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慢性心力衰竭患者血清 sST2、IL-6 和肽素水平的变化及临床意义 *

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摘要 目的:探讨慢性心力衰竭(CHF)患者血清可溶性人基质裂解素 2(sST2)、白细胞介素 -6(IL-6)、和肽素水平的变化及临床意义。**方法:**选取 2017 年 1 月 -2018 年 1 月期间我院收治的 CHF 患者 122 例纳入 CHF 组,根据纽约心脏协会(NYHA)心功能分级将患者分为 II 级组 34 例,III 级组 48 例,IV 级组 40 例。另选取同期住院的心律失常非 CHF 患者 35 例为对照组。检测并比较 CHF 组与对照组患者血清 sST2、和肽素、IL-6 水平,比较不同 NYHA 心功能分级 CHF 患者血清 sST2、和肽素、IL-6 水平,采用 Pearson 相关性分析血清 sST2、IL-6 及和肽素三指标间的相关性。**结果:**CHF 组患者血清 sST2、和肽素、IL-6 水平均高于对照组,差异有统计学意义 ($P<0.05$)。不同 NYHA 心功能分级的 CHF 患者血清 sST2、和肽素、IL-6 水平整体比较差异均有统计学意义 ($P<0.05$)。IV 级组、III 级组患者血清 sST2、和肽素、IL-6 水平均高于 II 级组患者,且 IV 级组高于 III 级组,差异有统计学意义 ($P<0.05$)。经 Pearson 相关性分析显示,血清 sST2、IL-6 水平与和肽素均呈正相关性 ($P<0.05$)。**结论:**血清 sST2、和肽素、IL-6 水平与 CHF 的严重程度密切相关,可考虑将其作为临床诊断 CHF 的生物学指标。

关键词:慢性心力衰竭;可溶性人基质裂解素 2;白介素 -6;和肽素;临床意义;相关性

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Changes and Clinical Significance of Serum Levels of sST2, IL-6 and Peptide in Patients with Chronic Heart Failure*

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ABSTRACT Objective: To investigate the changes and clinical significance of serum levels of Soluble human matrix lysin 2(sST2), Interleukin -6 (IL-6) and peptide in patients with chronic heart failure(CHF). **Methods:** 122 cases of CHF patients who were admitted in our hospital from January 2017 to January 2018 were included in CHF group. According to the New York Heart Association (NYHA), the patients were divided into II group with 34 cases, III group with 48 cases and IV group with 40 cases. Another 35 non arrhythmic patients hospitalized in the same period were selected as control group in the same period. The serum levels of sST2, peptide and IL-6 were detected and compared between the CHF group and the control group. The serum sST2, peptide and IL-6 levels in CHF patients with different NYHA heart function classification were compared, the correlation between serum sST2, IL-6 and peptide were analyzed by Pearson correlation analysis. **Results:** The serum levels of sST2, peptide and IL-6 in CHF group were higher than those in control group ($P<0.05$). There were significant differences in serum sST2, peptide and IL-6 levels in CHF patients with different NYHA cardiac function grades ($P<0.05$). The serum levels of sST2, peptide and IL-6 in the IV group and III group were higher than those in the II group, and the IV group was higher than that of the III group, the differences were statistically significant ($P<0.05$). Pearson correlation analysis showed that serum sST2 and IL-6 levels were positively correlated with peptide ($P<0.05$). **Conclusion:** The levels of serum sST2, peptide and IL-6 is closely related to the severity of CHF. It can be used as biological indexes for clinical diagnosis of CHF.

Key words: Chronic heart failure; Soluble suppression of tumorigenicity 2; Interleukin -6; Peptide; Clinical significance; Correlation

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前言

慢性心力衰竭 (chronic heart failure, CHF) 是由于心肌梗死、炎症、心肌病、血流动力学等原因引起的心肌损伤,临床主要表现为呼吸困难、乏力以及体液潴留等症状^[1,2]。虽然临床上关于治疗 CHF 取得了较大的进展,然而相关研究表明其 5 年

病死率仍高达 50%^[3]。目前临床用于评估 CHF 病情严重程度的指标较少,且超声心动图、X 射线等辅助性检查易受客观条件影响,由于 CHF 是由多种病理机制参与发生、发展的过程,因此,需联合多种生物学标记物对患者病情进行有效的评估^[4]。血清可溶性人基质裂解素 2(soluble suppression of tumorigenicity 2, sST2)是白介素 -1 受体家族成员之一,已有多项研究证明其

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在 CHF 患者体内呈现高表达^[5,6]。白细胞介素 -6(interleukin -6, IL-6)是一种炎性细胞因子,可激活溶胶原的基质金属蛋白酶系,继而影响心室重塑^[7,8]。和肽素作为血管加压素的前体,近年来有研究发现,其在心血管疾病、危重症以及下呼吸道感染等疾病的早期诊断及预后方面存在一定的临床价值^[9,10]。鉴于此,本文通过探讨 CHF 患者血清 sST2、IL-6、和肽素水平的变化及临床意义,旨在为 CHF 病情评估提供理论依据。现将结果整理如下。

1 资料与方法

1.1 一般资料

选取 2017 年 1 月 -2018 年 1 月期间我院收治的 CHF 患者 122 例纳入 CHF 组,纳入标准:(1)所有患者均符合 CHF 相关诊断标准并确诊^[11];(2)入院前半月内未使用抗炎药物或者糖皮质激素类药物者;(3)患者及其家属知情本研究并签署同意书。排除标准:(1)急性心肌梗死患者;(2)伴有严重肝肾功能障碍者;(3)合并自身免疫性疾病者;(4)伴有感染、高烧不退者;(5)伴有哮喘、脓毒症者。根据纽约心脏协会(New York Heart Association, NYHA)心功能分级将患者分为 II 级组 34 例, III 级组 48 例, IV 级组 40 例,其中 II 级组男 19 例,女 15 例,年龄 45-68 岁,平均(53.35± 2.48)岁。III 级组男 27 例,女 21 例,年龄 46-66 岁,平均(54.68± 3.09)岁。IV 级组男 21 例,女 19

例,年龄 43-69 岁,平均(52.71± 2.87)岁。另选取同期住院的心律失常非 CHF 患者 35 例为对照组,对照组男 20 例,女 15 例,年龄 46-65 岁,平均(54.22± 3.27)岁。四组患者一般资料比较差异无统计学意义($P>0.05$),提示组间可进行比较,本研究已通过医院伦理学委员会批准同意。

1.2 检测方法

所有研究对象均于入院第二天抽取清晨空腹静脉血 5 mL, 3000 r/min 离心 15 min,取上清液保存于 -20℃ 冰箱中待测。采用双抗体夹心酶联免疫吸附试验检测血清 sST2、和肽素、IL-6 水平,试剂盒来源于深圳晶美生物科技有限公司,按照试剂盒说明进行操作。

1.3 统计学方法

数据分析采用 SPSS 23.0 统计学软件。计数资料以率表示,实施 χ^2 检验,计量资料以均值± 标准差表示,多组数据应用单因素 F 分析,两组数据应用 t 检验,采用 Pearson 相关性分析血清 sST2、IL-6 与和肽素相关性,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 CHF 组与对照组患者血清 sST2、和肽素、IL-6 水平比较

CHF 组患者血清 sST2、和肽素、IL-6 水平均高于对照组,差异有统计学意义($P<0.05$),详见表 1。

表 1 CHF 组与对照组患者血清 sST2、和肽素、IL-6 水平比较($\bar{x} \pm s$)

Table 1 Comparison of serum sST2, peptide and IL-6 levels between CHF group and control group($\bar{x} \pm s$)

Groups	n	sST2(ng/mL)	Peptide(pg/mL)	IL-6(ng/L)
Control group	35	0.33± 0.08	1237.28± 218.21	40.51± 8.36
CHF group	122	1.28± 0.76	1984.07± 309.45	219.09± 19.84
t	-	13.652	16.147	78.458
P	-	0.000	0.000	0.000

2.2 不同 NYHA 心功能分级的 CHF 患者血清 sST2、和肽素、IL-6 水平比较

不同 NYHA 心功能分级的 CHF 患者血清 sST2、和肽素、

IL-6 水平整体比较差异均有统计学意义 ($P<0.05$), IV 级组、III 级组患者血清 sST2、和肽素、IL-6 水平均高于 II 级组患者,且 IV 级组高于 III 级组,差异有统计学意义($P<0.05$),详见表 2。

表 2 不同 NYHA 心功能分级的 CHF 患者血清 sST2、和肽素、IL-6 水平比较($\bar{x} \pm s$)

Table 2 Comparison of serum sST2, peptide and IL-6 levels in CHF patients with different NYHA cardiac function classification($\bar{x} \pm s$)

Groups	n	sST2(ng/mL)	Peptide(pg/mL)	IL-6(ng/L)
IIgroup	34	0.47± 0.18	1629.14± 421.37	141.54± 20.19
IIIgroup	48	0.85± 0.12*	1913.51± 381.46*	202.68± 18.22*
IVgroup	40	2.38± 0.35**	2316.69± 419.53**	248.85± 21.31**
F	-	10.587	19.482	20.412
P	-	0.000	0.000	0.000

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

2.3 CHF 患者血清 sST2、和肽素、IL-6 水平相关性分析

经 Pearson 相关性分析显示,血清 sST2、IL-6 水平与和肽素均呈正相关性($r=0.378, 0.413, P=0.000, 0.000$)。

3 讨论

心力衰竭是各种心血管疾病的转归结局,也是导致患者死亡的主要原因,随着我国人口老龄化趋势的加剧,其发病率呈现不断上升的趋势^[12,13]。CHF 是由多种生理学机制参与作用的一组临床综合征,需从多角度对 CHF 的诊断、预后进行评估,以获得更为全面的临床信息。近年来生物标记法作为一种简单

可靠的检测方法,已逐渐应用于 CHF 患者的早期诊断、治疗以及预后当中,与心肌细胞牵张相关的标志物已成为当前研究热点之一^[14,15]。目前为止,脑钠肽用于 CHF 的检测技术已较为成熟,然而其作为单一的生物标记物,仅仅只能反映 CHF 众多病理生理机制中的一种^[16,17]。因此,临床中需检测多种生物学标志物以反映不同的病理生理机制。

血清人基质裂解素 2(suppression of tumorigenicity 2,ST2)是心肌细胞受到机械应力时所产生一种心肌蛋白,主要编码两种形式的蛋白产物:sST2 和跨膜性 ST2 蛋白(transmembrane ST2 protein,ST2L)^[18]。白介素 -33(interleukin -33,IL-33)是 ST2 的功能性配体,可组成 ST2/IL-33 信号系统产生作用。已有研究证实 ST2/IL-33 信号系统在抗动脉粥样硬化^[19]、自身免疫性疾病^[20]以及抗心肌纤维化^[21]等过程中均发挥重要作用。另相关动物实验研究表明^[22],ST2/IL-33 信号系统具有减少心肌纤维化,抑制心肌细胞肥大、凋亡,改善心肌功能的作用,而上述保护心脏的作用均是通过蛋白产物 ST2L 与 IL-33 配体结合所产生,但是 sST2 与 IL-33 配体结合并不能发挥保护心脏的作用。当机体心肌受损时,sST2 则会竞争性的与 IL-33 配体结合,大大减弱了 ST2L 与其结合能力,从而引发心肌细胞凋亡、肥大及纤维化,加重机体损伤。有学者研究报道^[23],sST2 是通过机械应力诱导所产生的一种蛋白质,是心肌细胞肥厚以及纤维化的标志物,CHF 病情越严重,心肌细胞受到机械应力则越大,造成血清 sST2 水平越高,因此,sST2 可在一定程度上反映 CHF 病情严重程度。相关学者研究报道^[24,25],CHF 发生发展的主要机制为心肌重塑,当心肌重塑时神经内分泌被激活,从而分泌精氨酸加压素,其与众多心血管疾病的预后均存在密切联系,但由于精氨酸加压素半衰期短、结构不稳定,临床关于精氨酸加压素的检测技术并不十分成熟。和肽素是一种含有 39 个氨基酸的糖肽,属于精氨酸加压素的末端部分,在 CHF 的发生、发展过程中,和肽素的作用机制与精氨酸加压素类似^[26,27]。且与精氨酸加压素相比,和肽素具有稳定性好、易检测等优点,因此检测 CHF 患者和肽素水平可能为临床诊断、评估提供新的思路。

目前有研究认为^[28],CHF 的发生除了与神经内分泌激活有关,还与细胞因子失衡有关。IL-6 是第二类血管减压的前炎症细胞因子,其通过增加心肌细胞心钠肽、脑钠肽的表达,致使患者心功能不全。IL-6 在心肌损伤中的作用机制主要表现为提高交感神经活性,促进心肌蛋白质水解,导致心肌细胞凋亡加速继而损伤心功能,并且持续的细胞因子激活会不断加重患者心肌损伤^[29]。本次研究结果表明,CHF 组患者血清 sST2、和肽素、IL-6 高于对照组,且随着 NYHA 心功能分级越高,其体内 sST2、和肽素、IL-6 也越高,提示随着 CHF 患者病情的加重,sST2、和肽素、IL-6 水平均参与了 CHF 的发生、发展,且在患者体内呈现高表达,可见上述三种指标可作为 CHF 病情严重程度的生物学指标,这与 Shao D 等人研究结果基本一致^[30]。通过相关性分析显示血清 sST2、IL-6 水平与和肽素均呈正相关性,提示在心室重塑方面,sST2、IL-6 水平与和肽素可发挥协同作用。

综上所述,血清 sST2、IL-6 及和肽素水平可较为准确的反映不同 NYHA 心功能分级 CHF 患者病情进展状态,可作为临床上新的生物学检测补充手段,为提高 CHF 患者的诊断、病情评估以及预后具有一定的参考价值。

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