·临床研究·

老年射血分数保留的心力衰竭合并贫血患者心脏结构及功能分析

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【摘 要】 目的 分析老年射血分数保留的心力衰竭(HFpEF)合并贫血患者的心脏结构及功能特点。**方法** 选取2008年2月至2019年12月于中国人民解放军总医院第一医学中心住院的≥60岁的老年HFpEF患者2 281例,根据是否合并贫血,分为贫血组(n=949)和对照组(n=1 332)。分析2组患者的临床特征、心脏超声结构及功能差异。采用EmpowerStats统计软件(3.0版)和R软件进行数据分析。根据数据类型,组间比较分别采用独立样本t检验、Kruskal-Wallis H检验或χ^2检验。采用多元线性回归模型分析血红蛋白(HGB)的影响因素,以及HGB与心脏超声指标的相关性。**结果** 老年HFpEF住院患者中41.6%(949/2 281)合并贫血。贫血组男性[54.69%(519/949)和47.75%(636/1 332)]、年龄[(74.79±7.99)和(73.40±7.72)年]、收缩压[(140.06±23.80)和(136.77±23.05)mmHg(1 mmHg=0.133 kPa)]、院内全因死亡率[3.58%(34/949)和1.50%(20/1 332)]、空腹血糖[(7.68±3.35)和(7.02±3.38)mmol/L]、N末端B型利钠肽原(NT-proBNP)[3 118.01(1 137.21,8976.32)和1 333.34(596.32,2 777.11)ng/L]及肌钙蛋白T[0.04(0.02,0.08)和0.02(0.01,0.04)μg/L]显著高于对照组,体质量指数[(24.34±4.10)和(24.87±4.05)kg/m^2]、HGB[(9.37±1.65)和(13.32±1.45)g/dl]及估算肾小球滤过率[38.85(13.98,73.98)和76.26(57.79,95.87)ml/(min·1.73m^2)]显著低于对照组,差异均有统计学意义(均P<0.05)。2组间纽约心脏病协会心功能分级和慢性肾脏病(CKD)分期比较,差异均有统计学意义(均P<0.05)。心脏超声结果显示,与对照组相比,贫血组左心扩大更明显,表现为左心房前后径[(41.43±8.13)和(40.64±7.62)mm]、左心房容积指数[29.82(22.55,38.80)和28.38(20.55,38.96)ml/m^2]、左心室收缩末期内径[(32.63±4.48)和(31.64±4.89)mm]、左心室舒张末期内径[(46.87±5.78)和(45.75±6.47)mm]、左心室收缩末期容量[(44.98±23.97)和(41.15±15.75)ml]及左心室舒张末期容量[(103.69±30.07)和(97.36±31.03)ml]显著增大;左心室肥厚更显著,表现为左心室质量指数[(120.24±39.99)和(110.14±36.91)g/m^2]、左心室后壁厚度[(10.68±1.47)和(10.47±1.52)mm]显著增大;右心负荷加重,表现为右心室内径[(36.74±7.12)和(35.90±7.42)mm]、主肺动脉内径[(22.93±3.40)和(22.51±3.63)mm]及下腔静脉内径[(16.89±4.18)和(16.15±3.93)mm]显著增宽,差异均有统计学意义(均P<0.05)。多元线性回归分析显示,C-反应蛋白、NT-proBNP及CKD≥4期是HGB的独立危险因素。HGB是左心室收缩末期容量、左心室舒张末期容量、左心室收缩末期内径、左心室舒张末期内径、左心室质量指数及左心房容积指数的独立危险因素。**结论** 老年HFpEF住院患者贫血患病率高,合并贫血者心脏结构重构和舒张功能障碍更为显著。炎症、心肾功能差是贫血的独立危险因素,而贫血与心脏结构和功能改变密切相关。

【关键词】 老年人;射血分数保留的心力衰竭;贫血;心脏结构重构;左心室舒张功能

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Cardiac structure and function in elderly heart failure patients with preserved ejection fraction complicated with anemia

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【Abstract】 Objective To analyze the characteristics of cardiac structure and function in elderly heart failure patients with preserved ejection fraction (HFpEF) complicated with anemia. **Methods** A total of 2 281 elderly HFpEF patients ≥60 years old hospitalized in the First Medical Center of Chinese PLA General Hospital from February 2008 to December 2019 were enrolled and divided into anemia

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group (n=949) and control group (n=1 332) according to whether they were accompanied by anemia. The clinical characteristics, cardiac ultrasonic structure and function were analyzed and compared between the 2 groups. The data were analyzed with EmpowerStats statistical software (version 3.0) and R software. According to the data type, independent sample t-test, Kruskal Wallis H test or Chi-square test was used for comparison between groups. Multivariate linear regression model was employed to analyze the influencing factors of hemoglobin (HGB) and the correlation of HGB with cardiac ultrasound indexes. **Results** The prevalence of anemia was 41.6% (949/2 281) in the elderly HFpEF inpatients. The patients of the anemia group had significantly higher ratio of males [54.69% (519/949) *vs* 47.75% (636/1 332)], older age [(74.79±7.99) *vs* (73.40±7.72 years], higher systolic blood pressure [(140.06±23.80) *vs* (136.77±23.05) mmHg (1 mmHg=0.133 kPa)], increased hospital all-cause mortality [3.58% (34/949) *vs* 1.50% (20/1 332)], and higher levels of fasting blood glucose [(7.68±3.35) *vs* (7.02±3.38) mmol/L], N-terminal pro B-type natriuretic peptide [NT-proBNP, 3 118.01 (1 137.21, 8 976.32) *vs* 1 333.34 (596.32, 2 777.11) ng/L] and troponin T [0.04 (0.02, 0.08) *vs* 0.02 (0.01, 0.04) μg/L], but lower body mass index [(24.34±4.10) *vs* (24.87±4.05) kg/m^2], HGB level [(9.37±1.65] *vs* [13.32±1.45) g/dl] and estimated glomerular filtration rate [38.85 (13.98, 73.98) *vs* 76.26 (57.79, 95.87) ml/(min · 1.73m^2)] when compared with the patients in the control group (all P<0.05). There were statistical differences between the 2 groups in heart function classification and chronic kidney disease (CKD) stage (both P<0.05). Cardiac ultrasound results showed that compared with the control group, the left heart in the anemia group expanded more significantly, with larger left atrial anteroposterior diameter [(41.43±8.13) *vs* (40.64±7.62 mm], left atrial volume index [29.82(22.55,38.80) *vs* 28.38(20.55,38.96) ml/m^2], left ventricular end systolic diameter [(32.63±4.48) *vs* (31.64±4.89) mm], left ventricular end diastolic diameter [(46.87±5.78) *vs* (45.75±6.47) mm], left ventricular end systolic volume [(44.98±23.97) *vs* (41.15±15.75) ml] and left ventricular end diastolic volume [(103.69±30.07) *vs* (97.36±31.03) ml]; more significant left ventricular hypertrophy was observed, with increased left ventricular mass index [(120.24±39.99) *vs* (110.14±36.91) g/m^2] and left ventricular posterior wall thickness [(10.68±1.47) *vs* (10.47±1.52) mm]; the right heart load was aggravated, with widened diameter of the right ventricle [(36.74±7.12) *vs* (35.90±7.42) mm], diameter of the main pulmonary artery [(22.93±3.40) *vs* (22.51±3.63) mm] and diameter of the inferior vena cava [(16.89±4.18) *vs* (16.15±3.93) mm] (all P<0.05). Multiple linear regression analysis indicated that C-reactive protein, NT-proBNP and CKD ⩾4 were independent risk factors for lower HGB. Low HGB was an independent risk factor for left ventricular end systolic volume, left ventricular end diastolic volume, left ventricular end systolic diameter, left ventricular end diastolic diameter, left ventricular mass index and left atrial volume index. **Conclusion** Elderly HFpEF inpatients have a high prevalence of anemia, and cardiac structural remodeling and diastolic dysfunction were more evident in anemic patients. Inflammation and poor cardiac and renal function are independent risk factors for anemia, while anemia is closely related to cardiac structure and functional remodeling.

【Key words】 aged; heart failure with preserved ejection fraction; anemia; cardiac structural remodeling; left ventricular diastolic function

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老年人是心力衰竭和贫血的高患病人群,二者的共病现象在临床中较为常见。研究表明,急性或慢性心力衰竭(chronic heart failure,CHF)患者无论左心室射血分数(left ventricular ejection fraction,LVEF)[1,2]如何,贫血都是其死亡和再住院的独立预测因子[3]。射血分数保留的心力衰竭(heart failure with preserved ejection fraction,HFpEF)作为老年人最常见的心力衰竭类型,与贫血的关系密切,但机制不明[4]。研究表明,贫血与心脏前负荷相关的舒张功能障碍指标相关[5],目前国内尚缺乏老年 HFpEF 合并贫血患者超声心脏结构和功能特点的真实世界数据。本研究旨在探索合并贫血对 HFpEF 患者心脏结构及功能的影响,以期为贫血导致 HFpEF 不良预后的机制研究提供临床资料。

1 对象与方法

1.1 研究对象

通过解放军总医院住院患者电子病历系统,检索并收集 2008 年 2 月至 2019 年 12 月出院诊断中包含 CHF 的 4 650 例老年患者(年龄⩾60 岁)的临床资料。根据住院首次心脏超声及生化检验结果,最终纳入 2 281 例 HFpEF 患者为研究对象。纳入标准:(1)具备心力衰竭症状和体征;(2)纽约心脏病协会(New York Heart Association,NYHA)心功能分级⩾Ⅱ级;(3)符合我国《老年人慢性心力衰竭诊治中国专家共识(2021)》中 CHF 的诊断标准[6],即 N 末端 B 型利钠肽原(N-terminal pro-B-type natriuretic peptide,NT-proBNP)>220 pg/ml 诊断为窦性心律,NT-proBNP>660 pg/ml 诊断为心房颤动;(4)LVEF⩾50%。根据世界卫生组织对贫血的诊断标准[7](血红蛋白(hemoglobin,HGB)女性<12 g/dl,男性<13 g/dl),将 HFpEF 分为贫血组 949 例和对照组 1 332 例。

1.2 方法

(1)收集患者的一般资料包括年龄、性别、身高、体质量、血压及 NYHA 分级等;(2)实验室指标包括 HGB、C-反应蛋白(C-reactive protein,CRP)、空

腹血糖(fasting blood glucose, FBG)及NT-proBNP等;(3)超声心动图常用的心脏结构及功能指标包括心房/心室内径及容积、左心室后壁厚度、右心室内径、主肺动脉内径、下腔静脉内径及LVEF等。以下指标通过二次计算获得:体质量指数(body mass index, BMI)、体表面积、左心房容积指数(left atrial volume index, LAVI)、左心室质量指数(left ventricular mass index, LVMI)及相对室壁厚度[8]。估算肾小球滤过率(estimated glomerular filtration rate, eGFR)采用慢性肾脏病流行病学协作组公式计算[9]。

1.3 统计学处理

采用EmpowerStats统计软件(3.0版)和R软件进行数据分析。计量资料呈正态分布者以均数±标准差($\bar{x}\pm s$)表示,组间比较采用独立样本t检验;呈非正态分布者以中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,组间比较采用Kruskal-Wallis H检验。计数资料以例数(百分率)表示,组间比较采用χ^2检验。采用多元线性回归模型分析HGB的影响因素以及HGB与心脏超声指标的相关性。$P<0.05$为差异有统计学意义。

2 结 果

2.1 2组患者一般资料比较

2 281例老年HFpEF患者中合并贫血者949例(41.6%);合并CKD患者1 107例(48.5%),其中贫血组CKD患病率为67.8%(643/949),显著高于对照组34.8%(464/1 332),差异有统计学意义($P<0.05$)。贫血组男性、年龄、收缩压、院内全因死亡率、FBG、NT-proBNP、肌钙蛋白T显著高于对照组,BMI、HGB、eGFR显著低于对照组,差异均有统计学意义(均$P<0.05$)。2组间NYHA心功能分级和慢性肾脏病(chronic kidney disease, CKD)分期比较,差异均有统计学意义(均$P<0.05$;表1)。

2.2 HGB的影响因素分析

以HGB为因变量,将单因素分析中$P<0.05$的自变量(白蛋白、logCRP、年龄≥75岁、logNT-proBNP和CKD≥4期)纳入多元线性回归分析,结果显示CRP、NT-proBNP及CKD≥4期是HGB的危险因素,而白蛋白则是保护因素(均$P<0.05$;表2)。

2.3 2组患者心脏超声指标比较

心脏超声显示,与对照组相比,贫血组左心扩大更明显(左心房前后径、LAVI、左心室收缩末期内径、左心室舒张末期内径、左心室收缩末期容量及左心室舒张末期容量显著增大);左心室肥厚更显著(LVMI和左心室后壁厚度显著增加);右心负荷更重(右心室内径、主肺动脉内径和下腔静脉内径显著增加),差异均有统计学意义(均$P<0.05$;表3)。

2.4 HGB与心脏超声指标关系分析

以心脏超声指标为因变量,HGB为自变量,进行单因素及多元线性回归分析。结果显示,在调整性别、年龄、BMI、冠心病、高血压、糖尿病、高脂血症及CKD等因素后,HBG是左心室收缩末期容量、左心室舒张末期容量、左心室收缩末期内径、左心室舒张末期内径、左心室质量指数及LAVI的独立危险因素(均$P<0.05$;表4)。

表1 2组患者一般资料比较

Table 1 Comparison of baseline data between two groups

Item	Anemia group(n=949)	Control group(n=1332)	P value
Male[n(%)]	519(54.69)	636(47.75)	<0.001
Age(years, $\bar{x}\pm s$)	74.79±7.99	73.40±7.72	<0.001
BMI(kg/m^2, $\bar{x}\pm s$)	24.34±4.10	24.87±4.05	0.003
SBP(mmHg, $\bar{x}\pm s$)	140.06±23.80	136.77±23.05	<0.001
NYHA functional class[n(%)]			<0.001
Ⅱ	251(26.45)	572(42.94)	
Ⅲ	445(46.89)	581(43.62)	
Ⅳ	253(26.66)	179(13.44)	
CKD stage[n(%)]			<0.001
3	255(37.66)	370(79.74)	
4	161(25.04)	55(11.85)	
5	227(35.30)	39(8.41)	
In-hospital death[n(%)]	34(3.58)	20(1.50)	0.001
HGB(g/dl, $\bar{x}\pm s$)	9.37±1.65	13.32±1.45	<0.001
FBG(mmol/L, $\bar{x}\pm s$)	7.68±3.35	7.02±3.38	<0.001
eGFR[ml/(min·1.73m^2), $M(Q_1, Q_3)$]	38.85(13.98,73.98)	76.26(57.79,95.87)	<0.001
NT-ProBNP[ng/L, $M(Q_1, Q_3)$]	3 118.01(1 137.21,8 976.32)	1 333.34(596.32,2 777.11)	<0.001
TnT[μg/L, $M(Q_1, Q_3)$]	0.04(0.02,0.08)	0.02(0.01,0.04)	<0.001

BMI: body mass index; SBP: systolic blood pressure; NYHA: New York Heart Association; CKD: chronic kidney disease; HGB: hemoglobin; FBG: fasting blood glucose; eGFR: estimated glomerular filtration rate; NT-proBNP: N-terminal pro-B-type natriuretic peptide; TnT: Troponin T. 1 mmHg=0.133 kPa.

表 2 血红蛋白的影响因素分析

Table 2 Analysis of influencing factors of hemoglobin

Item	Univariate analysis			Multivariate analysis		
	OR	95%*CI*	*P* value	*OR*	95%*CI*	*P* value
Albumin	1.95	1.76–2.14	<0.000 1	1.93	1.75–2.11	<0.001
LogCRP	−3.08	−3.82–−2.35	<0.000 1	−2.93	−3.64–−2.21	<0.001
≥75 years old	−4.70	−6.73–−2.67	<0.000 1	−4.51	−9.90–0.88	0.101
LogNT-proBNP	−15.23	−16.9–−13.53	<0.000 1	−14.65	−16.30–−13.00	<0.001
CKD stage≥4	−26.74	−28.98–−24.51	<0.000 1	−26.25	−28.49–−24.02	<0.001

CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; CKD: chronic kidney disease.

表 3 2 组患者心脏超声指标比较

Table 3 Comparison of cardiac ultrasound indexes between two groups

Item	Anemia group(n=949)	Control group(n=1 332)	*P* value
Left atrial anterior-posterior diameter(mm, $\bar{x}\pm s$)	41.43±8.13	40.64±7.62	0.034
Left atrial volume index[ml/m^2, $M(Q_1, Q_3)$]	29.82(22.55,38.80)	28.38(20.55,38.96)	0.031
Left ventricular end systolic dimension(mm, $\bar{x}\pm s$)	32.63±4.48	31.64±4.89	<0.001
Left ventricular end diastolic dimension(mm, $\bar{x}\pm s$)	46.87±5.78	45.75±6.47	<0.001
Left ventricular end systolic volume(ml, $\bar{x}\pm s$)	44.98±23.97	41.15±15.75	<0.001
Left ventricular end diastolic volume(ml, $\bar{x}\pm s$)	103.69±30.07	97.36±31.03	<0.001
Left ventricular mass index(g/m^2, $\bar{x}\pm s$)	120.24±39.99	110.14±36.91	<0.001
Left ventricular posterior wall thickness(mm, $\bar{x}\pm s$)	10.68±1.47	10.47±1.52	0.004
Left ventricular ejection fraction(%, $\bar{x}\pm s$)	58.33±5.11	58.18±5.40	0.498
Right atrium diameter(mm, $\bar{x}\pm s$)	38.71±9.29	38.25±8.86	0.289
Right ventricle diameter(mm, $\bar{x}\pm s$)	36.74±7.12	35.90±7.42	0.017
Internal diameter of main pulmonary artery(mm, $\bar{x}\pm s$)	22.93±3.40	22.51±3.63	0.010
Internal diameter of ascending aorta(mm, $\bar{x}\pm s$)	32.34±4.41	32.41±4.58	0.743
Internal diameter of inferior vena cava(mm, $\bar{x}\pm s$)	16.89±4.18	16.15±3.93	<0.001
Interventricular septal thickness(mm, $\bar{x}\pm s$)	11.52±1.72	11.40±2.15	0.186
Relative wall thickness(mm, $\bar{x}\pm s$)	0.48±0.08	0.49±0.10	0.146

表 4 血红蛋白与心脏超声指标关系分析

Table 4 Relationship between hemoglobin and cardiac ultrasound index

Item	Univariate analysis			Multivariate analysis		
	OR	95%*CI*	*P* value	*OR*	95%*CI*	*P* value
Left ventricular end systolic volume	−0.40	−0.73–−0.06	0.020	−0.81	−1.19–−0.43	<0.001
Left ventricular end diastolic volume	−0.60	−1.13–−0.06	0.029	−1.26	−1.83–0.68	<0.001
Left ventricular end systolic dimension	−0.12	−0.2–−0.03	0.006	−0.20	−0.29–−0.11	<0.001
Left ventricular end diastolic dimension	−0.12	−0.22–0.01	0.035	−0.25	−0.37–−0.14	<0.001
Left ventricular mass index	−1.66	−2.31–−1.0	<0.001	−1.20	−1.85–−0.55	0.003
Left atrial volume index	−0.65	−1.07–−0.23	0.003	−0.68	−1.13–−0.23	0.003
Left ventricular posterior wall thickness	−0.03	−0.05–0.00	0.043	−0.04	−0.07–−0.01	0.066

3 讨 论

HFpEF 是老年 CHF 的最常见类型,其病因及病理机制复杂,缺乏有效的治疗措施。贫血作为老年 CHF 最重要并发疾病之一,是 CHF 恶化、再住院率及死亡率增加的重要影响因素。研究贫血对 HFpEF 患者心脏结构重构及功能的影响,可为心力衰竭-贫血共病的病理生理特点及机制研究提供资料。本研究回顾性分析了 HFpEF 合并贫血患者的临床特征及心脏结构和功能改变,发现 HFpEF 患者贫血的患病率高达 41.6%。多因素分析显示,CRP、NT-proBNP 升高,以及 CKD≥4 期是 HFpEF 患者合并贫血的独立危险因素,提示炎症状态及严重心、肾功能受损在 HFpEF 患者的贫血发生中的起重要作用。慢性炎症状态可导致机体免疫功能紊乱,营养状况变差,从而影响铁代谢,加重贫血。此外,炎症状态下单核吞噬细胞对红细胞的破坏增加,部分患者会出现胃肠道、泌尿系统或呼吸道的出血,导致机体失血[10]。CKD 是 HFpEF 的常见共病之一,本研究中 HFpEF 合并 CKD 患者共 1 107 例,患病率高达 48.5%,其中贫血组 CKD 患病率为 67.8%,显著高于对照组 34.8%。CKD 患者贫血的发病机制是多方面的,主要包括促红细胞生成素的相对缺乏、尿毒症毒素对红细胞膜的损伤以及尿毒症毒素和红细胞抑制因子对骨髓造

血的影响[11]。HFpEF通过多种通路与CKD发生交互作用,包括炎症、免疫反应、神经内分泌机制、代谢营养变化、容量及酸碱平衡等。有研究发现,心功能的恶化会加重肾脏损害,从而进一步加剧贫血。此外,严重心力衰竭患者因胃肠道淤血,也可引起营养不良性贫血[12]。

本研究还发现,2组患者心脏超声结构和功能存在显著差异。贫血组心脏结构重构更显著,表现为左心扩大、左心室肥厚,右心负荷加重等。与心脏舒张功能障碍有关的指标,如LAVI、相对室壁厚度及LVMI,在贫血组升高更为显著(均$P<0.05$),提示贫血组左心室舒张功能更差。多元线性回归分析显示,HGB与左心室收缩末期容量、左心室舒张末期容量、左心室收缩末期内径、左心室舒张末期内径、左心室质量指数以及LAVI等指标呈负相关,与Burns等[5]的研究结果基本一致。贫血对心脏结构和功能的影响主要表现在血液动力学及心脏负荷的变化上,会导致每搏输出量、心脏指数和心脏容积增加[13,14]。此外,贫血也会降低心肌细胞的携氧能力及能量效率[15],进而加剧心功能的恶化。研究发现,贫血与CHF患者运动能力降低、住院时间延长、住院次数增多、生活质量变低、病情恶化以及预后不良相关[15]。本研究也显示,贫血组院内全因死亡率为对照组的2.39倍。由此可见,心力衰竭与贫血互为因果,恶性循环,可能是导致不良预后的原因。因此,加强老年HFpEF患者贫血的筛查和干预是CHF综合管理的重要内容。

本研究存在一定局限性:(1)本研究的对象为老年HFpEF住院患者,不能代表所有年龄段、门诊或社区以及其他类型的CHF人群;(2)受回顾性资料的限制,用于HFpEF诊断的心脏舒张功能指标,如肺动脉收缩压等数据缺失,研究结果可能存在偏差;(3)缺乏血清铁等指标数据,未能系统分析贫血原因。纠正贫血能否逆转心脏重构、改善心脏功能,有待进一步研究。

综上,老年HFpEF住院患者合并贫血临床常见,炎症、严重的心肾功能损害是贫血的重要危险因素。合并贫血患者心脏结构重构和舒张功能障碍更显著,贫血可能是院内死亡风险增加的病理生理机制。

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