doi: 10.3978/j.issn.2095-6959.2021.11.004
View this article at: https://dx.doi.org/10.3978/j.issn.2095-6959.2021.11.004

重症肺炎合并脓毒症患者外周静脉血TLR–4、CRP、TNF–α、PCT表达水平及近期生存情况

王真[1]，张家艳[1]，王玉霞[2]，沈剑[1]

(1. 成都市第三人民医院呼吸与危重症医学科，成都 610031；2. 四川省医学科学院·四川省人民医院老年重症医学科，成都 610072)

[摘　要]　**目的：**观察重症肺炎合并脓毒症患者外周血单个核细胞(peripheral blood mononuclear cell，PBMC)表面Toll样受体4(TLR-4)表达水平、血清C反应蛋白(C-reaction protein，CRP)、肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)、降钙素原(procalcitonin，PCT)水平，并探索其临床意义。**方法：**回顾性分析成都市第三人民医院104例重症肺炎合并脓毒症患者及32例重症肺炎非脓毒症患者(对照组)临床资料，根据病情严重程度将合并脓毒症的患者分为重症脓毒症组(重症组)与非重症脓毒症组(非重症组)。比较3组基线资料及入院24 h PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平差异，使用受试者工作特征(receiver operating characteristic，ROC)曲线评估入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT及其联合检测对重症肺炎合并重症脓毒症的诊断价值，并记录3组入院28 d病死率。**结果：**3组性别、吸烟史、支气管扩张、合并支气管哮喘及高血压情况比较，差异无统计学意义(P>0.05)；但重症组年龄及慢性阻塞性肺疾病、糖尿病合并率高于非重症组及对照组(P<0.05)，非重症组年龄高于对照组(P<0.05)；3组入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平比较，均为重症组>非重症组>对照组(P<0.05)。入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT对重症肺炎合并重症脓毒症具有较高诊断价值(P<0.05)，且4项联合检测诊断价值最高。3组入院28 d病死率比较，重症组>非重症组>对照组(P<0.05)。**结论：**重症肺炎合并脓毒症患者入院早期外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平可显著升高，上述指标联合检测对重症脓毒症诊断价值较高，TLR-4信号通路可能是引起全身强烈炎症反应的重要途径，有望成为重症肺炎合并脓毒症诊疗新方向。

[关键词]　重症肺炎；脓毒症；重症脓毒症；Toll样受体4；C反应蛋白；肿瘤坏死因子-α；降钙素原

收稿日期 (Date of reception)：2021–01–22

通信作者 (Corresponding author)：沈剑，Email: sjfy12@163.com

基金项目 (Foundation item)：四川省干部保健科研课题 (川干研 2020-204)。This work was supported by Sichuan Provincial Cadre Health Research Project, China (Sichuan Ganyan 2020-204).

Expression levels of TLR-4, CRP, TNF-α and PCT in peripheral venous blood in patients with severe pneumonia complicated with sepsis and their recent survival status

WANG Zhen[1], ZHANG Jiayan[1], WANG Yuxia[2], SHEN Jian[1]

(1. Department of Respiratory and Critical Care Medicine, Chengdu Third People's Hospital, Chengdu 610031; 2. Department of Geriatric Critical Care Medicine, Sichuan Academy of Medical Sciences, Sichuan Provincial People's Hospital, Chengdu 610072, China)

Abstract **Objective:** To investigate the expression level of Toll-like receptor 4 (TLR-4) on peripheral blood mononuclear cell (PBMC) surface, levels of serum C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and procalcitonin (PCT) and their clinical significance in patients with severe pneumonia complicated with sepsis. **Methods:** The clinical data of 104 patients with severe pneumonia complicated with sepsis and 32 patients with severe pneumonia but without sepsis (the control group) in our hospital were retrospectively analyzed. The patients with sepsis were divided into a severe sepsis group (the severe group) and a non-severe sepsis group (the non-severe group) according to the disease severity. The baseline data and differences in expression level of PBMC surface TLR-4, levels of serum CRP, TNF-α and PCT at 24 h after admission were compared among the three groups, and the receiver operating characteristic (ROC) curve was used to evaluate the diagnostic value of expression level of peripheral venous blood PBMC surface TLR-4, serum CRP, TNF-α and PCT at 24 h after admission and their combined detection on severe pneumonia with severe sepsis, and the mortality rate at 28 d after admission was recorded among the three groups. **Results:** There were no significant differences in the gender, smoking history and concurrent rates of bronchiectasis, bronchial asthma and hypertension among the three groups (P>0.05). But the age and concurrent rates of chronic obstructive pulmonary obstruction and diabetes mellitus in severe group were higher than those in non-severe group and those in control group (P<0.05), and the age in non-severe group was higher than that in control group (P<0.05). Comparison of expression level of peripheral venous blood PBMC surface TLR-4 and levels of serum CRP, TNF-α and PCT in the three groups at 24 h after admission showed that the severe group > the non-severe group > the control group (P<0.05). After ROC curve analysis, it was found that expression level of peripheral venous blood PBMC surface TLR-4 and serum CRP, TNF-α and PCT at 24 h after admission had high diagnostic value on severe pneumonia with severe sepsis (P<0.05), and the combined detection of the four had the highest diagnostic value. Comparison of mortality rate of the three groups at 28 d after admission showed that the severe group > the non-severe group > the control group (P<0.05). **Conclusion:** The expression level of peripheral venous blood PBMC surface TLR-4 and levels of serum CRP, TNF-α and PCT of patients with severe pneumonia complicated with sepsis can be significantly increased in the early stage of admission, and the combined detection of the above indexes has a higher diagnostic value on severe sepsis, and TLR-4 signaling pathway may be an important way to cause strong systemic inflammatory response, and is expected to become a new direction for the diagnosis and treatment of severe pneumonia with sepsis.

Keywords severe pneumonia; sepsis; severe sepsis; Toll-like receptor 4; C-reactive protein; tumor necrosis factor-α; procalcitonin

重症肺炎是一种起病较急、病情危重的呼吸系统疾病，易出现全身炎症反应，诱发脓毒症，若机体存在细菌感染或感染灶，还能诱发脓毒性休克等重症脓毒症，使病死率升高[1]。Toll样受体(Toll-like receptors，TLRs)信号通路异常为近年发现的与脓毒症发病机制相关的信号通路，TLRs在脓毒症中异常活化，诱导炎症细胞因子表达，增强机体炎症反应[2]。然而，各种炎症诊断指标繁多，临床难以选取特征性指标判断重症肺炎的病情进展及预后。因此，寻找可快速检测、灵敏度高的诊断指标，以有效评估患者病情进展，指导临床诊疗，对患者预后有积极意义[3]。C反应蛋白(C-reactive protein，CRP)、肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)均为评估炎症反应的敏感指标，降钙素原(procalcitonin，PCT)则能灵敏反映机体感染状况，3项血清学检测操作方便，在临床普及度较高[4]。本研究拟分析上述4项指标联合检测在重症肺炎合并脓毒症病情判断中的应用价值，为临床诊疗提供指导意见。

1 对象与方法

1.1 对象

回顾性分析成都市第三人民医院104例重症肺炎合并脓毒症患者及32例重症肺炎非脓毒症患者(对照组)临床资料。纳入标准：符合美国胸科学会/美国传染病学会[5]制订的重症肺炎诊断标准；脓毒症则符合国际脓毒症定义会议关于脓毒症诊断标准[6]；临床资料完整。排除标准：入院24 h死亡；伴免疫功能缺陷、心血管疾病、激素分泌代谢紊乱；合并结核等传染性疾病；存在恶性肿瘤。根据病情严重程度将脓毒症患者分为重症脓毒症组(重症组)与非重症脓毒症组(非重症组)，重症脓毒症包括出现器官功能障碍或脓毒性休克[7]。本研究已获得成都市第三人民医院医学伦理委员会批准，患者均知情同意。

1.2 方法

患者均在入院24 h内采集外周静脉血3~5 mL；使用淋巴细胞分离液分离外周血单个核细胞(peripheral blood mononuclear cell，PBMC)，核糖核酸试剂提取其总核糖核酸，经试剂盒反转录，采用荧光免疫聚合酶链式反应，检测外周静脉血PBMC表面TLR-4表达水平；经3 500 r/min离心7~10 min获得血清，采用酶联免疫分析法检测血清CRP、TNF-α水平，采用半定量免疫色谱法检测血清PCT。

1.3 统计学处理

应用SPSS 21.0统计学软件进行数据分析；计量资料以均数±标准差($\bar{x}\pm s$)表示，多组间比较采用单因素方差分析，事后检验采用LSD-t检验；计数资料以例(%)表示，采用χ^2检验；采用受试者工作特征曲线(receiver operating characteristic curve，ROC)评估入院24 h血清CRP、TNF-α、PCT及其联合检测对重症肺炎合并重症脓毒症的诊断价值，计算曲线下面积(area under curve，AUC)，AUC值越高，诊断价值越高。P<0.05为差异有统计学意义。

2 结果

2.1 3组基线资料比较

104例重症肺炎合并脓毒症患者中，重症组28例，非重症组76例；3组性别、吸烟史、合并支气管扩张、支气管哮喘及高血压情况的差异无统计学意义(P>0.05)；重症组年龄及慢性阻塞性肺疾病、糖尿病合并率高于非重症组及对照组(P<0.05)，非重症组年龄高于对照组(P<0.05，表1)。

2.2 3组入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平比较

3组入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平比较，均为重症组>非重症组>对照组，组间差异有统计学意义(P<0.05，表2)。

2.3 入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT及其联合检测对重症肺炎合并重症脓毒症的诊断价值

ROC曲线分析结果显示：入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT对重症肺炎合并重症脓毒症具有较高诊断价值(P<0.05)，其cut-off值分别为15.89%、112.92 mg/L、62.49 pg/mL、4.92 ng/mL，且4项联合检测诊断价值最高(P<0.05；表3、图1)。

2.4 3组入院28 d病死率比较

重症组病死率为42.86%(12/28)，非重症组病死率为21.05%(16/76)，对照组病死率为6.25%(2/32)，3组入院28 d病死率比较，重症组>非重症组>对照组，组间差异有统计学意义(χ^2=11.741，P=0.003)。

表1 3组基线资料比较

Table 1 Comparison of baseline data among the three groups

组别	*n*	男/女	年龄/岁	吸烟史/[例(%)]	支气管扩张/[例(%)]	支气管哮喘/[例(%)]	慢性阻塞性肺疾病/[例(%)]	高血压/[例(%)]	糖尿病/[例(%)]
重症组	28	20/8	69.79 ± 7.25	12 (42.86)	3 (10.71)	0 (0.00)	7 (25.00)	11 (39.29)	12 (42.86)
非重症组	76	45/31	60.85 ± 8.11[a]	25 (32.89)	5 (6.58)	1 (1.32)	3 (3.95)[a]	28 (36.84)	8 (10.53)[a]
对照组	32	17/15	55.71 ± 8.24[ab]	9 (28.13)	2 (6.25)	1 (3.13)	2 (6.25)[a]	10 (31.25)	3 (9.38)[a]
χ^2/F		2.174	19.561	1.514	0.588	1.035	11.617	0.468	16.913
P		0.337	<0.001	0.469	0.745	0.596	0.003	0.791	<0.001

与重症组比较，[a]*P*<0.05；与非重症组比较，[b]*P*<0.05。

Compared with the severe group, [a]*P*<0.05; compared with the non-severe group, [b]*P*<0.05.

表2 3组入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平比较

Table 2 Comparison of expression level of peripheral venous blood PBMC surface TLR-4 and levels of serum CRP, TNF-α and PCT among the three groups at 24 h after admission

组别	*n*	TLR-4/%	CRP/(mg·mL^{-1})	TNF-α/(pg·mL^{-1})	PCT/(ng·mL^{-1})
重症组	28	19.85 ± 3.91	121.36 ± 20.47	69.96 ± 14.59	5.31 ± 1.72
非重症组	76	12.15 ± 3.20[a]	104.15 ± 17.22[a]	55.02 ± 10.81[a]	3.96 ± 0.95[a]
对照组	32	8.65 ± 1.74[ab]	79.36 ± 15.19[ab]	40.92 ± 8.86[ab]	2.55 ± 0.56[ab]
F		52.156	44.510	49.462	48.311
P		<0.001	<0.001	<0.001	<0.001

与重症组比较，[a]*P*<0.05；与非重症组比较，[b]*P*<0.05。

Compared with the severe group, [a]*P*<0.05; compared with the non-severe group, [b]*P*<0.05.

表3 入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT及其联合检测对重症肺炎合并重症脓毒症的诊断价值

Table 3 Diagnostic value of expression levels of peripheral venous blood PBMC surface TLR-4 and levels of serum CRP, TNF-α and PCT and their combined detection at 24 h after admission on severe pneumonia with severe sepsis

指标	Cut-off值	灵敏度/%	特异度/%	约登指数	AUC	95%CI
TLR-4	15.89%	100.00	98.25	0.983	0.947	0.907~0.987
CRP	112.92 mg/L	72.22	95.52	0.677	0.849	0.711~0.975
TNF-α	62.49 pg/mL	77.78	96.27	0.741	0.867	0.727~0.989
PCT	4.92 ng/mL	77.78	81.34	0.591	0.859	0.719~0.961
联合		94.44	88.06	0.825	0.995	0.982~0.999

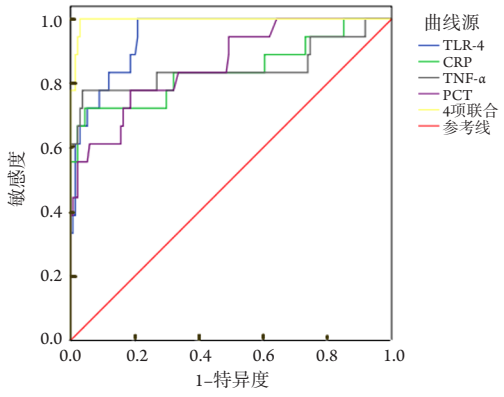

图1 入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT及其联合检测诊断重症肺炎合并重症脓毒症的ROC曲线

Figure 1 ROC curves of expression levels of TLR-4 on peripheral venous blood PBMC surface and levels of serum CRP, TNF-α and PCT and their combined detection at 24 h after admission in the diagnosis of severe pneumonia with severe sepsis

3 讨论

重症肺炎好发于中老年人群，患者常伴多种基础疾病，免疫力低下，感染较难控制，易诱发脓毒症[8]。而在出现低血压或低灌注及器官功能障碍时，即为重症脓毒症，以凝血功能紊乱、全身炎症反应为主要病理生理变化，是机体对感染失控的应答，具有较高病死率[9]。目前，临床对重症脓毒症的管理多提倡早识别、早诊断、针对性治疗，以降低病死率[10]。基于此，本研究分析TLR信号通路异常情况及CRP、TNF-α、PCT 3种血清学指标判断重症肺炎合并重症脓毒症的使用价值，评估上述指标应用于重症脓毒症防控及管理的可行性。

本研究结果显示：重症组、非重症组、对照组入院28 d病死率分别为42.86%、21.05%、6.25%，3组病死率比较，重症组>非重症组>对照组，说明合并重症脓毒症者，死亡风险显著升高，与既往研究[11]结果一致。这提示尽早识别、及时针对性治疗有其必要性。在脓毒症发病过程中，TLRs识别病原菌，TLRs信号通路异常活化，促进炎症介质释放，增强炎症反应，大量炎症因子释放入血，引起免疫细胞活化，诱发具有生物活性的细胞因子及炎症介质贯序性瀑布样释放，导致组织细胞损伤[12]。故早期评估TLRs信号异常情况及机体炎性水平，可判断患者病情进展，而利于尽早识别重症脓毒症[13]。TLRs中TLR-4主要介导内毒素信号转导，在脓毒症发生发展时表达水平迅速升高，并参与炎症反应进程[14]。CRP为肝脏合成分泌的急性时相蛋白，在炎症、创伤时可迅速分泌入血，且能抑制一氧化氮合成，使内皮功能障碍进一步恶化[15]。TNF-α则为小分子多肽类物质，可增加中性粒细胞CD18表面抗原，使中性粒细胞对内皮细胞的黏附及抗体依赖性细胞毒反应增强，也能促进巨噬细胞活化，并触发级联反应，介导炎症反应[16]。近年研究也指出[17]，细菌感染后TLR-4信号通路被激活，可刺激CRP、TNF-α等炎症介质及细胞因子大量合成及释放，加剧全身炎症反应。本研究也发现，3组入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α水平比较，均为重症组>非重症组>对照组，上述指标对重症肺炎合并重症脓毒症具有较高诊断价值。提示TLR-4信号通路可能参与脓毒症的发生发展，该信号通路对CRP、TNF-α的分泌有促进作用。CRP、TNF-α作为临床常用检测指标，可辅助判断重症肺炎患者病情进展情况，尽早识别重症脓毒症，为临床尽早诊疗提供指导意见，且检测项目简便、普及度较高，也适用于基层医院。本研究通过荧光定量PCR技术检测外周静脉血PBMC表面TLR-4表达水平，虽然检测步骤繁琐，普及度不高，但能准确评估感染后TLR-4表达情况，TLR-4信号通路可能是刺激炎症因子大量分泌的重要途径，有望作为脓毒症靶向治疗的新靶点，改善脓毒症治疗现状。

另外，PCT是反映机体细菌、真菌等外源微生物感染的敏感指标，在轻微感染或慢性炎症时，血清PCT不发生明显波动，而在细菌感染后炎症反应活跃时显著升高[18]。本研究中，3组入院24 h血清PCT水平比较，均为重症组>非重症组>对照组，入院24 h血清PCT对重症肺炎合并重症脓毒症具有较高诊断价值。也说明，在入院早期伴严重感染、炎症反应增强时，并发重症脓毒症风险较高，临床需尽早予以针对性干预措施，以降低病死率。不仅如此，本研究还发现，入院24 h外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT联合检测诊断重症肺炎合并重症脓毒症价值最高。提示临床可联合监测上述4项指标，发现4项指标高于上述范围时，积极抗感染、抗炎，并注意凝血功能，避免进展为重症脓毒症。

年龄较高及糖尿病等基础疾病是诱发重症脓毒症的危险因素[19-20]。在本研究中，重症组年龄及慢性阻塞性肺疾病、糖尿病合并率高于非重症

组及对照组，非重症组年龄高于对照组，提示年龄较高、合并慢性阻塞性肺疾病、糖尿病者并发重症脓毒症风险更高，与上述报道基本一致。因此，对于存在上述高危因素者，临床应加强积极开展外周静脉血PBMC表面TLR-4及血清CRP、TNF-α、PCT监测，以及时评估病情进展，给予针对性治疗，改善患者预后。

综上，重症脓毒症病死率较高，监测入院早期外周静脉血PBMC表面TLR-4表达水平及血清CRP、TNF-α、PCT水平能辅助判断重症肺炎患者病情进展，尽早识别重症脓毒症，TLR-4信号通路可能是引起CRP、TNF-α分泌增多的重要途径，有望作为重症肺炎合并脓毒症诊疗新方向。

参考文献

1. 刘丽红, 刘丽芬, 曾育英, 等. 肝素结合蛋白在肺炎并发脓毒症中的早期诊断价值[J]. 广东医学, 2018, 39(4): 601-603.
   LIU Lihong, LIU Lifen, ZENG Yuying, et al. Value of heparin binding protein in the early diagnosis of pneumonia with sepsis[J]. Guangdong Medical Journal, 2018, 39(4): 601-603.
2. 刘德义, 马胜喜, 刘雨婷, 等. 胸腺肽α1对重症肺炎合并脓毒症患者的疗效[J]. 中华医院感染学杂志, 2019, 29(18): 2771-2774.
   LIU Deyi, MA Shengxi, LIU Yuting, et al. Effect of thymosin α1 of severe pneumonia patients complicated with sepsis[J]. Chinese Journal of Nosocomiology, 2019, 29(18): 2771-2774.
3. 朱国清, 杨志军, 刘燕. HBP、PCT、CRP测定在肺炎合并脓毒症中的诊断价值[J]. 中国急救复苏与灾害医学杂志, 2020, 15(4): 460-462.
   ZHU Guoqing, YANG Zhijun, LIU Yan. Diagnostic value of HBP, PCT and CRP in pneumonia complicated with sepsis[J]. China Journal of Emergency Resuscitation and Disaster Medicine, 2020, 15(4): 460-462.
4. 斯妍娜, 鲍红光, 王晓亮, 等. 老年患者髋关节置换术后血清趋化因子CXC配体13的变化[J]. 临床麻醉学杂志, 2018, 34(3): 230-233.
   SI Yanna, BAO Hongguang, WANG Xiaoliang, et al. Changes of serum C-X-C motif ligand 13 concentration in senior patients undergoing total hip replacement[J]. Journal of Clinical Anesthesiology, 2018, 34(3): 230-233.
5. Phua J, See KC, Chan YH, et al. Validation and clinical implications of the IDSA/ATS minor criteria for severe community-acquired pneumonia[J]. Thorax, 2009, 64(7): 598-603.
6. 姚咏明, 盛志勇, 林洪远, 等. 2001年国际脓毒症定义会议关于脓毒症诊断的新标准[J]. 中华危重病急救医学, 2006, 18(11): 645.
   YAO Yongming, SHENG Zhiyong, LIN Hongyuan, et al. 2001 international conference on sepsis definition on new standards for sepsis diagnosis[J]. Chinese Critical Care Medicine, 2006, 18(11): 645.
7. 王宝权, 李男, 付海燕, 等. 重症医学科脓毒症和脓毒性休克患者影响预后相关因素分析[J]. 中国感染与化疗杂志, 2019, 19(5): 499-504.
   WANG Baoquan, LI Nan, FU Haiyan, et al. Analysis of prognostic factors in patients with sepsis and septic shock in intensive care unit[J]. Chinese Journal of Infection and Chemotherapy, 2019, 19(5): 499-504.
8. TItova EA, Eyrikh AR, Titova ZA. The role of presepsin in the diagnosis and assessment of severity of sepsis and severe pneumonia[J]. Ter Arkh, 2018, 90(11): 44-47.
9. Samuels JM, Moore HB, Moore EE. Coagulopathy in severe sepsis: interconnectivity of coagulation and the immune system[J]. Surg Infect (Larchmt), 2018, 19(2): 208-215.
10. Matan M, King D, Peled E, et al. Heparanase level and procoagulant activity are reduced in severe sepsis[J]. Eur J Haematol, 2018, 100(2): 182-188.
11. Kusakabe Y, Uchida K, Yamamura Y, et al. Early-phase innate immune suppression in murine severe sepsis is restored with systemic interferon-β[J]. Anesthesiology, 2018, 129(1): 131-142.
12. Hsiao SY, Kung CT, Tsai NW, et al. Concentration and value of endocan on outcome in adult patients after severe sepsis[J]. Clin Chim Acta, 2018, 483(8): 275-280.
13. Schwarzkopf D, Fleischmann-Struzek C, Rüddel H, et al. A risk-model for hospital mortality among patients with severe sepsis or septic shock based on German national administrative claims data[J]. PLoS One, 2018, 13(3): e0194371.
14. 丁小山, 吴亚军. 乌司他丁辅助高容量血液滤过对脓毒症患者血清TLR4、NT-proBNP水平的影响[J]. 内科急危重症杂志, 2018, 24(2): 143-145.
   DING Xiaoshan, WU Yajun. Effect of ulinastatin adjuvant to high-volume hemofiltration on serum levels of TLR4 and NT-proBNP in patients with sepsis[J]. Journal of Internal Intensive Medicine, 2018, 24(2): 143-145.
15. Sikorska D, Orzechowska Z, Rutkowski R, et al. Diagnostic value of salivary CRP and IL-6 in patients undergoing anti-TNF-alpha therapy for rheumatic disease[J]. Inflammopharmacology, 2018, 26(7): 1183-1188.
16. Marti A, Morell-Azanza L, Rendo-Urteaga T, et al. Serum and gene expression levels of CT-1, IL-6, and TNF-α after a lifestyle intervention in obese children[J]. Pediatr Diabetes, 2018, 19(2): 217-222.
17. 代晓茹, 张茹, 于玉兰, 等. 糖尿病足感染患者炎症因子和Toll样受体信号通路的表达及意义[J]. 中华医院感染学杂志, 2020, 30(2): 198-202.

DAI Xiaoru, ZHANG Ru, YU Yulan, et al. Expression of inflammatory factors and Toll-like receptors signaling pathways in diabetic foot infection patients and their significance[J]. Chinese Journal of Nosocomiology, 2020, 30(2): 198-202.

18. Huang DT, Yealy DM, Filbin MR, et al. Procalcitonin-guided use of antibiotics for lower respiratory tract infection[J]. N Engl J Med, 2018, 379(3): 236-249.

19. 康家旗, 杨永姣, 刘莉, 等. 输尿管结石致尿脓毒血症患者发生严重脓毒症或脓毒性休克的危险因素分析[J]. 重庆医科大学学报, 2018, 43(4): 556-559.
KANG Jiaqi, YANG Yongjiao, LIU Li, et al. Analysis of risk factors of severe sepsis or septic shock in patients with ureteric sepsis caused by ureteral calculi[J]. Journal of Chongqing Medical University, 2018, 43(4): 556-559.

20. 齐文旗, 黄椿媚, 边帆, 等. 肝脓肿致脓毒血症的危险因素及早期诊断[J]. 中华急诊医学杂志, 2019, 28(11): 1383-1389.
QI Wenqi, HUANG Chunmei, BIAN Fan, et al. Risk factors and early diagnosis of sepsis caused by liver abscess[J]. Chinese Journal of Emergency Medicine, 2019, 28(11): 1383-1389.

本文引用：王真, 张家艳, 王玉霞, 沈剑. 重症肺炎合并脓毒症患者外周静脉血TLR-4、CRP、TNF-α、PCT表达水平及近期生存情况[J]. 临床与病理杂志, 2021, 41(11): 2517-2523. doi: 10.3978/j.issn.2095-6959.2021.11.004

Cite this article as: WANG Zhen, ZHANG Jiayan, WANG Yuxia, SHEN Jian. Expression levels of TLR-4, CRP, TNF-α and PCT in peripheral venous blood in patients with severe pneumonia complicated with sepsis and their recent survival status[J]. Journal of Clinical and Pathological Research, 2021, 41(11): 2517-2523. doi: 10.3978/j.issn.2095-6959.2021.11.004