切除术）
ERAS（加速康复外科）
ESD（内镜黏膜下剥离术）
ESMO（欧洲肿瘤内科学会）
EUS（内镜超声检查术）
FDA（美国食品药品管理局）
GIST（胃肠间质瘤）
HR（风险比）
ICU（重症监护病房）
Ig（免疫球蛋白）
IL（白细胞介素）
ISR（经括约肌间切除术）
NOSES（经自然腔道取标本手术）
NOTES（经自然腔道内镜手术）
MRI（磁共振成像）
MDT（多学科综合治疗协作组）
NCCN（美国国立综合癌症网络）
NIH（美国国立卫生院）
NK细胞（自然杀伤细胞）
OS（总体生存率）
OR（比值比）
PET（正电子发射断层显像术）
PFS（无进展生存率）
PPH（吻合器痔上黏膜环切钉合术）
RCT（随机对照试验）
RNA（核糖核酸）
ROC曲线（受试者工作特征曲线）
RR（相对危险度）
PCR（聚合酶链反应）
taTME（经肛全直肠系膜切除术）
TME（全直肠系膜切除术）
TNF（肿瘤坏死因子）
UICC（国际抗癌联盟）
VEGF（血管内皮生长因子）
WHO（世界卫生组织）