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射血分数保留的老年心力衰竭患者的临床特征*

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摘要 目的:分析和比较射血分数保留的心力衰竭(HFpEF)、射血分数中间值(HFmrEF)及射血分数降低的老年心力衰竭(HFrEF)患者临床特征的差异。**方法:**选取2017年9月至2018年8月哈尔滨市第一医院收治的老年慢性心力衰竭患者共287例,根据心动超声所测左室舒张末期容积(LVEF)值将其分为3组:HFpEF组175例、HFmrEF组50例和HFrEF组62例。比较各组患者一般情况、心动超声检查结果、血清学指标的差异。**结果:**(1)与HFrEF组患者比较, HFpEF组患者年龄、性别、吸烟史、体重指数(BMI)、原发性冠心病、高血压、2型糖尿病患者比例、房颤发生率及心功能分级构成比均具有统计学差异($P<0.05$);(2)与HFrEF组相比较, HFpEF组患者的E/A比值,左房内径、肺动脉内径、LVEDD较小,而室间隔厚度较厚($P<0.05$);(3)与HFrEF组患者相比, HFpEF组血清总胆固醇、甘油三酯较高;血肌酐、血尿素氮、血尿酸、超敏C反应蛋白、N-末端脑钠肽前体水平较低,具有统计学差异($P<0.05$)。**结论:**老年HFpEF心力衰竭患者以女性居多,体重指数较大,以向心性肥胖为主,血压水平较高,心功能II级者比例高,有明显的舒张功能不全,易发生房性心律失常,房颤发生率高,主要病因为高血压。

关键词:射血分数保留的心力衰竭;射血分数中间值的心力衰竭;射血分数降低的心力衰竭;临床特征

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Clinical Feature of Elderly Heart Failure Patients with Ejection Fraction Retention*

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ABSTRACT Objective: To investigate and compare the clinical characteristics of heart failure with retained ejection fraction (HFpEF), heart failure with intermediate ejection fraction (HFmrEF) and heart failure with reduced ejection fraction (HFrEF) in the elderly patients. **Methods:** A total of 287 elderly patients with chronic heart failure admitted to the Harbin first hospital from September 2017 to August 2018 were selected. According to the LVEF value measured by echocardiography, they were divided into 3 groups: 175 patients in the HFpEF group; There were 50 cases in HFmrEF group and 62 cases in HFrEF group. The general situation, cardiac ultrasound, serology and other indicators of patients in each group were compared, and the clinical characteristics of the three groups were analyzed and compared. **Results:** (1) Compared with patients in the HFrEF group, the age, gender, smoking history, body mass index (BMI) proportion of patients in the HFpEF group, the proportion of coronary heart disease, hypertension, type 2 diabetes among the primary causes, the incidence rate of atrial fibrillation and the composition ratio of cardiac function classification were statistically different ($P<0.05$); (2) Compared with the HFrEF group, the E/A ratio of patients in the HFpEF group showed smaller left atrial diameter, pulmonary artery diameter and LVEDD, while thicker ventricular septal thickness ($P<0.05$). (3) Compared with patients in the HFrEF group, serum total cholesterol and triglyceride in the HFpEF group were higher; Serum creatinine, blood urea nitrogen, blood uric acid, hypersensitive c-reactive protein and n-terminal brain natriuretic peptide precursor levels were lower, with statistically significant differences ($P<0.05$). **Conclusion:** Among the elderly patients with heart failure, the majority of HFpEF patients are women. The body mass index (BMI) was large, and the centripetal obesity was the main one. High blood pressure. The main disease is hypertension, and the incidence of atrial fibrillation is high. In terms of cardiac function evaluation, patients in the HFpEF group have more level II cardiac function and are prone to atrial arrhythmia. There is obvious diastolic insufficiency.

Key words: Ejection fraction retention in heart failure; Median ejection fraction of heart failure; Decreased ejection fraction in heart failure; Clinical features

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前言

心力衰竭(heart failure, HF)是多种原因导致心脏结构和 /

或功能的异常改变,使心室收缩和 / 或舒张功能发生障碍,而引起的一组复杂临床综合征^[1],主要表现为呼吸困难、疲乏和液体潴留的症状,如肺淤血、体循环淤血及外周水肿等。根据左

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心室射血分数 (left ventricular ejection fraction, LVEF) 的不同, HF 可分为以下三类: 射血分数保留的心衰(heart failure with ejection fraction, HFpEF, LVEF $\geq$ 50%)、射血分数降低的心衰(heart failure with reduced ejection fraction, HFrEF, LVEF $<$ 40%)和射血分数中间值的心衰 (heart failure with mid-range ejection fraction, HFmrEF, LVEF40%-49%)^[2]。大量研究显示随着人口老龄化的加剧, 慢性 HF 患者中 HFpEF 患者所占比例明显增加^[3], 明确其临床特征对于改善患者预后具有重要的临床意义。本研究通过比较 HFpEF 组、HFrEF 组、HFmrEF 组患者的临床特征差异, 探讨了射血分数保留的老年心力衰竭临床特征, 结果如下。

1 资料与方法

1.1 一般资料

入选自 2017 年 9 月至 2018 年 8 月在我院住院的 60 岁以上已确诊为慢性心力衰竭的患者作为研究对象, 共 287 例。根据心动超声所测 LVEF 值, 将其分为 3 组: HFpEF 组 175 例, HFmrEF 组 50 例, HFrEF 组 62 例。心功能分级按照纽约心脏病协会(NYHA)的分级标准。

1.2 纳入及排除标准

纳入标准: (1) 慢性心力衰竭按照 2018 年中国心力衰竭诊断和治疗指南制定的诊断依据; (2) HFpEF、HFmrEF、HFrEF 各组的诊断按照 2018 年中国心力衰竭诊断和治疗指南: 依据患者症状与体征、超声心动图结果、相关的结构性心脏病变或舒张功能不全的证据。排除标准: 急性冠脉综合征、先天性心脏病、急慢性心包炎、瓣膜性心脏病、肺源性心脏病、严重的内分

泌疾病、结缔组织疾病、肿瘤、肝肾功能不全、严重感染性疾病。

1.3 观察指标

(1) 一般情况: 收集所有受试者的临床资料包括年龄、性别、吸烟史、病因、身高及体重、以计算体重指数(BMI)。(2) 应用飞利浦 IE-33 超声诊断仪作心动超声图, 检测指标包括: E 峰(二尖瓣早期血流速度)、A 峰(舒张晚期血流速度)、E/A 比值(二尖瓣早期血流速度 / 舒张晚期血流速度)、室间隔厚度、左房内径、肺动脉内径、LVEDD(左室舒张末期内径)、LVEF(左室射血分数)。(3) 血清学指标: 四组受试者均在禁食 12 小时后, 于次日晨起 6:30 分抽取空腹静脉血标本送我院检验科, 采用日本 Sysmex XN-1000 血液分析仪、美国 BECKMAN COULTER AU5800 生化分析仪、南京 FIA8000 系列免疫定量分析仪进行分析测定, 检测的项目包括血浆 BNP、血糖(GLU)、甘油三酯(TG)、血清总胆固醇(TC)、低密度脂蛋白(LDL)、高密度脂蛋白(HDL)、肌酐(Scr)、尿素氮 (BUN)、血清钾钠钙离子、N-末端脑钠肽前体 (NT-proBNP)。

1.4 统计学分析

采用 SPSS 19.0 版统计学分析软件对所得的各组数据进行正态性检验和方差齐性检验。计量资料数据以均数 $\pm$ 标准差($\bar{x} \pm s$)表示, 两组计量资料比较采用 LSD-t 检验, 如方差齐采用单因素方差分析 (one-way, ANOVA), 如方差不齐采用秩和检验, 运用 Pearson 法分析各个指标的相关性, 以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 各组一般情况比较

表 1 各组受试者一般情况比较

Table 1 Comparison of the general conditions of subjects in each group

Objection	HFpEF (n=60)	HFmrEF (n=50)	HFrEF (n=51)
Ages (years)	76.42 $\pm$ 7.75	74.62 $\pm$ 11.27	72.32 $\pm$ 7.73*
Sex			
Male (%)	76(43.42)	27(53.79)*	35(56.86)*
Female (%)	99(56.57)	23(46.22)*	27(43.14)*
Smoking (%)	32(18.35)	17(33.82)	26(41.18)*
BMI(kg/m ²)	24.53 $\pm$ 4.66	24.34 $\pm$ 5.87	22.51 $\pm$ 3.90* Δ
Coronary Artery Disease(%)	115(65.72)	43(86.67)*	61(98.04)*
Hypertension (%)	98(56.21)	32(64.62)	27(43.98)*
Diabetes (%)	46(26.11)	13(25.36)	15(24.14)
Atrial fibrillation(%)	81(46.21)	11(22.98)	16(25.99)*
Cardiac Function Levels			
II level (%)	76(43.33)	5(9.79)	5(8.06)* Δ
III level (%)	73(41.71)	24(48.11)	26(41.93)* Δ
IV level (%)	26(14.85)	21(42.00)	32(51.61)

在本研究中, HFpEF 组患者比例最高 (60.97%), HFrEF 组患者次之(21.61%), HFmrEF 组患者最少(17.42%)。HFpEF 组中, 女性和高龄患者较多, 体重指数、血压水平平均较高, 主要发

病原因为高血压, 心房颤动发生率高($P < 0.05$), 合并糖尿病者较多, 但组间差异无统计学意义。HFrEF 组患者主要为冠心病 ($P < 0.05$)。在心功能分级上, HFpEF 组患者 II 级较多, 而 HFrEF

组患者主要为 III-IV 级。而 HFmrEF 组患者临床特征介于二者之间,有些特征类似于 HFpEF 组患者,有些特征类似于 HFrEF 组患者。见表 1。

2.2 超声心动图指标比较

表 2 各组心脏超声测量参数比较

Table 2 Comparison of the cardiac ultrasound measurement parameters between different groups

Item	HFpEF	HFmrEF	HFrEF
Ventricular Septal Thickness (mm)	10.65± 1.44	10.38± 1.26	10.06± 1.12*
E/A	0.85± 0.32	1.25± 0.52*	1.41± 0.71*
Left Atrial Diameter (mm)	37.94± 8.26	39.54± 8.13*	41.32± 4.23* [△]
Pulmonary Artery Diameter (mm)	21.00± 3.01	21.68± 3.02*	22.38± 3.05* [△]
LVEDD(mm)	48.61± 6.91	59.71± 8.22*	64.52± 8.25* [△]
LVEF	58.67± 4.60	45.92± 2.5*	34.52± 5.88* [△]

Note: LVEDD = Left Ventricular End Diastolic Diameter; LVEF= Left Ventricular Ejection Fraction.

*HFrEF is compared with HFpEF group, P<0.05; [△]HFrEF is compared with HFmrEF group, P<0.05.

2.3 血清学指标比较

HFpEF 组患者与 HFmrEF 组患者血清总胆固醇、甘油三酯、低密度脂蛋白、空腹血糖、血尿酸、血清钾钠钙离子、超敏 C 反应蛋白水平比较差异均无统计学意义(P>0.05);而 HFpEF 组患者血肌酐、血尿素氮及 N- 末端脑钠肽前体水平均较 HFmrEF 组患者显著降低(P<0.05)。HFpEF 组患者与 HFrEF 组患者

HFpEF 组患者的室间隔厚度较 HFrEF 组患者大(P<0.05); HFrEF 组患者 E/A 比值、左房内径、肺动脉内径、LVEDD 较大, LVEF 较低。HFmrEF 组患者 E/A 比值、左房内径、肺动脉内径、LVEDD 比 HFpEF 组患者高, LVEF 较低(P<0.05)。见表 2。

相比较,低密度脂蛋白、空腹血糖、血清钾钠钙离子比较无统计学差异(P>0.05),血清总胆固醇、甘油三酯较高;血肌酐、血尿素氮、血尿酸、超敏 C 反应蛋白、N- 末端脑钠肽前体水平较低,具有统计学差异(P<0.05)。HFmrEF 组患者与 HFrEF 组患者比较:超敏 C 反应蛋白、N- 末端脑钠肽前体水平较低,具有统计学差异(P<0.05)。见表 3。

表 3 各组血生化指标的比较

Table 3 Comparison of the serum biochemical indexes between different groups

Objection	HFpEF	HFmrEF	HFrEF
Total cholesterol (mmol/L)	4.56± 1.12	4.39± 0.82	3.87± 1.39*
Triglycerides (mmol/L)	1.47± 0.67	1.2± 0.49	1.45± 0.78*
Low Density Lipoprotein (mmol/L)	2.78± 0.93	2.71± 0.64	3.06± 1.11
Fasting Plasma Glucose (mmol/L)	6.18± 2.52	7.93± 3.52	6.04± 1.54
Blood Urea Nitrogen (mmol/L)	6.53± 2.31	10.58± 6.27*	8.88± 7.25*
Serum Creatinine (umol/L)	118.75± 151.94	139.83± 98.38*	126.41± 119.57*
Serum Sodium (mmol/L)	141.00± 3.31	139.08± 4.5	141.39± 2.92
Potassium (mmol/L)	4.07± 0.45	4.32± 0.83	4.27± 0.41
Calcium (mmol/L)	2.22± 0.13	2.14± 0.18	2.31± 11.00
Blood Uric Acid (umol/L)	351.11± 100.22	378.15± 95.74	396.95± 134.23*
Hs-CRP (mg/L)	0.63± 0.58	1.82± 1.41	4.64± 2.04* [△]
NT-pro BNP (pg/ml)	1003.90± 981.90	4098.5± 2155.1*	2557.18± 1314.88* [△]

Note: Hs-CRP= Hypersensitive c-reactive protein; NT-proBNP =N-terminal brain natriuretic peptide precursor;

* HFrEF is compared with HFpEF group, P<0.05; [△]HFrEF is compared with HFmrEF group, P<0.05.

3 讨论

HFpEF 以心脏舒张功能异常、顺应性减低为特征,具有预后差、猝死风险大、死亡率高的特点,目前发病率呈逐年升高^[9]。据文献报道, HFpEF 患者占心力衰竭的比例波动较大, 约占 40-71%^[9], 常常发生在老龄肥胖的患者、往往有高血压病、冠心

病、心房颤动、糖尿病、肥厚性心肌病、限制性心肌病的病史,更加容易发生在老年女性、患有高血压、且体重指数较大的患者^[6-11], 主要与心室 - 血管耦合异常及其所导致的大动脉僵硬有关。本研究结论与以上观点相符。心功能分级是评价心脏受损严重程度的指标, 按照纽约心脏病学会心功能分为 I-IV 级, 其值越大表示心功能越差^[12]。本研究中, HFpEF 患者主要以心功

能 II 级为主, HFmrEF 患者主要以心功能 III 级为主, HFrEF 患者主要以心功能 IV 级为主, 提示三组患者中 HFpEF 组患者心功能受损最轻。

神经内分泌系统的激活导致心室重构是引起心衰发生和发展的关键因素。HFpEF 患者在病理学上的改变主要是向心性肥厚, 原因在于 HFpEF 患者心脏后负荷过重, 而增加了心室壁的张力。机体为了维持正常范围内的心室壁张力, 就会通过代偿机制而使心肌纤维复制, 久之出现心室壁的增厚, 室间隔的增厚^[13-15], 同时心肌纤维并不拉长, 最终导致向心性心室肥厚。在正常情况下, 因为在舒张早期左心室充盈量大于心房收缩期左心室的充盈量^[16,17], 所以心动超声测得 E/A 比值应大于 1, 正常值为 1.6 ± 0.5 。临床上往往用 E/A 比值评价左心室的舒张功能。本研究将三组测量参数进行比较, 发现 HFpEF 组、HFmrEF 组、HFrEF 组患者的室间隔厚度由大逐渐变小; E/A 比值、肺动脉内径、LVEDD 逐渐增大, 提示 HFpEF 患者有明显的舒张功能不全。

慢性心力衰竭的患者会出现中心静脉压的升高、消化系统的淤血、从而使脂质摄入和吸收减少, 而其中肝淤血又可影响脂质转运和合成, 导致脂质代谢紊乱, 机体总胆固醇水平降低^[18,19]。心力衰竭的发生与氧化应激、炎症反应密切相关^[20-22]。氧化应激是指机体在遭受各种有害刺激时, 体内会产生过多的高活性分子(活性氧自由基和活性氮自由基), 出现氧化系统和抗氧化系统失衡的现象, 即氧化程度超过氧化物的清除, 从而导致组织损伤^[23]。活性氧在体内可介导心肌细胞的肥大和凋亡, 从而导致内皮功能的障碍, 这些是通过信号通路及灭活一氧化氮等机制来完成的^[24]。血管内皮细胞能够保持血液正常流动、维持心血管的稳态, 当内皮功能障碍时会降低血管扩张反应能力, 从而损害内皮调节的一氧化氮生物利用度^[25]。Akiyama 等^[26]研究表明内皮功能障碍是 HFpEF 的独立危险因素, 能够独立预测 HFpEF 患者的预后。研究显示血尿酸可反映机体的氧化应激状况, 与心力衰竭的发生、发展及预后紧密相关^[27-29]。另外, 炎症反应也可促进心肌细胞坏死、内皮功能障碍、心室重构的发生, 这也是慢性心力衰竭的独立危险因素^[30]。研究表明^[31]超敏 C 反应蛋白与机体的炎症水平呈正相关。本研究结果提示 HFpEF 患者或许存在较高的氧化应激和炎症反应。

综上所述, HFpEF 老年心力衰竭患者具有以下特点: 女性居多、体重指数较大、血压水平较高、房颤发生率高、以向心性肥胖为主、有明显的舒张功能不全、心功能 II 级较多。或许存在较高的氧化应激和炎症反应。因本研究样本量有限, 研究结论仍有待于扩大样本量进一步研究证实。

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由于政府机构改革,经黑龙江省机构编制委员会批准,黑龙江省卫生厅更名为黑龙江省卫生健康委员会。由此,本刊的主管单位将由黑龙江省卫生厅更名为黑龙江省卫生健康委员会,相应的更名批文正在办理过程中!

特此告示!

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