

失代偿心力衰竭患者血钠水平与三尖瓣收缩期位移及肾小球滤过率的关系

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摘要 **目的** 研究失代偿心力衰竭患者血钠水平与三尖瓣收缩期位移及肾小球滤过率的关系。**方法** 选取经超声心动图证实的左心室射血分数(LVEF) $\leq 45\%$,且 NYHA 心功能分级在Ⅲ~Ⅳ级的失代偿心力衰竭患者 116 例,入院当天收集身高、体重、收缩压/舒张压等一般资料,第 2 日空腹抽血测定血电解质,尿素及肌酐等生化指标;血清 N 末端脑钠肽前体(NT-proBNP)水平。选用改良 MDRD 方程计算肾小球滤过率估算值(eGFR)。入院 48h 内行超声心动图测定三尖瓣收缩期位移(TAPSE)、左心室舒张末期内径(LVED)、右心室舒张末期内径(RVED)、肺动脉收缩压(PASP)及左心室射血分数(LVEF)。根据血清钠水平将全部入选病例分为低钠血症组(血清钠 $\leq 135\text{mmol/L}$, $n = 52$)与正常血钠组(血清钠 $> 135\text{mmol/L}$, $n = 64$)。对比两组上述一般资料、生化指标以及超声学指标差异。此外,对低钠血症组,以血钠水平分别与 TAPSE、eGFR 进行直线相关分析,同时将 TAPSE 与 eGFR 进行直线相关分析。**结果** ①低钠血症组 NT-proBNP 显著高于正常血钠组($P = 0.032$) ,TAPSE 降低及 eGFR 下降与血钠正常组相比,差异均有统计学意义($P = 0.015$, $P = 0.004$) ; ②直线相关分析显示,低钠血症组其血钠水平与 TAPSE 降低及 eGFR 下降均呈正相关($r = 0.785$; $r = 0.702$)。同时,低钠血症组 TAPSE 下降与 eGFR 下降亦呈正相关($r = 0.630$)。**结论** 失代偿心力衰竭患者低钠血症与 TAPSE 下降及 eGFR 降低之间密切相关,可作为早期识别此类患者发生肾功能恶化的简便而实用临床预测指标。

关键词 失代偿心力衰竭 低钠血症 三尖瓣收缩期位移 肾小球滤过率

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Association Between Serum Sodium Level and Tricuspid Annular Plane Systolic Excursion and Estimated Glomerular Filtration Rate in Patients with Decompensated Heart Failure. Yang Jingmin, Zhang Jieyu, Zhang Feifei. The First Affiliated Hospital of Zhengzhou University, Henan 450000, China

Abstract **Objective** To investigate the association between serum sodium level and tricuspid annular plane systolic excursion (TAPSE) and estimated glomerular filtration rate (eGFR) in patients with decompensated heart failure. **Methods** Totally 116 in-patients with decompensated heart failure who had left ventricular ejection fraction (LVEF) $\leq 45\%$ confirmed by echocardiogram and belonged to Ⅲ-Ⅳ degree of NYHA were enrolled. We collected height, weight, systolic/diastolic blood pressure and other general information on the first day of hospitalization. The dates of serum electrolyte, urea, creatinine and N-terminal pro-brain natriuretic peptide (NT-proBNP) level were detected in the second day of hospitalization on an empty stomach. Then eGFR were obtained by the modified MDRD equation. Tricuspid annular plane systolic excursion (TAPSE), left ventricular end diameter (LVED), right ventricular end diameter (RVED), pulmonary arterial systolic pressure (PASP) and left ventricular ejection fraction (LVEF) all were measured by echocardiography within 48 hours of hospitalization. All the patients were divided into two groups, the hyponatremia group and non-hyponatremia group, according to the serum sodium level (serum sodium $\leq 135\text{mmol/L}$ was defined as hyponatremia, $n = 52$; serum sodium $> 135\text{mmol/L}$ was defined as non-hyponatremia, $n = 64$). The NT-proBNP, LVEF, TAPSE and eGFR were compared between the two groups. Besides, for the hyponatremia group, the relevance between serum sodium level and TAPSE, eGFR were respectively analyzed. And we also analyzed the relevance between TAPSE and eGFR. **Results** ①The level of NT-proBNP in hyponatremia group was higher than non-hyponatremia group with statistical significance ($P = 0.032$), while TAPSE and eGFR were lower than non-hyponatremia group with statistical significance ($P = 0.015$, $P = 0.004$). ②Logistic regression analysis results showed that serum sodium level was positively correlated with the decrease of both TAPSE and eGFR ($r = 0.785$, $r = 0.702$). Meanwhile the decrease of TAPSE was also positively corre-

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lated with the decrease of eGFR ($r=0.630$). **Conclusion** Hyponatremia was positively correlated with the decrease of both TAPSE and eGFR in patients with decompensated heart failure. And hyponatremia maybe was considered as an easy and practical predictor for identifying those patients who would experience worsening renal function in early state.

Key words Decompensated heart failure; Hyponatremia; Tricuspid annular plane systolic excursion (TAPSE); Estimated glomerular filtration rate (eGFR)

心力衰竭因病因复杂,预后差等特点被称为心脏病难以攻克的堡垒。晚期失代偿心力衰竭患者出现利尿剂效果欠佳及肾功能恶化(即肾综合征)等情况,是导致治疗效果差且预后不良的重要原因^[1]。心肾综合征病理生理机制复杂迄今尚未完全阐明,且无简便实用预测手段。低钠血症是失代偿心力衰竭患者最常出现的电解质紊乱类型之一,多项研究表明其是导致心力衰竭患者预后不良及生存率下降的独立预测因素,但失代偿心力衰竭患者发生低钠血症是否与肾功能受损之间密切相关尚未明确确定论^[2,3]。因此,本研究通过研究血钠水平与三尖瓣收缩期位移(tricuspid annular plane systolic excursion, TAPSE)及肾小球滤过率(estimated glomerular filtration rate, eGFR)之间的关系旨在评估低钠血症在早期识别失代偿心力衰竭患者发生肾功能恶化的临床预测价值。

材料与方法

1. 研究对象:选取 2015 年 7 月 1 日~2016 年 5 月 20 日在郑州大学第一附属医院心内科住院,并经超声心动图证实左心室射血分数(left ventricular ejection fraction, LVEF) $\leq 45\%$,且 NYHA 心功能分级 III~IV 级的失代偿性心力衰竭患者 116 例,患者平均年龄 53 ± 28 岁。其中男性 64 例,女性 52 例。病因包括慢性缺血性心脏病 39 例,扩心病 36 例,酒精性心肌病 23 例,围生期心肌病 11 例及高血压性心脏病 7 例。患者诊断符合 Framingham 心力衰竭诊断标准^[4],病例排除标准:①单侧或双侧肾动脉狭窄者;入院前即患有严重肾功能不全甚至需要透析患者;②原发于肺及肺血管疾病引起的肺高压及右心力衰竭者;③舒张型心力衰竭及明显瓣膜病导致的心力衰竭患者;④合并重症结核、恶性肿瘤,感染性疾病、甲状腺疾病、严重肝脏疾病患者;⑤伴有消化道持续出血、严重脱水甚至休克等血容量严重不足者。

2. 一般资料收集:入院当天采集所有入选患者年龄、性别,收缩压/舒张压(systolic/diastolic blood pressure, SBP/DBP)及体重指数(body mass index, BMI)

等一般临床资料。

3. 血生化资料收集:入院第 2 日空腹抽血测定血清电解质,尿素,肌酐值等指标,应用美国 ROCHE 公司 Elecsy2010 全自动免疫分析仪采用双向侧流免疫法测定血清 N 末端 B 型脑钠肽前体(N-terminal proatriuretic peptide, NT-proBNP)水平。

4. 估测肾小球滤过率(eGFR):选用改良 MDRD 方程 $[eGFR = 175 \times SCR^{-1.234} \times \text{年龄}^{-0.179} \times 0.79(\text{女性})]$ 计算 eGFR。

5. 超声心动图检测:所有入选患者于入院 48h 内行超声心动图检测。取心尖四腔心切面,用改良的 Simpson 法计算左心室射血分数(LVEF),将 LVEF $\leq 45\%$ 定义为左心功能不全。常规测量左心室舒张末期内径(left ventricular end diameter, LVED)、右心室舒张末期内径(right ventricular end diameter, RVED),应用右房室瓣反流速度法估测肺动脉收缩压(pulmonary arterial systolic pressure, PASP)采用 M 型超声在右房室瓣与右心室游离壁交界处取样测量三尖瓣收缩期位移(TAPSE),TAPSE 参考值 $>20\text{mm}$,右心室功能不全时 $<16\text{mm}$ ^[5]。使用美国超声心动图学会推荐的方法。

6. 入选分组方法:根据血清钠水平将患者分为两组:低钠血症组(血清钠 $\leq 135\text{mmol/L}$, $n=52$)、血钠正常组(血清钠 $>135\text{mmol/L}$, $n=64$)。

7. 统计学方法:应用 SPSS 17.0 统计学软件对数据进行统计分析。主要检验指标均进行正态性检验,并以均数 $\pm$ 标准差($\bar{x} \pm s$)表示;组间差异的正态定量资料采用独立样本 t 检验分析;低钠血症组相关指标间相关性采用直线回归分析,非正态定量资料行线性分析前需将其数值进行对数转化,以 $P < 0.05$ 为差异有统计学意义。

结 果

1. 两组患者一般资料及生化指标比较:低钠血症组患者 NYHA 心功能分级、肌酐及 NT-proBNP 明显升高, eGFR 显著下降($P < 0.05$),而其他指标差异无统计学意义(表 1)。

2. 两组超声指标比较:低钠血症组患者 PASP 升

高及 TAPSE、eGFR 下降较血钠正常组差异有统计学意义 ($P < 0.05$)。而 LVED、RVED 及 LVEF 与正常血钠组对应超声学指标比较,差异无统计学意义 (表 2)。

表 1 两组患者一般资料及生化指标对比

项目	低钠血症组 ($n = 52$)	正常血钠组 ($n = 64$)	P
年龄 (岁)	47.73 ± 13.61	51.29 ± 15.17	0.368
女性: 男性	29: 35	23: 29	0.587
NYHA Ⅲ级: Ⅳ级	27: 37	19: 33	0.035
BMI (kg/m^2)	31.02 ± 10.04	29.04 ± 8.06	0.221
SBP (mmHg^Δ)	123 ± 32.85	122.48 ± 30.50	0.783
血清钾 (mmol/L)	4.17 ± 0.50	4.41 ± 0.49	0.121
血红蛋白含量 (g/L)	139.12 ± 18.87	145.71 ± 14.12	0.205
尿素 (mmol/L)	11.12 ± 5.91	14.06 ± 5.12	0.549
肌酐 ($\mu\text{mol}/\text{L}$)	76.82 ± 17.11	90.86 ± 26.92	0.032
eGFR [$\text{ml}/(\text{min} \cdot 1.73\text{m}^2)$]	95.89 ± 22.31	75.16 ± 25.92	0.004
NT-proBNP (pg/ml)	4526.11 ± 3173.47	6308.87 ± 3589.12	0.032

$^\Delta 1\text{mmHg} = 0.133\text{kPa}$

表 2 两组超声学指标对比

类别	钠正常组 ($n = 64$)	低钠血症组 ($n = 52$)	P
LVED (mm)	57.17 ± 11.31	58.06 ± 14.12	0.106
RVED (mm)	20.09 ± 3.25	26.58 ± 10.13	0.043
PASP (mmHg^Δ)	30.92 ± 13.88	43.35 ± 15.76	0.036
LVEF 值 (%)	37.80 ± 7.18	34.37 ± 10.62	0.063
TAPSE (mm)	17.88 ± 4.78	13.96 ± 4.62	0.015

$^\Delta 1\text{mmHg} = 0.133\text{kPa}$

3. 对低钠血症组患者,以血钠水平分别与 TAPSE 及 eGFR 进行直线相关分析:血清钠与 TAPSE 呈正相关 ($r = 0.785, P < 0.05$, 图 1), 与 eGFR 亦呈正相关 ($r = 0.702, P < 0.05$, 图 2), 同样的, TAPSE 与 eGFR 下降亦呈正相关 ($r = 0.630, P < 0.05$, 图 3)。

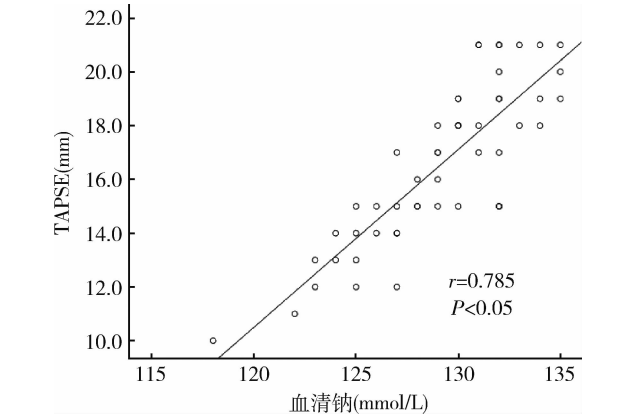


图 1 低钠血症组患者血钠水平与三尖瓣收缩期位移 (TAPSE) 下降呈正相关

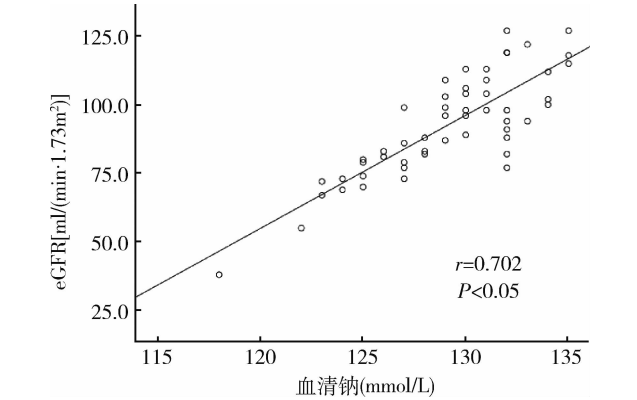


图 2 低钠血症组患者血钠水平与肾小球滤过率 (eGFR) 下降呈正相关

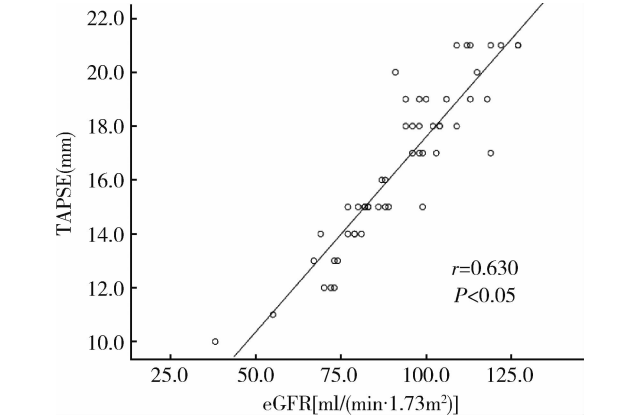


图 3 低钠血症组患者肾小球滤过率下降 (eGFR) 与三尖瓣收缩期位移 (TAPSE) 下降呈正相关

讨 论

本研究结果显示低钠血症发生率约为 44%, 与 Gheorghiade 等所报道低钠血症发生率 20% ~ 25% 相比较, 可能与本研究所纳入病例中 EF 值偏低且 NYHA 心功能分级 IV 级者所占比例较高有关^[2, 3]。本研究还发现, 低钠血症组患者 NT - proBNP 水平升高较正常血钠组差异有统计学意义。NT - proBNP 被认为是目前对心力衰竭患者进行危险分层, 指导治疗及预后判断的最佳指标, 其水平升高提示心室舒张末压增加及液体潴留, 故低钠血症在一定程度上可协同 NT - proBNP 作为评估失代偿心力衰竭患者心力衰竭严重程度的实用指标^[6]。

心力衰竭合并低钠血症的发生机制复杂, 一方面因心排出量降低导致血流动力学紊乱, 从而激活交感神经系统及肾素 - 血管紧张素 - 醛固酮系统 (renin - angiotensin - aldosterone system, RAAS), 促进体液再分布及水钠重吸收增加^[7, 8]。另一方面由于有效循环血容量减少, 导致下丘脑室上核和室旁核合成, 神经垂体后叶释放大量精氨酸加压素 (arginine vasopressin, AVP)。与正常人因血浆渗透压上升引起 AVP 释放不同, 心力衰竭患者 AVP 的非渗透性释放占据主导地位。研究表明, 当血容量下降 20% 以上, 激活肾素血管紧张素 II 及压力感受器, 引起 AVP 的非渗透性释放, 且 AVP 的非渗透性释放随血容量下降呈指数增长^[9, 10]。AVP 主要通过两种受体发挥作用。其中 V2 受体位于肾远端集合管主细胞, 与 AVP 结合后引起 cAMP 浓度增加, 激活蛋白激酶, 促使位于管腔膜上水通道蛋白合成与开放增加, 促进对自由水的重吸收, 进而形成稀释性低钠血症^[11, 12]。此外由于 AVP 分泌增加, 激活 V1A 受体, 导致血管收缩, 心脏后负荷增加, 降低了心力衰竭时 AVP 释放的阈值, 最终导致 AVP 所介导的低钠血症进一步恶化^[13]。

三尖瓣收缩期位移 (TAPSE) 是指右房室瓣环沿右心室长轴方向的收缩期位移 (TAPSE 正常值 > 20mm, 右心室功能受损 < 16mm), 因其测量不受限于几何形状及右心室心内膜的清晰度, 且多项研究证实它与右心室面积变化率及右心室射血分数呈正相关, 已被作为临床上评价右心室功能的良好指标^[5]。本研究发现血钠水平降低与 TAPSE 下降呈显著正相关, 提示左心失代偿心力衰竭患者继发右心室功能障碍时更易发生低钠血症。

进一步研究还发现, 血钠水平与 eGFR, 以及 TAPSR 与 eGFR 之间均存在显著正相关, 表明右心室

功能受损是导致肾功能恶化的重要原因。既往认可“前向衰竭”理论即心排出量降低导致肾灌注不足引起肾前性氮质血症和肾小管坏死^[14]。但近年来“后向衰竭”理论逐渐得到重视。ESCAPE 回顾性研究发现右心房压升高, 是导致肾功能恶化唯一危险因素^[15]。同样, Mulleins 等^[16]研究证实约 60% 的患者伴有腹内压升高, 且与肾功能恶化密切相关。左心室功能障碍继发右心室功能受损, 导致静脉系统淤血, 进而引起右心房压及中心静脉压升高, 进一步引起腹内压升高, 向后传导引起肾静脉淤血, 肾静脉压升高, 导致肾小球有效滤过压差减少, 从而使肾小球率过滤 (eGFR) 下降, 出现肾功能性损伤。此时若不能及时解除肾静脉淤血, 长期的肾灌注不足导致肾缺血缺氧加重, 激活炎症及氧化应激进一步导致肾小管间质纤维化而出现肾结构性损伤^[17-19]。

总之, 本研究表明血钠水平与三尖瓣收缩期位移下降及肾小球滤过率下降密切相关, 表明低钠血症 - 右心室功能受损 - 肾功能相互影响, 共同参与了复杂的“心肾综合征”的病理发展。同时证实低钠血症不仅是一种简单的电解质紊乱的临床表现, 而是神经内分泌高度激活及静脉系统淤血的标志物, 可为早期识别心力衰竭患者发生肾功能恶化的高危人群提供简便而又实用的临床指标, 需引起临床医生的高度重视^[20]。

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