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重度心力衰竭患者血清 RDW、CPP、NT-proANP 的临床意义 及其与预后相关性分析 *

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摘要 目的:探讨重度心力衰竭患者血清红细胞分布宽度(RDW)、和肽素(CPP)、氨基末端 A 型利钠肽(NT-proANP)的临床意义及其与预后相关性。**方法:**选取我院 2020 年 1 月与到 2022 年 12 月收治的 98 例心力衰竭患者作为研究对象,将所有患者应用 Killip 分级进行分组, I 级 16 例, II 级 23 例, III 级 21 例, IV 级 38 例,并选取同期来我院体检的 50 名健康志愿者作为对照组,对比五组患者血清 RDW、CPP、NT-proANP 表达水平,分析 RDW、CPP、NT-proANP 与重度心力衰竭的相关性。随后将 III 级与 IV 级重度心力衰竭的 59 例患者依照其预后情况分为死亡组(n=21)和存活组(n=38),对比两组患者临床一般情况与血清 RDW、CPP、NT-proANP 表达水平,并分析血清 RDW、CPP、NT-proANP 对重度心力衰竭的预后预测价值。**结果:**五组受检者血清 RDW、CPP、NT-proANP 水平对比差异显著, IV 级组明显高于 III 级、II 级、I 级和对照组($P<0.05$); Spearman 相关分析结果显示:血清 RDW、CPP、NT-proANP 与重度心力衰竭呈正相关 ($P<0.05$); 曲线下面积 (AUC) 从依次为 RDW (0.688)、CPP(0.667)、NT-proANP (0.656)、三者联合 (0.671)。RDW 诊断灵敏度为 67.61 %, 特异度为 66.85 %, CPP 诊断灵敏度为 60.03 %, 特异度为 67.53 %, NT-proANP 诊断灵敏度为 61.24 %, 特异度为 66.53 %, 三者联合诊断灵敏度为 74.58 %, 特异度为 86.32 %; 存活组与死亡组患者 Killip 分级、合并陈旧性心肌梗死、RDW、CPP、NT-proANP 水平对比差异显著($P<0.05$); logistic 回归分析结果表明: RDW、CPP、NT-proANP 为重度心力衰竭预后的独立预测指标($P<0.05$)。 **结论:**血清 RDW、CPP、NT-proANP 与重度心力衰竭具有明显相关性,其对于重度心力衰竭的诊断临界值分别为 17.58 %、1772.62 pg/mL、1.12 nmol/mL。同时三者为重度心力衰竭预后不良的独立影响因素。

关键词:重度心力衰竭;红细胞分布宽度;和肽素;氨基末端 A 型利钠肽

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Clinical Significance of Serum RDW, CPP and NT-proANP in Patients with Severe Heart Failure and Their Correlation with Prognosis*

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ABSTRACT Objective: To investigate the clinical significance of serum red blood cell distribution width (RDW), cardiac peptide (CPP) and amino-terminal type A natriuretic peptide (NT-proANP) in patients with severe heart failure and their correlation with prognosis. **Methods:** 98 patients with heart failure admitted to our hospital from January 2020 to December 2023 were selected as the study subjects. All patients were divided into groups according to Killip classification, including 16 patients with grade I, 23 patients with grade II, 21 patients with grade III, and 38 patients with grade IV. 50 healthy volunteers who came to our hospital for physical examination at the same time were selected as the control group. The expression levels of serum RDW, CPP, and NT-proANP in five groups were compared, and the correlation between RDW, CPP, NT-proANP and severe heart failure was analyzed. Subsequently, 59 patients with severe heart failure of grade III and IV were divided into death group (n=21) and survival group (n=38) according to their prognosis. The clinical general situation and the expression level of serum RDW, CPP, NT-proANP were compared between the two groups, and the prognostic value of serum RDW, CPP, NT-proANP for severe heart failure was analyzed. **Results:** The levels of serum RDW, CPP and NT-proANP were significantly different among the five groups. The level of serum RDW, CPP and NT-proANP in grade IV group was significantly higher than that in grade III, II, I and control group ($P<0.05$); Spearman correlation analysis showed that serum RDW, CPP, NT-proANP were positively correlated with severe heart failure ($P<0.05$); The area under the curve (AUC) is RDW (0.688), CPP (0.667),

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NT-proANP (0.656), and the combination of the three (0.671). The diagnostic sensitivity of RDW is 67.61 %, the specificity is 66.85%, the diagnostic sensitivity of CPP is 60.03 %, the specificity is 67.53 %, the diagnostic sensitivity of NT-proANP is 61.24 %, the specificity is 66.53%, the combined diagnostic sensitivity of the three is 74.58 %, the specificity is 86.32 %; There were significant differences in Killip grade, levels of RDW, CPP, NT proANP between the survival group and the death group ($P<0.05$); The results of logistic regression analysis showed that RDW, CPP and NT-proANP were independent predictors of the prognosis of severe heart failure ($P<0.05$). **Conclusion:** Serum RDW, CPP and NT-proANP are significantly correlated with severe heart failure, and their diagnostic thresholds for severe heart failure are 17.58 %, 1772.62 pg/mL and 1.12 nmol/mL, respectively. At the same time, the three factors are independent influencing factors for poor prognosis of severe heart failure.

Key words: Severe heart failure; Red blood cell distribution width; And peptide; Amino-terminal A-type natriuretic peptide

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前言

随着我国人口老龄化进程加深,心力衰竭发病率逐渐增高,成为了当前全球高死亡率的主要疾病之一,而且患者多预后较差,死亡率仅次于恶性肿瘤^[1]。重度心力衰竭为当前多种心血管病发展的终末期阶段,也是心脏病患者最主要的死亡原因,由于重度心力衰竭患者临床体征和症状特异性较差,因此需要采取超声心动图等手段进行检查,但总体准确性较低。随着血清生物学标记物的发展,越来越多学者推荐采取不同血清指标来诊断重度心力衰竭,并判断心力衰竭的严重程度^[2,3]。超敏C反应蛋白、N端脑钠肽原以及脑钠肽作为心力衰竭辅助诊断的标记物已经在临床上广泛应用,但对于诊断效能依然存在一定局限^[4]。近年来大量国外研究发现^[5-7],血清红细胞分布宽度(red cell distribution width, RDW)、和肽素(copeptin, CPP)、氨基末端A型利钠肽(N-terminal pro-B-type natriuretic peptide, NT-proANP)与慢性心力衰竭和其预后情况具有一定相关性,然而是否能够诊断重度心力衰竭目前尚无确切定论。另外,有研究发现^[8],Killip分级能够准确诊断心力衰竭的严重,但是对于预后的预测并无明显优势,同时分级方法需要结合临床多项检查,局限性较大。因此,为了辅助诊断重度心力衰竭,本研究选取98例心力衰竭患者作为研究对象,探讨重度心力衰竭患者血清RDW、CPP、NT-proANP的临床意义及其与预后相关性。

1 资料与方法

1.1 一般资料

选取我院2020年1月到2022年12月收治的98例心力衰竭患者作为研究对象,将所有患者应用Killip分级进行分组,I级16例,II级23例,III级21例,IV级38例,并选取同期来我院体检的50名健康志愿者作为对照组。I级患者男10例,女6例;年龄为48~79岁,平均(67.22±5.55)岁;II级患者男13例,女10例;年龄为45~78岁,平均(67.53±6.61)岁;III级患者男12例,女9例;年龄为46~80岁,平均(67.96±3.25)岁;IV级患者男21例,女17例;年龄为43~75岁,平均(68.62±5.37)岁。对照组患者男性27例,女性23例;年龄为43~75岁,平均(67.82±6.83)岁。五组患者一般资料对比无差异($P>0.05$)。本研究经我院伦理委员会批准。

1.2 纳排标准

纳入标准:符合《急性心衰诊疗指南》^[9]中关于心功能衰竭

的诊断标准;临床资料完整;对本研究知情并签署同意书。

排除标准:不配合研究或中途退出者;合并肺源性心脏病、先天性心脏病等;合并肺栓塞或急性心肌梗死者;合并严重重要脏器功能障碍者;合并恶性肿瘤者;合并严重心肌梗死需要搭桥的患者。

1.3 方法

Killip分级方法:I级:无明显心力衰竭表现,听诊无肺部啰音和第三心音。II级:有左心衰竭表现,肺部啰音<50%肺野。III级:有急性肺水肿表现,肺部啰音>50%肺野。IV级:有心源性休克表现^[10]。

血清RDW、CPP、NT-proANP水平检测方法:采取所有受试者的清晨空腹静脉血3 mL,以3000 r/min的速度离心5 min后分离血浆与血清,保存在零下80摄氏度的冰箱内待检。应用酶联免疫吸附法检测和CPP、NT-proANP表达水平,检测步骤严格依照试剂盒(生产企业:南京信帆生物技术有限公司)说明书进行。应用SYSMEX XE-2100血细胞分析仪检测RDW。

1.4 观察指标

收集所有患者一般临床资料,其中包括性别、年龄、体质量指数(BMI)、合并基础疾病、左心室射血分数。

1.5 统计学方法

采取SPSS 23.0分析,计数资料以(n/%)表示,进行 χ^2 检验;计量资料用($\bar{x}\pm s$)表示,采用t检验;Spearman相关分析方法分析RDW、CPP、NT-proANP与重度心力衰竭的相关性;采用logistic回归分析上述指标与患者预后的关系;建立ROC曲线判断三者对重度心力衰竭的诊断价值;以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 五组受检者血清RDW、CPP、NT-proANP水平对比

五组受检者血清RDW、CPP、NT-proANP水平对比差异显著,IV级组明显高于III级、II级、I级和对照组($P<0.05$),如表1所示。

2.2 血清RDW、CPP、NT-proANP与重度心力衰竭的相关性

Spearman相关分析结果显示:血清RDW、CPP、NT-proANP与重度心力衰竭呈正相关($P<0.05$),如表2所示。

2.3 血清RDW、CPP、NT-proANP对重度心力衰竭的诊断价值

通过绘制ROC曲线,结果显示,AUC依次为RDW(0.688)、CPP(0.667)、NT-proANP(0.656)、三者联合(0.671)。

RDW 诊断灵敏度为 67.61 %, 特异度为 66.85 %, CPP 诊断灵敏度为 60.03 %, 特异度为 67.53 %, NT-proANP 诊断灵敏度为 61.24 %, 特异度为 86.32%。三者联合诊断灵敏度为 74.58%, 特异度为 86.32%。见表 3、图 1。

表 1 五组受检者血清 RDW、CPP、NT-proANP 水平对比($\bar{x} \pm s$)

Table 1 Comparison of serum RDW, CPP and NT-proANP levels among five groups of subjects($\bar{x} \pm s$)

Groups	n	RDW(%)	CPP(pg/mL)	NT-proANP(nmol/mL)
Grade I	16	13.76± 3.29	1343.73± 231.24	0.74± 0.12
Grade II	23	15.28± 3.49	1622.85± 214.25	0.86± 0.26
Grade III	21	17.19± 3.78	1825.24± 221.34	1.28± 0.22
Grade IV	38	19.63± 4.73	2137.07± 315.36	1.93± 0.32
Control group	50	12.66± 2.01	1276.17± 351.24	0.24± 0.05
F	-	368.529	1048.470	
P	-	0.001	0.001	

表 2 血清 RDW、CPP、NT-proANP 与重度心力衰竭的相关性

Table 2 Correlation between serum RDW, CPP, NT-proANP and severe heart failure

Indexs	Severity of heart failure	
	r	P
RDW	0.586	0.005
CPP	0.374	0.019
NT-proANP	0.426	0.012

表 3 血清 RDW、CPP、NT-proANP 对重度心力衰竭的诊断价值

Table 3 Diagnostic Value of Serum RDW, CPP, NT-proANP in Senile Heart Failure

Indexs	AUC	Diagnostic threshold	Sensitivity(%)	Specificity(%)
RDW	0.688	17.58%	67.61	66.85
CPP	0.667	1772.62 pg/mL	60.03	67.53
NT-proANP	0.656	1.12 nmol/mL	61.24	66.53
Combination of the three	0.671	-	74.58	86.32

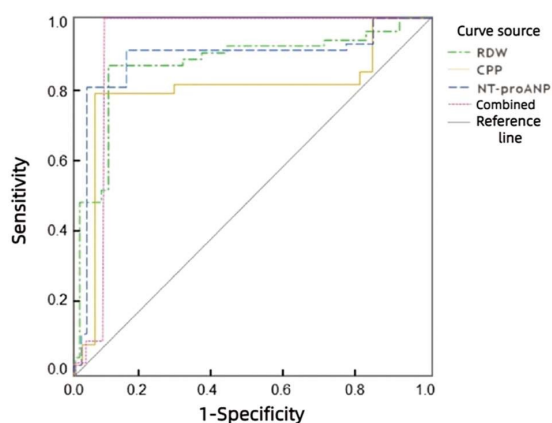


图 1 血清 RDW、CPP、NT-proANP 对重度心力衰竭的诊断 ROC 曲线图

Fig.1 ROC curve of serum RDW, CPP and NT-proANP in diagnosis of severe heart failure

2.4 存活组与死亡组一般临床情况

存活组与死亡组患者 Killip 分级、合并陈旧性心肌梗死、RDW、CPP、NT-proANP 水平对比差异显著($P<0.05$),如表 4

所示。

2.5 血清 RDW、CPP、NT-proANP 对重度心力衰竭的预后预测价值

logistic 回归分析结果表明:RDW、CPP、NT-proANP 为重度心力衰竭预后的独立预测指标($P<0.05$),如表 5 所示。

3 讨论

心力衰竭是各种原因导致的心脏舒张和收缩功能障碍,患者会出现心脏排血量无法满足于机体组织代谢需求情况,进而出现的相关体征与症状的慢性疾病^[1]。对于老年群体来说,心脏的舒张和收缩功能明显降低,同时合并高血压、糖尿病以及高脂血症等多种疾病后,容易在外伤、感染等多种因素刺激下引发心力衰竭,所以早期诊断,并评估心力衰竭病情和严重程度在诊断过程中具有重要价值^[12-14]。随着生物学指标的应用与研究进程加深,越来越多血清指标被用于老年心力衰竭的临床诊断之中。因此,本研究主要分析血清 RDW、CPP、NT-proANP 水平与重度心力衰竭的关系及其预后相关性,希望能够为临床提供参考意见。

表 4 存活组与死亡组一般临床情况

Table 4 General clinical conditions of survival group and death group

Categories	Survival group(n=38)	Death group(n=21)	χ^2/t	P
Gender (example)				
male	21	12	0.001	0.972
female	19	9		
Age	57.29± 3.42	57.30± 3.57	0.013	0.990
BMI(kg/m ²)	23.14± 2.34	23.19± 2.29	0.095	0.925
Killip				
III	24	7	4.820	0.028
IV	14	14		
Combined basic diseases				
Old myocardial infarction	6	9	5.230	0.022
Diabetes	12	6	1.573	0.210
hypertension	21	14	0.320	0.571
Hyperlipidemia	12	8	2.416	0.120
Left ventricular ejection fraction(%)	61.26± 7.84	63.63± 6.73	1.473	0.144
RDW(%)	16.39± 3.28	21.31± 4.34	1.243	0.217
CPP(pg/mL)	1783.47± 321.84	2314.02± 375.79	21.952	0.001
NT-proANP(nmol/mL)	1.30± 0.19	2.52± 0.73	17.826	0.001

表 5 血清 RDW、CPP、NT-proANP 对重度心力衰竭的预后预测价值

Table 5 Prognostic value of serum RDW, CPP and NT-proANP for severe heart failure

Factors	Parameter estimate	Standard error	Wald	P	OR	95% CI
Killip	0.635	0.108	10.484	0.108	0.464	0.210~1.347
Old myocardial infarction	0.847	0.304	13.274	0.124	0.747	0.314~1.249
RDW	0.463	0.096	8.096	0.023	2.546	1.364~3.475
CPP	0.526	0.028	5.736	0.016	0.326	0.251~0.765
NT-proANP	0.464	0.105	8.484	0.016	2.774	1.876~4.010

本研究结果表明,五组受检者血清 RDW、CPP、NT-proANP 水平对比差异显著,IV 级组明显高于 III 级、II 级、I 级和对照组($P<0.05$),与 Wu X 等^[15]研究相似。Wu X 等研究发现,冠心病患者血清 RDW 表达水平明显高于健康人群。这可能是因为,心血管疾病的发生与发展与机体炎症反应具有明显关系^[16]。而炎症因子会抑制红细胞生成素所介导红细胞的成熟情况,因此部分患者会出现 RDW 水平升高现象^[17]。本研究还发现心力衰竭程度越严重 CPP 水平越高,与 Combes A 等^[18]研究相似。另外,NT-proANP 与心力衰竭的相关研究较少,NT-proANP 是就是心房利钠肽前体中间片段,是心功能监测的新型指标^[19]。ANP 由心房细胞合成,当心肌细胞受到的牵拉增加时,心房细胞分泌和释放的 ANP 显著增多,与 Davidovski FS 等^[20]研究相似;Spearman 相关分析结果显示:血清 RDW、CPP、NT-proANP 与重度心力衰竭呈正相关($P<0.05$),与华娇等^[21]、吴淑彬等^[22]、吴超等^[23]研究相符。华娇等研究发现,RDW 与血液透析并发急性心力衰竭情况具有明显相关性。RDW 主

要反应了血液之中红细胞大小的异质性参数,多用于诊断缺铁性贫血^[24]。RDW 水平升高主要反应了机体的红细胞生成障碍,例如造血原料叶酸、铁等物质的缺乏。而近期有研究发现^[25],RDW 水平升高在选择性人群中属于心血管疾病的新型相关性因素。虽然其具体机制尚无确切定论,但推测可能与炎症反应、肝淤血、肾功能不全以及营养不良有关。吴淑彬等研究发现,血清和肽素表达水平与慢性心力衰竭具有明显相关性。这可能是因为, CPP 属于前体精氨酸加压素羧基端部分,比精氨酸加压素更加稳定,且容易检测。而精氨酸加压素属于神经垂体和丘脑合成的一种血浆容量与渗透压调节因素,经常在心血管疾病患者中表现出异常改变^[26]。吴超等研究显示,心力衰竭患者病情越严重 NT-proANP 水平越高。这主要是因为,NT-proANP 水平升高可能与心功能情况具有一定关系,有可能与本研究均为肌酐轻幅升高的患者有关,与肾小球损害引起的肾功能不全相比,肾前性氮质血症对利钠肽影响更大;AUC 从依次为 RDW (0.688)、CPP (0.667)、NT-proANP (0.656)、三者联合 (0.671)。

RDW 诊断灵敏度为 67.61 %, 特异度为 66.85 %, CPP 诊断灵敏度为 60.03 %, 特异度为 67.53 %, NT-proANP 诊断灵敏度为 61.24 %, 特异度为 66.53 %, 三者联合诊断灵敏度为 74.58 %, 特异度为 86.32 %。提示临床可选择应用 RDW、CPP、NT-proANP 三者联合来辅助诊断重度心力衰竭; 存活组与死亡组患者 Killip 分级、合并陈旧性心肌梗死、RDW、CPP、NT-proANP 水平对比差异显著 ($P < 0.05$)。提示, 合并陈旧性心肌梗死患者病死率较高, 与 Putthapiban P 等^[27]研究相符。这主要是因为, 合并陈旧性心肌梗死患者死亡率较高可能是因为该类患者一般自身合并有心律失常、心功能不全和劳力性心绞痛情况, 心肌损伤并没有完全恢复, 发生心功能衰竭后疾病严重程度更高, 预后更差^[28]。另外, 有研究发现^[29,30], Killip 分级可作为急性心肌梗死合并心功能衰竭的重要分级标准, 可用于预测患者预后情况; logistic 回归分析结果表明: RDW、CPP、NT-proANP 为重度心力衰竭预后的独立预测指标 ($P < 0.05$)。提示临床上针对 RDW、CPP、NT-proANP 水平升高的重度心力衰竭患者需及时改善治疗方案, 进一步预防其预后不良情况的发生, 降低患者死亡率。但本研究由于样本量过少与随访时间较短, 研究可能存在局限, 还需在日后研究中深入研究。

综上所述, 血清 RDW、CPP、NT-proANP 与重度心力衰竭具有明显相关性, 其对于重度心力衰竭的诊断临界值分别为 17.58 %、1772.62 pg/mL、1.12 nmol/mL。同时三者为重度心力衰竭预后不良的独立影响因素。

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