

不同射血分数类型心力衰竭患者肾功能恶化的发生率及相关因素分析

王婧欣 李 雷 张丹丹 徐 敏 陈思远

摘要 **目的** 比较肾功能恶化(WRF)在射血分数减低(HFrEF)、射血分数中间值(HFmrEF)和射血分数保留的心力衰竭(HFpEF)中的发生率及相关因素的分析。**方法** 对2015年5月~2020年5月徐州医科大学附属医院住院的130例慢性心力衰竭(CHF)患者的临床资料进行回顾性分析。根据射血分数分为射血分数减低的心力衰竭(HFrEF)组56例、射血分数中间值的心力衰竭(HFmrEF)组32例和射血分数保留的心力衰竭(HFpEF)组42例,统计分析3组CHF患者肾功能恶化发生率及相关因素。**结果** HFrEF组WRF发生率为23.2%,HFmrEF组WRF发生率为21.9%,HFpEF组WRF发生率为45.2%,HFpEF组WRF发生率与HFrEF组及HFmrEF组发生率比较,差异有统计学意义($P < 0.05$)。3组之间非参数检验显示,3组年龄、性别、肺动脉收缩压水平比较,差异有统计学意义($P < 0.05$),HFpEF组较HFmrEF组和HFrEF组,年龄较高,女性居多,肺动脉收缩压水平较高。3组各自的肾功能恶化危险因素的回归分析显示,年龄、性别、肺动脉收缩压均不是HFrEF和HFmrEF组肾功能恶化的危险因素($P > 0.05$)。而性别、年龄、肺动脉收缩压是HFpEF组肾功能恶化的危险因素($P < 0.05$)。**结论** HFpEF患者中WRF发生率高于HFrEF和HFmrEF患者。

关键词 心力衰竭 肾功能恶化 射血分数

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Study on the Incidence and Related Factors of Worsening Renal Function in Heart Failure with Different Ejection Fraction Categories.

Wang Jingxin, Li Lei, Zhang Dandan, et al. Graduate School, Xuzhou Medical University, Jiangsu 221002, China

Abstract **Objective** To compare the incidence and related factors of worsening renal function in patients with preserved (HFpEF), mid-range (HFmrEF), and reduced EF (HFrEF). **Methods** The clinical data of 130 patients with chronic heart failure (CHF) hospitalized in the affiliated Hospital of Xuzhou Medical University from May 2015 to May 2020 were analyzed retrospectively. According to the ejection fraction, the patients were divided into three groups: 56 patients with heart failure with decreased ejection fraction (HFrEF), 32 patients with heart failure with median ejection fraction (HFmrEF) and 42 patients with heart failure with preserved ejection fraction (HFpEF). Statistical analysis was made to find out the incidence and related factors of worsening renal function in the three groups of patients with CHF. **Results** The incidence of WRF was 23.2% in HFrEF group, 21.9% in HFmrEF group and 45.2% in HFpEF group. The incidence of WRF in HFpEF group was significantly higher than that in HFrEF group and HFmrEF group ($P < 0.05$). Nonparametric tests among the three groups showed that there were statistically significant differences in age, sex and pulmonary artery systolic pressure among the three groups ($P < 0.05$). Compared to HFrEF group and HFmrEF group, the patients in HFpEF group were older, mostly female and higher level of pulmonary artery systolic pressure ($P < 0.05$). Regression analysis showed that age, sex and pulmonary artery systolic pressure were not risk factors for renal function deterioration in HFrEF and HFmrEF groups ($P > 0.05$). However, sex, age and pulmonary artery systolic pressure were risk factors for renal function deterioration in HFpEF group ($P < 0.05$). **Conclusion** The incidence of WRF in patients with HFpEF is higher than that in patients with HFrEF and HFmrEF.

Key words Heart failure; Worsening renal function; Ejection fraction

随着人口老龄化和医疗水平的提高,慢性心力衰竭(CHF)的发生率逐年提高,而肾功能恶化(WRF)

在各种射血分数的慢性心力衰竭中均很常见,这给临床诊断和治疗均带来了挑战^[1]。多项研究表明WRF在不同射血分数的慢性心力衰竭中的发生机制可能不同^[2]。发生机制的不同可能导致WRF在不同射血分数中的发生率存在差异,因此本研究评估和比较了肾功能恶化(WRF)在射血分数减低(HFrEF)、射血分数中间值(HFmrEF)和射血分数保留的心力衰

作者单位:221002 徐州医科大学研究生院(王婧欣、张丹丹、徐敏、陈思远);221002 徐州医科大学附属医院全科医学科、老年医学科(李雷)

通讯作者:李雷,电子邮箱:Ligroup-999@126.com

竭(HFpEF)中的长期发生率,并检查了WRF在不同射血分数类型的HF中发生率不同的可能影响因素。

资料与方法

1. 一般资料: 回顾性分析2016年5月~2019年5月徐州医科大学附属医院住院治疗的130例慢性心力衰竭(CHF)患者的真实队列。根据《中国心力衰竭诊断和治疗指南2018》诊断研究对象是否为HF患者^[3]。依据2016年《欧洲心力衰竭指南(ESC)》根据左心室射血分数(LVEF)将心力衰竭患者分成3组, HFpEF组(LVEF ≥ 50%)、HFmrEF组(LVEF 40% ~ 49%)和 HFrEF组(LVEF < 40%)。排除标准: ①年龄 < 18岁; ②急性心肌梗死; ③合并恶性肿瘤; ④心包疾病; ⑤明显的心脏瓣膜病; ⑥严重感染; ⑦原发病为肝脏、肾脏疾病所导致的心力衰竭; ⑧原发性肾脏疾病或使用肾毒性药物; ⑨糖尿病、系统性红斑狼疮; ⑩出院后没有随访的患者。

2. 数据收集: 肾功能恶化(WRF)定义为血清肌酐(SCr)在初次检测的水平上增加超过0.3mg/dl(26.5 μmol/L)或血清肌酐(SCr)在初次检测的基线水平上增加超过25%。记录患者临床资料、生物化学指标、心脏彩超、入院前服用药物、住院治疗药物。采入院后第2天晨时空腹8h外周静脉血测定其实实验室指标。(1)临床资料: 年龄、性别、心律失常病史、脑卒中病史。(2)生物化学指标: 初次检测的脑钠肽(BNP)、血清胱抑素C(CysC)、血清肌酐(SCr)、血尿

素氮(BUN)、血尿酸(UA)、肾小球滤过率(eGFR)、血红蛋白(Hb); 半年或更长时间复查的血清肌酐(SCr)、肾小球滤过率(eGFR)。(3)心脏彩超: 左心室射血分数(LVEF)、肺动脉收缩压。(4)入院前服用药物: β受体阻滞剂、ACEI/ARB、袢利尿剂、螺内酯。(5)住院治疗药物: 螺内酯例数、托拉塞米例数、呋塞米例数、正性肌力药物例数。

3. 统计学方法: 采用SPSS 22.0统计学软件对数据进行统计分析。对3组患者基线资料进行比较, 对服从正态分布的连续型变量采用方差分析, 以均数 ± 标准差($\bar{x} \pm s$)表示, 对不服从正态分布的连续型变量采用 Kruskal - Wallis 检验, 以中位数(四分位数间距)[M(Q1, Q3)]表示; 对分类变量采用 χ^2 检验, 以例数(百分比)[n(%)]表示, 以 $P < 0.05$ 为差异有统计学意义。

结 果

1.3组基线资料比较: 3组患者年龄比较, 差异有统计学意义($P < 0.05$), HFpEF患者年龄水平较其他两组较高; 3组男性比例比较, 差异有统计学意义($P < 0.05$), HFpEF患者中女性比例较其他两组较多; 3组肺动脉收缩压水平比较, 差异有统计学意义($P < 0.05$), HFpEF患者肺动脉收缩压较其他两组较高; 3组的心功能分级、脑卒中病史、心力衰竭病史及药物治疗等比较, 差异无统计学意义($P > 0.05$), 详见表1、表2。

表1 3组基线资料的比较[n(%), $\bar{x} \pm s$, M(Q1, Q3)]

项目	HFrEF(n=56)	HFmrEF(n=32)	HFpEF(n=42)	F/ χ^2	P
年龄(岁)	70.0(50,88)	73.0(50,91)	75.5(53,87)	7.271	0.026
男性	36(64.3)	20(62.5)	17(40.5)	6.220	0.045
NYHA IV级	20(35.7)	8(25.0)	8(19.0)	3.483	0.175
脑卒中	7(12.5)	8(25.0)	11(26.2)	3.475	0.176
心律失常	22(39.3)	15(46.9)	23(54.8)	2.322	0.313
CysC(mg/L)	1.005(0.590,2.030)	1.020(0.610,2.280)	1.000(0.670,1.710)	0.223	0.894
肌酐(μmol/L)	72.0(46.0,178.0)	75.5(44.0,258.0)	65.0(43.0,118.0)	4.608	0.100
eGFR(ml/min)	90.51 ± 98.12	91.07 ± 27.16	94.03 ± 28.45	0.203	0.816
血尿酸(μmol/L)	375.0(192.0,738.0)	362.5(219.0,652.0)	334.0(129.0,759.0)	4.276	0.118
尿素氮(mmol/L)	6.105(2.100,19.900)	6.850(3.270,24.060)	5.645(3.520,15.250)	2.335	0.311
血红蛋白(g/L)	140.786 ± 18.970	131.563 ± 14.242	134.619 ± 18.852	3.057	0.051
脑钠肽(pg/ml)	3899.5(285,35000)	3378.5(135,17113)	2227.5(853,14129)	5.813	0.055
肺动脉收缩(mmHg ^Δ)	37.0(28,60)	37.0(30,65)	48.5(28,111)	6.150	0.046

^Δ1mmHg = 0.133kPa

2.3组肾功能恶化发生率比较: 56例HFrEF患者中13例(23.2%)发生肾功能恶化, 32例HFmrEF患者中7例(21.9%)发生肾功能恶化, 42例

HFpEF患者中19例(45.2%)发生肾功能恶化, 3组肾功能恶化的发生率比较, 差异有统计学意义($P = 0.032$)。

表2 3组用药情况的比较[n(%)]

项目	HFrEF(n=56)	HFmrEF(n=32)	HFpEF(n=42)	F/χ ²	P
入院前服用β受体阻滞剂	16(28.6)	11(34.4)	15(35.7)	1.832	0.400
入院前服用ACEI或ARB	20(35.70)	10(31.25)	16(38.10)	0.377	0.828
入院前服用螺内酯	16(28.6)	9(28.1)	13(31.0)	0.091	0.956
入院前服用利尿剂	15(26.8)	9(28.1)	15(35.7)	0.982	0.612
住院期间使用螺内酯	53(94.6)	28(87.5)	35(83.3)	3.327	0.189
住院期间使用托拉塞米	38(67.9)	25(78.1)	33(78.6)	1.829	0.401
住院期间使用呋塞米	16(28.6)	6(18.8)	10(23.8)	1.080	0.583
住院服用正性肌力药物	18(32.1)	9(28.1)	7(16.7)	3.062	0.216

3.3组肾功能恶化危险因素的Logistic回归分析:以心力衰竭患者肾功能恶化为因变量(0=无,1=有),以单因素分析有统计学意义的指标为自变量,对年龄、性别、肺动脉收缩压进行Logistic回归分析,分析3组不同射血分数类型心力衰竭各自发生肾

功能恶化的危险因素。回归分析结果显示年龄、性别、肺动脉收缩压均不是HFrEF和HFmrEF组肾功能恶化的危险因素(P>0.05),而性别、年龄、肺动脉收缩压是HFpEF组肾功能恶化的危险因素。

表3 HFpEF组肾功能恶化危险因素回归分析

项目	β	SE	Wald	P	OR	95% CI
性别	2.314	1.136	4.146	0.042	10.112	1.091~93.769
年龄	0.291	0.114	6.499	0.011	1.338	1.070~1.674
肺动脉收缩压	0.070	0.032	4.744	0.029	1.073	1.007~1.142

讨 论

心脏和肾脏在心力衰竭临床综合征中密切相关,由于共同的风险因素对这两种器官系统的影响^[4]。肾功能恶化常常发生在各种不同类型的心力衰竭中,当肾功能恶化发生时常常意味着更高的病死率和发生率^[5]。虽然对心力衰竭患者的心肾相互作用已有很多研究,但在临床治疗中仍有很多问题有待于进一步研究。

本研究中HFpEF患者年龄较HFrEF组和HFmrEF组年龄大,女性较多,与许多文献报道相一致^[6]。女性的预期寿命比较长,衰老又是肾功能恶化的独立危险因素,随着年龄的增长,肾脏的结构会发生改变,如肾小球硬化、肾小管萎缩、间质性纤维化等^[7]。

本研究发现,HFpEF组患者在随访期间发生WRF的发生率高于HFrEF组和HFmrEF组的心力衰竭患者,这与Lofman等^[8]研究一致。此外,本研究发现HFpEF组的肺动脉收缩压高于HFrEF和HFmrEF组。有研究显示,肺动脉高压在HFpEF患者中普遍存在^[9]。Unger等^[10]研究发现,WRF与HFpEF中较高的肺动脉压相关。这与本研究的结论一致。在本研究中HFpEF患者肺动脉压更高,肺动脉高压患者可能有更多的血管疾病和更高的肾功能减退风险,并且也与右心功能不全有关^[11]。

心脏和肾脏之间的相互作用一直是人们感兴趣的课题,但机制途径尚未完全阐明。连接心脏、肾脏的主要病理生理机制包括血流动力学因素,肾血管紧张素-醛固酮系统(RAAS)的激活,交感神经系统(SNS)的刺激,炎症以及一氧化氮(NO)和活性氧(ROS)之间的平衡失调^[12]。这些机制之间相互作用,进一步破坏心脏和肾脏功能^[13]。

在HFpEF患者中,左侧和右侧充盈压力升高是主要的血流动力学特征^[14]。HFpEF患者中肺动脉收缩压增高普遍存在,即右心室的后负荷增加,会引起右心室舒张功能障碍,继而增加右心房压力并引起静脉充血,将升高中心静脉压^[15]。中心静脉压的升高与肾功能受损有关,是肾功能恶化的危险因素^[16]。中心静脉压的升高降低了跨肾小球毛细血管网络的梯度,导致肾血流量和肾灌注压降低,从而激活RAAS和交感神经系统,并促进尿蛋白的渗漏,导致WRF。更高的中心静脉压和肾静脉压增加了肾间质内的压力,导致肾间质纤维化和肾小管压力增加,进一步降低了肾小球滤过率(GFR)^[17]。HFpEF患者中静脉充血是心力衰竭和肾衰竭的重要介体,这一概念得到了充血性心力衰竭和肺动脉插管有效性评估研究(EASH)试验结果的支持^[18]。右心衰竭是肺动脉高压患者预后不良的最重要标志之一,Mukherjee等

的研究发现,合并 WRF 的 HFpEF 患者与无 WRF 配对患者比较,右心功能显著下降。右心衰竭患者的神经激素激活和交感神经激活会导致慢性肾脏疾病。

综上所述,本研究中 HFpEF 发生 WRF 的发生率高于 HFrEF 组和 HFmrEF 组,可能的原因是 HFpEF 患者年龄水平较 HFrEF 组和 HFmrEF 组患者高,此外因肺动脉收缩压较高,导致中心静脉压升高及右心衰竭,从而促进 WRF 的发生。在临床治疗心力衰竭的诊疗过程中应重视 HFpEF 患者肾功能的变化。

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