

## 血清镁水平联合血小板与淋巴细胞比值用于辅助 诊断肢体创伤后骨髓炎的临床价值\*

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**摘要** 目的:探讨血清镁和血小板与淋巴细胞比值(PLR)在辅助诊断肢体创伤后骨髓炎(PTOM)的作用。方法:选取2013—2018年我院收治的78例肢体PTOM患者作为PTOM组,以89例无菌性骨不连(ABN)患者作为ABN组,以同期骨折愈合患者100例作为对照组。采用日立AU5832全自动生化分析仪和Sysmex XN-2800全自动血细胞分析仪检测血清镁水平和全血细胞计数,进一步计算PLR和中性粒细胞与淋巴细胞计数比值(NLR)。结果:PTOM组血清镁低于对照组和ABN组,PLR高于对照组和ABN组,而NLR高于对照组( $P<0.05$ )。PTOM组患者血清镁水平和PLR与年龄、性别分层无关( $P>0.05$ )。Logistic回归分析结果表明,血清镁和PLR为肢体PTOM的独立影响因素( $P<0.05$ )。PTOM患者血清镁水平与PLR无显著相关性( $r=-0.086, P>0.05$ )。ROC曲线下面积(AUC)表明血清镁水平(AUC=0.816, 95%CI: 0.753~0.879)和PLR(AUC=0.728, 95%CI: 0.649~0.808)的AUC可接受准确性较高(AUC>0.7)。二者联合预测AUC值为0.886(95%CI: 0.835~0.936),灵敏度和特异性分别为85.9%、78.0%。血清镁水平2.25 mg/dL和PLR181.35被确定为最佳截止值。结论:血清镁降低和PLR升高与PTOM密切相关,血清镁水平联合PLR检测有可能成为辅助诊断肢体PTOM的有效方法。

**关键词** 血清镁;血小板与淋巴细胞比值;创伤后骨髓炎;诊断

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### Clinical value of serum magnesium level combined with platelet-to-lymphocyte ratio in the auxiliary diagnosis of limb post-traumatic osteomyelitis

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**Abstract Objective:** To explore the role of serum magnesium and platelet-to-lymphocyte ratio (PLR) in the auxiliary diagnosis of limb post-traumatic osteomyelitis (PTOM). **Methods:** A total of 78 patients with limb PTOM treated in our hospital from 2013 to 2018 were included in the PTOM group, 89 patients with aseptic non-union (ABN) were included in the ABN group, and 100 patients with fracture healing in the same period were included in the control group. The serum magnesium level and whole blood cell counts were detected by Hitachi AU5832 automatic biochemical analyzer and Sysmex XN-2800 automatic blood cell analyzer, and PLR as well as neutrophil-to-lymphocyte ratio (NLR) were further calculated. **Results:** Serum magnesium in the PTOM group was lower than that in the control group and ABN group, PLR was higher than that in the control group and ABN group, and NLR was higher than that in the control group ( $P<0.05$ ). Serum magnesium level and PLR in the PTOM group were not related to age and gender stratification ( $P>0.05$ ). Logistic regression analysis showed that serum magnesium and PLR were independent influencing factors of limb PTOM ( $P<0.05$ ). There was no significant correlation between serum magnesium level and PLR in patients with PTOM ( $r=-0.086, P>0.05$ ). The area under ROC curve (AUC) showed that the acceptable accuracy of serum magnesium level (AUC=0.816, 95% CI: 0.753-0.879) and PLR (AUC=0.728, 95% CI: 0.649-0.808) was high (AUC>0.7). The combined prediction of

AUC was 0.886 (95% CI: 0.835-0.936), and the sensitivity and specificity were 85.9% and 78.0%, respectively. Serum magnesium levels of 2.25mg/dL

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and PLR of 181.35 were determined as the best cut-off values. **Conclusion:** The decrease of serum magnesium and the increase of PLR are closely related to PTOM. Serum magnesium level combined with PLR detection may be an effective method to assist the diagnosis of limb PTOM.

**Keywords** serum magnesium; platelet-to-lymphocyte ratio; post-traumatic osteomyelitis; diagnosis

创伤后骨髓炎(post-traumatic osteomyelitis, PTOM)是四肢慢性骨髓炎(chronic osteomyelitis, COM)最常见的类型之一,继发于机械损伤、交通事故造成的开放性骨折或者骨科手术感染<sup>[1]</sup>。诊断和治疗不及时或不规范,可导致临床治愈困难<sup>[2]</sup>。因此,鉴定潜在的生物标志物将有助于改善临床护理及预后。镁是人体必需的微量元素,是骨骼的重要组成部分,与炎症反应有关,在人体细胞的许多生理功能中发挥着重要作用<sup>[3]</sup>。据报道,血清镁水平降低与骨折风险增加有关<sup>[4-6]</sup>。尽管如此,人们对血清镁与PTOM风险之间的关系知之甚少。血小板与淋巴细胞比值(platelet-to-lymphocyte ratio, PLR)在当前许多临床研究中被认为是全身炎症的重要指标之一<sup>[7]</sup>。据报道,PLR在COM中显著升高,可以预测糖尿病足感染中的骨髓炎及截肢需要<sup>[8]</sup>。血清镁和PLR在PTOM中的诊断价值如何尚未清楚,为此,本研究对我院收治的78例肢体PTOM患者进行比较分析,以期对PTOM临床诊治提供参考。

## 1 资料与方法

### 1.1 研究对象

选取2013—2018年我院收治的78例肢体PTOM患者作为PTOM组,以89例无菌性骨不连(ABN)患者作为ABN组,以同期骨折愈合患者100例作为对照组。纳入研究的对象均符合相关的诊断标准<sup>[9-11]</sup>。PTOM组中,男54例,女24例,年龄31~87岁;ABN组中,男65例,女24例,年龄37~99岁;对照组中,男69例,女31例,年龄26~91岁。本研究方案经医院医学伦理委员会批准。

### 1.2 纳入和排除标准

纳入标准:(1)明确诊断为骨愈合、ABN或PTOM的患者;(2)患者具有正常的肾、肝和甲状腺功能;(3)具有完整的临床资料。排除标准:急性骨髓炎、关节炎、类风湿性关节炎、非暂时性骨感染或血源性或糖尿病足(DF)相关COM的患者;肾功能异常和肝功能异常、甲状腺功能亢进或甲状腺功能减退、共病、缺铁、癌症、肺结核、服用抗糖尿

病和抗疟药物、饮酒、激素缺乏性疾病、血液疾病以及服用可能影响血钙、磷、镁水平和血小板计数的药物者。

### 1.3 观察指标

1.3.1 一般资料 收集研究对象的人口统计学信息,包括年龄、性别、腰椎2~4(L2~L4)骨密度(bone mineral density, BMD)、桡骨BMD、全髌BMD、体质指数(body mass index,  $I_{bm}$ )、心血管疾病史、糖尿病史、甲状旁腺切除术、药物使用情况等。BMD采用美国LUNAR DPX-MD双能X线骨密度仪进行测定。

1.3.2 实验室指标 禁食8~12 h,于次日清晨在上臂根部从肘静脉采集所有研究对象外周血样本,置于4℃环境下,4 000 r/min离心15 min,分离血清,-80℃低温保存待测。采用贝克曼DXI800全自动化学发光免疫分析仪测定全段甲状旁腺激素。采用日立AU5832全自动生化分析仪测定白蛋白(albumin, ALB)、ALB校正血钙、血磷、尿素氮(blood urea nitrogen, BUN)、碱性磷酸酶(alkaline phosphatase, ALP)、C反应蛋白(C-reactive protein, CRP)、血红蛋白(hemoglobin, Hb)、血清镁水平。使用Sysmex XN-2800全自动血细胞分析仪器检测血小板(platelet count, PLT)、白细胞计数(white blood cell count, WBC)、中性粒细胞(neutrophil, NEU)、淋巴细胞(lymphocyte, LYM),计算中性粒细胞与淋巴细胞计数比值(neutrophil-to-lymphocyte ratio, NLR)及血小板与淋巴细胞比值(PLR)。

1.4 统计学方法 采用SPSS 26.0软件处理数据,正态分布的计量资料以均数±标准差( $\bar{x} \pm s$ )表示,组间比较采用单因素方差分析和两两比较的LSD-*t*检验。计数资料以百分率(%)表示,组间比较采用卡方检验。偏态分布数据以中位数[四分位间距( $M_{25} \sim M_{75}$ )]表示,并使用Kruskal-Wallis检验和事后Mann-Whitney *U*分析。采用二元logistic回归模型分析肢体PTOM的影响因素。采用受试者工作特征(receiver operating characteristic, ROC)曲线评估血清镁、PLR对肢体PTOM的诊断价值。采用Spearman相关分析方法分析血清镁水平与PLR的

相关性。所有检验均为双侧检验,以 $P<0.05$ 为差异有统计学意义。

2 结 果

2.1 一般资料比较 3组患者年龄、性别、全段甲状旁腺素、 $Ibm$ 、糖尿病史、甲状旁腺切除术、补充维生素D、磷结合剂、质子泵抑制剂(PPIs)、L2~L4段

BMD、桡骨BMD、全髌BMD、ALB校正血钙、血磷、ALP、CRP、Hb、BUN、WBC、NEU、PLT比较,差异无统计学意义( $P>0.05$ )。而心血管病史、ALB、LYM、NLR、PLR、血清镁水平比较,差异有统计学意义( $P<0.05$ );ABN组血清镁水平低于对照组,NLR高于对照组,而PTOM组血清镁水平低于对照组和ABN组,PLR高于对照组和ABN组,同时NLR高于对照组(均 $P<0.05$ ),见表1。

表1 3组一般资料比较

| 项目                                                                | 对照组( $n=100$ )        | ABN组( $n=89$ )                  | PTOM组( $n=78$ )                     | $\chi^2/u/F$ | $P$    |
|-------------------------------------------------------------------|-----------------------|---------------------------------|-------------------------------------|--------------|--------|
| 年龄/岁, $M(P_{25}\sim P_{75})$                                      | 65.00(49.00~71.75)    | 65.00(51.00~73.00)              | 66.50(50.00~74.25)                  | 3.290        | 0.201  |
| 男性, $n(\%)$                                                       | 69(69.0)              | 65(73.0)                        | 54(69.2)                            | 0.442        | 0.802  |
| $Ibm/(\text{kg}/\text{m}^2)$ , $M(P_{25}\sim P_{75})$             | 22.39(18.28~25.81)    | 21.30(18.01~24.06) <sup>a</sup> | 21.06(18.03~24.58) <sup>a</sup>     | 4.238        | 0.073  |
| 心血管病史, $n(\%)$                                                    | 24(24.0)              | 40(44.9) <sup>a</sup>           | 27(34.6)                            | 9.208        | 0.010  |
| 糖尿病史, $n(\%)$                                                     | 36(36.0)              | 38(42.6)                        | 38(48.7)                            | 2.941        | 0.230  |
| 甲状旁腺切除术, $n(\%)$                                                  | 5(5.0)                | 4(4.4)                          | 1(1.2)                              | 1.888        | 0.389  |
| 药物, $n(\%)$                                                       |                       |                                 |                                     |              |        |
| 维生素D                                                              | 72(72.0)              | 71(79.7)                        | 56(71.7)                            | 1.935        | 0.380  |
| PPIs                                                              | 56(56.0)              | 58(65.1)                        | 52(66.6)                            | 2.630        | 0.269  |
| 磷结合剂                                                              | 51(51.0)              | 39(43.8)                        | 36(46.1)                            | 1.022        | 0.200  |
| 全段甲状旁腺素/<br>( $\text{mg}/\text{L}$ ), $M(P_{25}\sim P_{75})$      | 163.00(104.00~231.00) | 137.00(98.50~205.50)            | 123.00(66.50~76.00)                 | 4.272        | 0.118  |
| L2-L4段BMD/<br>( $\text{mg}/\text{cm}^2$ ), $M(P_{25}\sim P_{75})$ | 0.99(0.86~1.10)       | 1.02(0.88~1.23)                 | 1.00(0.87~1.16)                     | 3.785        | 0.311  |
| 桡骨BMD/<br>( $\text{mg}/\text{cm}^2$ ), $M(P_{25}\sim P_{75})$     | 0.71(0.54~0.84)       | 0.81(0.60~0.92)                 | 0.77(0.55~0.87)                     | 4.888        | 0.104  |
| 全髌BMD/( $\text{mg}/\text{cm}^2$ ), $\bar{x}\pm s$                 | 0.72 $\pm$ 0.16       | 0.76 $\pm$ 0.20                 | 0.73 $\pm$ 0.15                     | 1.350        | 0.261  |
| 血钙/( $\text{mg}/\text{dL}$ ), $M(P_{25}\sim P_{75})$              | 8.90(8.60~79.30)      | 9.10(8.70~9.40)                 | 9.20(8.68~9.50)                     | 1.780        | 0.411  |
| 血磷/( $\text{mg}/\text{dL}$ ), $\bar{x}\pm s$                      | 5.20 $\pm$ 1.03       | 5.12 $\pm$ 1.20                 | 4.95 $\pm$ 1.33                     | 1.001        | 0.369  |
| 血镁/( $\text{mg}/\text{dL}$ ), $M(P_{25}\sim P_{75})$              | 2.75(2.40~2.95)       | 2.30(2.20~2.50) <sup>a</sup>    | 2.00(1.70~2.40) <sup>ab</sup>       | 84.572       | <0.001 |
| ALP/( $\text{U}/\text{L}$ ), $M(P_{25}\sim P_{75})$               | 240.50(189.25~323.75) | 266.00(199.75~331.50)           | 239.50(196.25~310.50)               | 1.678        | 0.432  |
| CRP/( $\text{mg}/\text{dL}$ ), $M(P_{25}\sim P_{75})$             | 0.10(0.05~0.22)       | 0.21(0.07~0.48)                 | 0.12(0.05~0.33)                     | 4.548        | 0.103  |
| ALB/( $\text{g}/\text{L}$ ), $M(P_{25}\sim P_{75})$               | 3.70(3.40~3.90)       | 3.50(3.30~3.70) <sup>a</sup>    | 3.50(3.30~3.80) <sup>a</sup>        | 13.381       | 0.001  |
| Hb/( $\text{g}/\text{L}$ ), $\bar{x}\pm s$                        | 11.21 $\pm$ 1.07      | 10.92 $\pm$ 1.05                | 10.95 $\pm$ 1.41                    | 1.744        | 0.177  |
| BUN/( $\text{mg}/\text{dL}$ ), $\bar{x}\pm s$                     | 56.54 $\pm$ 11.33     | 55.37 $\pm$ 12.58               | 53.13 $\pm$ 14.63                   | 1.579        | 0.208  |
| WBC/( $\times 10^9/\text{L}$ ), $M(P_{25}\sim P_{75})$            | 6.19(5.41~7.56)       | 5.97(5.11~8.58)                 | 5.98(4.71~7.58)                     | 2.570        | 0.277  |
| NEU/( $\times 10^9/\text{L}$ ), $M(P_{25}\sim P_{75})$            | 3.96(3.16~5.18)       | 4.02(2.96~5.82)                 | 4.03(2.92~5.10)                     | 1.223        | 0.543  |
| LYM/( $\times 10^9/\text{L}$ ), $M(P_{25}\sim P_{75})$            | 1.85(1.61~2.35)       | 1.60(1.18~2.10) <sup>a</sup>    | 1.57(1.24~2.05) <sup>a</sup>        | 14.316       | 0.001  |
| PLT/( $\times 10^9/\text{L}$ ), $M(P_{25}\sim P_{75})$            | 237.50(203.00~265.00) | 239.00(181.00~278.00)           | 258.00(184.00~311.75)               | 0.353        | 0.838  |
| NLR, $M(P_{25}\sim P_{75})$                                       | 2.14(1.62~2.67)       | 2.40(1.77~3.39) <sup>a</sup>    | 2.87(1.78~4.11) <sup>a</sup>        | 14.241       | 0.001  |
| PLR, $M(P_{25}\sim P_{75})$                                       | 125.84(102.15~150.23) | 138.81(105.39~188.97)           | 165.17(114.75~271.15) <sup>ab</sup> | 18.418       | <0.001 |

与对照组相比,<sup>a</sup> $P<0.05$ ;与ABN组相比,<sup>b</sup> $P<0.05$ 。

2.2 PTOM组血镁水平和PLR的亚组分析 由于年龄和性别可能会影响血镁水平和全血细胞计数,因此按年龄(60岁以下和60岁以上)和性别进行亚组分析。由于ABN组和PTOM组NLR无显著差异,因此未对该指标进行进一步分层分析。结果显示,两个年龄组之间的血清镁水平[1.95(1.70~2.40)mg/dL vs. 2.05(1.78~2.40)mg/dL,  $Z=-0.770$ ,  $P=0.441$ ]和PLR[185.10(117.15~256.59) vs. 163.84(106.38~285.58),  $Z=-0.544$ ,  $P=0.586$ ]均无显著差异。男性患者和女性患者之间血清镁水平[2.10(1.85~2.45)mg/dL vs. 2.00(1.75~2.45)mg/dL,  $Z=-1.021$ ,  $P=0.307$ ]和PLR[146.09(95.30~264.46) vs. 213.33(144.32~287.02),  $Z=-1.095$ ,  $P=0.274$ ]比较差异亦无统计学意义( $P>0.05$ )。

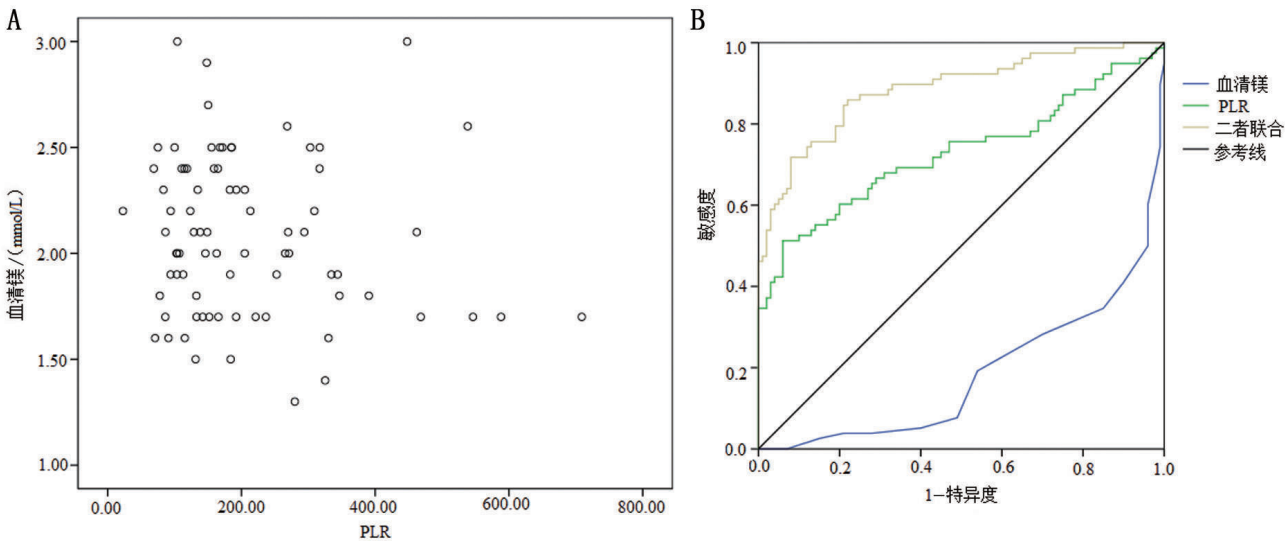
2.3 肢体PTOM影响因素的多因素logistic回归分

析 以是否发生PTOM作为因变量,将表1中 $P<0.01$ 的变量作为自变量纳入多因素回归模型,经logistic回归分析,血清镁和PLR均为肢体PTOM的独立影响因素( $P<0.05$ ),见表2。

2.4 血清镁水平与PLR在PTOM诊断中的相关性 及预测价值 Spearman秩相关系数分析结果显示,PTOM患者血清镁水平与PLR之间没有相关性( $r=-0.086$ ,  $P>0.05$ ),见图1A。ROC曲线的AUC表明,血清镁水平(AUC=0.775,  $P<0.001$ , 95%CI: 0.703~0.829)和PLR(AUC=0.728,  $P<0.001$ , 95%CI: 0.649~0.808)的AUC可接受准确性较高(AUC>0.7)。二者联合检测,AUC升高至0.886(95%CI: 0.835~0.936),灵敏度和特异性分别为85.9%、78.0%。血清镁水平2.25 mg/dL和PLR 181.35为最佳截止值(图1B)。

表2 多因素logistic回归分析影响肢体PTOM的临床因素

| 指标     | PTOM组 vs. ABN组 |       |        |                    |        | PTOM组 vs. 对照组 |       |        |                    |        |
|--------|----------------|-------|--------|--------------------|--------|---------------|-------|--------|--------------------|--------|
|        | $\beta$        | SE    | Walds  | OR(95%CI)          | P      | $\beta$       | SE    | Walds  | OR(95%CI)          | P      |
| Ibm    | -0.110         | 0.046 | 5.691  | 0.896(0.818~1.981) | 0.217  | -0.141        | 0.073 | 3.731  | 0.869(0.753~1.002) | 0.053  |
| 心血管疾病史 | -0.344         | 0.352 | 0.958  | 0.709(0.356~1.412) | 0.328  | 0.736         | 0.542 | 1.848  | 2.088(0.722~6.037) | 0.174  |
| 血镁     | -2.467         | 0.610 | 16.366 | 0.085(0.026~0.280) | <0.001 | -4.910        | 0.876 | 31.436 | 0.007(0.001~0.041) | <0.001 |
| ALB    | -              | -     | -      | -                  | -      | -0.903        | 0.629 | 2.064  | 0.405(0.118~1.390) | 0.151  |
| NLR    | -              | -     | -      | -                  | -      | 0.306         | 0.178 | 2.955  | 1.358(0.958~1.925) | 0.086  |
| PLR    | 0.005          | 0.002 | 5.979  | 1.005(1.001~1.009) | 0.015  | 0.014         | 0.005 | 7.842  | 1.015(1.004~1.025) | 0.005  |



A: 血清镁水平与PLR相关性分析; B: 血清镁水平、PLR及二者联合诊断PTOM的ROC曲线。  
图1 血清镁水平和PLR在PTOM中的诊断价值



### 3 讨 论

PTOM作为最常见的肢体COM类型之一,是开放性骨折和骨科手术后的后遗症或并发症<sup>[1]</sup>,由于病程长、感染复发率高、身心残疾风险高,对临床治疗构成巨大挑战<sup>[2]</sup>。而因其发生过程中损伤机制的不同,目前关于PTOM发病机制也未完全阐明,使得临床上准确的早期发现和诊断PTOM仍然面临较大的困难。

影像学检查作为临床诊断的主要手段之一,在PTOM的诊断中具有重要的地位,X线平片、MRI、三相骨显像、WBC显像、抗粒细胞抗体显像、氟代脱氧一葡萄糖正电子发射断层扫描、CT等经常用于诊断或排除PTOM,虽然这些方法很大程度上有助于评估金属内固定物的位置及骨折愈合程度,但往往难以鉴别感染,到目前为止,在最佳的影像学检查上也尚无公认的专家共识<sup>[12]</sup>。此外,还有许多生物标记物,如血沉、降钙素原、WBC等和分泌物细菌培养被报道用于辅助诊断PTOM,但由于特异性较低、细菌培养所需时间较长且敏感度不高而难以早期诊断<sup>[13-14]</sup>。血清镁水平和PLR是临床诊断的常见指标。最近,一些细菌性传染病已被证明与血清镁水平降低和PLR增加有关<sup>[15-16]</sup>。此外,在患有包括骨髓炎、化脓性关节炎等在内的细菌感染疾病的患儿中,PLR显著升高,在疾病诊断中具有较高的预测价值<sup>[17-18]</sup>。在本研究中,与对照组和ABN组相比,PTOM患者更容易出现低镁血症和PLR升高,且不受年龄、性别等客观因素的干扰。提示血清镁水平和PLR能更好地反应机体感染情况,参与机体炎症反应。

本研究logistic回归分析结果发现,血清镁水平和PLR均为肢体PTOM的独立影响因素,提示血清镁和PLR可能参与PTOM的发病机制,理由是:许多传染病在发展过程中伴有PLR、NLR、血钙、血镁、血磷等水平的异常<sup>[19-20]</sup>,一方面镁缺乏引起人体炎症,其机制包括启动促炎因子白细胞介素-1 $\beta$ 和肿瘤坏死因子- $\alpha$ 的过度产生和释放以及激活吞噬细胞、打开钙通道、激活N-甲基-D-天冬氨酸受体和NF- $\kappa$ B信号传导,以及刺激一氧化氮和炎症标志物的合成<sup>[21]</sup>。另一方面,镁缺乏还会增加人体中血小板聚集和黏附性,并抑制内皮细胞的生长和迁移,改变微血管功能<sup>[8]</sup>。PLR是血小板和淋巴细胞计数比值,在当前许多临床研究中被认为是全身炎症的

指标,其水平升高表明人体处于持续的炎症状态<sup>[7,22]</sup>。本研究ROC曲线结果显示,血清镁水平和PLR在PTOM诊断中均具有较高预测价值,AUC分别为0.775和0.728,这与Demirdal等<sup>[8]</sup>研究结果相似,PLR预测骨髓炎的最佳切点为141.57,较本研究PLR最佳截止值(181.35)稍微降低,推测可能与PLR在不同患者中分布差异或纳入患者的严重程度及样本量有关。但单独用于预测PTOM诊断的AUC较低,若二者联合检测,可将AUC提高至0.886,表明二者联合检测可显著提高其临床应用价值。提示应密切监测病情和早期规范化干预和管理,必要时补充镁,并降低PLR,以避免PTOM发生。

综上所述,血清镁水平降低和PLR升高与PTOM密切相关,血清镁水平联合PLR检测有可能成为辅助诊断肢体PTOM的有效方法。但是本研究也存在一定的局限性,如患者人数较少和没有将血沉、CRP、WBC等典型炎症指标与血清镁水平和PLR结合起来进行骨髓炎诊断,仍需要更多的临床研究来进一步明确。

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