

• 临床研究 •

肥胖减弱心力衰竭患者标准药物治疗后的心脏逆重构

李皓阳¹, 钱芷君², 曾嘉欣¹, 张恩瑞¹, 王 焱¹, 钱智勇¹, 侯小锋¹, 朱晓梅², 邹建刚^{1*}

¹南京医科大学第一附属医院心血管内科, ²放射科, 江苏 南京 210029

[摘要] 目的: 探讨肥胖对接受指南指导的药物治疗(guideline-directed medical therapy, GDMT)的射血分数降低和轻度降低的心力衰竭(heart failure with reduced and mildly reduced ejection fraction, HFrEF/HFmrEF)患者心脏逆重构的影响。方法: 回顾性分析2022年1月—2024年10月在南京医科大学第一附属医院就诊且左心室射血分数(left ventricular ejection fraction, LVEF)<50%的心衰患者。所有患者均接受GDMT治疗, 并于基线时接受心脏磁共振检查(cardiac magnetic resonance, CMR), 通过延迟钆增强(late gadolinium enhancement, LGE)和细胞外容积分数(extracellular volume fraction, ECV)评估心肌纤维化。肥胖定义为体重指数(body mass index, BMI)≥28 kg/m²。在基线和GDMT治疗6个月后采用超声心动图评估心脏逆重构, 治疗有反应定义为LVEF绝对增加≥5%。结果: 共纳入80例患者(肥胖组31例, 非肥胖组49例)。与非肥胖组相比, 肥胖组LVEF改善幅度及治疗反应率均较低[ΔLVEF: (14.45±2.08)% vs. (20.80±1.81)%, *P*=0.024; 反应率: 76.80% vs. 93.58%, *P*=0.036]。多因素回归分析显示BMI是LVEF改善的独立负向预测因素(β =-0.90, *P*=0.004)。LGE(*OR*=0.68, *P*=0.025)和ECV(*OR*=0.89, *P*=0.012)均为治疗应答降低的独立预测因素。整合BMI与ECV的预测模型对低反应者的识别能力最佳, 曲线下面积为0.923, 且显著优于基线模型(*P*=0.043)。结论: 在HFrEF/HFmrEF患者中, 肥胖与GDMT治疗后心脏逆重构减弱及治疗反应性降低相关, 联合BMI与ECV有助于识别治疗反应降低的高风险患者。

[关键词] 肥胖; 心力衰竭; 心脏逆重构; 指南指导的药物治疗; 心肌纤维化; 心脏磁共振

[中图分类号] R541.6

[文献标志码] A

[文章编号] 1007-4368(2026)04-551-10

doi: 10.7655/NYDXBNSN260036

Obesity attenuates cardiac reverse remodeling following guideline - directed medical therapy in patients with heart failure

LI Haoyang¹, QIAN Zhijun², ZENG Jiabin¹, ZHANG Enrui¹, WANG Yao¹, QIAN Zhiyong¹, HOU Xiaofeng¹, ZHU Xiaomei², ZOU Jiangang^{1*}

¹Department of Cardiology, ²Department of Radiology, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China

[Abstract] **Objective:** To investigate the impact of obesity on cardiac reverse remodeling in patients with heart failure with reduced or mildly reduced ejection fraction (HFrEF/HFmrEF) receiving guideline-directed medical therapy (GDMT). **Methods:** A retrospective analysis was conducted on heart failure patients with a left ventricular ejection fraction (LVEF)<50% treated at the First Affiliated Hospital of Nanjing Medical University between January 2022 and October 2024. All patients received GDMT and underwent baseline cardiac magnetic resonance (CMR) imaging at baseline. Myocardial fibrosis was assessed *via* late gadolinium enhancement (LGE) and extracellular volume fraction (ECV). Obesity was defined as a body mass index (BMI) ≥28 kg/m². Cardiac reverse remodeling was evaluated by echocardiography at baseline and after 6 months of GDMT. Treatment response was defined as an absolute increase in LVEF ≥5%. **Results:** A total of 80 patients were included (31 in the obese group and 49 in the non-obese group). Compared to the non-obese group, the obese group showed a smaller improvement in LVEF and a lower treatment response rate [ΔLVEF: (14.45 ± 2.08)% vs. (20.80 ± 1.81)%, *P*=0.024; response rate: 76.80% vs. 93.58%, *P*=0.036]. Multivariable regression analysis confirmed that BMI was an independent negative predictor of LVEF improvement (β =-0.90, *P*=0.004). Both LGE (*OR*=0.68, *P*=0.025) and ECV (*OR*=0.89, *P*=0.012) were independent predictors of reduced treatment response. A predictive model combining BMI and ECV demonstrated the

[基金项目] 江苏省医学新技术专项(JX233C202103)

*通信作者(Corresponding author), E-mail: jgzou@njmu.edu.cn (ORCID: 0000-0001-5891-6589)

highest accuracy for identifying poor responders, with an area under the curve (AUC) of 0.923, which was significantly superior to the baseline model ($P=0.043$). **Conclusion:** In HFrEF/HFmrEF patients, obesity is associated with attenuated cardiac reverse remodeling and reduced responsiveness to GDMT. The combination of BMI and ECV improves the identification of patients at risk for diminished treatment response.

[Key words] obesity; heart failure; cardiac reverse remodeling; guideline-directed medical therapy; myocardial fibrosis; cardiac magnetic resonance

[J Nanjing Med Univ, 2026, 46(04): 551-560]

心力衰竭(heart failure, HF)仍然是全球性的健康挑战,具有高发病率和 high 病死率^[1]。尽管指南指导的药物治疗(guideline-directed medical therapy, GDMT)取得了显著进展,总体预后有所改善,但治疗反应存在明显的个体异质性,这凸显了识别临床结局影响因素的重要性^[2-3]。

肥胖是射血分数保留的心力衰竭(heart failure with preserved ejection fraction, HFpEF)中已明确的预后决定因素,但其在射血分数降低和轻度降低的心力衰竭(heart failure with reduced and mildly reduced ejection fraction, HFrEF/HFmrEF)中的作用仍不明确且存在争议,部分原因在于“肥胖悖论”^[4-7]。肥胖影响 HFrEF/HFmrEF 患者心脏逆重构和治疗反应的机制尚不明确^[8-9]。心脏磁共振(cardiac magnetic resonance, CMR)通过延迟钆增强(late gadolinium enhancement, LGE)和细胞外容积分数(extracellular volume fraction, ECV)评估心肌纤维化,可能有助于描述肥胖相关的心肌重构并优化预后评估^[10-12]。因此,本研究旨在探讨肥胖是否会减弱 HFrEF/HFmrEF 患者的心脏逆重构和治疗反应,并评估联合体重指数(body mass index, BMI)与心肌纤维化指标的价值。

1 对象和方法

1.1 对象

回顾性分析 2022 年 1 月—2024 年 10 月在南京医科大学第一附属医院行 CMR 检查的 HFrEF/HFmrEF 患者。纳入标准:①左心室射血分数(left ventricular ejection fraction, LVEF)≤40%(HFrEF)或 LVEF 41%~49%(HFmrEF);②存在符合纽约心脏协会(New York Heart Association, NYHA)心功能分级 II~IV 级的心力衰竭体征或症状;③年龄≥18 周岁且<70 周岁。为专门评估肥胖对初始治疗反应的影响,研究纳入新诊断且在入组时未接受过任何前期 GDMT 的患者。排除标准:①缺血性心脏病,包括心绞痛、心肌梗死病史或既往有经皮冠状动脉介入治疗史;

②其他特定结构性心脏病,包括心肌炎、肥厚型心肌病、严重瓣膜性心脏病、心脏内血栓等;③严重的系统性合并症,如重度慢性阻塞性肺疾病、严重肾功能不全(或终末期肾病)、活动性恶性肿瘤等;④关键临床资料缺失或 CMR 图像质量不佳无法进行分析。在连续纳入的 150 例患者中,排除 4 例心肌炎、5 例肥厚型心肌病、9 例心脏血栓、10 例心肌梗死病史和 42 例失访患者后,最终共纳入 80 例患者。本研究通过了南京医科大学第一附属医院伦理委员会批准(2024-SR-091),患者均知情同意。

1.2 方法

从电子病历中收集所有纳入患者的基线临床和影像学数据。CMR 检查使用 3.0T 扫描仪(Skya and Vida, Siemens Healthcare 公司,德国)。采用平衡稳态自由进动序列,在屏气时获取短轴和长轴(二腔、三腔、四腔)电影图像。按照心血管磁共振学会标准测量左心室舒张末期容积(end-diastolic volume, EDV)和收缩末期容积(end-systolic volume, ESV)以及左心室质量(left ventricular mass, LVMass)^[13]。在注射对比剂后 10~15 min 采集 LGE 图像,采用反转恢复梯度回波序列。ECV 计算公式为:ECV=(1-血细胞比容)×(ΔR1 心肌/ΔR1 血液),其中 ΔR1 为对比剂注射后弛豫率(1/T1)的变化。

依据现行指南评估标准二维超声心动图参数^[14],包括采用双平面 Simpson 法测量的 LVEF、左心房内径(left atrial diameter, LAD)、左心室舒张末期内径(left ventricular end-diastolic dimensions, LVDd)和收缩末期内径(left ventricular end-systolic dimension, LVDs)。随访超声心动图测量数据在基线评估至少 6 个月后获取。左心室内径变化量化如下:ΔLVDd 和 ΔLVDs 定义为舒张末和收缩末内径的绝对减少值(基线值减随访值),而 ΔLVDd% 和 ΔLVDs% 表示相应的相对变化[(ΔLVDd 或 ΔLVDs)÷基线值×100%]。治疗有反应定义为指南指导的药物治疗后 LVEF 绝对增加≥5%,该阈值被既往多项研究采

用,作为判断具有临床意义的心脏逆重构标准^[15]。

1.3 统计学方法

使用 R 4.3.3 和 SPSS 27.0 进行统计学分析,计数资料以例数(百分比)[$n(\%)$]表示,组间比较采用卡方检验或 Fisher 精确检验。定量资料先行正态性检验,正态分布资料以均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较采用独立样本 t 检验,非正态分布资料以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,组间比较采用秩和检验。为校正基线不平衡,组间比较采用逆概率加权(inverse probability of treatment weighting, IPTW)法,纳入的协变量包括年龄、性别、高血压、冠心病、心房颤动和糖尿病。将倾向评分的倒数作为权重,创建一个基线特征平衡的伪人群。所有组间比较均基于 IPTW 校正后的模型。采用多因素线性回归(用于连续心超参数变化)和逻辑回归(用于治疗反应)校正潜在混杂因素以评估 BMI 与结局的独立关联。使用受试者工作特征(receiver operating characteristic, ROC)曲线评估模型对治疗反应的预测性能,并通过 DeLong 检验进行比较。采用中介分析探讨 LGE 和 ECV 在 BMI 与治疗反应关系中的潜在中介作用。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基线特征与药物治疗

最终 80 例 HFrEF/HFmrEF 患者纳入分析。以 BMI 28 kg/m^2 为界值,将患者分为肥胖组(31 例)和非肥胖组(49 例)。两组基线特征比较显示,肥胖组患者更年轻, BMI、收缩压、舒张压、心率、LAD 及高血压患病率均更高,而高密度脂蛋白胆固醇水平较低($P < 0.05$)。CMR 显示,肥胖组患者的 LGE、EDV、ESV 和 LVMass 均显著高于非肥胖组($P < 0.05$)。在药物治疗方面,两组患者 GDMT 药物的使用比例无显著差异,但肥胖组沙库巴曲缬沙坦和琥珀酸美托洛尔的平均剂量显著高于非肥胖组,其余药物剂量在两组间差异无统计学意义(表 1)。IPTW 校正后,两组间纳入加权的协变量(年龄、性别、合并症)均达到了良好的平衡(表 2)。

2.2 肥胖对心脏逆重构的影响

经过至少 6 个月 GDMT 后,采用 IPTW 校正年龄、性别和合并症等混杂因素后评估心脏逆重构情况。如图 1 所示,肥胖组患者在射血分数及心室内径改善方面均显著低于非肥胖组: $\Delta\text{LVEF}(14.45 \pm 2.08)\% \text{ vs. } (20.80 \pm 1.81)\% (P=0.024)$; $\Delta\text{LVDs}(9.20 \pm 1.53) \text{ mm vs. } (13.40 \pm 1.32) \text{ mm } (P=0.042)$; $\Delta\text{LVDd}\%$

$(8.58 \pm 1.77)\% \text{ vs. } (13.21 \pm 1.29)\% (P=0.037)$ 和 $\Delta\text{LVDs}\%$ $(16.56 \pm 2.63)\% \text{ vs. } (24.41 \pm 2.02)\% (P=0.024)$ 。 ΔLVDd 的组间差异未达统计学意义 [$(5.80 \pm 1.26) \text{ mm vs. } (8.70 \pm 0.94) \text{ mm}, P=0.070$]。肥胖组治疗反应率显著低于非肥胖组($76.80\% \text{ vs. } 93.58\%, P=0.036$)。

进一步进行性别分层分析发现,肥胖对心脏逆重构的不利影响在男性患者中更为显著。肥胖男性患者在 $\Delta\text{LVEF}[(14.00 \pm 2.20)\% \text{ vs. } (23.44 \pm 1.85)\%, P=0.002]$ 、 $\Delta\text{LVDd}[(5.73 \pm 1.40) \text{ mm vs. } (9.66 \pm 1.09) \text{ mm}, P=0.031]$ 、 $\Delta\text{LVDs}[(8.94 \pm 1.68) \text{ mm vs. } (15.07 \pm 1.39) \text{ mm}, P=0.007]$ 、 $\Delta\text{LVDd}\%[(8.40 \pm 1.94)\% \text{ vs. } (14.55 \pm 1.46)\%, P=0.014]$ 及 $\Delta\text{LVDs}\%[(15.96 \pm 2.85)\% \text{ vs. } (26.98 \pm 2.11)\%, P=0.003]$ 等参数上均改善较差。而在女性亚组中,肥胖与非肥胖患者之间各项参数差异均无统计学意义(表 3)。敏感性分析结果支持上述发现的稳健性。

2.3 BMI 作为心脏功能恢复的独立预测因子

多因素回归分析评估了 BMI 与心脏参数变化之间的关联(表 4)。在调整年龄、性别、基线心功能指标、合并症以及关键 GDMT 药物剂量后(模型 3), BMI 与 $\Delta\text{LVEF}(\beta=-0.90, P=0.004)$ 、 $\Delta\text{LVDs}(\beta=-0.51, P=0.030)$ 、 $\Delta\text{LVDd}\%(\beta=-0.57, P=0.043)$ 和 $\Delta\text{LVDs}\%(\beta=-0.98, P=0.019)$ 均呈独立负相关。此外,较高的 BMI 也可独立预测较低的治疗反应($\text{OR}=0.70, P=0.013$)。

2.4 LGE 和 ECV 作为治疗反应的预测因子

逻辑回归分析显示,在调整 BMI、年龄、性别、基线心功能指标及合并症后, LGE($\text{OR}=0.68, P=0.025$) 与 ECV($\text{OR}=0.89, P=0.012$) 均为治疗反应降低的独立负向预测因素(表 5)。

2.5 整合模型的预测性能

通过 ROC 曲线分析比较不同预测模型对治疗反应的判别性能(图 2)。模型 1 作为基线模型,包含了已知与心力衰竭预后相关的临床因素(年龄、性别、基线 LVEF、LVMass 及合并症),旨在评估这些因素对治疗反应的基本预测能力,并为后续模型的比较提供基准。这有助于验证新变量(如 BMI 和纤维化标志物)的增量预测价值。基线模型 1 的 AUC 为 0.782。加入 BMI 后(模型 2), AUC 提升至 0.874,但差异无统计学意义($P=0.172$)。进一步纳入 LGE 的模型(模型 3) AUC 为 0.893,与基线模型相比无显著增量增益($P=0.126$)。而同时整合 BMI 与 ECV 的模型(模型 4)表现出最优的预测性能, AUC 达 0.923,且显著优于基线模型($P=0.043$)。

表1 按肥胖状况分组的HFrEF/HFmrEF患者基线特征

Table 1 Baseline characteristics stratified by obesity status in HFrEF/HFmrEF patients

Characteristic	Total(n=80)	OB(n=31)	Non-OB(n=49)	P
Demographics				
Age(years, $\bar{x} \pm s$)	49.73 \pm 13.94	38.55 \pm 9.21	56.80 \pm 11.62	<0.001
Male[n(%)]	56(70.00)	27(87.10)	29(59.18)	0.008
BMI(kg/m ² , $\bar{x} \pm s$)	27.90 \pm 6.57	34.69 \pm 5.04	23.60 \pm 2.56	<0.001
Clinical parameters				
Systolic BP(mmHg, $\bar{x} \pm s$)	126.11 \pm 19.72	132.87 \pm 20.43	121.84 \pm 18.18	0.014
Diastolic BP(mmHg, $\bar{x} \pm s$)	83.05 \pm 15.71	89.58 \pm 14.17	78.92 \pm 15.36	0.003
Heart rate(bpm, $\bar{x} \pm s$)	83.53 \pm 16.12	90.81 \pm 13.60	78.92 \pm 16.00	<0.001
NYHA class($\bar{x} \pm s$)	2.88 \pm 0.58	2.94 \pm 0.51	2.84 \pm 0.62	0.463
Echocardiography				
LVEF(%, $\bar{x} \pm s$)	32.14 \pm 7.71	33.45 \pm 7.76	31.31 \pm 7.65	0.229
LAD(mm, $\bar{x} \pm s$)	46.88 \pm 6.46	49.26 \pm 6.61	45.37 \pm 5.95	0.008
LVDd(mm, $\bar{x} \pm s$)	64.64 \pm 7.97	65.71 \pm 8.08	63.96 \pm 7.90	0.341
LVDs(mm, $\bar{x} \pm s$)	54.46 \pm 8.40	55.00 \pm 8.56	54.12 \pm 8.37	0.652
Biomarkers				
NT-proBNP(pg/mL, $\bar{x} \pm s$)	1 043.30(504.75, 3 150.43)	1 038.60(335.20, 2 858.35)	1 053.00(649.00, 3 106.00)	0.427
Fasting glucose(mmol/L, $\bar{x} \pm s$)	4.81(4.26, 5.72)	5.16(4.28, 6.11)	4.79(4.24, 5.58)	0.521
Total cholesterol(mmol/L, $\bar{x} \pm s$)	4.47(4.05, 5.05)	4.61(4.08, 5.17)	4.38(4.06, 5.01)	0.486
Triglycerides(mmol/L, $\bar{x} \pm s$)	1.40(1.08, 2.16)	1.57(1.09, 2.69)	1.37(1.08, 2.03)	0.192
HDL-C(mmol/L, $\bar{x} \pm s$)	0.96(0.85, 1.16)	0.88(0.78, 1.00)	1.05(0.91, 1.20)	0.001
LDL-C(mmol/L, $\bar{x} \pm s$)	2.83(2.44, 3.28)	2.90(2.46, 3.49)	2.74(2.45, 3.18)	0.319
Comorbidities[n(%)]				
Hypertension	32(40.00)	20(64.52)	12(24.49)	<0.001
Coronary artery disease	24(30.00)	6(19.35)	18(36.73)	0.098
Atrial fibrillation	20(25.00)	5(16.13)	15(30.61)	0.145
Diabetes mellitus	19(23.75)	9(29.03)	10(20.41)	0.377
Medications				
Sacubitril/Valsartan[n(%)]	69(86.25)	29(93.55)	40(81.63)	0.240
Dose(mg, $\bar{x} \pm s$)	100.00(100.00, 200.00)	200.00(100.00, 200.00)	100.00(100.00, 200.00)	<0.001
Metoprolol succinate[n(%)]	73(91.25)	28(90.32)	45(91.84)	1.000
Dose(mg, $\bar{x} \pm s$)	47.50(47.50, 47.50)	47.50(47.50, 71.25)	47.50(47.50, 47.50)	0.001
Spirolactone[n(%)]	75(93.75)	30(96.77)	45(91.84)	0.678
Dose(mg, $\bar{x} \pm s$)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	0.231
Furosemide[n(%)]	63(78.75)	25(80.65)	38(77.55)	0.742
Dose(mg, $\bar{x} \pm s$)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	0.320
Dapagliflozin[n(%)]	77(96.25)	28(90.32)	49(100.00)	0.106
Dose(mg, $\bar{x} \pm s$)	10.00(10.00, 10.00)	10.00(10.00, 10.00)	10.00(10.00, 10.00)	0.276
Vericiguat[n(%)]	30(37.50)	10(32.26)	20(40.82)	0.441
Dose(mg, $\bar{x} \pm s$)	5.00(2.50, 5.00)	3.75(2.50, 5.00)	5.00(2.50, 5.00)	0.819
CMR parameters				
LGE(%, $\bar{x} \pm s$)	6.14(4.59, 9.35)	8.84(5.94, 10.51)	5.35(4.39, 7.41)	0.003
EDV(mL)	262.79(196.62, 319.60)	296.87(238.33, 356.20)	231.33(185.21, 302.94)	0.003
ESV(mL)	196.50(137.97, 262.15)	225.40(174.50, 290.00)	186.00(128.00, 242.00)	0.040
LVMass(g)	152.51(120.63, 192.17)	187.96(160.35, 232.82)	134.23(105.31, 160.00)	<.001
ECV(%)	32.45(28.78, 40.05)	33.90(29.80, 41.30)	31.50(28.75, 36.60)	0.292

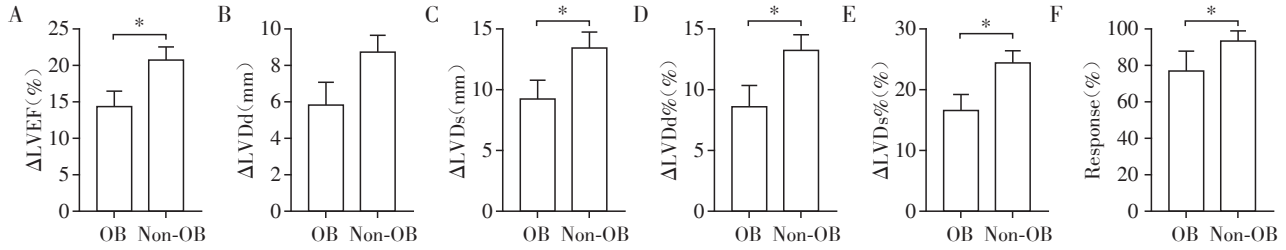
BMI: body mass index; BP: blood pressure; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; LAD: left atrial diameter; LVDd: left ventricular end-diastolic dimension; LVDs: left ventricular end-systolic dimension; NT-proBNP: N-terminal pro-B-type natriuretic peptide; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; LGE: late gadolinium enhancement; EDV: end-diastolic volume; ESV: end-systolic volume; LV: left ventricular; ECV: extracellular volume fraction.

表2 IPTW校正后按肥胖状况分组的HFrEF/HFmrEF患者基线特征

Table 2 Baseline characteristics of HFrEF/HFmrEF patients stratified by obesity status after IPTW adjustment

Characteristic	Total(n=70.75)	OB(n=21.52)	Non-OB(n=49.23)	P
Demographics				
Age(years, $\bar{x} \pm s$)	47.10 \pm 19.21	42.53 \pm 11.72	49.10 \pm 23.83	0.122
Male[n(%)]	54.63(77.21%)	18.97(88.15%)	35.66(72.43%)	0.123
BMI(kg/m ² , $\bar{x} \pm s$)	26.90 \pm 5.46	33.63 \pm 3.62	23.96 \pm 3.44	<0.001
Clinical parameters				
Systolic BP(mmHg, $\bar{x} \pm s$)	125.35 \pm 26.82	130.91 \pm 16.10	122.92 \pm 30.35	0.151
Diastolic BP(mmHg, $\bar{x} \pm s$)	82.79 \pm 26.88	88.66 \pm 11.00	80.22 \pm 31.29	0.097
Heart rate(bpm, $\bar{x} \pm s$)	83.83 \pm 19.73	87.84 \pm 10.32	82.08 \pm 23.27	0.151
NYHA class($\bar{x} \pm s$)	2.75 \pm 0.78	2.88 \pm 0.48	2.70 \pm 0.85	0.263
Echocardiography				
LVEF(% , $\bar{x} \pm s$)	32.03 \pm 7.38	33.46 \pm 5.91	31.40 \pm 7.91	0.227
LAD(mm, $\bar{x} \pm s$)	46.93 \pm 6.25	49.28 \pm 5.68	45.91 \pm 6.47	0.029
LVDd(mm, $\bar{x} \pm s$)	64.72 \pm 8.12	65.41 \pm 6.29	64.41 \pm 9.00	0.591
LVDs(mm, $\bar{x} \pm s$)	54.55 \pm 8.34	54.73 \pm 6.31	54.46 \pm 9.17	0.887
Biomarkers				
NT-proBNP(pg/mL)	901.00(489.00, 1 889.00)	1 038.60(179.00, 2 317.00)	885.00(510.00, 1 888.00)	0.740
Fasting glucose(mmol/L)	4.66(3.97, 5.71)	5.64(4.48, 6.52)	4.49(3.75, 5.22)	0.029
Total cholesterol(mmol/L, $\bar{x} \pm s$)	4.44(4.09, 5.11)	4.61(4.15, 5.23)	4.35(4.09, 5.11)	0.715
Triglycerides(mmol/L)	1.36(1.06, 2.16)	1.84(1.17, 2.72)	1.24(1.06, 2.03)	0.084
HDL-C(mmol/L, $\bar{x} \pm s$)	0.95(0.86, 1.14)	0.91(0.80, 0.99)	1.04(0.90, 1.16)	0.026
LDL-C(mmol/L)	2.87(2.48, 3.30)	2.87(2.55, 3.50)	2.83(2.48, 3.29)	0.877
Comorbidities[n(%)]				
Hypertension	27.64(39.06%)	10.87(50.51%)	16.77(34.06%)	0.284
Coronary artery disease	23.23(32.84%)	5.34(24.83%)	17.89(36.34%)	0.415
Atrial fibrillation	17.76(25.10%)	4.12(19.14%)	13.64(27.70%)	0.466
Diabetes mellitus	15.09(21.32%)	5.76(26.74%)	9.33(18.95%)	0.480
Medications				
Sacubitril/Valsartan[n(%)]	63.24(89.38%)	19.95(92.69%)	43.29(87.94%)	0.522
Dose(mg)	100.00(100.00, 200.00)	200.00(100.00, 200.00)	100.00(100.00, 200.00)	0.102
Metoprolol succinate[n(%)]	65.61(92.74%)	19.06(88.56%)	46.55(94.56%)	0.338
Dose(mg)	47.50(47.50, 47.50)	47.50(47.50, 95.00)	47.50(47.50, 47.50)	0.029
Spironolactone[n(%)]	67.31(95.14%)	20.94(97.30%)	46.37(94.20%)	0.487
Dose(mg, $\bar{x} \pm s$)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	0.327
Furosemide[n(%)]	48.22(68.15%)	17.46(81.13%)	30.76(62.47%)	0.172
Dose(mg, $\bar{x} \pm s$)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	20.00(20.00, 20.00)	0.266
Dapagliflozin[n(%)]	68.83(97.29%)	19.61(91.10%)	49.23(100.00%)	0.018
Dose(mg, $\bar{x} \pm s$)	10.00(10.00, 10.00)	10.00(10.00, 10.00)	10.00(10.00, 10.00)	0.252
Vericiguat[n(%)]	27.89(39.42%)	9.21(42.79%)	18.68(37.94%)	0.747
Dose(mg, $\bar{x} \pm s$)	5.00(2.50, 5.00)	5.00(2.50, 5.00)	5.00(2.50, 5.00)	0.659
CMRparameters				
LGE(% , $\bar{x} \pm s$)	6.09(4.69, 8.97)	8.04(6.10, 9.82)	5.25(4.35, 7.72)	0.024
EDV(mL)	268.77(209.81, 331.92)	324.76(239.48, 338.56)	250.61(192.20, 304.03)	0.025
ESV(mL)	204.90(139.00, 258.00)	209.00(169.00, 263.00)	197.00(139.00, 250.00)	0.309
LVMass(g)	157.18(121.30, 186.35)	171.76(154.79, 229.62)	140.20(116.64, 177.72)	0.014
ECV(%)	32.20(28.70, 38.30)	37.20(29.80, 41.09)	31.47(28.60, 36.50)	0.106

IPTW: inverse probability of treatment weighting; BMI: body mass index; BP: blood pressure; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; LAD: left atrial diameter; LVDd: left ventricular end-diastolic dimension; LVDs: left ventricular end-systolic dimension; NT-proBNP: N-terminal pro-B-type natriuretic peptide; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; LGE: late gadolinium enhancement; EDV: end-diastolic volume; ESV: end-systolic volume; LV: left ventricular; ECV: extracellular volume fraction.



Bar graphs illustrate adjusted mean changes (Δ) in echocardiographic parameters (Panels A-E) and the proportion of treatment responders (Panel F) among obese (OB) and non-obese (Non-OB) patients with heart failure with reduced or mildly reduced ejection fraction (HFReF/HFmrEF) following inverse probability of treatment weighting (IPTW) adjustment. Error bars indicate standard deviation (SD) for Panels A-E and 95% confidence intervals (95% CI) for Panel F. * $P < 0.05$.

图1 IPTW校正后肥胖与非肥胖HFReF/HFmrEF患者超声心动图参数变化与治疗反应的比较

Figure 1 Comparison of echocardiographic parameter changes and treatment response between the obese and non-obese HFReF/HFmrEF patients after IPTW adjustment

表3 IPTW校正后按性别分层的HFReF/HFmrEF患者超声心动图参数变化

Table 3 Echocardiographic parameter changes in HFReF/HFmrEF patients stratified by sex after IPTW adjustment

Variable	Male				Female			
	Total(n=56)	OB(n=27)	Non-OB(n=29)	P	Total(n=24)	OB(n=4)	Non-OB(n=20)	P
Δ LVEF	17.60 \pm 12.28	14.00 \pm 2.20	23.44 \pm 1.85	0.002	16.43 \pm 11.88	19.90 \pm 7.42	12.46 \pm 2.03	0.344
Δ LVDd	7.79 \pm 7.35	5.73 \pm 1.40	9.66 \pm 1.09	0.031	7.10 \pm 6.98	7.00 \pm 3.56	5.20 \pm 1.24	0.637
Δ LVDs	11.75 \pm 8.99	8.94 \pm 1.68	15.07 \pm 1.39	0.007	10.75 \pm 8.61	12.00 \pm 4.70	7.75 \pm 1.48	0.397
Δ LVDd%	11.52 \pm 10.26	8.40 \pm 1.94	14.55 \pm 1.46	0.014	8.84 \pm 9.10	10.96 \pm 5.19	8.42 \pm 1.96	0.651
Δ LVDs%	20.81 \pm 15.12	15.96 \pm 2.85	26.98 \pm 2.11	0.003	16.30 \pm 13.08	22.80 \pm 7.92	15.00 \pm 2.69	0.361

OB: obese patients; Non-OB: non-obese patients. P values were derived from Student's t-test after IPTW adjustment. The sample sizes presented are effective sample sizes after IPTW adjustment and therefore may be non-integers.

表4 HFReF/HFmrEF患者BMI与心脏结局相关性的回归分析

Table 4 Regression analyses of association between BMI and cardiac outcomes in HFReF/HFmrEF patients

Predictor variable	Outcome variable	Unadjusted		Model 1		Model 2		Model 3	
		β /OR(95% CI)	P	β /OR(95% CI)	P	β /OR(95% CI)	P	β /OR(95% CI)	P
BMI	Δ LVEF	-0.28(-0.68-0.12)	0.171	-0.74(-1.25--0.23)	0.006	-0.74(-1.25--0.22)	0.006	-0.90(-1.49--0.32)	0.004
	Δ LVDd	-0.11(-0.34-0.12)	0.361	-0.23(-0.54-0.08)	0.149	-0.36(-0.68--0.05)	0.028	-0.36(-0.73-0.01)	0.061
	Δ LVDs	-0.14(-0.43-0.15)	0.353	-0.37(-0.75-0.01)	0.062	-0.46(-0.85--0.08)	0.022	-0.51(-0.95--0.06)	0.030
	Δ LVDd%	-0.21(-0.54-0.12)	0.219	-0.39(-0.83-0.05)	0.086	-0.55(-1.02--0.08)	0.025	-0.57(-1.12--0.03)	0.043
	Δ LVDs%	-0.31(-0.80-0.18)	0.218	-0.73(-1.37--0.09)	0.027	-0.84(-1.53--0.15)	0.019	-0.98(-1.77--0.19)	0.019
	Treatment response [n(%)]	0.89(0.81-0.97)	0.008	0.79(0.67-0.93)	0.005	0.76(0.62-0.94)	0.011	0.70(0.53-0.93)	0.013

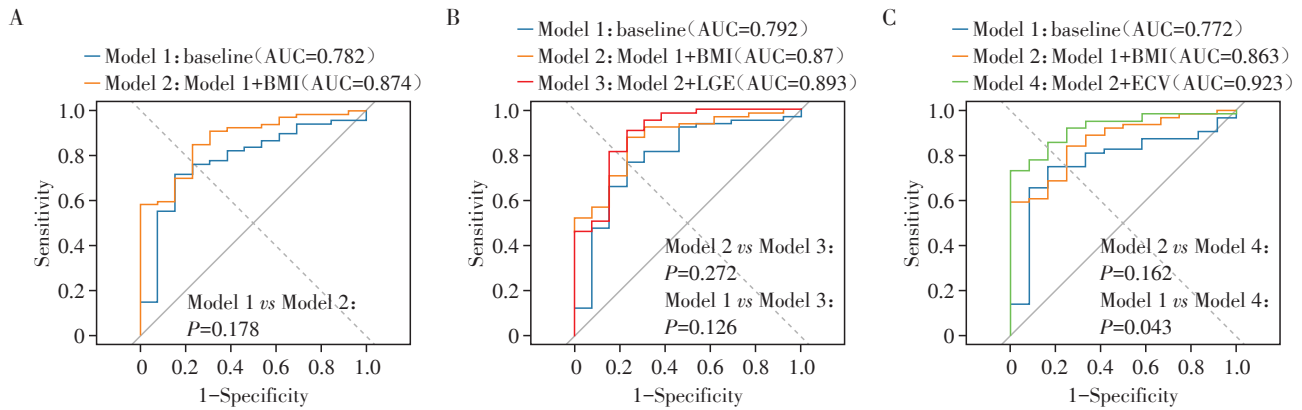
Model specifications: Model 1: adjusted for age and sex; Model 2: Model 1 plus baseline LVEF and left ventricular mass; Model 3: Model 2 plus comorbidities (hypertension, coronary heart disease, atrial fibrillation, diabetes) and key GDMT medication doses (sacubitril/valsartan and metoprolol succinate doses). β denotes regression coefficient for continuous outcomes; OR represents odds ratio for binary outcomes.

表5 LGE与ECV作为HFReF/HFmrEF患者治疗反应预测因子的逻辑回归分析

Table 5 Logistic regression analysis of LGE and ECV as predictors of treatment response in HFReF/HFmrEF patients

Predictor variable	Outcome variable	OR(95% CI)	P	Adjusted OR(95% CI)	Adjusted P
LGE	Treatment response	0.92(0.79-1.06)	0.257	0.68(0.49-0.95)	0.025
ECV		0.94(0.88-0.99)	0.023	0.89(0.81-0.97)	0.012

Adjusted variables: BMI, age, sex, baseline LVEF, left ventricular mass, and comorbidities (hypertension, coronary artery disease, atrial fibrillation, diabetes). OR, odds ratio; CI, confidence interval.



This composite figure presents three ROC curve analyses evaluating the performance of logistic regression models for predicting treatment outcomes in the HFrEF/HFmrEF patients. A: Comparisons between the Model 1 (baseline) and Model 2 (baseline+BMI). B: Comparisons between the Model 1, Model 2, and Model 3 (Model 2+LGE). C: Comparisons between the Model 1, Model 2, and Model 4 (Model 2+ECV). Model 1 includes age, sex, baseline LVEF, left ventricular mass, and comorbidities.

图2 HFrEF/HFmrEF患者预测模型比较的复合ROC曲线

Figure 2 Composite ROC curves comparing sequential predictive models in HFrEF/HFmrEF patients

2.6 BMI与纤维化指标的中介分析

中介分析旨在探讨心肌纤维化标志物(LGE、ECV)是否在BMI与治疗反应之间起中介作用(表6)。结果显示,BMI与治疗反应之间存在直接负向关联。LGE($\beta=-0.38, P=0.025$)和ECV($\beta=-0.12, P=$

0.012)也与治疗反应呈负相关。然而,BMI对LGE($\beta=0.08, P=0.368$)和ECV($\beta=0.49, P=0.088$)的影响均无统计学意义,提示肥胖对治疗反应的不利影响在很大程度上独立于心肌纤维化程度。未发现LGE或ECV存在显著的中介效应。

表6 HFrEF/HFmrEF患者BMI通过LGE与ECV影响治疗反应的中介分析路径系数

Table 6 Path coefficients from mediation analysis of BMI on treatment response via LGE and ECV in HFrEF/HFmrEF patients

Mediator	Path	SE	Beta	95% CI	P
LGE	BMI to mediator	0.09	0.08	-0.09-0.25	0.368
	BMI to outcome(direct effect)	0.14	-0.36	-0.63--0.09	0.008
	Mediator to outcome	0.17	-0.38	-0.72--0.05	0.025
ECV	BMI to mediator	0.28	0.49	-0.06-1.04	0.088
	BMI to outcome(direct effect)	0.13	-0.31	-0.56--0.05	0.018
	Mediator to outcome	0.05	-0.12	-0.21--0.03	0.012

SE: standard error; CI: confidence interval. All models were adjusted for age, sex, hypertension, coronary heart disease, atrial fibrillation, diabetes, left ventricular ejection fraction, and left ventricular mass. The path "BMI to outcome" indicates the direct effect of BMI on treatment response.

3 讨论

研究发现,在HFrEF/HFmrEF患者中,即使关键药物的使用情况相似,肥胖仍与心脏逆重构减弱及对GDMT的反应性降低相关。BMI是左心功能及内径改善的独立负向预测因素,且该影响在男性患者中更为显著。尽管心肌纤维化标志物(LGE和ECV)与较差的治疗反应独立相关,但它们并未介导肥胖的不利效应,提示可能存在不依赖于纤维化的潜在机制。联合BMI与ECV的预测模型显著提升

了对低治疗反应患者的识别能力。

3.1 肥胖与肥胖悖论

心力衰竭领域中广泛报道的“肥胖悖论”指出,超重或轻度肥胖患者可能具有更优的生存率。然而,该悖论的内在机制尚未完全阐明,且其不同疾病进程和终点事件中的适用性仍存争议^[5-6]。本研究并非旨在重新界定肥胖悖论,而是从影像学角度出发,通过聚焦HFrEF/HFmrEF患者的心脏逆重构及治疗反应性,为此现象提供补充性见解。

本研究发现,肥胖组患者虽然接受了更高剂量

的沙库巴曲缬沙坦与琥珀酸美托洛尔,但其心脏逆重构程度与治疗反应率却显著低于非肥胖组。这一看似矛盾的结果引出了两个关键问题。首先,这种“药物剂量增加”很可能是临床医生针对肥胖患者所采取的一种补偿性调整策略。临床医生可能基于其更重的病情负荷评估,而上调了核心治疗药物的剂量。这与既往注册研究中肥胖心衰患者往往能耐受并接受更强化GDMT的现象是一致的^[16]。其次,本研究发现,这种剂量调整在肥胖表型中并未完全转化为预期的生物学效应,即未能使心脏逆重构达到与非肥胖者相当的水平。多因素回归分析表明,肥胖对治疗反应的削弱作用独立于所使用的药物剂量。因此,尽管剂量上调可能部分反映了更好的临床耐受性,但并未能有效克服肥胖本身对心肌恢复过程的不利影响。这一发现提示,对于肥胖的心衰患者,标准的“剂量强化”策略在促进心脏逆重构方面可能存在局限性。

3.2 NT-proBNP水平无显著组间差异

本研究发现肥胖与非肥胖心衰患者的基线NT-proBNP水平无显著差异,这与经典“肥胖悖论”描述中肥胖者利钠肽水平通常较低的现象不同。多项研究证实,在心力衰竭患者及一般人群中,更高的BMI与更低的BNP及NT-proBNP水平独立相关^[17-18]。本研究出现不同结果的可能原因如下:首先,检测时机与心衰状态是需要考虑的因素。利钠肽水平动态变化,受心衰急性发作、失代偿加重或稳定期状态的影响^[19]。本研究所有心衰患者均为新诊断且在入组时未接受过任何前期GDMT。这意味着基线NT-proBNP的测量是在患者处于明确的疾病活动期、且未经治疗的状态下进行的。在这种临床背景下,心肌产生的应激信号可能非常强烈,从而部分掩盖了肥胖带来的利钠肽水平降低效应。其次,NT-proBNP水平取决于心肌生成与全身清除的平衡。肥胖通常通过脂肪组织高表达利钠肽清除受体等机制增强清除,导致水平降低。然而,本研究中肥胖组患者伴有更严重的左心室扩张、心肌肥厚及纤维化,提示其心肌应激与损伤更重,可能增强了NT-proBNP的生成,从而抵消了肥胖相关的清除增强效应。再次,两组间年龄、性别、合并症等基线特征不均衡,可能作为混杂因素影响了关联。最后,仅用BMI定义肥胖存在局限。既往研究指出,BMI与NT-proBNP的负相关主要由体重而非脂肪质量驱动^[20]。而BMI无法区分身体成分,可能掩盖了脂肪分布(如向心性肥胖)与利钠肽系统的特异性

关联。未来研究需结合更精确的身体成分测量指标进行深入探讨。

3.3 心脏逆重构的性别特异性差异

亚组分析显示,肥胖对心脏逆重构的不利影响在男性患者中更为显著,而在女性中未观察到明显差异。例如,Fu等^[21]报道腹型肥胖与男性(而非女性)HFpEF患者病死率增加独立相关,提示存在性别特异性。

多种机制可能参与上述差异的形成。男性多倾向于内脏脂肪堆积,此类脂肪组织代谢活跃且具促炎性,与微血管功能障碍及不良心脏重构相关^[22]。相比之下,女性更常见外周皮下脂肪分布,其对心血管系统的负面影响可能较小^[23]。此外,既往实验表明,雌激素相关通路可能通过减轻纤维化及促进血管生成等机制,对女性肥胖相关的心肌损伤发挥保护作用^[24]。

尽管这些机制仍属推测,但本研究强调了在评估肥胖对心脏逆重构影响时考量性别特异性的重要性。未来需进一步探索其生物学通路,为HFrEF/HFmrEF患者的性别特异性治疗策略提供依据。

3.4 心肌纤维化作为预测因子而非中介因子

本研究的一项重要发现是,心肌纤维化标志物并未介导肥胖与心力衰竭治疗反应降低之间的关联。我们证实LGE与ECV均为GDMT治疗反应降低的独立负向预测因子,这强化了纤维化与心力衰竭预后的关联^[10-11]。然而,中介分析并未支持这些纤维化标志物在肥胖与治疗反应减弱关系中的显著中介效应。

这表明,肥胖对心脏逆重构的不利影响可能主要通过非间质纤维化途径实现。尽管有限的样本量可能降低了对轻中度中介效应的检测力,但本研究结果不支持纤维化主导的机制。此外,本研究的局限性在于未纳入系统性炎症与代谢指标。肥胖常伴随慢性低度炎症状态、脂肪因子分泌失调以及胰岛素抵抗,这些因素均可直接或间接促进心肌纤维化、内皮功能障碍和心肌细胞代谢紊乱,从而可能抵消GDMT带来的获益^[25]。未来的前瞻性研究应着重于动态监测炎症标志物、脂肪因子谱及胰岛素抵抗相关指标,以明确这些肥胖相关的关键病理生理途径是否介导了其对抗心脏逆重构的负面影响,从而为肥胖心衰患者探索新的治疗靶点提供理论依据。

3.5 对病因异质性的考量

本研究的一项重要优势在于关注了非缺血性

病因为主的HFrEF/HFmrEF患者。通过严格的排除标准,最大程度地减少了缺血性心肌病这一对治疗反应和预后具有显著影响的病因干扰^[26]。尽管如此,非缺血性心衰内部仍存在病因异质性,如高血压性心脏病、心动过速心肌病等。值得注意的是,多因素回归分析已将高血压、心房颤动等关键病因和合并症作为协变量进行了校正。分析结果表明,即使在控制了这些因素后,BMI仍然是心脏逆重构减弱的独立危险因素。这提示肥胖对心脏逆重构的不利影响,可能超越了本研究所评估的这些常见病因差异,其机制可能更多地与肥胖相关的代谢、炎症等通路相关^[25]。当然,基于临床记录的病因分类可能无法完全捕捉其复杂性,且本研究样本量限制了更精细的病因亚组分析。未来前瞻性研究在更大样本中纳入更详细的病因学分型,将有助于进一步阐明该问题。

3.6 研究局限性

本研究存在若干局限性。首先,作为一项回顾性、单中心观察性研究,尽管采用逆概率加权及多变量调整,仍难以完全排除残留混杂因素。其次,本研究的样本量相对较小($n=80$),可能降低统计检验效能,增加Ⅱ类错误(假阴性)的风险。这一点在性别亚组分析中较为突出:女性肥胖亚组仅包含4例患者。因此,“在女性中未观察到明显差异”的结果应被谨慎解读,这更可能反映了检验效能不足,而非确实不存在性别差异。未来需要更大规模的前瞻性研究以验证或修正本研究关于性别特异性影响的初步发现。最后,采用BMI评估肥胖未能区分身体成分及脂肪分布^[27-28];未来研究中使用更精确的肥胖指标可能提供更深入的机制见解。

综上,肥胖独立损害HFrEF/HFmrEF患者的心脏逆重构并降低治疗反应性。虽然心肌纤维化(LGE、ECV)可预测低反应,但它并未显著介导肥胖效应关系。整合BMI和ECV的模型显著提高了对治疗反应的预测准确性。

利益冲突声明:

所有作者声明无利益冲突。

Conflict of Interests:

All authors declare no conflict of interests.

作者贡献声明:

李皓阳、邹建刚负责设计研究方案,确定研究方法,李皓阳负责数据分析及撰写论文;钱芷君和朱晓梅负责影像学数据收集与分析;曾嘉欣、张恩瑞参与设计研究方案,撰写和审阅论文;王焱、钱智勇、侯小锋参与文章审阅与修改;邹建刚负责文章审阅及修订。

Author's Contributions:

LI Haoyang and ZOU Jiangang were responsible for designing the research plan, determining research methods. LI Haoyang was responsible for data analysis and writing the paper; QIAN Zhijun and ZHU Xiaomei were responsible for data collection and analysis; ZENG Jiixin and ZHANG Enrui also participated in designing the research plan, writing, and reviewing the paper; WANG Yao, QIAN Zhiyong, and HOU Xiaofeng also participated in reviewing the paper; ZOU Jiangang was responsible for article review and revision.

参考文献

- [1] SHAHIM B, KAPELIOS C J, SAVARESE G, et al. Global public health burden of heart failure: an updated review [J]. *Card Fail Rev*, 2023, 9: e11
- [2] MCDONAGH T A, METRA M, ADAMO M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure [J]. *Eur Heart J*, 2021, 42(36): 3599-3726
- [3] MCDONAGH T A, METRA M, ADAMO M, et al. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure [J]. *Eur J Heart Fail*, 2024, 26(1): 5-17
- [4] REINHARDT M, SCHUPP T, ABUMAYYALEH M, et al. Obesity paradox in heart failure with mildly reduced ejection fraction [J]. *Pragmat Obs Res*, 2024, 15: 31-43
- [5] SALVINO N F A, SOUSA L T D, ABRAHAO F M, et al. Is the obesity paradox in outpatients with heart failure reduced ejection fraction real? [J]. *Front Cardiovasc Med*, 2023, 10: 1239722
- [6] SIMATI S, KOKKINOS A, DALAMAGA M, et al. Obesity paradox: fact or fiction? [J]. *Curr Obes Rep*, 2023, 12(2): 75-85
- [7] BUTT J H, PETRIE M C, JHUND P S, et al. Anthropometric measures and adverse outcomes in heart failure with reduced ejection fraction: revisiting the obesity paradox [J]. *Eur Heart J*, 2023, 44(13): 1136-1153
- [8] THYAGATURU H, SHAH K, LI S, et al. Obesity paradox in HFrEF hospitalizations: analysis of national inpatient sample 2016-2018 [J]. *Eur J Prev Cardiol*, 2021, 28(Supplement 1): i50
- [9] PACKER M. Do obesity and visceral adiposity promote heart failure with reduced ejection fraction? [J]. *Eur Heart J*, 2026, 47(1): 12-21
- [10] FRANGOGIANNIS N G. Cardiac fibrosis [J]. *Cardiovasc Res*, 2021, 117(6): 1450-1488
- [11] GHAZAL R, WANG M, LIU D, et al. Cardiac fibrosis in the multi-omics era: implications for heart failure [J]. *Circ Res*, 2025, 136(7): 773-802

- [12] 计雨佳,张恩瑞,钱雯,等. 心肌瘢痕与药物治疗反应对非缺血性心肌病心衰患者室性心律失常风险的影响[J]. 南京医科大学学报(自然科学版), 2025, 45(5): 671-677
JI Y J, ZHANG E R, QIAN W, et al. The impact of myocardial scarring and drug treatment response on the risk of ventricular arrhythmia in patients with nonischemic cardiomyopathy [J]. Journal of Nanjing Medical University (Natural Sciences), 2025, 45(5): 671-677
- [13] SCHULZ-MENGER J, BLUEMKE D A, BREMERICH J, et al. Standardized image interpretation and post-processing in cardiovascular magnetic resonance-2020 update[J]. J Cardiovasc Magn Reson, 2020, 22(1): 19
- [14] NAGUEH S F, SMISETH O A, APPLETON C P, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging [J]. Eur Heart J Cardiovasc Imaging, 2016, 17(12): 1321-1360
- [15] NAKAI T, IKEYA Y, KOGAWA R, et al. What are the expectations for cardiac resynchronization therapy? A validation of two response definitions[J]. J Clin Med, 2021, 10(3): 514
- [16] CAPPELLETTO C, STOLFO D, ORSINI N, et al. Use of and association between heart failure pharmacological treatments and outcomes in obese versus non-obese patients with heart failure with reduced ejection fraction: data from the Swedish Heart Failure Registry [J]. Eur J Heart Fail, 2023, 25(5): 698-710
- [17] LAVIE C J, ALPERT M A, ARENA R, et al. Impact of obesity and the obesity paradox on prevalence and prognosis in heart failure[J]. JACC Heart Fail, 2013, 1(2): 93-102
- [18] MEHRA M R, UBER P A, PARK M H, et al. Obesity and suppressed B-type natriuretic peptide levels in heart failure[J]. J Am Coll Cardiol, 2004, 43(9): 1590-1595
- [19] MCKITTRICK M M K, MCKITTRICK S M K, CONWAY R C, et al. The prognostic implications of serum NT-pro B-type natriuretic peptide (NT-proBNP) in emergency medical admissions [J]. Eur Heart J, 2025, 46 (Supplement 1): ehaf784.1160
- [20] DAS S R, DRAZNER M H, DRIES D L, et al. Impact of body mass and body composition on circulating levels of natriuretic peptides: results from the dallas heart study[J]. Circulation, 2005, 112(14): 2163-2168
- [21] FU L, ZHOU Y, SUN J, et al. Abdominal obesity is associated with an increased risk of all-cause mortality in males but not in females with HFpEF [J]. Cardiovasc Ther, 2022, 2022: 2950055
- [22] LUMISH H S, O'REILLY M, REILLY M P. Sex differences in genomic drivers of adipose distribution and related cardiometabolic disorders: opportunities for precision medicine [J]. Arterioscler Thromb Vasc Biol, 2020, 40(1): 45-60
- [23] JAYEDI A, SOLTANI S, ZARGAR M S, et al. Central fatness and risk of all cause mortality: systematic review and dose-response meta-analysis of 72 prospective cohort studies[J]. BMJ, 2020, 370: m3324
- [24] IORGA A, LI J, SHARMA S, et al. Rescue of pressure overload-induced heart failure by estrogen therapy [J]. J Am Heart Assoc, 2016, 5(1): e002482
- [25] CHIN J F, AGA Y S, ABOU KAMAR S, et al. Association between epicardial adipose tissue and cardiac dysfunction in subjects with severe obesity [J]. Eur J Heart Fail, 2023, 25(11): 1936-1943
- [26] LING L F, MARWICK T H, FLORES D R, et al. Identification of therapeutic benefit from revascularization in patients with left ventricular systolic dysfunction: inducible ischemia versus hibernating myocardium [J]. Circ Cardiovasc Imaging, 2013, 6(3): 363-372
- [27] HOBACH A J, FELD J, LINKE W A, et al. BMI-stratified exploration of the 'obesity paradox': heart failure perspectives from a large german insurance database [J]. J Clin Med, 2024, 13(7): 2086
- [28] HUANG C, LI Y, XU Y, et al. Body mass index, regional adipose deposition, and clinical outcomes in non-ischaemic dilated cardiomyopathy: a prospective cohort study [J]. Eur J Prev Cardiol, 2025, 32(12): 1043-1053

(收稿: 2026-01-09; 修回: 2026-03-06; 录用: 2026-03-09)

(本文编辑: 唐震)