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子宫肌瘤外周血生物标记物的研究进展

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摘 要

子宫肌瘤(uterine leiomyoma, UL)是女性最常见的生殖系统良性肿瘤，约50% UL患者出现临床症状，严重影响生活质量，且尚无明确的实验室检查作为辅助检查手段。炎症反应在子宫平滑肌瘤发病机制中发挥重要作用。血小板－淋巴细胞比值、中性粒细胞－淋巴细胞比值、淋巴细胞－单核细胞比值和系统免疫炎症指数是炎症反应的综合反射，很容易从完整的血细胞计数中测量得出，也是临床可以使用的新兴炎症标志物，同时可作为多种疾病的生物标志物。因此，探讨PLR、NLR、LMR和SII在子宫肌瘤发生发展中的作用，可以更好地指导临床工作，对子宫肌瘤进行有效的一级和二级预防，延缓疾病的发展。

关键词

子宫肌瘤，生物标记物，PLR，NLR，LMR，SII

Advances in the Study of Peripheral Blood Biomarkers for Uterine Leiomyoma

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Abstract

Uterine leiomyoma (UL) is the most common benign tumour of the reproductive system in women. Approximately 50% of patients with UL present with clinical symptoms that severely affect quality of life, and there are no definitive laboratory tests available as an adjunct. The inflammatory re-

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sponse plays an important role in the pathogenesis of uterine smooth muscle tumours. The platelet-lymphocyte ratio, neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio and systemic immune inflammatory index are comprehensive reflections of the inflammatory response that can be easily measured from a complete blood count and are emerging inflammatory markers that can be used clinically, as well as being used as biomarkers for a variety of diseases. Therefore, exploring the role of PLR, NLR, LMR and SII in the development of uterine fibroids can better guide clinical efforts to provide effective primary and secondary prevention of fibroids and delay the progression of the disease.

Keywords

Uterine Leiomyoma, Biomarkers, PLR, NLR, LMR, SII

1. 引言

子宫肌瘤(uterine leiomyoma, UL)是女性最常见的生殖系统良性肿瘤，其特点是子宫平滑肌细胞增殖紊乱，细胞外基质(ECM)沉积改变以及对性类固醇激素的反应增强[1] [2]。流行病学调查显示，中国女性子宫肌瘤 2016 年负担较 1990 年明显增加，其患病率随年龄增加而增加，并于 45~49 岁达顶峰，之后随年龄增加而降低[3]。出现临床症状的子宫肌瘤女性约占一半，包括经期延长、经量增多、腹痛腹胀等，严重影响了患者生活质量[4] [5]；同时，粘膜下肌瘤和多数肌壁间肌瘤导致不育和不良妊娠结局也成为子宫肌瘤手术指征之一，严重影响生活质量[6] [7] [8]。UL 早期诊断方法包括影像学检查、临床症状及体格检查，其金标准为病理学检查，仍无明确的实验室检查作为辅助诊断方法。所以，寻找 UL 早期诊断的生物标记物显得尤为重要。随着子宫平滑肌瘤研究的深入，炎症反应在子宫平滑肌瘤发病机制中发挥重要作用[9]。因此，探讨适用于 UL 早期诊断的炎症标记物成为广大临床工作者亟待解决的问题。

2. 外周血炎症指标

越来越多的研究发现，免疫炎症反应在 UL 发生发展中发挥关键作用，包括激活免疫系统细胞通路及释放细胞因子、趋化因子和炎症介质等[10] [11] [12]。但机体炎症介质检测方法较为复杂，尚无简便易得且经济的方法进行检测。血小板－淋巴细胞比值(Platelet-Lymphocyte Ratio, PLR)、中性粒细胞－淋巴细胞比值(Neutrophil-Lymphocyte Ratio, NLR)、淋巴细胞－单核细胞比值(Lymphocyte-Monocyte Ratio, LMR)和系统免疫炎症指数(systemic immune-inflammation index, SII)是炎症反应的综合反射，很容易从完整的血细胞计数中测量得出，也是临床可以使用的新兴炎症标志物，同时可作为多种疾病的生物标志物[13]。

2.1. 血小板－淋巴细胞比值(PLR)

血小板存在于血管外微环境中，激活的血小板可以分泌转化生长因子 β (TGF-β)，血管内皮生长因子(VEGF)等因子促进肿瘤新生血管的形成及肿瘤生长[14] [15]。同时，血小板包裹肿瘤细胞以及诱导肿瘤细胞表达 MMP-9，从而抑制免疫系统监视杀伤肿瘤细胞[16]。淋巴细胞产生于淋巴器官，在淋巴管中循环的淋巴液中进行储存，在肿瘤免疫微环境中调节免疫应答。此外，可以分泌 IL-6、VEGF 等免疫生长

因子及抑制因子，促进肿瘤细胞免疫逃逸[17] [18]。

血小板－淋巴细胞比值(Platelet-Lymphocyte Ratio, PLR)是可以反应机体炎症状态的重要指标，也是转化淋巴细胞计数与中性粒细胞计数之间变化的生物标记物。当肿瘤细胞触发机体免疫防御反应，导致淋巴细胞相对减少及血小板计数相对增加，从而引起外周血 PLR 值增加[19]。Templeton 等人结合 20 余项研究使用荟萃分析，探讨了 PLR 在 12754 名实体肿瘤患者预后中的作用。分析结果显示，高 PLR 和多种实体肿瘤的生存率呈负相关，也就是说，PLR 值越高，机体肿瘤负荷越重，抗肿瘤能力越弱，预后越差[20]。研究指出，高 PLR 是肺癌死亡的重要因素[21]。既往研究[22] [23]表明，PLR 是 COVID-19 预后的一个独立危险因素，患者的死亡与较高的 PLR 有明显关系。一项临床研究[24]认为，PLR 是恶性肿瘤术后转移的独立危险因素，高 PLR 意味着术后转移率高。在针对平滑肌瘤的鉴别诊断研究中[25] [26]指出，PLR 是建立诊断平滑肌瘤预测模型的重要指标。

2.2. 中性粒细胞－淋巴细胞比值(NLR)

中性粒细胞来源于骨髓静脉窦深处的髓系祖细胞，具有调节炎症反应、肿瘤免疫微环境、急慢性损伤等多种免疫功能，也是抵御病原体入侵的第一道防线[27]。中性粒细胞作为炎症细胞的重要组成部分，参与机体急慢性炎症反应、损伤修复、肿瘤免疫微环境的调节及自身免疫力调节等多个免疫环节[28]。实体肿瘤组织产生后，巨噬细胞演化为肿瘤相关巨噬细胞(TAM)，可以将中性粒细胞聚集于实体肿瘤微环境中。在炎症介质、细胞因子 TNF、IL-8 等介导下，中性粒细胞分化为不同作用类型的中性粒细胞，释放多种调控实体肿瘤增殖代谢的物质如活性氧、白介素因子以及 VEGF 等，从而达到抑制免疫反应、促进实体肿瘤血管生成及肿瘤转移的作用[29] [30]。淋巴细胞产生细胞毒性酶穿孔素、颗粒酶 B 等多种细胞因子，从而抑制实体肿瘤细胞增殖、转移。Ruan、Silatha Sakamuru 等人[31] [32]研究认为抑制免疫反应时，导致肿瘤治疗相关性和非肿瘤治疗相关性淋巴细胞减少症，均会影响小细胞肺癌的预后。

中性粒细胞－淋巴细胞比值(Neutrophil-Lymphocyte Ratio, NLR)与血小板－淋巴细胞比值(PLR)一样，也是机体防御能力与炎症免疫之间变化的综合反应[33]。机体对肿瘤细胞产生免疫防御反应时，相对于中性粒细胞，淋巴细胞相对减少。最终免疫细胞为能识别肿瘤细胞，造成了肿瘤细胞免疫逃逸，使肿瘤出现转移或浸润，反映在外周血表现则是 NLR 值增高[34]。Xu 等人通过 NHANES 数据库进行了一项横断面研究[35]，结果显示 NLR 值与高血压患病率呈正相关关系，研究认为高 NLR 值是高血压患病的危险因素。NLR、PLR 可以用于早期实体肿瘤的诊断，一项针对胃癌患者的研究结果显示，在早期诊断中 NLR、PLR 等新兴炎症标记物的精确度高于 CA199 等传统肿瘤标记物，对其进行分层分析显示，男性发病人群中，联合 NLR 与 PLR 进行检测效果更佳[36]。NLR 和 PLR 除了用于实体肿瘤的早期诊断，还用于预测实体肿瘤患者不良预后结局，近期关于乳腺癌和胆管癌等多项研究均提及了 NLR 和 PLR 用于预测实体肿瘤预后的重要作用[37] [38]。

2.3. 淋巴细胞－单核细胞比值(LMR)

单核细胞是血液中最大血细胞，也是体积最大白细胞，是机体防御系统的重要组成部分。在机体中，巨噬/单核细胞存在于不同组织，其功能也有所差异，分布于组织中为巨噬细胞，分布于血液中为单核细胞。组织中的巨噬细胞及时发现侵袭机体的病原体，并且对他们进行攻击、吞噬，然后启动体液免疫功能及机体修复功能。同时，当巨噬/单核细胞被激活后产生炎症反应，对机体造成不可逆转的损害[39]。

淋巴细胞－单核细胞比值(Lymphocyte-Monocyte Ratio, LMR)作为新兴炎症指标，简便易得，可以反应多种疾病的炎症状态。近期研究[40]显示，浸润性乳腺癌患者术前低 LMR 值是影响患者预后的独立危险因素，且 LMR 值与预后呈正相关。一项针对胃癌淋巴结转移的研究[41]认为，低 LMR 值与胃癌患者

淋巴结转移数量呈正相关关系，且对于胃癌患者淋巴结转移情况有预测价值。

2.4. 系统免疫炎症指数(SII)

系统免疫炎症指数(systemic immune-inflammation index, SII)是一种基于中性粒细胞、淋巴细胞及血小板计数的新兴免疫标记物，在实体肿瘤的诊疗中发挥了重要作用。同时，Meta 分析[42]指出，高 SII 值与非小细胞肺癌总生存期短、无病生存期短及无复发生存期短存在显著相关性，因此 SII 值对于非小细胞肺癌患者的预后具有重要预测意义。此外，SII 值较高也是多种实体肿瘤及肿瘤转移的独立危险因素[43] [44]。

3. 展望

子宫肌瘤是最常见的妇科良性肿瘤，严重影响了患者的生活质量，给家庭和患者带来严重的经济和社会问题。因此，找到一个有效的监测指标来指导子宫肌瘤的一级和二级治疗显得尤为重要。PLR、NLR、LMR 和 SII 是新兴的炎症标志物，可作为多种疾病的生物标志物，也可以反映肿瘤微环境的免疫细胞浸润状况。虽然其简单易得价廉，在临床上可以大规模得到，但易受外界因素影响，特异性较差，仍需大量临床研究进一步确定。因此，探讨 PLR、NLR、LMR 和 SII 在子宫肌瘤发生发展中的作用，可以更好地指导临床工作，对子宫肌瘤进行有效的一级和二级预防，延缓疾病的发展。

参考文献

[1] McWilliams, M.M. and Chennathukuzhi, V.M. (2017) Recent Advances in Uterine Fibroid Etiology. *Seminars in Reproductive Medicine*, **35**, 181-189. https://doi.org/10.1055/s-0037-1599090

[2] Giuliani, E., As-Sanie, S. and Marsh, E.E. (2020) Epidemiology and Management of Uterine Fibroids. *International Journal of Gynecology & Obstetrics*, **149**, 3-9. https://doi.org/10.1002/ijgo.13102

[3] 吉宁, 王黎君, 刘世炜, 刘敏, 曾新颖, 周脉耕. 1990 年与 2016 年中国女性子宫纤维瘤的疾病负担研究[J]. 中华流行病学杂志, 2019, 40(2): 160-164.

[4] 李雅. 中药化癥汤治疗子宫肌瘤的临床疗效分析[J]. 当代临床医刊, 2022, 35(3): 49-50.

[5] Borah, B.J., Nicholson, W.K., Bradley, L. and Stewart, E.A. (2013) The Impact of Uterine Leiomyomas: A National Survey of Affected Women. *American Journal of Obstetrics & Gynecology*, **209**, 319.e1-319.e20. https://doi.org/10.1016/j.ajog.2013.07.017

[6] Lu, B., Wang, Q., Yan, L., Yu, K. and Cai, Y. (2022) Analysis of Pregnancy Outcomes after Laparoscopic Myomectomy: A Retrospective Cohort Study. *Computational and Mathematical Methods in Medicine*, **2022**, Article ID: 9685585. https://doi.org/10.1155/2022/9685585

[7] Zhu, W., Mao, S., Chen, Y. and Kong, X. (2022) Analysis of Clinical Efficacy of Laparoendoscopic Single-Site Surgery for Uterine Fibroids. *Journal of Healthcare Engineering*, **2022**, Article ID: 5606998. https://doi.org/10.1155/2022/5606998

[8] Perutelli, A., Domenici, L., Garibaldi, S., Albanesi, G., Baroni, C., Salvati, L., Salvati, N., Cecchi, E., Bottone, P. and Salerno, M.G. (2022) Efficacy and Safety of Robotic-Assisted Surgery in Challenging Hysterectomies—A Single Institutional Experience. *European Review for Medical and Pharmacological Sciences*, **26**, 1235-1240.

[9] Islam, M. S., Ciavattini, A., Petraglia, F., Castellucci, M. and Ciarmela, P. (2018) Extracellular Matrix in Uterine Leiomyoma Pathogenesis: A Potential Target for Future Therapeutics. *Human reproduction Update*, **24**, 59-85. https://doi.org/10.1093/humupd/dmx032

[10] Orciani, M., Caffarini, M., Biagini, A., Lucarini, G., Delli Carpini, G., Berretta, A., Di Primio, R. and Ciavattini, A. (2018) Chronic Inflammation May Enhance Leiomyoma Development by the Involvement of Progenitor Cells. *Stem Cells International*, **2018**, Article ID: 1716246. https://doi.org/10.1155/2018/1716246

[11] Yang, Q., Ali, M., El Andaloussi, A. and Al-Hendy, A. (2018) The Emerging Spectrum of Early Life Exposure-Related Inflammation and Epigenetic Therapy. *Cancer Studies and Molecular Medicine*, **4**, 13-23. https://doi.org/10.17140/CSMMOJ-4-125

[12] Cetin, E., Al-Hendy, A. and Ciebiera, M. (2020) Non-Hormonal Mediators of Uterine Fibroid Growth. *Current Opinion in Obstetrics and Gynecology*, **32**, 361-370. https://doi.org/10.1097/GCO.0000000000000650

[13] Tang, Y., Peng, B., Liu, J., Liu, Z., Xia, Y. and Geng, B. (2022) Systemic Immune-Inflammation Index and Bone Mineral Density in Postmenopausal Women: A Cross-Sectional Study of the National Health and Nutrition Examination Survey (NHANES) 2007-2018. *Frontiers in Immunology*, **13**, Article 975400. https://doi.org/10.3389/fimmu.2022.975400

[14] Schlesinger, M. (2018) Role of Platelets and Platelet Receptors in Cancer Metastasis. *Journal of Hematology & Oncology*, **11**, Article No. 125. https://doi.org/10.1186/s13045-018-0669-2

[15] Zufferey, A., Fontana, P., Reny, J.L., Nolli, S. and Sanchez, J.C. (2012) Platelet Proteomics. *Mass Spectrometry Reviews*, **31**, 331-351. https://doi.org/10.1002/mas.20345

[16] Palumbo, J.S., Talmage, K.E., Massari, J.V., *et al*. (2005) Platelets and Fibrin(ogen) Increase Metastatic Potential by Impeding Natural Killer Cell-Mediated Elimination of Tumor Cells. *Blood*, **105**, 178-185. https://doi.org/10.1182/blood-2004-06-2272

[17] Rahir, G. and Moser, M. (2012) Tumor Microenvironment and Lymphocyte Infiltration. *Cancer Immunology, Immunotherapy*, **61**, 751-759. https://doi.org/10.1007/s00262-012-1253-1

[18] Sakamuru, S., Attene-Ramos, M.S. and Xia, M. (2016) Mitochondrial Membrane Potential Assay. In: Zhu, H. and Xia, M., Eds., *High-Throughput Screening Assays in Toxicology*. *Methods in Molecular Biology*, Vol. 1473, Humana Press, New York, 17-22. https://doi.org/10.1007/978-1-4939-6346-1_2

[19] Damar Çakırca, T., Torun, A., Çakırca, G. and Portakal, R.D. (2021) Role of NLR, PLR, ELR and CLR in differentiating COVID-19 patients with and without pneumonia. *International Journal of Clinical Practice*, **75**, e14781. https://doi.org/10.1111/ijcp.14781

[20] Templeton, A.J., Ace, O., McNamara, M.G., *et al*. (2014) Prognostic Role of Platelet to Lymphocyte Ratio in Solid Tumors: A Systematic Review and Meta-Analysis. *Cancer Epidemiology, Biomarkers & Prevention*, **23**, 1204-1212. https://doi.org/10.1158/1055-9965.EPI-14-0146

[21] Mandaliya, H., Jones, M., Oldmeadow, C. and Nordman, I.I. (2019) Prognostic Biomarkers in Stage IV Non-Small Cell Lung Cancer (NSCLC): Neutrophil to Lymphocyte Ratio (NLR), Lymphocyte to Monocyte Ratio (LMR), Platelet to Lymphocyte Ratio (PLR) and Advanced Lung Cancer Inflammation Index (ALI). *Translational Lung Cancer Research*, **8**, 886-894. https://doi.org/10.21037/tlcr.2019.11.16

[22] Zhu, S., Dong, L. and Cai, W. (2020) Predictive Value of Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratio in COVID-19. *Critical Care*, **24**, Article No. 532. https://doi.org/10.1186/s13054-020-03258-x

[23] Sarkar, S., Kannan, S., Khanna, P. and Singh, A.K. (2022) Role of Platelet-to-Lymphocyte Count Ratio (PLR), as a Prognostic Indicator in COVID-19: A Systematic Review and Meta-Analysis. *Journal of Medical Virology*, **94**, 211-221. https://doi.org/10.1002/jmv.27297

[24] Chen, Y., Zeng, J., Guo, P., Zeng, J. and Liu, J. (2021) Prognostic Significance of Platelet-to-Lymphocyte Ratio (PLR) in Extrahepatic Metastasis of Hepatocellular Carcinoma after Curative Resection. *Cancer Management and Research*, **13**, 1395-1405. https://doi.org/10.2147/CMAR.S290738

[25] Zhai, Y.-H., Zheng, Z., Deng, W., Yin, J., Bai, Z.-G., Liu, X.-Y., Zhang, J. and Zhang, Z.-T. (2022) Inflammation-Related Indicators to Distinguish between Gastric Stromal Tumors and Leiomyomas: A Retrospective Study. *World Journal of Clinical Cases*, **10**, 458-468. https://doi.org/10.12998/wjcc.v10.i2.458

[26] Jing, X., Li, C., Sun, J., Peng, J., Dou, Y., Xu, X., Ma, C., Dong, Z., Liu, Y., Zhang, H., Shao, Q., Zhang, H., Wang, L., Zhang, Y. and Qu, X. (2020) Systemic Inflammatory Response Markers Associated with Infertility and Endometrioma or Uterine Leiomyoma in Endometriosis. *Therapeutics and Clinical Risk Management*, **16**, 403-412. https://doi.org/10.2147/TCRM.S232849

[27] 徐茵, 王玉月, 徐婷, 董伟民, 顾伟英. 中性粒细胞 CD64 在恶性血液病伴感染诊断中应用的研究进展[J]. 白血病·淋巴瘤, 2020, 29(10): 630-633.

[28] Liew, P.X. and Kubes, P. (2019) The Neutrophil's Role during Health and Disease. *Physiological Reviews*, **99**, 1223-1248. https://doi.org/10.1152/physrev.00012.2018

[29] Comen, E., Wojnarowicz, P., Seshan, V.E., *et al*. (2016) TNF Is a Key Cytokine Mediating Neutrophil Cytotoxic Activity in Breast Cancer Patients. *NPJ Breast Cancer*, **2**, Article No. 16009. https://doi.org/10.1038/npjbcancer.2016.9

[30] Ramakrishnan, G., Augustine, T.A., Jagan, S., Vinodhkumar, R. and Devaki, T. (2007) Effect of Silymarin on N-Nitrosodiethylamine Induced Hepatocarcinogenesis in Rats. *Experimental Oncology*, **29**, 39-44.

[31] Sen, T., Rodriguez, B.L., Chen, L., *et al.* (2019) Targeting DNA Damage Response Promotes Antitumor Immunity through STING-Mediated T-Cell Activation in Small Cell Lung Cancer. *Cancer Discovery*, **9**, 646-661. https://doi.org/10.1158/2159-8290.CD-18-1020

[32] Ruan, J.-S., Liu, Y.-P., Zhang, L., *et al*. (2012) Luteolin Reduces the Invasive Potential of Malignant Melanoma Cells by Targeting Beta-3-Integrin and the Epithelial-Mesenchymal Transition. *Acta Pharmacologica Sinica*, **33**, 1325-1331. https://doi.org/10.1038/aps.2012.93

[33] Capone, M., Giannarelli, D., Mallardo, D., Madonna, G., Festino, L., Grimaldi, A.M., Vanella, V., Simeone, E., Paone, M., Palmieri, G., Cavalcanti, E., Caracò, C. and Ascierto, P.A. (2018) Baseline Neutrophil-to-Lymphocyte Ratio (NLR) and Derived NLR Could Predict Overall Survival in Patients with Advanced Melanoma Treated with Nivolumab. *Journal for ImmunoTherapy of Cancer*, **6**, Article No. 74. https://doi.org/10.1186/s40425-018-0383-1

[34] Karantanos, T., Karanika, S., Seth, B. and Gignac, G. (2019) The Absolute Lymphocyte Count Can Predict the Overall Survival of Patients with Non-Small Cell Lung Cancer on Nivolumab: A Clinical Study. *Clinical and Translational Oncology*, **21**, 206-212. https://doi.org/10.1007/s12094-018-1908-2

[35] Xu, J.-P., Zeng, R.-X., Zhang, Y.-Z., Lin, S.-S., Tan, J.-W., Zhu, H.-Y., Mai, X.-Y., Guo, L.-H. and Zhang, M.-Z. (2023) Systemic Inflammation Markers and the Prevalence of Hypertension: A NHANES Cross-Sectional Study. *Hypertension Research*. https://doi.org/10.1038/s41440-023-01195-0

[36] Fang, T., Wang, Y., Yin, X., *et al*. (2020) Diagnostic Sensitivity of NLR and PLR in Early Diagnosis of Gastric Cancer. *Journal of Immunology Research*, **2020**, Article ID: 9146042. https://doi.org/10.1155/2020/9146042

[37] Ge, M.-Y., Liu, Z.-P., Pan, Y., Wang, J.-Y., Wang, X., Dai, H.-S., Gao, S.-Y., Zhong, S.-Y., Che, X.-Y., Zuo, J.-H., Liu, Y.-H., Liu, X.-C., Fan, H.-N., Chen, W.-Y., Wang, Z.-R., Yin, X.-Y., Bai, J., Zhang, Y.-Q., Jiang, Y., Gong, Y. and Chen, Z.-Y. (2023) Assessment of the Prognostic Value of the Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Perihilar Cholangiocarcinoma Patients Following Curative Resection: A Multicenter Study of 333 Patients. *Frontiers in Oncology*, **12**, Article 1104810. https://doi.org/10.3389/fonc.2022.1104810

[38] Ren, Z., Yang, J., Liang, J., Xu, Y., Lu, G., Han, Y., Zhu, J., Tan, H., Xu, T. and Ren, M. (2023) Monitoring of Postoperative Neutrophil-to-Lymphocyte Ratio, D-Dimer, and CA153 in: Diagnostic Value for Recurrent and Metastatic Breast Cancer. *Frontiers in Surgery*, **9**, Article 927491. https://doi.org/10.3389/fsurg.2022.927491

[39] 靳宇. 单核细胞在新型冠状病毒引发的细胞因子风暴中的作用和机制研究[D]: [硕士学位论文]. 长春: 吉林大学, 2022. https://doi.org/10.27162/d.cnki.gjlin.2022.004042

[40] 孙琳, 刘佳嘉, 尹光浩, 王丹. 乳腺癌患者术前淋巴细胞/单核细胞比值与临床病理特征及预后的相关性[J]. 中国临床研究, 2022, 35(9): 1233-1236.

[41] 赵成, 纪澄华, 马雷, 李德辉. 淋巴细胞与单核细胞比值和进展期胃癌淋巴结转移的相关性[J]. 中国现代普通外科进展, 2022, 25(10): 825-828.

[42] 陈梦琪, 刘珂萌, 赵华琴, 贺霞. 术前系统免疫炎症指数对非小细胞肺癌患者预后价值的系统评价与 Meta 分析[J/OL]. 中国胸心血管外科临床杂志: 1-7. http://1.15.146.118/kcms/detail/51.1492.R.20230117.1218.007.html, 2023-02-22.

[43] 张小磊, 江晓晖, 吴金东. 系统免疫炎症指数和血小板/淋巴细胞比值与胃癌患者术后预后的关系[J]. 现代医学与健康研究电子杂志, 2022, 6(24): 24-28.

[44] 唐敏, 李桂香. 系统免疫炎症指数和肿瘤标志物与肺癌骨转移的相关性[J]. 肿瘤防治研究, 2022, 49(12): 1252-1257.