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血清降钙素原用于烧伤脓毒症早期诊断的临床研究 *

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摘要 目的:分析特重度烧伤患者血清降钙素原(PCT)水平,探讨其在烧伤脓毒症早期诊断中的应用价值。**方法:**回顾性分析 2014 年 1 月至 2018 年 1 月解放军总医院第一附属医院烧伤整形科收治的 259 例特重度烧伤患者的病例资料,根据患者烧伤 ICU 住院期间是否发生脓毒症分为脓毒症组(86 例,359 个检测时间点)与非脓毒症组(173 例,1591 个检测时间点),收集患者年龄、性别、烧伤面积、烧伤深度、合并有吸入性损伤情况等一般资料,记录每个检测时间点的血常规、肝肾功、血气分析及血清 PCT 值等实验室检查结果。比较两组患者基线情况及各项脓毒症相关生物学指标,分析各项生物学指标脓毒症诊断能力及不同 PCT 截断值的诊断效能,并绘制受试者工作特征(ROC)曲线,评估各项生物学指标烧伤脓毒症的诊断效能。**结果:**两组体温、心率、呼吸频率、血小板计数、胆碱酯酶、脑钠肽差异无统计学意义(*P>0.05*),脓毒症组血清 PCT 水平[4.52(2.35~8.83) vs 1.33(0.74~3.24)]、白细胞计数[24.28 (17.48~33.09) vs 20.11 (16.01~25.4)]、血糖[13.12 (9.66~17.28) vs 10.45 (8.31~13.13)]、肌酐[71.60 (57.94~89.62) vs 61.48 (48.87~73.48)]、总胆红素差[30.07(22.63~38.69) vs 21.04(15.53~28.4)]显著高于非脓毒症组,差异有统计学意义(*P<0.05*),其区分脓毒症与非脓毒症的 ROC 曲线下面积分别为 0.801 (95 %CI 为 0.776~0.824,*P<0.01*)、0.617 (95 %CI 为 0.581~0.652,*P<0.01*)、0.658 (95% CI 为 0.624~0.691,*P<0.01*)、0.671(95 %CI 为 0.640~0.702,*P<0.01*)、0.722(95% CI 为 0.694~0.691,*P<0.01*)。PCT 的有效截断值为 2.0 ng/mL(敏感度 84.4 %、特异度 62.1 %)、3.0 ng/mL(敏感度 70.8 %、特异度 71.8 %)、4.0 ng/mL(敏感度 58.1 %、特异度 81.2 %)。**结论:**PCT 可作为烧伤脓毒症早期诊断的有效生物学指标。

关键词:烧伤;脓毒症;早期诊断;降钙素原

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Clinical Analysis of Serum Procalcitonin for the Early Diagnosis of Sepsis in Burn Patients*

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ABSTRACT Objective: To analyze the level of serum procalcitonin (PCT) in extremely severe burn patients, and to evaluate its clinical significance in the early diagnosis of sepsis. **Methods:** From January 2014 to January 2018, we retrospectively analyzed 259 extremely severe burn patients admitted to the Burn and Plastic Surgery Department of the First Hospital Affiliated to the Chinese PLA General Hospital. The patients were divided into sepsis group (86 cases, 359 timepoints) and non-sepsis group (173 cases, 1591 timepoints) according to whether sepsis occurred during hospitalization in burn ICU. The baseline data such as patient's basic conditions, vital signs, and the laboratory examination results of routine blood test, liver and kidney function, blood gas analysis and serum PCT were collected. Baseline and sepsis related biomarkers were compared between the two groups. The diagnostic ability of each biomarker was compared and the diagnostic capacity of different PCT cut-off values was analyzed. Data were processed with t test, Mann-Whitney U test and chi-square test. Receiver operating characteristic (ROC) curves were performed to evaluate the capacity for burn sepsis diagnosis of each biomarker. **Results:** There was no significant difference in temperature, heart rate, respiratory frequency, platelet count, cholinesterase and brain natriuretic peptide between the two groups (*P>0.05*). PCT[4.52(2.35~8.83) vs. 1.33(0.74~3.24)], leucocyte count [24.28(17.48~33.09) vs. 20.11(16.01~25.4)], blood glucose[13.12(9.66~17.28) vs. 10.45(8.31~13.13)], urea nitrogen[71.60(57.94~89.62) vs. 61.48(48.87~73.48)] and total bilirubin[30.07(22.63~38.69) vs 21.04(15.53~28.4)] were significantly higher in septic patients than non-septic patients, and the areas under the ROC curve were 0.801 (95% CI, 0.776~0.824, *P<0.01*), 0.617 (95% CI, 0.581~0.652, *P<0.01*), 0.658 (95% CI, 0.624~0.691, *P<0.01*), 0.671 (95% CI, 0.640~0.702, *P<0.01*), 0.722 (95% CI, 0.694~0.691, *P<0.01*). The effective cut-off values of PCT for burn sepsis diagnosis were 2.0 ng/mL (sensitivity of 84.4 % and specificity of 62.1 %), 3.0 ng/mL (sensitivity of 70.8 % and specificity of 71.8 %), 4.0 ng/mL (sensitivity of 58.1 % and specificity of 81.2 %). **Conclusions:** PCT can be a useful

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biomarker for the early diagnosis of sepsis, which can be considered as a guide for rational use of antibiotics and provide as a reference for treatment.

Key words: Burn; Sepsis; Diagnosis; Procalcitonin

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前言

脓毒症是危重烧伤患者常见的合并症，是其死亡的主要病因[1,2]。严重烧伤后，皮肤屏障广泛性破坏、吸入性气道损伤、免疫抑制、菌群移位、留置各种导管和其他侵入性设备，以及暴露于医院菌群等因素皆可显著增加全身性感染发生的风险并促进其发展，增加了严重烧伤脓毒症的易感性[3-5]。相关文献报道，烧伤患者脓毒症的发病率为 8 %~42 %，病死率高达 28 %~65 %[6]。早期识别烧伤脓毒症并采取有效的抗菌治疗方案是降低其发病率和病死率的关键[7]。严重烧伤常伴有较高的炎症反应基线及免疫功能障碍，仅依据临床表现很难鉴别脓毒症与非感染全身炎症反应综合征。目前，烧伤脓毒症诊断的金标准仍然是血液微生物培养，其结果回报通常需要 48~72 小时，从而延迟了抗菌治疗的开始。因此，临床中需要能够早期诊断烧伤脓毒症的生物学指标。1993 年，Assicot[8]首次报道全身性细菌感染患者血清降钙素原(Procalcitonin，PCT)水平升高。此后，PCT 作为一个新兴的鉴别感染性疾病的生物学标记物被广泛应用[9]。本研究主要探讨了 PCT 在烧伤脓毒症早期诊断中的应用价值。

1 材料与方法

1.1 病例纳入与排除标准

1.1.1 **纳入标准** 年龄≥ 18 岁；烧伤面积≥ 50 % TBSA(total body surface area，TBSA)；烧伤 ICU 住院期间有连续的血清 PCT、脑钠肽(Brain natriuretic peptide，BNP)、血常规、肝肾功电解质及血气分析的检验记录 (各项指标每周至少检测 3 次；达到烧伤脓毒症诊断标准时，每日至少检测 1 次)；在院期间均按照指南予以有效液体复苏、手术清除创面坏死组织、免疫调理、代谢调理、营养支持、脏器功能保护与支持等治疗[10]。

1.1.2 **排除标准** 患有严重基础疾病及烧伤时合并重要脏器损伤者；中途放弃治疗者；病历资料记录不完全者。

1.2 临床资料

本研究应用回顾性分析方法，收集解放军总医院第一附属医院烧伤整形科 2014 年 1 月至 2018 年 1 月收治的 259 例特重度烧伤患者的病例资料。分析结果的每一天定义为一个检测时间点。同一天有两次以上检测结果时，选取最差结果为该检测点数值。本研究共统计 1950 个检测时间节点，其中脓毒症检测时间点 359 个，非脓毒症检测时间点 1591 个。根据烧伤脓毒症诊断标准[9]将纳入患者分为脓毒症组(86 例)和非脓毒症组(173 例)。两组患者年龄、性别比较无统计学差异($P>0.05$)，烧伤面积(三度烧伤面积 + 二度烧伤面积)、烧伤指数(三度烧伤面积 +2/3 深二度烧伤面积 +1/2 浅二度烧伤面积)、合并吸入性损伤情况、APACHE II 评分、SOFA 评分差异有统计学意义 ($P<0.05$)。见表 1。

表 1 脓毒症组与非脓毒症组基线资料比较

Table 1 Comparisons of the baseline date between septic and non-septic burn patients

Variables	Sepsis(n=86)	Non sepsis(n=173)	t	x^2	P
Gender(male/female)	61/25	124/49	—	0.016	0.902
Age(years, $\bar{x}\pm s$)	41.57± 12.03	42.12± 15.06	-0.293	—	0.771
Burn size(%TBSA, $\bar{x}\pm s$)	80.88± 15.25	72.69± 16.13	3.921	—	＜0.01
Burn index($\bar{x}\pm s$)	76.49± 18.36	66.24± 18.14	4.269	—	＜0.01
Inhalation injury(yes/no)	64/22	105/68	—	4.772	0.029
APACHE II score($\bar{x}\pm s$)	25.2± 5.3	21.8± 6.4	-2.287	—	0.013
SOFA score($\bar{x}\pm s$)	11.5± 3.3	9.4± 2.8	-1.974	—	0.046

Note: APACHE II score: Acute Physiology and Chronic Health Evaluation II; SOFA Score: Sequential Organ Failure Assessment Score.

1.3 观察指标

记录患者烧伤 ICU 住院期间每个检测时间点的体温、心率、呼吸频率、白细胞计数、血小板计数、血糖、肌酐、总胆红素、胆碱酯酶、BNP 及血清 PCT 水平。

1.4 统计学分析

应用 SPSS 20.0 软件进行数据处理和统计学分析。符合正态分布的定量变量采用均数± 标准差($\bar{x}\pm s$)表示，两组间比较行 t 检验；不符合正态分布的定量变量采用中位数 M(P25~P75)表示，行 Mann-Whitney U 检验；定性变量行 x^2 检验。绘制受试者工作特征(receiver operating characteristic，ROC)曲线，通过比较曲线下面积(AUC)大小评估各项生物学指标烧伤脓毒症的诊断效能，比较 Youden 指数获得 PCT 的有效截断值，并计算相应的敏感度及特异度。$P<0.05$ 为差异有统计学意义。

2 结果

2.1 脓毒症组与非脓毒症组各项生物学指标差异性比较

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脓毒症组血清 PCT 水平 [4.52 (2.35~8.83) vs. 1.33 (0.74~3.24)]、白细胞计数 [24.28 (17.48~33.09) vs. 20.11 (16.01~25.4)]、血糖[13.12(9.66~17.28) vs. 10.45(8.31~13.13)]、肌酐 [71.60 (57.94~89.62) vs. 61.48 (48.87~73.48)]、总胆红素差[30.07(22.63~38.69) vs. 21.04(15.53~28.4)]显著高于非脓毒症组，差异有统计学意义(*P<0.05*)；两组体温、心率、呼吸频率、血小板计数、胆碱酯酶、血清 BNP 水平比较差异无统计学意义(*P>0.05*)。见表 2。

表 2 脓毒症组与非脓毒症组各项生物学指标差异性比较

Table 2 Comparisons of the biomarkers levels between septic and non-septic burn patients

Variables	Sepsis [Nr. of timepoints: 359, M(P25~P75)]	Non sepsis [Nr. of timepoints: 1591, M(P25~P75)]	Z	*P*
PCT(ng/mL)	4.52(2.35~8.83)	1.33(0.74~3.24)	-17.818	＜0.01
Temp(℃)	37.6(36.8~37.9)	37.1(36.5~37.5)	-1.017	0.309
HR(bmp)	112(93~124)	103(90~116)	-0.778	0.437
RF(breaths/min)	22(21~24)	21(20~23)	-1.496	0.135
WBC(10^9/L)	24.28(17.48~33.09)	20.11(16.01~25.4)	-6.923	＜0.01
PLT(10^9/L)	217.2(189.1~278.4)	236.1(192.5~300.5)	-0.405	0.686
GLU(mmol/L)	13.12(9.66~17.28)	10.45(8.31~13.13)	-9.355	＜0.01
CR(μmol/L)	71.60(57.94~89.62)	61.48(48.87~73.48)	-10.135	＜0.01
TBIL(μmol/L)	30.07(22.63~38.69)	21.04(15.53~28.4)	-13.175	＜0.01
CHE(ku/L)	8.5(5.5~9.8)	7.4(6.6~8.4)	-1.089	0.276
BNP(pg/mL)	126.3(54.5~364.6)	79.2(38.9~213.5)	-1.826	0.068

Note: PCT: procalcitonin; Temp: temperature; HR: heart rate; RF: respiratory frequency; WBC: leucocyte count; PLT: platelet count; GLU: blood glucose; CR: urea nitrogen; TBIL: total bilirubin; CHE: cholinesterase; BNP: brain natriuretic peptide.

2.2 各项生物学指标诊断烧伤脓毒症的效能比较

PCT、白细胞计数、血糖、肌酐、总胆红素区分脓毒症与非脓毒症的 ROC 曲线下面积分别为 0.801 (95 % CI 为 0.776~0.824，*P<0.01*)、0.617 (95 %CI 为 0.581~0.652，*P<0.01*)、0.658 (95% CI 为 0.624~0.691，*P <0.01*)、0.671 (95 % CI 为 0.640~0.702，*P<0.01*)、0.722(95% CI 为 0.694~0.691，*P<0.01*)。见表 3、图 1。

表 3 各项生物学指标诊断烧伤脓毒症的效能比较

Table 3 Comparison of the AUCs of different biomarkers for the diagnosis of in burn patients with sepsis

Variables	PCT	WBC	GLU	CR	TBIL
AUC	0.801	0.617	0.658	0.671	0.722
95% CI	0.776~0.824	0.581~0.652	0.624~0.691	0.640~0.702	0.694~0.691
P	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01

表 4 血清降钙素原诊断烧伤脓毒症的效能分析

Table 4 Sensitivity and specificity of PCT cut-offs for the diagnosis of sepsis in burn patients.

Cut-off(ng/mL)	Sensitivity(%)	Specificity(%)	Youden index	PPV(%)	NPV(%)
2.0	84.4	62.1	0.466	32.8	94.6
3.0	70.8	71.8	0.427	35.7	91.2
4.0	58.1	81.2	0.393	41.1	89.5

Note: PCT: procalcitonin; PPV: positive predictive value; NPV: negative predictive value.

2.3 血清降钙素原诊断烧伤脓毒症的效能分析

以 2.0 ng/mL 为血清 PCT 区分脓毒症与非脓毒症的最佳截断值(约登指数最大)，其敏感度为 84.4 %，特异度为 62.1 %。选取 3.0 ng/mL 作为截断值时，敏感度为 70.8 %，特异度为 71.8 %；选取 4.0 ng/mL 作为截断值时，敏感度为 58.1 %，特异度为 81.2 %。见表 4。

3 讨论

脓毒症是机体对感染的反应失调，继而产生的危及生命的多器官功能障碍，其病情进展迅速，常因早期诊治不及时进一

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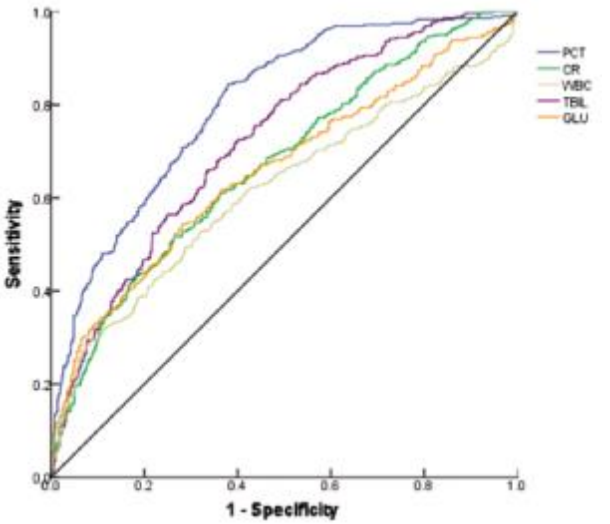

图 1 各项生物学指标早期诊断烧伤脓毒症的 ROC 曲线

Fig.1 Receiver operating characteristic (ROC) curves for the biomarkers used for early diagnosis of sepsis in burn patients

Note: PCT: procalcitonin; WBC: leucocyte count; GLU: blood glucose; CR: urea nitrogen; TBIL: total bilirubin.

步发展为脓毒症休克,病死率较高[11,12]。随着复苏技术和重症监护技术的不断发展,严重烧伤患者因早期休克发生死亡的风险得到了显著改善,脓毒症已成为烧伤患者死亡的首要病因[5]。严重烧伤时,机体的病理生理反应复杂,常伴随非感染全身炎症反应综合征,与脓毒症具有相似的临床表现,仅仅根据临床诊断标准来识别烧伤脓毒症非常困难[14]。目前,诊断烧伤脓毒症的金标准仍然是血液微生物培养鉴定,但血液培养耗时较长,从取样到结果回报通常需要 48~72 小时,且阳性率较低[13]。因此,单独或联合使用有效生物学标记物是提高临床早期烧伤脓毒症识别能力和及时启动有效抗菌治疗的重要策略。

PCT 是由 116 个氨基酸组成的降钙素前体,正常情况下由甲状腺 C 细胞合成,参与钙代谢,在健康人中其血清含量极低(< 0.1 ng/mL)。然而,在机体出现系统性细菌感染或严重真菌感染的情况下,其血清含量可随感染进程急剧上升,并在感染得到有效控制后迅速下降。多项研究结果表明,PCT 可用于区分非感染性全身炎症反应和微生物引起的全身性感染,并且是指导社区获得性肺炎和重症监护病房脓毒症患者合理应用抗生素的可靠手段[16-18]。1998 年,von Heimburg[19]首次提出 PCT 可应用于烧伤患者脓毒症的诊断,该报道得到了一些相关研究的证实[20,21],同时也存在反对的观点[22]。本研究对脓毒症组与非脓毒症组所有检测时间点临床常用烧伤脓毒症诊断指标的差异性进行了分析,两组间 PCT、白细胞计数、血糖、肌酐、总胆红素具有统计学差异。通过绘制 ROC 曲线进一步评价各项生物学指标烧伤脓毒症的诊断效能,PCT、白细胞计数、血糖、肌酐、总胆红素曲线下面积分别为 0.801、0.617、0.658、0.671、0.722,提示 PCT 与常规脓毒症相关指标相比,在区别烧伤脓毒症与非脓毒症中具有最好的诊断效能。

临床上,选取一个最佳的 PCT 诊断断阈值是其早期识别烧伤脓毒症并指导有效抗菌治疗的关键。但是,烧伤患者病情复杂,烧伤面积、深度、手术及检测设备等的差异均导致确定一个具体的诊断阈值较为困难。Ren H 等[20]一项评估 PCT 烧伤脓毒症诊断效能的 Meta 分析中显示,PCT 诊断脓毒症的最佳截断值波动在 0.53~3 ng/mL,相应的敏感度为 11 %~100 %,特异度为 76 %~100 %。另一项相关 Meta 分析显示,PCT 的合并 ROC 曲线下面积为 0.87,敏感度为 77 %,特异度为 65 %,平均截断值 1.5 ng/mL 是怀疑脓毒症发生并建议开始经验性抗生素治疗的有力指标[21]。各项研究具有相似的研究方法,区别主要体现在纳入病例的数量及烧伤总面积的不同。

本研究纳入病例均为烧伤面积≥ 50 % TBSA 的特重度烧伤患者,且创新性引入检测时间点为研究对象,显著增加了样本量并缩小了烧伤面积区间,提高了实验结果的可靠性。本研究中,PCT 区别烧伤脓毒症与非脓毒症约登指数最大的截断值为 2.0 ng/mL,具有高敏感度(84.4 %),但特异度(62.1 %)不高。选取4.0 ng/mL 作为截断值时,具有高特异度(81.2 %),但敏感度(58.1 %) 较低。选取 3.0 ng/mL 作为截断值,可获得敏感度(70.8 %)和特异度(71.8 %)的最好组合,其阳性预测值为 35.7 %,阴性预测值为 91.2 %。实际应用中,可将 2.0 ng/mL 作为警报截断值,继而每天检测 PCT 值并动态监测其变化;将 4.0 ng/mL 作为高危预警值,提示应立即使用高阶梯广谱抗菌药物,待血培养及药敏结果回报后再调整为敏感药物。同时,临床医生可将 PCT 与临床表现及传统生物标记物相结合,并通过动态连续检测的方式来提高烧伤脓毒症的诊断效力[24]。

本研究为单中心回顾性研究,存在一定的局限性,所得结论仍需联合其他烧伤中心开展大规模前瞻性临床研究进行论证。但本研究样本量较大且纳入排除标准严格,很大程度上避免了统计偏倚。本研究表明,PCT 动态监测有助于烧伤脓毒症的早期诊断,对指导临床医生及时采取有效抗菌治疗、提高危重烧伤患者救治成功率具有重要价值。

参 考 文 献(References)

[1] Krishnan P, Frew Q, Green A, et al. Cause of death and correlation with autopsy findings in burns patients [J]. Burns Including Thermal Injury, 2013, 39(8): 1649-1650

[2] Chipp E, Milner C S, Blackburn A V. Sepsis in burns: a review of current practice and future therapies [J]. Annals of Plastic Surgery, 2010, 65(2): 228

[3] Appelgren P, Björnhagen V, Bragderyd K, et al. A prospective study of infections in burn patients[J]. Burns, 2002, 28(1): 39-46

[4] Englert N C, Ross C. The older adult experiencing sepsis [J]. Critical Care Nursing Quarterly, 2015, 38(2): 175

[5] Fitzwater J, Purdue G F, Hunt J L, et al. The risk factors and time course of sepsis and organ dysfunction after burn trauma [J]. Journal of Trauma, 2003, 54(5): 959-966

[6] Mann E A, Baun M M, Meininger J C, et al. Comparison of mortality associated with sepsis in the burn, trauma, and general intensive care unit patient: a systematic review of the literature [J]. Shock, 2012, 37 (1): 4

[7] Hardwicke J. The influence of outcomes on the provision and practice of burn care [J]. Burns Journal of the International Society for Burn Injuries, 2016, 42(2): 307-315

[8] Assicot M, Gendrel D, Carsin H, et al. High serum procalcitonin concentrations in patients with sepsis and infection [J]. Lancet, 1993, 341(8844): 515-518

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[9] Safiri S, Ayubi E, Mansori K. Comments on procalcitonin for the early diagnosis of sepsis in burn patients: A retrospective study [J]. Burns, 2018, 44(4)

[10] 柴家科. 烧伤脓毒症诊断与综合防治策略[J]. 中华烧伤杂志, 2013, 29(2): 105-108

[11] Seymour C W, Liu V X, Iwashyna T J, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[J]. Jama, 2016, 315 (8): 762-774

[12] Shankar-Hari M, Singer M. Caring for Sepsis Patients: An Update[J]. Critical Care Clinics, 2018, 34(1): xiii

[13] Zheng Z, Jiang L, Ye L, et al. The accuracy of presepsin for the diagnosis of sepsis from SIRS: a systematic review and meta-analysis [J]. Annals of Intensive Care, 2015, 5(1): 48

[14] Gille J, Dietz A, Taha H, et al. A sirs-based automated alarm system for the diagnosis of sepsis after burn injury[J]. Annals of Fires & Burn Disaster, 2017, 30(3): 177-184

[15] Maruna P, Nedelníková K, Gürlich R. Physiology and genetics of procalcitonin[J]. Physiological Research, 2000, 49 Suppl 1(Suppl 1): S57

[16] Vincent J L, Nuffelen M V, Lelubre C. Host Response Biomarkers in Sepsis: The Role of Procalcitonin [J]. Methods in Molecular Biology, 2015, 1237(1237): 213

[17] Meisner M. Pathobiochemistry and clinical use of procalcitonin[J]. Clinica Chimica Acta, 2003, 323(1): 17-29

[18] Liu Y, Yang W, Wei J. Guiding Effect of Serum Procalcitonin (PCT) on the Antibiotic Application to Patients with Sepsis [J]. Iranian Journal of Public Health, 2017, 46(11): 1535-1539

[19] Heimburg D V, Stieghorst W, Khorram-Sefat R, et al. Procalcitonin-a sepsis parameter in severe burn injuries [J]. Burns Journal of the International Society for Burn Injuries, 1998, 24(8): 745

[20] Ren H, Li Y, Han C, et al. Serum procalcitonin as a diagnostic biomarker for sepsis in burned patients: a meta-analysis [J]. Burns, 2015, 41(3): 502-509

[21] Cabral L, Afreixo V, Almeida L, et al. The Use of Procalcitonin (PCT) for Diagnosis of Sepsis in Burn Patients: A Meta-Analysis[J]. Plos One, 2016, 11(12)

[22] Seoane L, Pértega S, Galeiras R, et al. Procalcitonin in the burn unit and the diagnosis of infection[J]. Burns, 2014, 40(2): 223

[23] Huang M Y, Chen C Y, Chien J H, et al. Serum Procalcitonin and Procalcitonin Clearance as a Prognostic Biomarker in Patients with Severe Sepsis and Septic Shock [J]. BioMed research international, 2016, 2016(2): 1758501

[24] Van T E, Wiersinga W J, Scicluna B P, et al. Biomarkers in Sepsis[J]. Critical Care Clinics, 2018, 34(1): 139

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[21] Liu W, Yin NC, Liu H, et al. Cav-1 promote lung cancer cell proliferation and invasion through lncRNA HOTAIR[J]. Gene, 2018, 641: 335-340

[22] Zhang Y, Wang LJ, Li WF, et al. The prognostic value of HOTAIR for predicting long-term prognosis of patients with gastrointestinal cancers[J]. Medicine (Baltimore), 2018, 97(26): e11139

[23] Chang YT, Lin TP, Tang JT, et al. HOTAIR is a REST-regulated lncRNA that promotes neuroendocrine differentiation in castration resistant prostate cancer[J]. Cancer Lett, 2018[Epub ahead of print]

[24] Tang Q, Hann SS. HOTAIR: An Oncogenic Long Non-Coding RNA in Human Cancer[J]. Cell Physiol Biochem, 2018, 47(3): 893-913

[25] Lei B, Yu L, Jung TA, et al. Prospective Series of Nine Long Noncoding RNAs Associated with Survival of Patients with Glioblastoma [J]. J Neurol Surg A Cent Eur Neurosurg, 2018[Epub ahead of print]

[26] Xia H, Jing H, Li Y, et al. Long noncoding RNA HOXD-AS1 promotes non-small cell lung cancer migration and invasion through regulating miR-133b/MMP9 axis [J]. Biomed Pharmacother, 2018, 106: 156-162

[27] Yang Q, Yu Y, Sun Z, et al. Long non-coding RNA PVT1 promotes cell proliferation and invasion through regulating miR-133a in ovarian cancer[J]. Biomed Pharmacother, 2018, 106: 61-67

[28] Jing N, Huang T, Guo H, et al. LncRNA CASC15 promotes colon cancer cell proliferation and metastasis by regulating the miR4310/LGR5/Wnt/betacatenin signaling pathway [J]. Mol Med Rep, 2018 [Epub ahead of print]

[29] Wang H, Qin R, Guan A, et al. HOTAIR enhanced paclitaxel and doxorubicin resistance in gastric cancer cells partly through inhibiting miR-217 expression[J]. J Cell Biochem, 2018[Epub ahead of print]

[30] Wang LP, Wang JP, Wang XP. HOTAIR contributes to the growth of liver cancer via targeting miR-217[J]. Oncol Lett, 2018, 15(5): 7963-7972

[31] Portoso M, Ragazzini R, Brencic Z, et al. PRC2 is dispensable for HOTAIR-mediated transcriptional repression [J]. EMBO J, 2017, 36 (8): 981-994

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