

doi: 10.13241/j.cnki.pmb.2018.19.011

慢性心力衰竭患者彩色多普勒超声心功能参数与血清同型半胱氨酸水平的相关性研究*

宋桂仙 阮中宝 朱 莉 王如珠 李建民 林 杰

(南通大学第五附属医院 / 泰州市人民医院心血管内科 江苏 泰州 225300)

摘要 目的:探讨慢性心力衰竭(CHF)患者彩色多普勒超声的心功能参数与血清同型半胱氨酸水平的相关性。**方法:**选取 2016 年 2 月至 2017 年 6 月期间我院收治的 CHF 患者 73 例作为研究组,选取同期体检的健康志愿者 70 例作为对照组。检测两组血清同型半胱氨酸(Hcy)及氨基末端 B 型利钠肽前体(NT-proBNP)水平,采用彩色多普勒超声测定两组心脏左室射血分数(LVEF)及左室舒张末期内径(LVEDd)。分析 CHF 患者血清 Hcy 水平与 NT-proBNP、LVEF、LVEDd 的相关性,观察不同血清 Hcy 水平 CHF 患者心血管事件发生情况。**结果:**研究组血清 Hcy、NT-proBNP 及 LVEDd 显著高于对照组,LVEF 显著低于对照组($P<0.05$)。IV 级患者血清 Hcy、NT-proBNP、LVEDd 水平高于 II 级与 III 级,且 III 级高于 II 级 ($P<0.05$);IV 级患者 LVEF 水平低于 II 级与 III 级,且 III 级低于 II 级 ($P<0.05$)。由 Pearson 相关性分析可得,CHF 患者血清 Hcy 水平与血清 NT-proBNP、LVEDd 呈正相关,与 LVEF 呈负相关 ($P<0.05$)。血清 Hcy 水平高于 $25\text{ }\mu\text{mol/L}$ 的患者心血管事件发生率为 31.43%,血清 Hcy 水平在 $15\text{ }\mu\text{mol/L}$ - $25\text{ }\mu\text{mol/L}$ 范围内的患者心血管事件发生率为 10.53%,差异有统计学意义 ($P<0.05$)。**结论:**CHF 患者血清 Hcy、NT-proBNP、LVEDd 随心功能恶化程度增加而升高,LVEF 随之降低,且 Hcy 水平越高,患者预后越差。

关键词:慢性心力衰竭;彩色多普勒超声;心功能;同型半胱氨酸;相关性

中图分类号:R541.61;R540.45 **文献标识码:**A **文章编号:**1673-6273(2018)19-3653-04

Correlation between Cardiac Function Parameters of Color Doppler Ultrasound and Serum Homocysteine Level in Patients with Chronic Heart Failure*

SONG Gui-xian, RUAN Zhong-bao, ZHU Li, WANG Ru-zhu, LI Jian-min, LIN Jie

(Department of Cardiovascular Medicine, The Fifth Affiliated Hospital of Nantong University/Taizhou People's Hospital, Taizhou, Jiangsu, 225300, China)

ABSTRACT Objective: To investigate the correlation between cardiac function parameters of color Doppler ultrasound and serum homocysteine level in patients with chronic heart failure (CHF). **Methods:** 73 patients with CHF who were treated in our hospital from February 2016 to June 2017 were selected as the study group, and 70 healthy volunteers in the same period were selected as the control group. The levels of serum homocysteine (Hcy) and N-terminal pro-brain natriuretic peptide (NT-proBNP) in two groups were detected, left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDd) in two groups were measured by color Doppler ultrasound. The correlation between serum Hcy level and NT-proBNP, LVEF and LVEDd in patients with CHF was analyzed, the occurrence of cardiovascular events in CHF patients with different serum Hcy levels was observed. **Results:** The serum levels of Hcy, NT-proBNP and LVEDd in the study group were significantly higher than those in the control group, and the LVEF was significantly lower than that of the control group ($P<0.05$). The level of serum Hcy, NT-proBNP and LVEDd in patients with IV grade was higher than that of II grade and III grade, and the level of III grade was higher than that of II grade ($P<0.05$). The level of LVEF in patients with IV grade was lower than that of II grade and III grade, and the level of III grade was lower than that of II grade ($P<0.05$). Pearson correlation analysis showed that the level of serum Hcy in patients with CHF was positively correlated with serum NT-proBNP and LVEDd, and it was negatively correlated with LVEF ($P<0.05$). The incidence of cardiovascular events in patients with serum Hcy level above $25\text{ }\mu\text{mol/L}$ was 31.43%, and the incidence of cardiovascular events in patients with the serum Hcy level in $15\text{ }\mu\text{mol/L}$ - $25\text{ }\mu\text{mol/L}$ was 10.53%, the difference was statistically significant ($P<0.05$). **Conclusion:** The serum levels of Hcy, NT-proBNP, and LVEDd in patients with CHF is increased with the increase of the severity of cardiac function deterioration, and the LVEF is decreasing. The level of serum Hcy is positively correlated with serum NT-proBNP and LVEDd, and the higher the Hcy level, the worse the patient's prognosis.

Key words: Chronic heart failure; Color doppler ultrasound; Cardiac function; Homocysteine; Correlation

Chinese Library Classification(CLC): R541.61; R540.45 **Document code:** A

Article ID: 1673-6273(2018)19-3653-04

* 基金项目:国家自然科学基金项目(81600223)

作者简介:宋桂仙(1983-),男,博士,主治医师,从事心血管内科方面的研究,E-mail:plouit@163.com

(收稿日期:2018-04-27 接受日期:2018-05-23)

前言

心力衰竭是心脏结构和功能发生异常而引起心室充盈和射血功能受损的临床综合征,慢性心力衰竭(Chronic heart failure, CHF)是心脏疾病发展到严重和最终阶段的临床表现,患者主要表现为呼吸困难、乏力和体液潴留^[1-3]。CHF的发生往往会伴随着心肌负荷过重、心肌细胞损伤、凋亡等变化,最后导致心室泵血功能低下^[4,5],其发生机制较为复杂,因此临床需对CHF发病机制进行深入的研究,进一步帮助CHF的诊断和治疗。同型半胱氨酸(Homocysteine, Hcy)是蛋氨酸代谢过程中产生的中间产物,近来有报道发现CHF患者的血清Hcy水平高于健康人群,提示Hcy可能是诱发CHF的临床危险因素^[6]。氨基末端B型利钠肽前体(N-terminal pro-brain natriuretic peptide, NT-proBNP)是一种心血管肽类激素,其数值可以反应左心室舒张末期压力的升高,可作为临床上反映心力衰竭的常用标志物^[7,8]。彩色多普勒超声在临床工作中常称为B超,由于其具有无创性且能够准确判断出心脏结构、室壁厚度、室壁运动、是否存在缺损、静脉动脉是否存在异常结构,因此可广泛应用于心血管疾病的辅助诊断^[9,10]。本文就CHF患者彩色多普勒超声心功能参数、NT-proBNP与其血清Hcy含量进行相关性研究,整理结果如下。

1 资料与方法

1.1 一般资料

选取我院于2016年2月~2017年6月期间收治的73例CHF患者作为研究组。纳入标准:(1)患者均经影像学、心电图等辅助检查确诊为CHF,符合2016欧洲心脏病学会(ESC)急、慢性心力衰竭诊断和治疗指南中对CHF的诊断标准^[11];(2)美国纽约心脏病协会(American heart association, NYHA)分级在II-IV级范围内;(3)患者或家属同意本研究,并签署知情同意书。排除标准:(1)合并肝、肾、肺功能严重不全者;(2)伴

有甲亢、急性心肌梗死、恶性肿瘤者;(3)伴有感染性疾病、血液疾病及全身免疫性疾病者。研究组患者女32例,男41例,年龄35-70岁,平均(59.23±10.46)岁,NYHA分级II级32例,III级26例,IV级15例。选取同期体检的健康志愿者70例作为对照组,其中女28例,男42例,年龄34-68岁,平均(58.17±9.37)岁。两组的性别、年龄比较无统计学差异($P>0.05$),具有可比性。本研究已通过本院伦理委员会批准同意。

1.2 方法

采集两组禁食12h后清晨空腹静脉血3mL,4000 r/min转速下离心5min得到血清,-80℃冻存待测。采用贝克曼全自动生化分析仪检测血清Hcy水平,采用罗氏COBAS e601电化学发光免疫分析仪检测NT-proBNP水平,均采用罗氏诊断试剂盒进行测定,严格按照试剂盒说明书进行,其中血清Hcy>15 μmol/L为正常,血清Hcy≥15 μmol/L为异常,NT-proBNP<300 pg/mL为正常,NT-proBNP≥300 pg/mL为异常^[12]。采用PhilipseE33心脏彩色多普勒超声仪检测两组心脏左室射血分数(Left ventricular ejection fractions, LVEF)及左室舒张末期内径(Left ventricular end-diastolic diameter, LVEDd)。对研究组患者出院后进行6个月的电话随访,记录患者心血管事件发生情况。

1.3 统计学方法

采用SPSS 21.0进行统计分析,计量资料以($\bar{x} \pm s$)表示,采用t检验,多组间比较采用F检验,计数资料以[n(%)]表示,采用 χ^2 检验,采用Pearson相关性进行相关性分析,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组Hcy、NT-proBNP、LVEF及LVEDd水平比较

研究组血清Hcy、NT-proBNP及LVEDd显著高于对照组,LVEF显著低于对照组($P<0.05$),见表1。

表1 两组Hcy、NT-proBNP、LVEF及LVEDd水平比较($\bar{x} \pm s$)

Table 1 Comparison of serum Hcy, NT-proBNP, LVEF and LVEDd levels of two groups($\bar{x} \pm s$)

Groups	n	Hcy(μmol/L)	NT-proBNP(pg/mL)	LVEF(%)	LVEDd(mm)
Study Group	73	26.13±5.64	2246.23±642.19	41.53±3.54	58.18±5.29
Control Group	70	10.44±7.03	156.46±59.30	67.26±4.27	46.21±3.83
t	-	14.301	33.012	28.147	13.204
P	-	0.000	0.000	0.000	0.000

2.2 不同NYHA分级患者Hcy、NT-proBNP、LVEF及LVEDd水平比较

研究组NYHA各级Hcy、NT-proBNP、LVEDd水平整体比较差异有统计学意义($P<0.05$);IV级患者血清Hcy、NT-proBNP、LVEDd水平高于II级与III级,且III级高于II级($P<0.05$);IV级患者LVEF水平低于II级与III级,且III级低于II级($P<0.05$),见表2。

2.3 血清Hcy水平与NT-proBNP、LVEF、LVEDd的相关性分析

由Pearson相关性分析可得,CHF患者血清Hcy水平与血清NT-proBNP、LVEDd呈正相关,与LVEF呈负相关($P<0.$

05),见表3。

2.4 不同血清Hcy水平CHF患者心血管事件发生情况比较

血清Hcy水平高于25 μmol/L的患者共35例,心血管事件发生例数为11例,占31.43%(11/35);血清Hcy水平在15 μmol/L-25 μmol/L范围内的患者共38例,心血管事件发生例数为4例,占10.53%(4/38),差异有统计学意义($\chi^2=4.876$, $P=0.027$)。

3 讨论

CHF是心内科中常见的危重病症,是心血管疾病患者丧失

表 2 不同 NYHA 分级患者 Hcy、NT-proBNP、LVEF 及 LVEDd 水平比较($\bar{x} \pm s$)Table 2 Comparison of serum Hcy, NT-proBNP, LVEF and LVEDd in patients with different NYHA grade($\bar{x} \pm s$)

NYHA grade	n	Hcy($\mu\text{mol/L}$)	NT-proBNP(pg/mL)	LVEF(%)	LVEDd(mm)
II grade	32	20.43 $\pm$ 4.02	1102.72 $\pm$ 528.36	42.19 $\pm$ 2.91	49.58 $\pm$ 4.28
III grade	26	24.29 $\pm$ 5.28*	1992.58 $\pm$ 729.24*	38.41 $\pm$ 3.17*	55.29 $\pm$ 5.13*
IV grade	15	28.92 $\pm$ 5.92**	2917.47 $\pm$ 902.63**	32.17 $\pm$ 4.01**	59.37 $\pm$ 4.81**
F	-	9.397	6.372	7.291	11.284
P	-	0.000	0.001	0.000	0.000

Note: compared with II grade, * $P < 0.05$; compared with III grade, ** $P < 0.05$.

表 3 血清 Hcy 水平与 NT-proBNP、LVEF、LVEDd 的相关性分析

Table 3 Correlation analysis of serum Hcy level and NT-proBNP, LVEF and LVEDd levels

Indexes	Hcy	
	r	P
NT-proBNP	0.725	0.001
LVEF	-0.610	0.003
LVEDd	0.842	0.000

自理能力、导致最终死亡的重要原因,CHF 并非是一个静止状态,而是一种进行性疾病,其病理和生理机制十分复杂^[13,14]。目前研究报道认为,CHF 与心室重构、神经交感神经系统的变化、多种体液因子(利钠肽、Hcy、一氧化氮、内皮素)存在相关性^[15-17]。有研究报道,血清 Hcy 是含巯基的氨基酸,其可促进机体内氧自由基和过氧化氢产生,对血管内皮细胞和血管功能造成直接损伤,并且可以提高血管内平滑肌生长速度,导致血管内膜增厚僵硬,从而引发动脉粥样硬化^[18,19]。NT-proBNP 是心室肌细胞产生的多肽类物质,主要由左心室分泌,其分泌含量随心室充盈高低而变化,当心室负荷增加时可以促进 NT-proBNP 的分泌增加,从而降低心室充盈和射血功能,增加体循环和肺循环的阻力^[20-22]。

本研究结果显示,研究组血清 Hcy、NT-proBNP 及 LVEDd 显著高于对照组,LVEF 显著低于对照组($P < 0.05$),说明血清 Hcy 和 NT-proBNP 水平在 CHF 患者和健康对照人群中具有显著性差异,CHF 的发生和发展过程中,血清 Hcy 和 NT-proBNP 呈现出高表达,可能是在 CHF 发病过程中,血管内皮细胞损伤和氧自由基增加致使 Hcy、NT-proBNP 异常表达。此外,随着 NYHA 分级增加,CHF 患者心功能受损越严重,血清 Hcy、NT-proBNP、LVEDd 呈增加趋势,LVEF 呈降低趋势。NYHA 分级是按诱发心力衰竭症状的活动程度将心功能的受损状况分级,级别越高表示心力衰竭症状越严重^[23,24]。LVEF 及 LVEDd 是心功能常用指标,LVEF 是心室每搏量与心室舒张末期容积的比值,当着心脏功能受损时,射血分数会显著地降低,心输出量会降低^[25,26]。正常情况下,左心室舒张后充盈的血液为 140 mL 左右,收缩时能将 70 mL 以上的血液射向主动脉。LVEDd 是指收缩末期间隔即左室面与左室后壁心内膜的垂直距离,通常在左室后壁向上运动的顶峰处测量,该指标可反应左心室舒张末期的心脏状态,心功能受损,心肌负荷增大,内径也会病理性增大^[27,28]。Pearson 相关性分析显示,CHF 患者血清 Hcy 水平与血清 NT-proBNP、LVEDd 呈正相关,与 LVEF 呈负相关

($P < 0.05$),说明 CHF 患者机体内血清 NT-proBNP、LVEDd 增加时,LVEF 降低,血清 Hcy 水平增加,符合心脏病理性代偿的过程,这可能与 Hcy 参与 CHF 激活基质金属蛋白酶,促进心肌间质纤维化,参与心肌及血管重构的过程相关^[29,30]。本研究结果还显示,血清 Hcy 水平高于 25 $\mu\text{mol/L}$ 的患者心血管事件发生率为 31.43%,血清 Hcy 水平在 15 $\mu\text{mol/L}$ -25 $\mu\text{mol/L}$ 范围内的患者心血管事件发生率为 10.53%,说明患者血清 Hcy 水平越高,心血管事件发生率越高,提示血清 Hcy 水平也是影响 CHF 患者预后的一个危险因素,需要引起重视。

综上所述,CHF 患者血清 Hcy 与 NT-proBNP、LVEDd、LVEF 密切相关,同时血清高 Hcy 水平也是心血管事件发生率的危险因素,因此 Hcy 可以作为分析 CHF 疾病发展与预后的指标。

参考文献(References)

- [1] Sharma A, Lavie CJ, Borer JS, et al. Meta-analysis of the relation of body mass index to all-cause and cardiovascular mortality and hospitalization in patients with chronic heart failure [J]. Am J Cardiol, 2015, 115(10): 1428-1434
- [2] Pham D, Grodin JL. Dilemmas in the Dosing of Heart Failure Drugs: Titrating Diuretics in Chronic Heart Failure[J]. Card Fail Rev, 2017, 3 (2): 108-112
- [3] Wang KH, Wu JR, Zhang D, et al. Comparative efficacy of Chinese herbal injections for treating chronic heart failure: a network meta-analysis[J]. BMC Complement Altern Med, 2018, 18(1): 41
- [4] Chen YW, Wang CY, Lai YH, et al. Home-based cardiac rehabilitation improves quality of life, aerobic capacity, and readmission rates in patients with chronic heart failure [J]. Medicine (Baltimore), 2018, 97 (4): e9629
- [5] Kotecha D, Lam CS, Van Veldhuisen DJ, et al. Heart Failure With Preserved Ejection Fraction and Atrial Fibrillation: Vicious Twins[J]. J Am Coll Cardiol, 2017, 68(20): 2217-2228
- [6] Fournier P, Fourcade J, Roncalli J, et al. Homocysteine in Chronic

- Heart Failure[J]. Clin Lab, 2015, 61(9): 1137-1145
- [7] Pan Y, Li D, Ma J, et al. NT-proBNP test with improved accuracy for the diagnosis of chronic heart failure[J]. Medicine (Baltimore), 2017, 96(51): e9181
- [8] Ozmen C, Deniz A, Deveci OS, et al. Association among tenascin-C and NT-proBNP levels and arrhythmia prevalence in heart failure[J]. Clin Invest Med, 2017, 40(6): E219-E227
- [9] Su D, Zheng W, Liu Y, et al. Different Combinations of Right Ventricular Longitudinal Velocity and Displacement Can Be Applied Effectively for Diagnosis of Right Heart Failure in Chinese Patients[J]. Heart Surg Forum, 2016, 19(4): E153-E159
- [10] Banasik G, Segiet O, Elwart M, et al. LV mechanical dispersion as a predictor of ventricular arrhythmia in patients with advanced systolic heart failure : A pilot study[J]. Herz, 2016, 41(7): 599-604
- [11] 边圆,王甲莉,程凯,等.2016年欧洲心脏病学会急性心力衰竭指南解读[J].中华急诊医学杂志, 2016, 25(7): 849-853
Bian Yuan, Wang Jia-li, Cheng Kai, et al. Interpretation of 2016 ESC guidelines for the diagnosis and treatment of acute heart failure[J]. Chinese Journal of Emergency Medicine, 2016, 25(7): 849-853
- [12] 邵俊良,孙剑,韦勇,等.冠心病患者血清同型半胱氨酸和脂蛋白 a 联合检测的临床意义[J].国际检验医学杂志, 2015, 36(2): 255-256
Shao Jun-liang, Sun Jian, Wei Yong, et al. Clinical significance of combined detection of serum homocysteine and lipoprotein a in patients with coronary heart disease[J]. International Journal of Laboratory Medicine, 2015, 36(2): 255-256
- [13] Aimo A, Januzzi JL Jr, Vergaro G, et al. Prognostic Value of High-Sensitivity Troponin T in Chronic Heart Failure: An Individual Patient Data Meta-Analysis[J]. Circulation, 2018, 137(3): 286-297
- [14] Wildeboer JA, Van de Ven ART, De Boer D. Substitution of care for chronic heart failure from the hospital to the general practice: patients' perspectives[J]. BMC Fam Pract, 2018, 19(1): 8
- [15] Almufleh A, Marbach J, Chih S, et al. Ejection fraction improvement and reverse remodeling achieved with Sacubitril/Valsartan in heart failure with reduced ejection fraction patients [J]. Am J Cardiovasc Dis, 2017, 7(6): 108-113
- [16] Wu Q, Cao Y, Mao G, et al. Effects of forest bathing on plasma endothelin-1 in elderly patients with chronic heart failure: Implications for adjunctive therapy[J]. Geriatr Gerontol Int, 2017, 17(12): 2627-2629
- [17] Kiuchi S, Hisatake S, Kabuki T, et al. Effect of Switching from Cilnidipine to Azelnidipine on Cardiac Sympathetic Nerve Function in Patients with Heart Failure Preserved Ejection Fraction [J]. Int Heart J, 2018, 59(1): 120-125
- [18] Gundam SS. Study of relationship between plasma homocysteine levels and congestive heart failure in patients with acute myocardial infarction[J]. J Assoc Physicians India, 2016, 64(1): 81
- [19] Muthuramu I, Singh N, Amin R, et al. Selective homocysteine-lowering gene transfer attenuates pressure overload-induced cardiomyopathy via reduced oxidative stress [J]. J Mol Med (Berl), 2015, 93(6): 609-618
- [20] Gao YH, Liu L. The relationship between NT-proBNP and Depression in Patients with Heart Failure[J]. J Geriatr Cardiol, 2017, 14(11): 715-716
- [21] Goudarzipour K, Alizadeh P, Tavassol HH, et al. A Comparison Between MRIT2 and NT-ProBNP in Early Detection of Heart Diseases in Thalassemia Major Patients: A Cross-Sectional Study [J]. Indian J Hematol Blood Transfus, 2017, 33(4): 541-544
- [22] Täger T, Wiedergren AK, Fröhlich H, et al. Hemodynamic Determinants of the Biologic Variation of N-Terminal Pro-B-Type Natriuretic Peptide in Patients With Stable Systolic Chronic Heart Failure [J]. J Card Fail, 2017, 23(12): 835-842
- [23] Chanchai R, Kanjanavanit R, Leemasawat K, et al. Clinical tolerability of generic versus brand beta blockers in heart failure with reduced left ventricular ejection fraction: a retrospective cohort from heart failure clinic[J]. J Drug Assess, 2018, 7(1): 8-13
- [24] Xia T, Chai X, Shen J. Pancreatic exocrine insufficiency in patients with chronic heart failure and its possible association with appetite loss[J]. PLoS One, 2017, 12(11): e0187804
- [25] 韩宝华,吕珊珊,罗晓婷,等.扩张型心肌病慢性心力衰竭患者血浆脑利钠肽水平的临床意义 [J]. 现代生物医学进展, 2017, 17(23): 4576-4578, 4513
Han Bao-hua, Lv Shan-shan, Luo Xiao-ting, et al. Clinical Significance of Dynamic Analysis of Plasma Brain Natriuretic Peptide in Patients with Dilated Cardiomyopathy with Chronic Heart Failure [J]. Progress in Modern Biomedicine, 2017, 17(23): 4576-4578, 4513
- [26] Xiaojing C, Yanfang L, Yanqing G, et al. Thymopentin improves cardiac function in older patients with chronic heart failure [J]. Anatol J Cardiol, 2017, 17(1): 24-30
- [27] Venero JV, Doyle M, Shah M, et al. Mid wall fibrosis on CMR with late gadolinium enhancement may predict prognosis for LVAD and transplantation risk in patients with newly diagnosed dilated cardiomyopathy-preliminary observations from a high-volume transplant centre[J]. ESC Heart Fail, 2015, 2(4): 150-159
- [28] Duan F, Qi Z, Liu S, et al. Effectiveness of bone marrow mononuclear cells delivered through a graft vessel for patients with previous myocardial infarction and chronic heart failure: an echocardiographic study of left ventricular remodeling [J]. Med Ultrason, 2015, 17(2): 160-166
- [29] Muthuramu I, Jacobs F, Singh N, et al. Selective homocysteine lowering gene transfer improves infarct healing, attenuates remodelling, and enhances diastolic function after myocardial infarction in mice[J]. PLoS One, 2013, 8(5): e63710
- [30] 周扬,陈良余.血浆同型半胱氨酸水平与慢性心力衰竭的相关性分析[J].安徽医学, 2017, 38(11): 1413-1416
Zhou Yang, Chen Liang-yu. Analysis of correlation between plasma homocysteine level and chronic heart failure[J]. Anhui Medical Journal, 2017, 38(11): 1413-1416