

急性冠脉综合征患者血清 sST2 及 NLRP3 水平与介入术后无复流 - 慢血流的相关性分析

雷 锐^a, 殷 实^a, 李 志^b (佳木斯市中心医院 a. 心内三科; b. 心内二科, 黑龙江佳木斯 154002)

摘要: **目的** 探讨急性冠脉综合征 (acute coronary syndrome, ACS) 患者血清可溶性生长刺激表达基因蛋白 2 (soluble growth stimulation expression gene 2 protein, sST2), 核苷酸寡聚化结构域样受体热蛋白结构域相关蛋白 3 (nucleotide oligomerization domain like receptor heat protein domain associated protein 3, NLRP3) 水平与经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 术后无复流 - 慢血流的关系。**方法** 选择 2020 年 1 月~2022 年 12 月佳木斯市中心医院收治的 97 例急性冠脉综合征患者, 所有患者均接受 PCI 治疗, 根据术后无复流 - 慢血流发生情况分为无复流 - 慢血流组 ($n=20$) 和对照组 ($n=77$)。术前检测血清 sST2 及 NLRP3 水平, 分析影响急性冠脉综合征患者 PCI 术后无复流 - 慢血流的因素以及 sST2, NLRP3 预测急性冠脉综合征患者 PCI 术后无复流 - 慢血流的价值。**结果** 无复流 - 慢血流组血清 sST2 (14.32 ± 2.65 ng/ml vs 11.02 ± 2.13 ng/ml), NLRP3 (68.23 ± 10.17 pg/ml vs 42.05 ± 8.23 pg/ml) 水平高于对照组, 差异具有统计学意义 ($t=5.860, 12.055$, 均 $P < 0.05$)。多因素 Logistic 回归分析显示高血栓负荷 (OR: 7.791, 95% CI: 2.834~21.421)、高水平 sST2 (OR=2.071, 95% CI: 1.146 ~ 3.743)、高水平 NLRP3 (OR=2.008, 95% CI: 1.228 ~ 3.284) 是急性冠脉综合征患者 PCI 术后无复流 - 慢血流的危险因素 (均 $P < 0.05$)。sST2, NLRP3 诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的临界值分别为 12.91 ng/ml, 55.39 pg/ml, 曲线下面积分别为 0.737, 0.686, 联合 sST2, NLRP3 诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的曲线下面积为 0.907, 高于单独诊断 ($Z=2.662, 2.856$, 均 $P < 0.05$)。**结论** 急性冠脉综合征患者血清 sST2, NLRP3 水平增高与 PCI 术后无复流 - 慢血流的发生有关, 联合检测 sST2 和 NLRP3 可提高对术后无复流 - 慢血流的诊断效能。

关键词: 急性冠脉综合征; 经皮冠状动脉介入术; 无复流 - 慢血流; 可溶性生长刺激表达基因蛋白 2; 核苷酸寡聚化结构域样受体热蛋白结构域相关蛋白 3

中图分类号: R541.4; R392.11 文献标志码: A 文章编号: 1671-7414 (2024) 04-121-06

doi:10.3969/j.issn.1671-7414.2024.04.022

Correlation Analysis between Serum sST2 and NLRP3 Levels in Patients with Acute Coronary Syndrome and No Reflow or Slow Re-Flow after Interventional Surgery

LEI Rui^a, YIN Shi^a, LI Zhi^b (a. the Third Department of Cardiology; b. the Second Department of Cardiology,

Jiamusi Central Hospital, Heilongjiang Jiamusi 154002, China)

Abstract: Objective To investigate the relationship between serum soluble growth stimulation expression gene 2 protein (sST2) and nucleotide oligomerization domain like receptor heat protein domain associated protein 3 (NLRP3) levels in patients with acute coronary syndrome (ACS) and postoperative no reflow or slow re-flow after percutaneous coronary intervention (PCI). **Methods** A total of 97 patients with acute coronary syndrome admitted to Jiamusi Central Hospital from January 2020 to December 2022 were selected. All patients received PCI treatment and were divided into no reflow or slow re-flow group ($n=20$) and control group ($n=77$) based on the occurrence of postoperative no reflow or slow re-flow. The serum levels of sST2 and NLRP3 were detected before surgery, and the factors affecting no reflow or slow re-flow in patients with acute coronary syndrome after PCI were analyzed. The value of sST2 and NLRP3 in predicting no reflow or slow re-flow in patients with acute coronary syndrome after PCI was also analyzed. **Results** The serum levels of sST2 (14.32 ± 2.65 ng/ml vs 11.02 ± 2.13 ng/ml) and NLRP3 (68.23 ± 10.17 pg/ml vs 42.05 ± 8.23 pg/ml) in the no reflow or slow re-flow group were higher than those in the control group, and the differences were statistically significant ($t=5.860, 12.055$, all $P < 0.05$). Multivariate logistic regression analysis showed that high thrombotic burden (OR=7.791, 95% CI: 2.834~21.421), high levels of sST2 (OR=2.071, 95%

基金项目: 黑龙江卫生健康委科研课题 (2020-368)。

作者简介: 雷锐 (1982-), 女, 硕士研究生, 副主任医师, 研究方向: 心血管疾病, leirui98464@126.com。

通讯作者: 李志 (1982-), 男, 硕士研究生, 副主任医师, 研究方向: 心血管疾病。

CI=1.146~3.743), and high levels of NLRP3 (OR=2.008, 95% CI: 1.228~3.284) were risk factors for no reflow or slow re-flow in patients with acute coronary syndrome after PCI (all $P<0.05$). The critical values of sST2 and NLRP3 for diagnosing no reflow or slow re-flow in patients with acute coronary syndrome after PCI were 12.91 ng/ml and 55.39 pg/ml, with areas under the curve of 0.737 and 0.686, respectively. The area under the curve of combined with sST2 and NLRP3 for diagnosing no reflow or slow re-flow in patients with acute coronary syndrome after PCI was 0.907, which was higher than that of individual diagnosis ($Z=2.662$, 2.856, all $P<0.05$). **Conclusion** The elevated levels of serum sST2 and NLRP3 in patients with acute coronary syndrome were related to the occurrence of no reflow or slow re-flow after PCI. The combination of sST2 and NLRP3 could improve the diagnostic efficacy of postoperative no reflow or slow blood flow.

Keywords: acute coronary syndrome; percutaneous coronary intervention; no reflow or slow re-flow; soluble growth stimulation expression gene 2 protein; nucleotide oligomerization domain like receptor heat protein domain associated protein 3

经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)是急性冠脉综合征的标准和首选治疗方法,在恢复心肌梗死溶栓(thrombolysis in myocardial infarction, TIMI)Ⅲ级血流和降低死亡率方面优于溶栓治疗,但是并非所有的急性冠脉综合征(acute coronary syndrome, ACS)患者PCI术后均可达到TIMIⅢ级血流^[1-2]。无复流-慢血流是PCI术后常见的并发症,定义为心外膜闭塞的冠状动脉开通后,在没有心外膜血管阻塞、痉挛或剥离前提下,缺血心肌微循环血流未完全恢复正常,部分心肌组织无有效的再灌注现象^[3-4]。无复流-慢血流增加再次心肌梗死、恶性室性心律失常、心力衰竭和死亡等不良临床结果的风险,因此准确识别无复流-慢血流对改善患者预后至关重要。可溶性生长刺激表达基因蛋白2(soluble growth stimulation expression gene protein 2, sST2)是白细胞介素(interleukin, IL)-1受体超家族成员,在不良心血管事件应激下表达升高,在急性心力衰竭和急性冠状动脉综合征风险分层和预后分析中具有较高的价值^[5-6]。核苷酸寡聚化结构域样受体热蛋白结构域相关蛋白3(nucleotide oligomerization domain like receptor heat protein domain associated protein 3, NLRP3)是一种细胞内先天免疫受体, NLRP3炎性小体是动脉粥样硬化的关键驱动因素,与心血管疾病的发生发展密切相关^[7]。但是目前sST2, NLRP3在无复流-慢血流的报道较为少见,鉴于其与心血管事件的关系,本研究拟探讨sST2, NLRP3与急性冠脉综合征患者PCI术后无复流-慢血流的关系,旨在为临床治疗提供参考。

1 材料与方法

1.1 研究对象 选择2020年1月~2022年12月佳木斯市中心医院收治的97例急性冠脉综合征患者。纳入标准:①符合《急性冠脉综合征急诊快速诊治指南(2019)》诊断标准^[8];②接受PCI治疗;③至少植入一枚支架,术后行冠状动脉造影检查;④年龄18周岁以上。排除标准:①恶性肿瘤,感染性疾病或其他全身性炎症;②无PCI指征的患者;③

并发自身免疫性疾病、恶性肿瘤、严重肝肾功能不全;④接受冠状动脉搭桥手术治疗。无复流-慢血流诊断:PCI术后冠状动脉造影结果结合校正TIMI帧数(corrected TIMI frame count, CTFC)提示经冠状动脉注射硝酸甘油排除冠状动脉痉挛引起的血流缓慢,残余狭窄 $<10\%$,但CTFC >30 帧^[4]。根据术后是否发生无复流-慢血流现象将患者分为无复流-慢血流组和对照组。本研究已经获得所有患者的知情同意和佳木斯市中心医院伦理委员会的批准(批号:2019-K12-067),遵循《赫尔辛基宣言》指导方针。本研究共20例患者发生无复流-慢血流现象,无复流-慢血流组年龄大于对照组,糖尿病、术前TIMI分级0级、高血栓负荷、多支病变比例、SYNTAX评分高于对照组,发病至梗死血管开通时间长于对照组,差异具有统计学意义(均 $P<0.05$);其它资料比较,差异无统计学意义(均 $P>0.05$),见表1。

1.2 仪器与试剂 Infinite F50酶标仪(瑞士Tecan公司), sST2试剂盒(上海研启生物科技有限公司,货号YSRIBIO-4501), NLRP3试剂盒(泉州市九邦生物科技有限公司,货号QZ-11855)。

1.3 方法

1.3.1 血清sST2及NLRP3水平检测:所有患者PCI术前采集肘静脉血5ml置于无抗凝剂的真空管中,将血标本在室温下静置60min左右,待血液凝固后取上层液3000r/min离心5min,离心半径10cm。离心后取上清液 -80°C 保存待检。采用酶联免疫吸附试验法检测sST2, NLRP3水平,试剂盒组和组间变异系数为8%~10%。

1.3.2 临床资料收集:收集患者年龄、性别、体质指数、吸烟史、饮酒史、基础疾病、发病至梗死血管开通时间、梗死部位、血管病变支数、术前TIMI分级、SYNTAX评分、高血栓负荷、支架长度、支架数量、支架直径。高血栓负荷:血栓直径大于冠状动脉管腔1/2,长度大于病变冠状动脉管腔直径^[3]。

1.4 统计学分析 采用SPSS 25.00分析数据,正

态分布计量资料以均值 ± 标准差 ($\bar{x} \pm s$) 表示, 组间比较行独立样本 t 检验, 计数资料以率表示, 组间比较采用卡方检验。多因素 Logistic 回归分析影响急性冠脉综合征患者 PCI 术后无复流 - 慢血流的因素, 受试者工作特征 (receiver operating characteristic, ROC) 曲线分析 sST2, NLRP3 预测急性冠脉综合征患者 PCI 术后无复流 - 慢血流的价

值。检验水准 $\alpha=0.05$ 。

表 1 无复流 - 慢血流组和对照组基线资料比较 [$\bar{x} \pm s, n (\%)$]

类 别		无复流 - 慢血流组 ($n=20$)	对照组 ($n=77$)	χ^2 值	P 值
年龄 (岁)		64.02 ± 10.63	57.03 ± 11.81	2.404	0.018
性别	男	13 (65.00)	47 (61.04)	0.106	0.745
	女	7 (35.00)	30 (38.96)		
体质量指数 (kg/m^2)		24.15 ± 2.09	23.97 ± 2.11	0.341	0.734
基础疾病	吸烟史	12 (60.00)	51 (66.23)	0.271	0.603
	饮酒史	10 (50.00)	48 (62.34)	1.005	0.316
	高血压	13 (65.00)	52 (67.53)	0.046	0.830
	糖尿病	16 (80.00)	41 (53.25)	4.689	0.030
	高脂血症	11 (55.00)	38 (49.35)	0.203	0.653
发病至梗死血管开通时间 (h)		4.21 ± 1.02	4.09 ± 0.93	0.504	0.615
梗死部位	左前降支	11 (55.00)	38 (49.35)	0.224	0.894
	左回旋支	3 (15.00)	12 (15.58)		
	右冠状动脉	6 (30.00)	27 (35.06)		
血管病变支数	单支	4 (20.00)	29 (37.66)	7.055	0.029
	双支	6 (30.00)	32 (41.56)		
	多支	10 (50.00)	16 (20.78)		
术前 TIMI 分级	0 级	9 (45.00)	15 (19.48)	5.553	0.018
	I 级及以上	11 (55.00)	62 (80.52)		
SYNTAX 评分 (分)		25.12 ± 2.62	23.21 ± 1.06	5.049	0.001
高血栓负荷		12 (60.00)	15 (19.48)	12.977	0.002
支架长度 (mm)		33.02 ± 2.65	33.51 ± 2.76	0.713	0.478
支架数量 (个)		1.65 ± 0.24	1.59 ± 0.21	1.105	0.272
支架直径 (mm)		3.02 ± 0.65	2.78 ± 0.53	1.720	0.089

2 结果

2.1 无复流 - 慢血流组与对照组血清 sST2 及 NLRP3 水平比较 无复流 - 慢血流组血清 sST2 ($14.32 \pm 2.65\text{ng}/\text{ml}$), NLRP3 ($68.23 \pm 10.17\text{ng}/\text{ml}$) 水平高于对照组 ($11.02 \pm 2.13\text{ng}/\text{ml}$, $42.05 \pm 8.23\text{ng}/\text{ml}$), 差异具有统计学意义 ($t=5.860, 12.055, P < 0.05$)。

表 2 影响急性冠脉综合征患者 PCI 术后无复流 - 慢血流的因素分析

因 素	β	SE	Wald χ^2	OR(95%CI)	P 值
常数项	9.352	2.845	10.805	-	0.001
高血栓负荷	2.053	0.516	15.830	7.791 (2.834 ~ 21.421)	0.001
sST2	0.728	0.302	5.811	2.071 (1.146 ~ 3.743)	0.021
NLRP3	0.697	0.251	7.711	2.008 (1.228 ~ 3.284)	0.006

2.2 影响急性冠脉综合征患者 PCI 术后无复流 - 慢血流的因素 见表 2。回归分析显示高血栓负荷、高水平 sST2, 高水平 NLRP3 是急性冠脉综合征患者 PCI 术后无复流 - 慢血流的危险因素 (均 $P < 0.05$)。

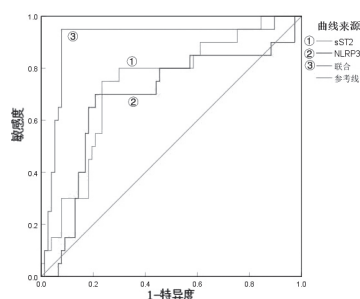


图1 sST2, NLRP3 诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的 ROC 曲线

2.3 sST2, NLRP3 诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的值分析 见表3和图1。sST2, NLRP3 联合诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的曲线下面积高于单独诊断, 差异具有统计学意义 ($Z=2.662, 2.856$, 均 $P < 0.05$)。

3 讨论

表3 sST2, NLRP3 诊断急性冠脉综合征患者 PCI 术后无复流 - 慢血流的效能

类别	临界值	曲线下面积 (95%CI)	P 值	敏感度 (%)	特异度 (%)	约登指数
sST2	12.91ng/ml	0.737 (0.638 ~ 0.821)	0.000	75.00	75.32	0.503 2
NLRP3	55.39pg/ml	0.686 (0.584 ~ 0.776)	0.002	70.00	78.62	0.486 2
联合检测	-	0.907 (0.831 ~ 0.957)	0.000	95.00	92.21	0.872 1

sST2 是一个诱饵受体, 属于 ST2 的可溶性形式, 主要表达于心肌细胞, 反映心室壁的应激反应, 与心脏重塑和免疫炎症反应有关。本研究发现血清 sST2 水平增高与急性冠脉综合征患者 PCI 术后无复流 - 慢血流有关。sST2 的天然配体是 IL-33, 属于 IL-1 家族的成员, 由内皮细胞、肺和肠上皮细胞、角质形成细胞、成纤维细胞和平滑肌细胞等不同类型的细胞产生, 在炎症条件下调节核因子- κ B 的转录活性, 协调免疫反应。IL-33 可通过与跨膜 ST2 (transmembrane ST2 isoform, ST2L) 相互作用防止脂肪组织炎症、抑制心脏重塑、心肌肥厚和心肌凋亡、发挥心脏保护作用。而 sST2 通过充当诱饵受体将 IL-33 从循环中清除, 减弱 IL-33/ST2L 的潜在心脏保护作用, 促进心脏肥厚、纤维化和心室功能障碍^[12]。既往研究也显示 sST2 与心血管疾病有关, sST2 水平随着心血管压力和心脏纤维化而增加, 急性心力衰竭患者较高的循环 sST2 浓度与病情加重和较差的临床结果相关^[13]。对于急性冠脉综合征患者, 基线时 sST2 浓度较高预示着死亡风险增加^[14]。本研究进一步通过回归分析发现高水平 sST2 是急性冠脉综合征患者 PCI 术后无复流 - 慢血流的危险因素, sST2 诊断无复流 - 慢血流曲线下面积为 0.737, 表明 sST2 可作为急性冠脉综合征患者 PCI 术后无复流 - 慢血流的标志物。分析高水平 sST2 导致 PCI 术后无复流 - 慢血流的原因为 sST2

冠状动脉无复流 - 慢血流指梗死相关心外膜冠状动脉恢复通畅后心肌不能达到足够的灌注, 在 PCI 围术期无复流 - 慢血流的发生率约为 30%~50%, 与未出现无复流 - 慢血流的患者比较, 无复流 - 慢血流患者出现早期梗死后并发症、左心室重构不良、住院时间延长、心源性休克的机率更高, 死亡风险也更高^[9]。目前治疗无复流 - 慢血流的方法非常有限, 探寻可预测无复流 - 慢血流的标志物可预防其发生, 改善患者预后。介入术后冠状动脉无复流 - 慢血流的发病机制复杂, 目前尚不清楚, 涉及远端动脉粥样硬化血栓栓塞、炎症反应、心肌缺血 - 再灌注损伤、微循环功能障碍、冠状动脉微循环对损伤的易感性增高等^[3,10]。冠脉阻塞血管开通后由于组织水肿、微血栓、中性粒细胞积聚和自由基形成引起的冠状动脉灌注后炎症反应与无复流 - 慢血流密切相关^[11]。

可促使冠状动脉管壁中巨噬细胞释放促炎细胞因子, 引起血管炎症反应和氧自由基过度产生, 导致微循环功能障碍甚至形成血栓栓塞, 最终影响冠状动脉血流灌注, 引起无血流 - 慢血流现象^[15]。

NLRP3 是一种细胞内先天免疫受体, 可识别来自病原体、受损或死亡细胞和刺激物的多种刺激, 以 NLRP3 为主形成的炎症小体可导致 IL-1 β 和 IL-18 的分泌, 并诱导炎症细胞死亡。本研究发现无复流 - 慢血流组血清 NLRP3 水平增高, 表明 NLRP3 可能参与急性冠脉综合征冠脉复流异常过程。研究显示在动脉粥样硬化中, 核因子- κ B 信号通路激活 NLRP3 和 IL-1 β , 诱导巨噬细胞浸润和吞噬氧化低密度脂蛋白 - 胆固醇, 促使动脉粥样硬化斑块的形成^[16]。既往临床报道证实急性冠脉综合征患者血清 NLRP3 水平显著增高, 且与动脉粥样硬化斑块易损性^[17]、冠状动脉粥样硬化严重程度以及出院后发生主要心脏不良事件有关^[18]。本研究回归分析显示高水平 NLRP3 是急性冠脉综合征患者 PCI 术后无复流 - 慢血流的危险因素, 表明 NLRP3 水平增高可能促使急性冠脉综合征患者 PCI 术后无复流 - 慢血流的发生。分析原因为: PCI 缺血再灌注过程中随着氧气和血液的恢复, 心脏处于高度应激状态, Toll 样受体 4/ 髓样分化因子 88/ 核因子- κ B 信号通路激活, NLRP3 通过与凋亡相关斑点样蛋白相互作用启动炎症小体的形成, 产生大量细胞因子、

趋化因子,驱使大量中性粒细胞被募集到狭窄的毛细血管上,巨大的白细胞不能通过狭窄的毛细血管,可能造成微血管阻塞,导致冠脉无复流-慢血流现象的发生^[19]。另外,NLRP3炎症小体的激活导致IL-1 β 和IL-18的产生,促使炎症细胞在心脏内浸润、黏连、聚集等,促使梗死心肌细胞凋亡,诱导心肌缺血再灌注损伤和冠脉无复流现象^[20]。

ROC曲线分析结果证实sST2,NLRP3预测急性冠脉综合征PCI术后无复流-慢血流均具有一定价值,联合sST2,NLRP3预测曲线下面积较单独指标预测显著增加,表明sST2,NLRP3联合检测可提高对术后无复流-慢血流的识别效能,对临床治疗策略调整和治疗反应评估提供更多参考。回归分析结果中高血栓负荷也是急性冠脉综合征PCI术后无复流-慢血流的危险因素,推测原因为血栓负荷加重导致远端血管缺血和心肌灌注不良导致。

综上,急性冠脉综合征PCI术后无复流-慢血流患者血清sST2,NLRP3水平均增高,高水平sST2,NLRP3是急性冠脉综合征PCI术后无复流-慢血流的危险因素,sST2,NLRP3联合检测在急性冠脉综合征患者PCI术后无复流-慢血流预测中具有较高的效能,能更好地指导临床治疗。本研究局限性在于这是一项单中心研究,样本例数偏少,可能会导致选择偏差,未来研究仍需进一步开展多中心、大样本研究加以证实。

参考文献:

- [1] 丁锦,贯芳,梁小涵,等.急性冠脉综合征患者血浆外泌体NEAT1,miR-204和MMP-9的表达水平及临床意义[J].现代检验医学杂志,2023,38(1):59-65.
DING Jin, GUAN Fang, LIANG Xiaohan, et al. Expression levels and clinical significance of plasma exosomal NEAT1, miR-204 and MMP-9 in patients with acute coronary syndrome[J]. Journal of Modern Laboratory Medicine, 2023, 38(1): 59-65.
- [2] WANG Le, CONG Hongliang, ZHANG Jingxia, et al. Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome[J]. Cardiovascular Diabetology, 2020, 19(1): 80.
- [3] FAJAR J K, HERIANSYAH T, ROHMAN M S. The predictors of no reflow phenomenon after percutaneous coronary intervention in patients with ST elevation myocardial infarction: a meta-analysis[J]. Indian Heart Journal, 2018, 70 (Suppl 3): S406-S418.
- [4] 刘艳杰,高宇平,赵晨.STEMI病人急诊介入无复流-慢血流危险因素及高危病变特征分析[J].中西医结合心脑血管病杂志,2020,18(12):1935-1939.
LIU Yanjie, GAO Yuping, ZHAO Chen. Analysis of risk factors of no reflow-slow flow and characteristics of high risk lesions in patients with STEMI after emergency intervention[J]. Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease, 2020, 18(12): 1935-1939.
- [5] ALEKSOVA A, PALDINO A, BELTRAMI A P, et al. Cardiac biomarkers in the emergency department: the role of soluble ST2 (sST2) in acute heart failure and acute coronary syndrome-there is meat on the bone[J]. Journal of Clinical Medicine, 2019, 8(2): 270.
- [6] SUN Yuan, PAVEY H, WILKINSON I, et al. Role of the IL-33/ST2 axis in cardiovascular disease: asystematic review and meta-analysis[J]. PLoS One, 2021, 16(11): e0259026.
- [7] TAKAHASHI M. NLRP3 inflammasome as a key driver of vascular disease[J]. Cardiovascular Research, 2022, 118(2): 372-385.
- [8] 中国医师协会急诊医师分会,国家卫健委能力建设与继续教育中心急诊学专家委员会,中国医疗保健国际交流促进会急诊急救分会.急性冠脉综合征急诊快速诊治指南(2019)[J].临床急诊杂志,2019,20(4):253-262.
Emergency Doctor Branch of Chinese Medical Doctor Association, Committee of Emergency Medicine Experts of National Health Commission Capacity Building and Continuing Education Center, Emergency First Aid Branch of China International Exchange and Promotive Association for Medical Healthcare. Guidelines for rapid emergency diagnosing acute coronary syndrome[J]. Journal of Clinical Emergency, 2019, 20(4): 253-262.
- [9] HU Xiangming, YANG Xing, LI Xida, et al. Elevated uric acid is related to the no-/slow-reflow phenomenon in STEMI undergoing primary PCI[J]. European Journal of Clinical Investigation, 2022, 52(4): e13719.
- [10] KAUR G, BAGHDASARYAN P, NATARAJAN B, et al. Pathophysiology, diagnosis, and management of coronary no-reflow phenomenon[J]. International Journal of Angiology, 2021, 30(1): 15-21.
- [11] CAIAZZO G, MUSCI R L, FREDIANI L, et al. State of the art: no-reflow phenomenon[J]. Cardiology Clinics, 2020, 38(4): 563-573.
- [12] LI Junpei, CAO Tianyu, WEI Yaping, et al. A review of novel cardiac biomarkers in acute or chronic cardiovascular diseases: the role of soluble ST2 (sST2), lipoprotein-associated phospholipase A2 (Lp-PLA2), myeloperoxidase (MPO), and procalcitonin (PCT)[J]. Disease Markers, 2021, 2021: 6258865.
- [13] 蒋美燕,黄恒贵,袁仕国.QRS波群时限联合血清angptl2, angpt17, sST₂对急性心力衰竭患者短期预后的评估价值[J].天津医药,2023,50(10):1136-1140.
JIANG Meiyun, HUANG Henggui, YUAN Shiguo. Evaluation value of QRS complex time limit combined with serum angptl2, angpt17 and sST₂ for short-term prognosis of patients with acute heart failure[J]. Tianjin Medical Journal, 2023, 50(10): 1136-1140.
- [14] GU Linlin, LI Jing. Short-term and long-term prognostic value of circulating soluble suppression of tumorigenicity-2 concentration in acute coronary syndrome: a meta-analysis[J]. Bioscience Reports, 2019, 39(6): BSR20182441.

- Enzymology, 2019, 629: 151-176.
- [12] 吴艳蓉, 梁跃波, 彭发兵, 等. 新生儿早发型败血症与晚发型败血症病原菌分布及炎症因子变化比较[J]. 现代医学, 2022, 50(1): 90-94.
- WU Yanrong, LIANG Yuebo, PENG Fabing, et al. Comparison of pathogen distribution and inflammatory factors in neonates with early-onset sepsis and late-onset sepsis [J]. Modern Medical Journal, 2022, 50(1): 90-94.
- [13] 张江玲. 个性化干预模式对新生儿败血症的影响[J]. 中国妇幼保健, 2023, 38(6): 1129-1132.
- ZHANG Jiangling. Effect of individualized intervention mode on neonatal sepsis[J]. Maternal and Child Health Care of China, 2023, 38(6): 1129-1132.
- [14] 陈明娟, 冯琳. 血清 AT-Ⅲ, G6PD 检测对新生儿败血症早期诊断及预后评估的价值分析[J]. 蚌埠医学院学报, 2023, 48(2): 174-177.
- CHEN Mingjuan, FENG Lin. Value analysis of the serum levels of AT-Ⅲ and G6PD in the early diagnosis and prognosis of neonatal sepsis [J]. Journal of Bengbu Medical College, 2023, 48(2): 174-177.
- [15] 吴小红, 颜海峰, 古裕鸟, 等. 感染标志物、炎症因子、血小板参数诊断新生儿早发型败血症的价值[J]. 中华医院感染学杂志, 2023, 33(7): 1090-1093.
- WU Xiaohong, YAN Haifeng, GU Yuniao, et al. Value of infectious markers, inflammatory factors and platelet parameters in the diagnosis of neonatal early-onset sepsis [J]. Chinese Journal of Nosocomiology, 2023, 33(7): 1090-1093.
- [16] BERARDI A, TREVISANI V, DI CAPRIO A, et al. Timing of symptoms of early-onset sepsis after intrapartum antibiotic prophylaxis: can it inform the neonatal management? [J]. Pathogens, 2023, 12(4): 588.
- [17] 康茹, 孟改利, 周雪红. 呼吸道感染患儿肠道菌群紊乱与 Th17/Treg 及其分泌炎症细胞因子免疫平衡的相关性研究[J]. 现代检验医学杂志, 2021, 36(6): 95-100.
- KANG Ru, MENG Gaili, ZHOU Xuehong. Correlation analysis between intestinal flora disturbance and immune balance of Th17/Treg and its secretion of inflammatory cytokines children with respiratory tract infection [J]. Journal of Modern Laboratory Medicine, 2021, 36(6): 95-100.
- [18] LIU Chunmei, FANG Chengzhi, HE Qi, et al. The value of interleukin-6 (IL-6) within 6 hours after birth in the prompt diagnosis of early-onset neonatal sepsis [J]. Translational Pediatrics, 2020, 9(5): 629-635.
- [19] LI Zhaohui, SHENG Lei. Significance of dynamic evolution of TNF- α , IL-6 and intestinal fatty acid-binding protein levels in neonatal necrotizing enterocolitis [J]. Experimental and Therapeutic Medicine, 2018, 15(2): 1289-1292.
- [20] WAN Jie, WU Yingqiu, JI Xiaoyun, et al. IL-9 and IL-9-producing cells in tumor immunity [J]. Cell Communication and Signaling, 2020, 18(1): 50.
- [21] ROY S, RIZVI Z A, CLARKE A J, et al. EGFR-HIF1 α signaling positively regulates the differentiation of IL-9 producing T helper cells [J]. Nature Communications, 2021, 12(1): 3182.
- [22] LONG Zhenyi, ZHOU Yifeng, YUAN Hao, et al. Expression and correlation of IgG4 and IL-21 in collagen-induced arthritis rats[J]. Journal of Inflammation Research, 2021, 14: 5051-5058.
- [23] HEIM J, ALMANZAR G, SCHMALZING M, et al. Induction of IL-9 in peripheral lymphocytes of rheumatoid arthritis patients and healthy donors by Th17-inducing cytokine conditions [J]. Frontiers Immunology, 2021, 12: 668095.
- [24] LIN Xuan, YE Longyun, WANG Xu, et al. Follicular helper T cells remodel the immune microenvironment of pancreatic cancer via secreting CXCL13 and IL-21 [J]. Cancers (Basel), 2021, 13(15): 3678.
- [25] HARPER J, HUOT N, MICCI L, et al. IL-21 and IFN- α therapy rescues terminally differentiated NK cells and limits SIV reservoir in ART-treated macaques [J]. Nature Communications, 2021, 12(1): 2866.
- [26] CAPITANI N, PATRUSSI L, BALDARI C T. Nature vs. Nurture: the two opposing behaviors of cytotoxic T lymphocytes in the tumor microenvironment [J]. International Journal of Molecular Sciences, 2021, 22(20): 11221.

收稿日期: 2023-11-07

修回日期: 2023-12-18

(上接第125页)

- [15] SOMUNCU M U, AKGUN T, CAKIR M O, et al. The elevated soluble ST2 predicts no-reflow phenomenon in ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention[J]. Journal of Atherosclerosis and Thrombosis, 2019, 26(11): 970-978.
- [16] ZHOU Wenyi, CHEN Chunyuan, CHEN Zhiheng, et al. NLRP3: a novel mediator in cardiovascular disease[J]. Journal of Immunology Research, 2018, 2018: 5702103.
- [17] XUE Chao, CHEN Qizhi, BIAN Ling, et al. The relationships between cholesterol crystals, NLRP3 inflammasome, and coronary atherosclerotic plaque vulnerability in acute coronary syndrome: an optical coherence tomography study[J]. Frontiers in Cardiovascular Medicine, 2022, 9: 905363.
- [18] AFRASYAB A, QU Peng, ZHAO Yang, et al. Correlation of NLRP3 with severity and prognosis of coronary atherosclerosis in acute coronary syndrome patients[J]. Heart and Vessels, 2016, 31(8): 1218-1229.
- [19] YU Ping, LI Yuangeng, FU Wenwen, et al. Panax quinquefolius L. Saponins protect myocardial ischemia reperfusion no-reflow through inhibiting the activation of NLRP3 inflammasome via TLR4/MyD88/NF- κ B signaling pathway[J]. Frontiers in Pharmacology, 2020, 11: 607813.
- [20] NIE Chaoqun, DING Xue, A Rong, et al. Hydrogen gas inhalation alleviates myocardial ischemia-reperfusion injury by the inhibition of oxidative stress and NLRP3-mediated pyroptosis in rats[J]. Life Sciences, 2021, 272: 119248.

收稿日期: 2023-07-14

修回日期: 2024-01-14