

doi: 10.13241/j.cnki.pmb.2018.18.021

甲状腺功能亢进性心脏病患者血清 BNP 及 CRP 水平 及其与心功能的关系 *

龚华平¹ 李 威¹ 宋文荣¹ 晏益民² 赵 涛²

(1 武汉大学人民医院汉川医院 湖北 汉川 431600; 2 武汉科技大学附属孝感医院 湖北 武汉 432000)

摘要 目的:研究甲亢性心脏病患者血清 BNP(B-type natriuretic peptide)与 CRP(C-reactive protein)水平及其与心功能的关系。**方法:**选择 2015 年 10 月至 2017 年 3 月在我院进行治疗的甲亢性心脏病患者 68 例作为观察组,同期选择在我院进行常规体检的健康者 35 例作为对照组。采用免疫放射法检测血清 BNP 水平,免疫比浊法检测血清 CRP 水平。比较两组血清 BNP、CRP 水平的差异及不同心功能甲亢性心脏病患者血清 BNP、CRP 水平,分析血清 BNP、CRP 水平与甲亢性心脏病患者心功能的相关性。**结果:**观察组血清 BNP、CRP 水平明显高于对照组,差异具有统计学意义($P<0.05$);观察组心功能 II 级患者血清 BNP、CRP 水平明显高于心功能 I 级患者 ($P<0.05$);心功能 III 级患者血清 BNP、CRP 水平明显高于心功能 II 级患者 ($P<0.05$);心功能 IV 级患者血清 BNP、CRP 水平明显高于心功能 III 级患者($P<0.05$);观察组治疗后血清 BNP、CRP 水平较治疗前显著降低,差异具有统计学意义($P<0.05$)。甲亢性心脏病患者血清 BNP、CRP 水平均与其心功能等级呈显著正相关($r=0.742, P=0.037; r=0.857, P=0.011$)。**结论:**甲亢性心脏病患者血清 BNP 与 CRP 水平均显著升高,可能用于甲亢并发甲亢性心脏病的早期诊断及心功能评估的重要参考指标。

关键词:甲状腺功能亢进症;甲亢性心脏病;B 型尿钠肽;C 反应蛋白

中图分类号:R541.85 **文献标识码:**A **文章编号:**1673-6273(2018)18-3498-04

Serum BNP and CRP Levels in the Patients with Hyperthyroid Heart Disease and Their Correlation with the Cardiac Function*

GONG Hua-ping¹, LI Wei¹, SONG Wen-rong¹, YAN Yi-min², ZHAO Tao²

(1 Hanchuan Hospital of people's Hospital of Wuhan University, Hanchuan, Hubei, 431600, China;

2 Xiaogan Hospital Affiliated to Wuhan University of Science and Technology, Wuhan, Hubei, 432000, China)

ABSTRACT Objective: To study the serum BNP and CRP Levels in the Patients with hyperthyroid heart disease and their correlation with the cardiac function. **Methods:** 58 patients of hyperthyroid heart disease who were treated from October 2015 to March 2017 in our hospital were selected as the observation group, 35 cases of healthy subjects in the hospital for regular physical examination were selected as the control group. The serum CRP and BNP levels were detected by immunoradiometric assay and immunoturbidimetry respectively and compared among patients with different heart function, the correlation of serum CRP and BNP levels with heart function of hyperthyroidism heart disease patient were analyzed. **Results:** The serum BNP, CRP levels of observation group were higher than those of the control group ($P<0.05$). The serum BNP, CRP levels of patients with cardiac function II in the observation group was higher than that of the patients with cardiac function grade I ($P<0.05$); the serum BNP, CRP levels of patients with cardiac function III in the observation group were higher than those of the patients with cardiac function grade II ($P<0.05$); the serum BNP, CRP levels of patients with cardiac function IV in Observation group were higher than those of the patients with cardiac function grade III ($P<0.05$). After treatment, the serum BNP, CRP level of observation group were lower than those before treatment($P<0.05$). The serum BNP and CRP levels of patients with hyperthyroid heart disease were positively correlated with the cardiac function ($r=0.742, P=0.037; r=0.857, P=0.011$). **Conclusion:** The serum BNP and CRP levels were significantly elevated in the patients with hyperthyroid heart disease, detecting the serum BNP and CRP levels can contribute to the early diagnosis of hyperthyroidism complicated with hyperthyroidism heart disease and effectively evaluate the cardiac function classification.

Key words: Hyperthyroidism; Hyperthyroid heart disease; BNP; CRP.

Chinese Library Classification(CLC): R541.85 **Document code:** A

Article ID: 1673-6273(2018)18-3498-04

* 基金项目:湖北省自然科学基金项目(2010HL053)

作者简介:龚华平(1969-),女,副主任医师,本科,研究方向:糖尿病发病相关因素的研究,电话:13871872345, E-mail:jlala309@21cn.com

(收稿日期:2018-04-07 接受日期:2018-04-30)

前言

甲亢性心脏病(Hyperthyroid heart disease, HHD)是由于机体过量分泌甲状腺激素对心脏造成一定的毒副作用,从而出现心律失常、心绞痛、心力衰竭等症状的内分泌紊乱性的心脏病,可发生于任何甲状腺功能亢进症患者中。据相关统计学研究显示甲亢性心脏病约占甲亢患者的 10%^[1-3],属于甲状腺危重症疾病,甚至可威胁患者生命。因此,早发现、早治疗对其预后具有重要的临床价值。对于甲亢性心脏病患者而言,除去怕热、多汗等典型的甲亢症状外,还容易出现心悸、呼吸困难、心房纤颤等症状。目前,甲亢性心脏病的诊断标准尚未统一,临床通常根据患者的症状给予判断,极易发生漏诊^[4]。因此,寻找早期诊断的血清标志物对患者预后具有重要意义。BNP 是在心室受到过度压力或扩张时所释放的一种激素,临床已证实 BNP 水平可反映患者的心功能受损情况^[5]。CRP 为一种由肝脏细胞合成的急性蛋白,多项研究显示 CRP 在评价患者心脏病严重程度具有较为重要的作用^[6]。本研究主要检测了甲亢性心脏病患者血清 BNP 与 CRP 水平并分析其与患者心功能的关系。现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 10 月至 2017 年 3 月在我院治疗的甲亢性心脏病患者 68 例作为观察组,纳入标准:(1)实验室检测及临床症状符合甲亢并发甲亢性心脏病诊断标准并确诊;(2)对本研究知情并同意。排除标准:(1)伴有高血压或慢性阻塞性肺炎;(2)因其他原因所致的心脏病;(3)患有精神障碍。其中,男 17 例,女 51 例,年龄 18~57 岁,平均年龄(38.45±5.76)岁;按照 NYHA 进行心功能分级,其中心功能 I 级患者 20 例,II 级患者 12 例,III 级患者 22 例,IV 级患者 14 例。选择同时期选择在我院进行常规

体检健康者 35 例作为对照组,其中男 14 例,女 21 例,年龄 18~59 岁,平均年龄(60.43±5.31)岁。两组在性别、年龄等方面相比具有可比性。

1.2 方法

收集两组空腹静脉静脉血 3 mL,置于 4℃ 环境中静置半小时至 1 h,待血液凝集后进行离心处理,取血清保存于 -80℃ 环境待检。采用免疫放射法检测血清 BNP,CRP 检测则使用免疫比浊法。上述检测步骤严格按照相关试剂盒要求进行。对本研究观察组患者进行抗甲状腺药物治疗,必要时可进行甲状腺次全切除术,在控制甲亢的同时,给予患者强心、利尿、扩血管等治疗,治疗 2 周后,再次检测患者血清 BNP、CRP 水平。

1.3 观察指标

观察治疗前后观察组血清 BNP、CRP 水平变化,并与对照组进行比较。心功能分级参照美国纽约心脏病学会提出方案进行,即 I 级:有心脏病但一般活动下不会引起疲乏、心悸、呼吸困难或心绞痛;II 级:体力活动受到轻微限制,一般活动有时可出现上述症状;III 级:体力活动明显受到限制,一般活动可出现上述症状;IV 级:无法从事任何体力活动,即使在休息状态下也可出现以上症状,活动后症状加重。

1.4 统计学分析

本研究数据选择 SPSS18.0 进行统计,计量资料比较采用 t 检验,计数资料比较采用 χ^2 检验,以 $P<0.05$ 时表示差异具有统计学意义。

2 结果

2.1 两组血清 BNP、CRP 水平比较

观察组血清 BNP、CRP 水平与对照组相比明显增高,差异具有统计学意义($P<0.05$);观察组治疗后血清 BNP、CRP 水平均显著低于治疗前,差异具有统计学意义($P<0.05$)。见表 1。

表 1 两组治疗前后血清 BNP、CRP 水平比较($\bar{x} \pm s$)

Table 1 Comparison of the serum BNP and CRP levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Time	BNP(pg/mL)	CRP(mg/L)
Observation group	68	Before treatment	652.78±74.23 ^a	32.76±3.76 ^a
		After treatment	76.64±5.21	8.16±0.92
Control group	35	-	30.52±3.45	6.67±0.73

Note: Compared with the control group, ^a $P<0.05$; Compared with after treatment, ^a $P<0.05$.

2.2 不同心功能甲亢性心脏病患者血清 BNP、CRP 水平比较

心功能 II 级甲亢性心脏病患者血清 BNP、CRP 水平明显高于心功能 I 级患者($P<0.05$);心功能 III 级患者 BNP、CRP 水

平明显高于心功能 II 级患者 ($P<0.05$); 心功能 IV 级患者 BNP、CRP 水平明显高于心功能 III 级患者($P<0.05$),见表 2。

表 2 不同心功能甲亢性心脏病患者血清 BNP、CRP 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the serum BNP and CRP levels of hyperthyroid heart disease patients with different heart function($\bar{x} \pm s$)

Cardiac function stages	n	BNP(pg/mL)	CRP(mg/L)
I	20	105.21±11.65	8.78±0.92
II	12	328.43±35.11 ^b	23.75±3.42 ^b
III	22	672.67±73.26 ^b	34.18±3.76 ^b
IV	14	1029.11±114.12 ^b	56.43±6.35 ^b

Note: Compared with the up-group, ^b $P<0.05$.

2.3 甲亢性心脏病患者血清 BNP、CRP 水平与功能之间的关系

甲亢性心脏病患者血清 BNP、CRP 水平均与心功能等级呈显著正相关($r=0.742, P=0.037; r=0.857, P=0.011$)。

3 讨论

甲亢是指由于机体甲状腺合成大量的释放甲状腺激素,从而使机体出现交感神经兴奋、代谢亢进,由于甲状腺激素可促进新陈代谢与机体氧化还原反应,从而使机体进食增多,但氧化反应的增强促进了机体能力消耗,从而使患者出现体重减轻,大多数患者同时会出现突眼、视力减退及眼睑水肿等症状^[7-9]。若甲亢患者长时间未得到有效的治疗,从而会诱发甲亢性心脏病。甲亢性心脏病是指患者在甲亢基础上发生心律失常、心脏扩大等心脏病症状,但要排除因其它原因所导致的心脏病^[10]。其发病机制是因为甲状腺激素可使心肌细胞对儿茶酚胺的敏感性增加,从而增强心肌收缩力,而甲亢病理状态下,机体全身处于代谢亢进,产热与散热均为增加,从而扩张了毛细血管,增加血管容量,导致心脏长时间处于高负荷状态,最终诱发心力衰竭、心脏扩张等症状^[11-13]。甲亢性心脏病的发生发展是一个持续积累的过程,临床症状未显示出现之前,患者的病理实则是—直存在,但目前对于甲亢性心脏病的诊断通常要等到患者病情发展到一定程度,因此对于处于早期甲亢性心脏病患者而言极其不利^[4]。然而在此期间,患者体内相关指标的水平表达可以反应出病情变化,对甲亢性心脏病患者心功能具有一定影响。

BNP 为临床常见的多肽激素,内含 32 个氨基酸,是利钠肽系统中重要的组成结构,最初是从猪脑分离出来,但研究显示其主要通过心室肌细胞合成^[15]。BNP 具有非常重要的生理作用,与 ANP 相似,具有调节水电平衡,利尿、利钠、扩张血管等作用^[16,17]。机体心室充盈压增高时可促进其合成分泌^[18]。近年来,BNP 被广泛运用于心功能状态的评价。国内外均有文献显示甲亢性心脏病患者血清 BNP 表达显著增高^[19-21]。本研究结果也显示与健康者相比,甲亢性心脏病患者血清 BNP 水平明显上升。由此可见,甲状腺功能的异常可影响 BNP 的代谢,临床研究显示其途径主要有以下几种:甲状腺毒症可直接促进心肌细胞分泌 BNP;甲亢患者血液动力学的改变可促进静脉回流量增加,从而使心脏容量处于超负荷状态,最终可致 BNP 水平增加;通过增加肾上腺素的活性从而使 BNP 的分泌增加。有学者通过研究已证实甲状腺素可作为 BNP 水平的调节因素^[22]。多项研究显示心脏病患者病情越严重其体内 BNP 水平表达越显著^[23-25]。本研究结果显示心功能等级越高患者 BNP 水平则越高,与上述文献结论一致。可见,血清 BNP 水平的增高可加重心脏负荷,从而导致患者心功能恶化。

CRP 为一种典型的急性反应蛋白,存在于机体肝脏,当机体出现感染、损伤、炎症反应时其水平会急速升高;可激活补体,加强吞噬细胞的吞噬而起一定的调节作用,可对入侵机体的病原微生物进行清除,在机体的天然免疫过程中发挥重要的保护作用^[26-28]。甲亢属于一种自身免疫性疾病,细胞免疫受损产生病理性的改变使血管内皮功能损伤,机体血清 CRP 水平显著上升。此外,患者处于心力衰竭、心律失常等症状下,机体会通过调节自身状态从而大量分泌 IL-6、TNF- α 等炎症因子,使肝细胞合成大量的 CRP,最终损伤血管内皮细胞,致心肌细胞

缺氧,促进心功能的恶化^[29-31]。本研究结果显示:与健康者相比,甲亢性心脏病患者血清 CRP 水平异常升高,且患者心功能分级越高其 CRP 水平越高,提示患者血清 CRP 水平的增高可影响患者心功能等级。

综上所述,甲亢性心脏病患者血清 BNP、CRP 水平与健康者相比显著升高,且水平增加幅度越大患者心功能等级越高。因此,可通过检测 BNP、CRP 水平对甲亢性心脏病进行早期诊断,同时可用作评估心功能分级的有效指标。

参考文献(References)

- [1] Sano M, Homma T, Ishige T, et al. An autopsy case of hyperthyroid cardiomyopathy manifesting lethal congestive heart failure [J]. *Pathol Int*, 2017, 67(2): 110-112
- [2] Schwensen C. Restoration of the Normal Auricular Rhythm in a Patient, Suffering from Graves' Disease and Auricular Fibrillation, after X-Ray Treatment[J]. *Acta Radiol*, 2016, 57(12): e238-e242
- [3] Raus I, Coroiu RE. McCune Albright syndrome - association of fibrous dysplasia, café-au-lait skin spots and hyperthyroidism case report [J]. *Clujul Med*, 2016, 89(4): 559-564
- [4] Habib H, Hawatmeh A, Rampal U, et al. Left ventricular noncompaction diagnosed following Graves' disease [J]. *Avicenna J Med*, 2016, 6(4): 113-116
- [5] Zăgreanu VM, Pop D, Zdrengea M, et al. Plasmatic Levels of N-terminal Pro-BNP in Elderly Patients with Atrial Fibrillation and Heart Failure with Preserved Ejection Fraction [J]. *Iran J Public Health*, 2017, 46(4): 568-570
- [6] Park Y, Kim KH, Kang MG, et al. Antiplatelet Therapy Combinations and Thrombogenicity in Patients with Non-Valvular Atrial Fibrillation[J]. *Korean Circ J*, 2017, 47(3): 366-376
- [7] Hasosah M, Alsaleem K, Qurashi M, et al. Neonatal Hyperthyroidism with Fulminant Liver Failure: A Case Report [J]. *J Clin Diagn Res*, 2017, 11(4): SD01-SD02
- [8] Vieira FF, Olivoto RR, Silva POD, et al. Functional Effects of Hyperthyroidism on Cardiac Papillary Muscle in Rats[J]. *Arq Bras Cardiol*, 2016, 107(6): 542-549
- [9] Nordio M. A novel treatment for subclinical hyperthyroidism: a pilot study on the beneficial effects of L-carnitine and selenium[J]. *Eur Rev Med Pharmacol Sci*, 2017, 21(9): 2268-2273
- [10] Gorenk Chair B, Pelliccia Co-Chair A. European Heart Rhythm Association (EHRA)/European Association of Cardiovascular Prevention and Rehabilitation (EACPR) position paper on how to prevent atrial fibrillation endorsed by the Heart Rhythm Society (HRS) and Asia Pacific Heart Rhythm Society (APHRS) [J]. *Eur J Prev Cardiol*, 2017, 24(1): 4-40
- [11] Leo M, Bartalena L, Rotondo Dottore G, et al. Effects of selenium on short-term control of hyperthyroidism due to Graves' disease treated with methimazole: results of a randomized clinical trial [J]. *J Endocrinol Invest*, 2017, 40(3): 281-287
- [12] Abdel-Salam M, Ibrahim S, Pessar SA, et al. The relationship between serum homocysteine and highly sensitive C-reactive protein levels in children on regular hemodialysis [J]. *Saudi J Kidney Dis Transpl*, 2017, 28(3): 483-490
- [13] Liao Z, Xiong Y, Luo L. Low-dose spinal-epidural anesthesia for Ce-

- sarean section in a parturient with uncontrolled hyperthyroidism and thyrotoxic heart disease[J]. *J Anesth*, 2016, 30(4): 731-734
- [14] Ozbek M, Gungunes A, Sahin M, et al. Serum heart type fatty acid binding protein levels are not changed in hyperthyroidism[J]. *Minerva Endocrinol*, 2016, 41(3): 298-301
- [15] Bando S, Soeki T, Matsuura T, et al. Plasma brain natriuretic peptide levels are elevated in patients with cancer[J]. *PLoS One*, 2017, 12(6): e0178607
- [16] Leufgen C, Gembruch U, Stoffel-Wagner B, et al. N-terminal pro-B-type natriuretic peptide in amniotic fluid of fetuses with known or suspected cardiac load[J]. *PLoS One*, 2017, 12(5): e0177253
- [17] Li H, Yuan Z, Li S, et al. Plasma levels of matrix metalloproteinase 9 in patients undergoing off-pump coronary artery bypass grafting [J]. *J Thorac Dis*, 2017, 9(4): 1100-1106
- [18] Yoshida J, Kawai M, Minai K, et al. Associations between Left Ventricular Cavity Size and Cardiac Function and Overload Determined by Natriuretic Peptide Levels and a Covariance Structure Analysis[J]. *Sci Rep*, 2017, 7(1): 2037
- [19] Yüksel IO, Arslan S, Cagirci G, et al. Assessment of left ventricular function with tissue Doppler echocardiography and of B-type natriuretic peptide levels in patients undergoing transcatheter aortic valve implantation[J]. *Rev Port Cardiol*, 2017, 36(5): 377-383
- [20] Pan Y, Lu Z, Hang J, et al. Effects of Low-Dose Recombinant Human Brain Natriuretic Peptide on Anterior Myocardial Infarction Complicated by Cardiogenic Shock [J]. *Braz J Cardiovasc Surg*, 2017, 32(2): 96-103
- [21] Yan W, Li RJ, Jia Q, et al. Neutrophil-to-lymphocyte ratio compared to N-terminal pro-brain natriuretic peptide as a prognostic marker of adverse events in elderly patients with chronic heart failure[J]. *J Geriatr Cardiol*, 2017, 14(2): 127-134
- [22] Tsutsumi J, Minai K, Kawai M, et al. Manifold implications of obesity in ischemic heart disease among Japanese patients according to covariance structure analysis: Low reactivity of B-type natriuretic peptide as an intervening risk factor[J]. *PLoS One*, 2017, 12(5): e0177327
- [23] Bartus K, Podolec J, Lee RJ, et al. Atrial natriuretic peptide and brain natriuretic peptide changes after epicardial percutaneous left atrial appendage suture ligation using LARIAT device[J]. *J Physiol Pharmacol*, 2017, 68(1): 117-123
- [24] Bando S, Soeki T, Matsuura T, et al. Plasma brain natriuretic peptide levels are elevated in patients with cancer[J]. *PLoS One*, 2017, 12(6): e0178607
- [25] Rasche FM, Stoebe S, Ebert T, et al. Modern peptide biomarkers and echocardiography in cardiac healthy haemodialysis patients [J]. *BMC Nephrol*, 2017, 18(1): 175
- [26] Shin HC, Jang JS, Jin HY, et al. Combined Use of Neutrophil to Lymphocyte Ratio and C-Reactive Protein Level to Predict Clinical Outcomes in Acute Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention[J]. *Korean Circ J*, 2017, 47(3): 383-391
- [27] Brammen L, Palestro CJ, Holinka J, et al. A retrospective analysis of the accuracy of radioactively labeled autologous leukocytes in patients with infected prosthetic joints[J]. *Nucl Med Rev Cent East Eur*, 2015, 20(2): 81-87
- [28] Matsumoto M, Nakabayashi Y, Fujiwara Y, et al. Duration of Preoperative Biliary Drainage as a Prognostic Factor After Pancreaticoduodenectomy for Pancreatic Head Cancer [J]. *Anticancer Res*, 2017, 37(6): 3215-3219
- [29] Nakamura T, Katagiri H, Shido Y, et al. Analysis of Factors for Predicting Survival in Soft-tissue Sarcoma with Metastatic Disease at Initial Presentation[J]. *Anticancer Res*, 2017, 37(6): 3137-3141
- [30] Pizzini A, Lunger F, Sahanic A, et al. Diagnostic and Prognostic Value of Inflammatory Parameters Including Neopterin in the Setting of Pneumonia, COPD, and Acute Exacerbations[J]. *COPD*, 2017, 14(3): 298-303
- [31] Brunvand L, Heier M, Brunborg C, et al. Advanced glycation end products in children with type 1 diabetes and early reduced diastolic heart function[J]. *BMC Cardiovasc Disord*, 2017, 17(1): 133
- (上接第 3479 页)
- [25] Hojs R, Ekart R, Bevc S, et al. Markers of Inflammation and Oxidative Stress in the Development and Progression of Renal Disease in Diabetic Patients[J]. *Nephron*, 2016, 133(3): 159-162
- [26] Siddiqi Z, Karoli R, Kaul A, et al. Evaluation of neutrophil gelatinase-associated lipocalin and cystatin C as early markers of diabetic nephropathy[J]. *Ann Afr Med*, 2017, 16(3): 101-106
- [27] Yuan Y, Sun H, Sun Z. Advanced glycation end products (AGEs) increase renal lipid accumulation: a pathogenic factor of diabetic nephropathy (DN) [J]. *Lipids Health Dis*, 2017, 16(1): 126
- [28] Aghadavod E, Khodadadi S, Baradaran A, et al. Role of Oxidative Stress and Inflammatory Factors in Diabetic Kidney Disease[J]. *Iran J Kidney Dis*, 2016, 10(6): 337-343
- [29] Jiang Y, Zhang W, Xu S, et al. Transplantation of human fetal pancreatic progenitor cells ameliorates renal injury in streptozotocin-induced diabetic nephropathy[J]. *J Transl Med*, 2017, 15(1):147
- [30] Srinivasan S, Dehghani C, Pritchard N, et al. Optical coherence tomography predicts 4-year incident diabetic neuropathy [J]. *Ophthalmic Physiol Opt*, 2017, 37(4): 451-459