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外周血血小板/淋巴细胞比值在肺腺癌诊断中的价值

汪向海,潘贤慧,邢 敏
(皖南医学院第一附属医院 弋矶山医院 呼吸内科,安徽 芜湖 241001)

【摘 要】目的:探讨外周血中血小板/淋巴细胞比值(PLR)在肺腺癌诊断中的价值。方法:收集80例肺腺癌患者和100例健康对照者外周血中PLR、中性粒细胞/淋巴细胞比值(NLR)、淋巴细胞/单核细胞比值(LMR)及血清癌胚抗原(CEA),观察外周血PLR与肺腺癌临床病理特征的相关性,运用受试者工作特征(ROC)曲线评价PLR在肺腺癌患者中的诊断效能。结果:与健康体检者相比较,肺腺癌患者PLR值升高,而NLR、LMR在肺腺癌患者和健康对照组间差异无统计学意义。肺腺癌患者PLR表达水平与患者吸烟及TNM分期具有相关性($P=0.025$和$P=0.039$),ROC曲线结果显示,采用PLR诊断肺腺癌的曲线下面积(AUC)为0.752,灵敏度为0.600,特异度为0.830,节点值为134.840,95%*CI*:0.677~0.825;采用CEA诊断肺腺癌的AUC为0.753,灵敏度为0.563,特异度为0.880,节点值为4.375,95%*CI*:0.679~0.827;PLR和CEA联合检测诊断肺腺癌的AUC为0.861,灵敏度为0.750,特异度为0.850,95% *CI*:0.803~0.919;结论:PLR表达水平具有初步诊断肺腺癌的价值,且诊断能力不亚于CEA,两者联合检测可以提高诊断的准确性,同时PLR表达水平与肺腺癌患者的吸烟状态及TNM分期具有相关性。

【关键词】血小板与淋巴细胞比值;肺腺癌;TNM分期;癌胚抗原
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Value of peripheral blood platelet and lymphocyte ratio in the diagnosis of lung adenocarcinoma

WANG Xianghai, PAN Xianhui, XING Min
Department of Respiratory Medicine, The First Affiliated Hospital of Wannan Medical College, Wuhu 241001, China

【**Abstract**】***Objective***: To assess the value of platelet-lymphocyte ratio in peripheral blood in the diagnosis of lung adenocarcinoma. ***Methods***: Peripheral blood samples were obtained from 80 patients of adenocarcinoma of lung and 100 healthy volunteers, and measured concerning platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR) and serum carcinoembryonic antigen (CEA) to observe the correlation between peripheral blood PLR and clinicopathological features of lung adenocarcinoma. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficacy of PLR in patients with lung adenocarcinoma. ***Results***: Elevated PLR value was found in patients of lung adenocarcinoma, whereas NLR and LMR were not significantly different between lung adenocarcinoma patients and healthy controls. PLR was associated with history of cigarette smoking and TNM staging in patients of lung adenocarcinoma ($P=0.025$, $P=0.039$). ROC curve results showed that the area under the curve of lung adenocarcinoma by PLR was 0.752, and the sensitivity, specificity and cutoff was 0.600, 0.830 and 134.840, respectively (95% *CI*: 0.677-0.825). The area under the curve for diagnosis of lung adenocarcinoma by CEA was 0.753, and the sensitivity, specificity and cutoff was 0.563, 0.880 and 4.375, respectively (95% *CI*: 0.679-0.827). The area under the curve by combined PLR with CEA for lung adenocarcinoma was 0.861, and the sensitivity, specificity and cutoff was respectively 0.750 and 0.850 (95% *CI*: 0.803-0.919). ***Conclusion***: PLR can be valuable in preliminary diagnosis of lung adenocarcinoma, and the diagnostic potency is as good as CEA level. Importantly, combined use of the two indicators can improve the accuracy of diagnosis. PLR is correlated with the history of cigarette smoking and TNM staging in patients of lung adenocarcinoma.

【**Key words**】platelet-lymphocyte ratio; lung adenocarcinoma; TNM stage; carcinoembryonic antigen

肺癌已经成为我国发病率及病死率位居首位的恶性肿瘤,其中大部分的肺癌是非小细胞肺癌(non-small cell lung cancer,NSCLC),NSCLS中又以肺腺癌居多,因肺腺癌早期无明显症状,患者就诊时大多已经是晚期,5年生存率很低,因此积极寻找肺腺癌早期诊断指标尤其重要。目前,肺腺癌诊断指标仍然局限于一些肿瘤标志物,其中血清癌胚抗原(carcinoembryonic antigen,CEA)在临床上使用最为广泛,但因肿瘤标志物检测费用高,检验设备复杂,因此在广大基层医院难以推广使用。国外研究认为,全身炎症反应与肿瘤的治疗效果和预后密切相关,Song等[1]发现血小板/淋巴细胞比值(platelet-to-

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作者简介:汪向海(1982-),男,主治医师,讲师,(电话)13965154483,(电子信箱)wxhwxpcyy@163.com。

lymphocyte ratio,PLR)和中性粒细胞/淋巴细胞比值(neutrophil-to-lymphocyte ratio,NLR)是影响结肠癌患者预后的独立预测因素,Eo 等[2]认为淋巴细胞/单核细胞比值(lymphocyte-to-monocyte ratio,LMR)在预测卵巢癌患者的生存期有重要意义。然而目前关于 PLR、NLR、LMR 与肺腺癌的关系仍不明确,Lan 等[3]认为外周血中高表达的 PLR 和 NLR 肺腺癌患者放疗效果不佳且预后差,而 Wu 等[4]研究认为肺腺癌患者 PLR 表达水平与肺腺癌侵袭无关,所以 PLR 是否可以作为肺腺癌患者的预测因子尚需进一步研究。为此,本研究比较外周血 PLR、NLR、LMR 在肺腺癌患者和健康对照组中的表达水平,并分析 PLR 表达水平与肺腺癌患者临床病理特征的相关性,运用受试者工作特征(receiver operating characteristic,ROC)曲线探讨 PLR 在肺腺癌患者中的诊断效能。

1　资料和方法

1.1　对象　收集弋矶山医院呼吸内科确诊且未经治疗的肺腺癌患者 80 例,男 57 例,女 23 例,平均年龄(66.700±8.781)岁,收集我院健康服务中心体检健康者 100 例作为健康对照组(以下简称对照组),男 60 例,女 40 例,平均年龄(64.250±8.174)岁。

1.2　方法　采集初诊肺腺癌患者和健康体检者外周静脉血,应用迈瑞 BC-5000 血细胞分析仪进行血常规检测,通过血常规结果分别计算出 PLR、NLR、LMR。血清 CEA 用雅培 i-2000 化学发光分析仪及配套试剂检测。

1.3　统计学分析　实验结果均用 SPSS 18.0 和 GraphPad Prism 6.0 软件进行统计分析,两组间数据比较采用独立样本 t 检验;患者临床病理特征与分组之间的相关性分析采用卡方检验,绘制 ROC 曲线,计算曲线下面积(area under the curve,AUC),并计算灵敏度和特异度;$P<0.05$ 为差异有统计学意义。

2　结果

2.1　外周血 PLR 表达水平比较　肺腺癌患者外周血 PLR 为(176.335±99.863),对照组为(107.918±34.870),肺腺癌患者组外周血 PLR 表达水平高于对照组,差异有统计学意义($t=5.849$,$P<0.001$),而肺腺癌患者外周血 NLR 为(4.182±3.245),对照组为(3.878±2.433),差异无统计学意义($t=0.478$,$P>0.05$),肺腺癌患者外周血 LMR 为(2.982±1.365),对照组为(3.588±2.130),差异无统计学意义($t=1.494$,$P>0.05$)。

2.2　PLR 表达水平与肺腺癌临床病理特征的相关性　收集 80 例肺腺癌患者的临床病理资料,进一步分析 PLR 表达与肺腺癌临床病理特征之间的相关性。根据 PLR 在 80 例肺腺癌患者中的表达水平的中位数,分为 PLR 低表达组(<154.280)和高表达组(≥154.280),经卡方检验分析显示 PLR 表达水平与肺腺癌患者吸烟状态及 TNM 分期具有相关性($P=0.025$和$P=0.039$,表 1),PLR 在肺腺癌吸烟患者和晚期肺腺癌患者外周血中表达水平较高。

表 1　PLR 表达水平与肺腺癌患者临床病理特征的相关性

临床病理特征	n	PLR		χ^2	P
		低(<154.280)	高(≥154.280)		
性别					
男	57	26	31	1.526	0.217
女	23	14	9		
年龄/岁					
<60	15	10	5	2.051	0.152
≥60	65	30	35		
吸烟					
是	42	16	26	5.013	0.025
否	38	24	14		
饮酒					
是	26	11	15	0.912	0.340
否	54	29	25		
分化程度					
高/中	55	27	28	0.058	0.809
低	25	13	12		
TNM 分期					
Ⅰ,Ⅱ	20	14	6	4.267	0.039
Ⅲ,Ⅳ	60	26	34		

2.3　PLR 在肺腺癌患者中的诊断效能　为进一步评价 PLR 在肺腺癌中的诊断效能,利用 ROC 曲线分析了 PLR、CEA 及两者联合检测在肺腺癌中的诊断效能,如图 1 所示,区别正常对照组与肺腺癌患者的 PLR 表达的节点值是 134.840,灵敏度为 0.600,特异度为 0.830,95% *CI*:0.677~0.825;AUC 为 0.752;区别对照组与肺腺癌患者的 CEA 表达的节点值是 4.375,灵敏度为 0.563,特异度为0.880,95% *CI*:0.679~0.827;AUC 为 0.753;PLR 和 CEA 联合检测灵敏度为 0.750,特异度为 0.850,95% *CI*:0.803~0.919,AUC 为 0.861;结果提示外周血中检测 PLR 作为肺腺癌的诊断标志物效能不亚于肿瘤标志物 CEA,且两者联合检测(串联)可提高诊断的准确度,减少漏诊。

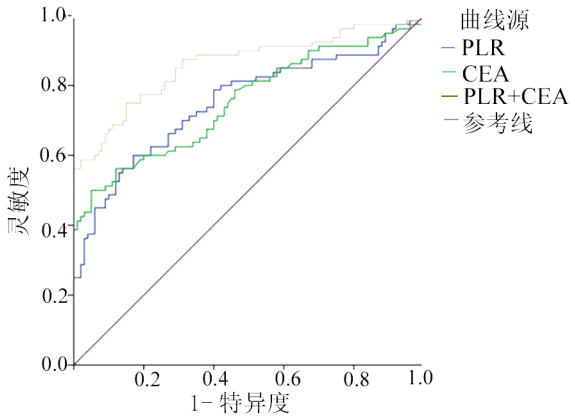

图1 ROC曲线分析PLR、CEA及两者联合检测在肺腺癌患者中的诊断效能

3 讨论

炎症指标与肿瘤之间的关系是近年来临床研究的热点，外周血PLR、NLR及LMR是近年来研究较多的炎症指标[5-8]，国内外的研究表明，PLR、NLR及LMR与膀胱癌[9]、乳腺癌[10]、食管癌[11]、恶性胸膜间皮瘤[12]、骨肉瘤[13]、结直肠癌[14]等疾病的发生发展有密切联系，目前关于PLR、NLR及LMR与肺癌之间的相关性研究结果具有一定的争议，Cannon等[15]研究认为PLR与接受化疗的NSCLC患者生存期密切相关，Liu等[16]通过单因素分析发现，PLR和NLR均与肺癌患者的预后相关，但多因素分析发现，NLR可作为肺癌患者预后的独立预测指标，而PLR没有独立预测价值。而Pinato等[17]通过研究认为PLR表达水平与肺癌患者的诊断及预后无相关性。目前关于PLR、NLR及LMR与肺腺癌诊断及肺腺癌患者临床病理特征之间关系的研究不多，本研究将外周血PLR、NLR及LMR在肺腺癌患者和对照组中的表达水平进行比较，分析PLR表达水平与肺腺癌患者临床病理特征的相关性，并评估PLR对肺腺癌患者的诊断价值，为肺腺癌的诊断寻找新的预测因子。

本研究结果认为，肺腺癌组患者外周血中PLR表达水平较对照组增加，而外周血NLR和LMR表达水平在肺腺癌组和对照组之间的差异无统计学意义，这与既往Unal等[18]研究结论不一致，他们认为肺腺癌患者外周血中PLR和NLR表达水平均升高。PLR表达水平与肺腺癌患者临床病理特征的相关性尚未见报道，本研究发现PLR表达水平与肺腺癌患者吸烟状态具有相关性，PLR在肺腺癌吸烟患者外周血中表达水平高于不吸烟患者，同时PLR与肺腺癌的TNM分期具有相关性，晚期的肺腺癌患者外周血中往往高表达PLR，预示着患者多伴有远处转移，说明PLR有助于对肺腺癌患者的病情评估，在以后的临床工作中，PLR可以辅助判断肺腺癌患者是否有远处转移的可能性。

在对同一种疾病的两种或两种以上诊断指标进行比较时，可将各指标的ROC曲线绘制到同一坐标中，以直观地鉴别优劣，靠近左上角的ROC曲线所代表的诊断效能最高，亦可通过分别计算各个诊断指标的AUC进行比较，哪一种指标的AUC最大，则哪一种诊断指标的诊断价值最佳。通过ROC曲线分析发现，PLR诊断肺腺癌的灵敏度为0.600，特异度为0.830，95% *CI*: 0.677~0.825，AUC为0.752，CEA诊断肺腺癌的灵敏度为0.563，特异度为0.880，95% *CI*: 0.679~0.827; AUC为0.753，提示PLR对肺腺癌患者的诊断效能不亚于CEA，在以后的临床工作中，尤其是基层及社区医院，可以使用PLR对人民群众进行肺腺癌的早期筛查，不仅检测方便，检测结果快捷，还可以大大减少群众的经济负担，易于被广泛推广。PLR和CEA联合检测灵敏度为0.750，特异度为0.850，95% *CI*: 0.803~0.919，AUC为0.861; 说明两者联合检测可提高肺腺癌诊断的准确度，减少漏诊。由于研究期限较短，样本量少，在以后的研究中需继续增加标本量，进一步探讨外周血PLR表达水平对肺腺癌患者诊断和预后的价值。

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影响了统计结果,但是 ROMA 诊断价值仍然最高。CA125 和 ROMA 采用临床建议的 cut-off 值较最佳 cut-off 值偏低,突出的问题是在临床诊断中其特异性偏低,而 HE4 临床建议的 cut-off 值较最佳 cut-off 值在绝经后患者偏高,这与文献报道基本一致[9]。3 项指标的 cut-off 值与临床建议的 cut-off 值有一定的出入,这可能需要增加研究病例数进行大样本的研究以确定最佳 cut-off 值。另外,我们还研究了 CA125、HE4 及 ROMA 在绝经前后与卵巢癌的临床 FIGO 分期之间的关系,Ⅰ~Ⅱ期 3 项指标水平明显低于Ⅲ~Ⅳ期患者,说明其可以反映患者的分期状况,对于卵巢癌患者的治疗评估具有一定的潜在价值[10]。

通过上述研究,我们认为 CA125、HE4 及 ROMA 在卵巢癌临床诊断、分期中具有重要价值,尤其以 ROMA 临床价值为最大,有利于卵巢癌的临床鉴别诊断并有助于判断卵巢癌的临床分期。

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