doi: 10.13241/j.cnki.pmb.2020.16.018

外周血中性粒细胞 CD4(nCD4)在白血病合并细菌感染患者检测中的应用价值*

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摘要 目的:观察外周血中性粒细胞 CD4(neutrophil CD4,nCD4)在白血病合并细菌感染患者检测中的准确度和灵敏度,评价其临床应用价值。**方法:**筛选我院在 2016 年 1 月至 2019 年 1 月期间收治的 100 例白血病患者作为研究对象并纳入研究组,其中合并 47 例合并细菌感染者纳入研究Ⅰ组,其余 53 例未合并细菌感染者纳入研究Ⅱ组,另外根据血培养检查结果将研究Ⅰ组分为阳性组(n=12)和阴性组(n=35),同时,筛选同时期进行健康体检者 50 例纳入对照组;对比降钙素原(Procalcitonin,PCT)、C- 反应蛋白(C-reactive protein,CRP)及 nCD4 水平,并比较阳性组和阴性组的 PCT、CRP、nCD4 的诊断准确度和灵敏度。**结果:**研究组的 PCT、CRP、nCD4 高于对照组($P<0.05$),研究Ⅰ组的 PCT、CRP、nCD4 高于研究Ⅱ组($P<0.05$);研究Ⅰ组中,阳性组的 nCD4 荧光强度高于阴性组($P<0.05$);nCD4 诊断白细胞细菌感染的准确度、灵敏度、特异度优于 CRP 及 PCT 诊断。**结论:**nCD4 在白血病合并细菌感染患者检测中具有较好的临床参考价值,联合 PCT、CRP 检测能够显著提高检测准确性,可以作为诊断白血病合并细菌感染的诊断指标。

关键词:中性粒细胞 CD4(nCD4);白血病,细菌感染;临床检测;应用价值

中图分类号:R733.7;R446.1 **文献标识码:**A **文章编号:**1673-6273(2020)16-3087-04

Application Value of Peripheral Blood Neutrophil CD4 (nCD4) in Detection of Natients with Leukemia Complicated by Bacterial Infection*

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ABSTRACT Objective: Observe the accuracy and sensitivity of peripheral blood neutrophil CD4 (nCD4) in the detection of patients with leukemia complicated by bacterial infection, and evaluate its clinical application value. **Methods:** 100 patients with leukemia admitted in our hospital from January 2016 to January 2019 were selected as the research object and included in the study group. Among them, 47 patients with bacterial infection were included in study group Ⅰ, and the remaining 53 patients without bacterial infection were included. Study Ⅱ group, according to the results of blood culture examination, the study Ⅰ components were positive group (n=12) and negative group (n=35). At the same time, 50 cases of healthy physical examination at the same period were screened into the control group; The levels of PCT, CRP and nCD4 were compared, and the diagnostic accuracy and sensitivity of PCT, CRP, and nCD4 in the positive and negative groups were compared. **Results:** The PCT, CRP, and nCD4 in the study group were higher than those in the control group (all $P<0.05$), and the PCT, CRP, and nCD4 in the study group Ⅰ were higher than those in the study Ⅱ group (all $P<0.05$). The intensity was higher than that of the negative group ($P<0.05$). nCD4 is better than CRP and PCT in the accuracy, sensitivity and specificity of leukocyte bacterial infection. **Conclusion:** nCD4 has good accuracy and sensitivity in the detection of patients with leukemia complicated by bacterial infection, and combined with PCT and CRP detection can significantly improve the detection accuracy, which can be used as a diagnostic indicator for the diagnosis of leukemia combined with bacterial infection.

Key words: Neutrophil CD4 (nCD4); leukemia, bacterial infection; clinical detection; application value

Chinese Library Classification(CLC): R733.7; R446.1 Document code: A

Article ID: 1673-6273(2020)16-3087-04

前言

白血管是造血系统的一种恶性肿瘤,因疾病、化疗、骨髓造血功能下降等因素,白血病患者的免疫功能大幅度降低,对细

* 基金项目:国家自然科学基金项目(81500219);陕西省科学技术研究发展计划项目(2016SF-217)

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(收稿日期:2020-02-06 接受日期:2020-02-28)

菌侵入的抵抗地下降，易发生感染，因此患者合并细菌感染风险较高，是导致白血病患者死亡的主要原因，严重威胁患者生命健康[1,2]。白血病合并细菌感染无典型症状，发展迅速，且患者普遍预后不佳，因此早期明确诊断、早期积极治疗对于及时治疗和改善预后而言至关重要[3-5]。由于临床很难通过患者的临床症状区分感染病原体的不同，目前普遍借助 PCT、CRP 进行检测，但是上述指标具有与一定的局限性，难以明确诊断细菌感染，诊断价值较低，且会增加细菌耐药性、菌群紊乱的风险[6,7]。有文献[8]报告 nCD4 是诊断败血症和细菌感染的可靠指标[9,10]。因此，在本研究中，为了能够为临床工作提供指导，我们观察了 nCD4 在白血病合并细菌感染患者检测中的准确度和灵敏度。现将有关资料整理报告如下。

1 临床资料

1.1 一般资料

筛选我院在 2016 年 1 月至 2019 年 1 月期间收治的 100 例白血病患者为研究组。纳入标准：① 初次确诊者，无既往相关病史；② 未接受相关治疗；③ 都同样采用细菌血培养确诊是否存在感染；④ 患者及家属均知情同意，经医院伦理委员批准。排除标准：① 已经明确诊断感染病原体（细菌、真菌感染等）者；② 合并恶性肿瘤者；③ 存在免疫缺陷者；④ 不同意本研究内容者；⑤ 依从性差者。其中男 67 例，女 33 例；年龄 24～54 岁，平均 35.29± 5.22 岁。其中 47 例合并细菌感染者纳入研究Ⅰ组，男 22 例，女 15 例；年龄 26～54 岁，平均 36.22± 5.27 岁；其余 53 例未合并细菌感染者纳入研究Ⅱ组，男 25 例，女 28 例；年龄 24～52 岁，平均 35.48± 5.24 岁。另外根据血培养检查结果，将研究Ⅰ组中 12 例纳入阳性组，男 7 例，女 5 例；年龄 27～54 岁，平均 35.35± 5.22 岁；35 例纳入阴性组，男 15 例，女 10 例；年龄 25～54 岁，平均 36.24± 5.19 岁。另选择同时期进行健康体检者 50 例纳入对照组，男 28 例，女 22 例；年龄 25～51 岁，平均 36.25± 5.25 岁。各组一般资料比较无差异（$P>0.05$），具有可比性。

1.2 研究方法

1.2.1 检测方法 两组入院之后常规抽取空腹静脉血。PCT 以免疫层析法进行检测，CRP 以酶联免疫吸附法进行检测，均应用广州健仑生物科技有限公司提供的试剂盒，nCD4 采用上海迪普生物技术有限公司提供的 BDFACSAria Ⅱ 流式细胞仪提供，平均荧光强度采用流式细胞术检测，试剂盒采用美国 Becton Dickinson 公司提供的 nCD4 流式细胞试剂盒。所有操作严格按照说明书进行。

1.2.2 指标判定 对照组检查者的 PCT、CRP、nCD4 检测数值符合正态分布曲线（$\bar{x}\pm$ SD），试验组各个亚组的检查结果以高于均值两个标准差（≥ $\bar{x}\pm$ SD）及以上者判定为阳性，据此判定上述各个指标在判断白血病合并细菌感染的准确度、灵敏度、特异度。

1.3 观察内容

观察不同组的 PCT、CRP、nCD4 水平以及阳性组和阴性组的准确度、灵敏度、特异度。

1.4 统计学方法

应用 SPSS 21.0，计量资料以（$\bar{x}\pm s$），两组间对比行 t 检验，多组间行方差分析，$P<0.05$ 为有统计学意义。PCT、CRP、nCD4 诊断准确性、灵敏度、特异度比较采用 ROC 曲线检查，准确度=（真阳性 + 真阴性）/ 总例数× 100%；灵敏度 = 真阳性 /（真阳性 + 假阴性）/ 总例数× 100%；特异度 = 真阴性 /（假阳性 + 真阴性）× 100%。

2 结果

2.1 各组 PCT、CRP、nCD4 比较

研究组的 PCT、CRP、nCD4 水平均显著高于对照组（$P<0.05$），研究Ⅰ组的 PCT、CRP、nCD4 高于研究Ⅱ组（$P<0.05$），见表 1。

表 1 各组的 PCT、CRP、nCD4 比较（$\bar{x}\pm s$）

Table 1 Comparison of PCT, CRP and nCD4 in each group ($\bar{x}\pm s$)

Groups		n	PCT（ng/mL）	CRP（mg/L）	nCD4
Study group	Ⅰ group	47	10.24± 1.26*#	72.58± 10.68*#	185.67± 66.24*#
	Ⅱ group	53	3.29± 0.85*	15.22± 2.48*	43.95± 10.37*
Control group		50	0.45± 0.09	2.11± 0.12	25.35± 6.49

Note: Compared with the control group, *$P<0.05$; compared with the study Ⅱ group, #$P<0.05$.

2.2 阳性组和阴性组 nCD4 荧光强度比较

研究Ⅰ组中，阳性组的 nCD4 荧光强度为 248.65± 77.35，显著高于阴性组的 55.63± 12.29，两组对比差异有统计学意义（$t=9.638$，$P=0.000$，$P<0.05$）。

2.3 诊断准确度、灵敏度、特异度比较

经过比较 nCD4 诊断白细胞细菌感染的准确度、灵敏度和特异度均优于 CRP 及 PCT 诊断，见表 2。

表 2 诊断准确度、灵敏度、特异度比较[例(%)]

Table 2 Comparison of the accuracy, sensitivity, and specificity of diagnosis [n (%)]

Testing indicators	Accuracy	Sensitivity	Specificity
nCD4	91.00（91/100）	95.74（45/47）	86.79（46/53）
CRP	72.00（72/100）	70.21（33/47）	73.58（39/53）
PCT	75.00（75/100）	74.47（35/47）	75.47（40/53）

3 讨论

白血病是一种造血干细胞恶性克隆性疾病,会对骨髓的正常造血功能产生抑制，联合化疗是临床治疗该病的重要方法[11,12],但由于缺乏治疗靶向性,在杀死肿瘤细胞的同时,也会杀伤正常血细胞,出现各种并发症,降低患者自身免疫力,极易继发感染,造成系统性炎症反应,严重威胁患者生命健康[13,14]。感染是白血病最为棘手的并发症之一[15]。联合化疗会导致白血病患者白细胞数量显著降低,造成感染症状不典型,有些合并感染患者只单纯有发热症状,难以早期明确诊断,容易延误治疗时机[16,17]。为改善患者预后,早期明确诊断是否合并细菌感染非常必要。

细菌培养、白细胞计数、CRP、PCT 是临床诊断感染性疾病的传统指标,其中,细菌培养是金标准,是当前临床诊断感染性疾病最为客观的指标,但存在一些不足,如检查时间长、某些细菌只有在晚期可以培养出甚至无法培养,另外标本采集时间、部位以及送检时间等因素也一定程度上限制了它的临床应用[18-20]。白细胞计数、CRP 是当前临床上诊断感染性疾病的常用辅助指标，但容易受到其他因素影响，检测的灵敏度普遍不高[21,22]。PCT 是较好的感染指示指标,但存在其指示作用存在一定延迟反应,另外,由于白血病患者受输血、集落因子的影响,血清PCT水平诊断感染情况的准确性、灵敏性、特异性均相对不高[23,24]。在本研究中,CRP、PCT 诊断白血病合并细菌感染的准确度、灵敏度、特异度分别为 72.00%、70.21%、73.58%和 75.00%、74.47%、75.47%,这 2 项指标的准确度、灵敏度、特异度的绝对值也相对较低,证实了上述观点。

近年来的研究发现，中性粒细胞膜表面的 CD4 分子与感染存在密切关系[25]。中性粒细胞是机体抵抗感染的主要防御细胞,CD4 分子参与了中性粒细胞的噬菌作用[26]。在正常情况下,中性粒细胞表面分子在外周血中呈低水平表达,一旦机体组织发生感染，中性粒细胞被激活，在 4～6 h 会大量表达 CD4。nCD4 与其配体结合之后,会启动并放大免疫效应,在细胞因子的调节下,通过免疫复合物清除作用、细胞吞噬作用、细胞毒性作用来进一步发挥清除病原体、释放介导炎症介质以及抗原递呈的作用[27-29]。所以,nCD4 对细菌感染的诊断意义重大。另外,有研究结果[30]证实,nCD4 表达与患者的年龄、性别无关,其表达水平高低仅与细菌感染有关，因此，可以适用于新生儿、儿童、成年人不同年龄段以及不同性别的群体。在本研究中,nCD4 诊断白血病合并细菌感染的准确度、灵敏度、特异度分别为 91.00 %、95.74 %、86.79 %,其中准确度、灵敏度不仅均优于 CRP、PCT,其结果的绝对值也相对较高。本研究也存在一定的不足,样本量少,没有对比 nCD4、CRP、PCT 联合诊断价值,在后续研究中需要加大样本量,进一步的深入研究,明确白血病合并细菌感染患者检测中有效的诊断手段,为其诊断提供检测指标。

综上所述,临床研究表明,nCD4 在白血病合并细菌感染患者检测中具有较好的准确度和灵敏度,联合 PCT、CRP 检测能够显著提高检测准确性,可以作为诊断白血病合并细菌感染的敏感的诊断指标。

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（上接第 3184 页）

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