

宫颈癌预后临床病理因素研究进展

苏梦媛^{1,2}, 王 锐^{2*}

¹承德医学院研究生学院, 河北 承德

²承德医学院附属医院放射科, 河北 承德

收稿日期: 2025年12月9日; 录用日期: 2026年1月2日; 发布日期: 2026年1月14日

摘 要

目的: 综述影响宫颈癌患者预后的关键临床病理因素及其研究进展, 特别关注组织学类型(包括HPV相关性)、肿瘤大小以及淋巴脉管间隙浸润(LVSI)与淋巴结转移(LNM)的相互关系及预后价值。方法: 通过梳理相关文献, 总结和分析上述相关临床病理因素在宫颈癌预后评估中的作用及存在的争议。结果: 组织学类型及其HPV相关性是重要的独立预后因素。肿瘤大小是FIGO分期的重要依据, 与局部浸润深度、LVSI、LNM风险及不良预后显著相关。LVSI作为预测LNM的关键危险因素之一, 其阳性显著增加LNM风险及复发风险, 但其能否作为独立预后因素仍存在争议。LNM是明确的不良预后因素, 已被纳入FIGO 2018分期系统。LVSI、肿瘤大小和浸润深度是预测LNM的核心指标。分子标志物和肿瘤微环境等因素同样会影响患者的预后。结论: 组织学类型、肿瘤大小、LNM、LVSI状态、分子标志物及肿瘤微环境是评估宫颈癌患者预后和制定个体化治疗策略的关键临床病理因素。深入了解这些因素及其相互关系对改善患者预后至关重要。

关键词

宫颈癌, 预后, 淋巴脉管间隙浸润, 淋巴结转移

Research Advances in Clinicopathological Prognostic Factors for Cervical Cancer

Mengyuan Su^{1,2}, Rui Wang^{2*}

¹Graduate School of Chengde Medical University, Chengde Hebei

²Department of Radiology, Affiliated Hospital of Chengde Medical University, Chengde Hebei

Received: December 9, 2025; accepted: January 2, 2026; published: January 14, 2026

*通讯作者。

文章引用: 苏梦媛, 王锐. 宫颈癌预后临床病理因素研究进展[J]. 临床医学进展, 2026, 16(1): 1304-1310.
DOI: 10.12677/acm.2026.161168

Abstract

Objective: To review the key clinicopathological factors influencing the prognosis of cervical cancer patients and the research progress in this field, with a particular focus on histological type (including HPV association), tumor size, and the interrelationship as well as prognostic significance of lymphovascular space invasion (LVSI) and lymph node metastasis (LNM). **Methods:** By reviewing relevant literature, we summarize and analyze the role of the aforementioned clinicopathological factors in the prognostic assessment of cervical cancer and the existing controversies. **Results:** Histological type and its association with HPV are important independent prognostic factors. Tumor size serves as a critical basis for FIGO staging and is significantly associated with local invasion depth, LVSI, LNM risk, and poor prognosis. LVSI, as a key risk factor for predicting LNM, significantly increases the risk of LNM and recurrence when positive. However, whether it can be considered an independent prognostic factor remains controversial. LNM is a well-established poor prognostic factor and has been incorporated into the FIGO 2018 staging system. LVSI, tumor size, and invasion depth are core indicators for predicting LNM. Factors such as molecular biomarkers and the tumor microenvironment also influence patient prognosis. **Conclusion:** Histological type, tumor size, LNM, LVSI status, molecular biomarkers, and the tumor microenvironment are key clinicopathological factors for assessing the prognosis of cervical cancer patients and formulating individualized treatment strategies. A deeper understanding of these factors and their interrelationships is crucial for improving patient prognosis.

Keywords

Cervical Cancer, Prognosis, Lymphovascular Space Invasion, Lymphatic Metastasis

Copyright © 2026 by author(s) and Hans Publishers Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

1. 引言

宫颈癌是女性最常见的恶性肿瘤之一[1]。持续的 HPV 感染是宫颈癌发病的主要因素[2][3]。近年来,随着 HPV 疫苗和宫颈癌筛查技术的逐步普及,有效地预防了 HPV 相关宫颈癌的发生,并促进早期无症状病例的诊断。即使目前已有有效的预防措施和规范的治疗方法,但宫颈癌的全球发病率和死亡率仍然居高不下,2020 年数据显示,全球宫颈癌新发病例估计为 604,127 例,死亡病例达 341,831 例,其中发展中国家的病例数占全球总数的 83% [4]。为了解决这一困境,研究者们展开了大量研究以改善宫颈癌患者的预后。目前一些研究表明,某些危险因素会影响宫颈癌患者的治疗结果和预后,包括组织学类型、肿瘤大小、宫颈间质浸润深度、LNM 及 LVSI 在内的临床病理因素,以及。值得注意的是,近年来有多个新的预后因素被提出。因此,本文旨在综述临床病理因素对宫颈癌患者预后的影响。

2. 组织学类型

鳞状细胞癌(SCC)、腺癌(AC)和腺鳞癌(ASC)是宫颈癌常见的三种组织学类型,约占所有组织学类型的 95%。近几十年来,宫颈鳞状细胞癌的发病率和死亡率有所下降,但在同一时期腺癌及腺鳞癌的发病率和死亡率却在升高[5][6]。J. M. Noh 等人的研究结果显示鳞状细胞癌(SCC)、腺癌(AC)和腺鳞癌(ASC)患者的 5 年无进展生存期(RFS)率分别为 83.7%、66.5%和 79.6% ($P < 0.0001$),腺癌和腺鳞癌相较于鳞状

细胞癌有较差的预后[7]。这是由于腺癌细胞更易向宫颈深层组织浸润, 侵犯血管和淋巴管, 导致早期淋巴结转移和远处转移的风险较高, 并且宫颈腺癌对放疗和化疗的敏感度低于鳞癌, 治疗效果相对较差。

总而言之, 组织学类型是影响宫颈癌患者预后的独立危险因素, 腺癌的预后相对较差, 这可能与其生物学特性相关, 致使传统治疗手段的效果不佳。因此, 为了提高患者的生存率, 未来有望开发更具针对性的药物, 使患者从个体化辅助治疗中获益。

3. 肿瘤大小

肿瘤的大小可以作为预测远处转移以及不良预后的危险因素之一, 其与 FIGO 分期、LNM 及肿瘤复发率相关。肿瘤大小(以最大直径 4 cm 为界)已被纳入宫颈癌 FIGO 分期。与此同时, Hiroyuki Yamazaki 等研究表明, 宫颈肿瘤直径 ≥ 25 mm 是宫旁浸润的独立危险因素[8]。此外, Chen 等人的研究发现肿瘤体积与 LNM 和 LVSI 密切相关, 并且是宫颈癌发生 LNM 和 LVSI 的独立危险因素[9] [10]。

肿瘤大小对临床分期具有重要的指示作用, 同时指导临床选择合适的诊疗方案。并且, 肿瘤大小还与宫旁浸润、LNM 和 LVSI 的发生密切相关, 肿瘤体积越大, 越容易侵犯周围组织内的血管和淋巴管, 进而发生 LNM 和宫旁浸润, 最终出现远处转移和复发, 造成患者不良的预后。因此, 早发现、早诊断、早治疗显得尤为重要, 高危人群要做好定期筛查。

4. 宫颈间质浸润深度

宫颈间质浸润深度是影响宫颈癌患者预后的重要组织病理学指标[11]。深层间质浸润是指肿瘤细胞侵犯宫颈间质外 1/3 的组织, 其与肿瘤大小和 LNM 等因素有关。一项研究指出磁共振成像上肿瘤最大直径是发生深层间质浸润的独立危险因素[12]。另一项研究表明, 宫颈癌患者的宫颈间质浸润深度与发生盆腔淋巴结转移有关[13]。

关于间质浸润深度与宫颈癌患者预后的关系, 主要在于宫颈癌肿瘤体积或直径越大, 间质浸润程度越深, 发生盆腔淋巴结转移可能性越大, 患者的预后越差。对此, 应将深层间质浸润纳入早期宫颈癌的预后因素, 并重视此类患者的综合治疗。

5. LVSI 与 LNM: 对预后的影响及相互关系

LVSI 的定义是在原发侵袭性肿瘤外的内皮血管或淋巴间隙内存在恶性细胞[14]。经免疫组化染色后, 在光学显微镜下可见由扁平内皮细胞围绕成的血管或淋巴间隙内存在至少一团附壁的肿瘤细胞时, 可认为存在 LVSI。多年来, LVSI 能否作为预后不良的独立危险因素一直是研究者们争论的主题。

5.1. LVSI 作为预后因素的研究证据与争议

早期研究者们对血管侵犯进行了初步研究, 研究发现血管侵犯对宫颈癌患者的预后有显著影响, 伴有血管侵犯的患者有转移的倾向[15]。1990 年, 妇科肿瘤组(GOG-49)对 FIGO I 期宫颈癌患者进行了第一项前瞻性研究, 证实肿瘤大小、间质浸润深度和毛细血管淋巴间隙浸润(CLS)是影响生存率的独立危险因素($P < 0.0001$)。该项研究认为当盆腔淋巴结阴性患者伴有 CLS 时, 相比于 CLS 阴性的患者 3 年无病间隔显著降低(89.9% VS 78.1%) [16]。后续众多研究(如 Eikelder, Yu Liu 等) [17]-[19]支持 LVSI 是影响早期宫颈癌的预后因素, 并发现 LVSI 阳性显著增加淋巴结转移(LNM)风险, LVSI 阳性者发生淋巴结转移的风险是阴性者的 5 倍。

但是, 有少部分研究认为, LVSI 并不是宫颈癌的独立预后因素[20] [21], 其原因可能包括病例选择偏倚, 如在选择病例时患者接受的治疗并不均匀, LVSI 患者接受的辅助治疗明显多于 LVSI 阴性的患者, 这一因素影响了研究的结果。同时, 对于哪种组织学类型更易发生 LVSI, 研究者们持有不同的观点。

Mohamud 等人认为在 LVSI 阳性的患者中鳞状细胞癌与 LNM 之间存在显著关联($p = 0.014$) [22]。然而, Figge 和 Tamimi 的研究发现腺癌相比于鳞癌更容易伴有 LVSI, 并且腺癌显著增加了疾病复发的风险[23]。对于此矛盾点, 需进行更全面、多中心的研究, 进一步探讨组织学类型与 LVSI 的关系, 从生物学行为等方面进行合理的解释。

除 LVSI 的存在与否外, 其量化程度(数量和范围)也被认为具有预后意义。据报道, Sykes P 首先试图量化 LVSI 的程度, 并将其与手术治疗的 IB 期和 IIA 期宫颈癌患者的复发风险联系起来, 但是由于病例数量较少, 最终未得到有意义的结果[24]。随后 Roman 等人的研究表明, 不仅 LVSI 的存在是宫颈癌预后的相关因素, 而且 LVSI 的数量是影响早期宫颈鳞癌患者复发时间的独立预后因素, 在手术缘阴性且含有 LVSI 的患者(65%)中, LVSI 的病灶总数 > 5 与复发时间有显著相关性($P = 0.006$) [25]。Praiss 等人进行了一项全面的国际、多中心、回顾性临床病理研究, 将宫颈鳞状细胞癌的 LVSI 量化为局灶性和广泛性以及阴性, 研究结果表明, 与阴性 LVSI 相比, 广泛 LVSI 和局灶性 LVSI 的预后更差(HR: 2.38 [95% CI: 1.26~4.47]和 HR: 1.54 [95% CI: 0.76~3.11]; $P = 0.02$) [26]。这些研究表明, 对 LVSI 进行量化有助于更准确地预测宫颈癌的预后。目前尚无宫颈鳞状细胞癌 LVSI 量化的标准方法, 仍需通过大量的临床研究, 进一步验证局灶性与广泛性 LVSI 的界值, 并将其他组织学类型纳入研究。

5.2. LNM

LNM 是公认的宫颈癌不良预后因素[27]。发生盆腔 LNM 的患者 5 年总生存率(52%)远低于未转移者(89%) [28], 而发生主动脉旁 LNM 的患者具有极差的预后(2 年 OS 仅 14%) [29]。LNM 已被纳入 2018 FIGO 分期, 仅有盆腔 LNM 转移为 IIIC1 期, 发生主动脉旁 LNM 转移的为 IIIC2 期。

目前, 越来越多的研究验证了 LNM 数目对宫颈癌患者的预后价值[30] [31]。一个相对较新的预后因素被提出, 即阳性淋巴结比值(LNR), 即切除淋巴结中阳性数目与切除淋巴结总数目的比值, LNR 在结直肠恶性肿瘤[32]、胰腺癌[33]、甲状腺癌[34]中也被证实为预后相关重要因素。有研究证实伴有 LNM 的宫颈癌患者, LNR 与复发率成正比[35]。另外, 有研究进一步分析, $LNR \geq 0.177$ 提示较差的预后[31]。这一指标有望优化治疗策略, 在预测宫颈癌不良预后中具有一定的临床价值。但有一问题值得思考, 即增大或缩小淋巴结清扫范围, 切除淋巴结总数目随之发生变化, 是否会影响比值, 从而影响对较差预后的判断。

5.3. LVSI 与 LNM 的紧密关联及其临床意义

LVSI 与 LNM 两者之间具有密切的相关性。Widschwendter 及 Olthof 等多项研究证实 LVSI 是淋巴结受累的显著独立预测因素($p < 0.001$) [18] [36]。并且多项研究已证明, 广泛的 LVSI 会增加淋巴结转移的风险, 从而影响生存结果[37]。Roman 等人发现, 当超过 45% 的肿瘤切片有 LVSI 时, 早期宫颈癌发生盆腔 LNM 的风险增加至 54% [38]。LVSI 提示肿瘤细胞已经进入淋巴脉管系统, 增加了通过淋巴途径转移至淋巴结乃至远处的可能性; 肿瘤细胞在淋巴脉管内分布地越广泛, 发生淋巴结转移及远处转移的风险越大。

6. 分子标志物和肿瘤微环境

肿瘤抑制基因 p16 的活性与宫颈癌的发生、发展及预后密切相关[39], p16 蛋白阴性表达患者的生存情况优于 p16 蛋白阳性表达患者[40]。程序性死亡配体 1 (PD-L1)是一种在肿瘤细胞表面表达的蛋白质, 其可以与 T 细胞表面的受体 PD-1 结合, 抑制 T 细胞的活性, 从而使肿瘤细胞逃避免疫系统的攻击[41]。在宫颈癌患者中, PD-L1 的高表达可能与晚期或转移性宫颈癌患者的预后较差有关[42]。

肿瘤浸润淋巴细胞亚群(TILs)是肿瘤微环境重要的组成部分, TILs 的数量和功能是决定抗癌效果的关键, 与患者预后密切相关[43], 在实体肿瘤浸润前沿中 CD8+TILs 介导了抗肿瘤效应, 它的密度在很大程度上影响预后。NI 的研究发现, 宫颈癌中 CD8+TILs 下降会导致更差的预后[44]。

7. 小结与展望

组织学类型、肿瘤大小、宫颈间质浸润、LVSI 与 LNM 等是影响宫颈癌预后的关键临床病理因素。但不同临床病理因素对患者生存和疾病进展的影响各异, 综合这些因素构建预后评估模型可以更全面、准确地预测患者的预后, 帮助医生和患者了解疾病发展趋势, 并指导医生为不同风险组的患者制定个性化的治疗方案。

在未来, 有望开展多中心前瞻性研究来进一步验证 LVSI 量化标准及其临床价值。另外, 影像组学作为一种非侵入式检测方法在宫颈癌疾病诊断及预后等领域发挥重要作用, 之后可通过整合宫颈癌患者的临床病理信息、图像特征和基因组数据探索之间的关联, 发现能够反映肿瘤属性特征的影像生物学标志物, 并构建整合了分子标志物的列线图(Nomogram)预测模型。

参考文献

- [1] Nadeem, R. (2023) NCCN Guidelines® Insights: Cervical Cancer, Version 1. *Journal of the National Comprehensive Cancer Network*, **21**, 1-10.
- [2] Kjaer, S.K., Frederiksen, K., Munk, C. and Iftner, T. (2010) Long-Term Absolute Risk of Cervical Intraepithelial Neoplasia Grade 3 or Worse Following Human Papillomavirus Infection: Role of Persistence. *JNCI Journal of the National Cancer Institute*, **102**, 1478-1488. <https://doi.org/10.1093/jnci/djq356>
- [3] Rodríguez, A.C., Schiffman, M., Herrero, R., Hildesheim, A., et al. (2010) Longitudinal Study of Human Papillomavirus Persistence and Cervical Intraepithelial Neoplasia Grade 2/3: Critical Role of Duration of Infection. *Journal of the National Cancer Institute*, **102**, 315-324.
- [4] Parkin, D.M., Bray, F., Ferlay, J. and Pisani, P. (2005) Global Cancer Statistics, 2002. *CA: A Cancer Journal for Clinicians*, **55**, 74-108. <https://doi.org/10.3322/canjclin.55.2.74>
- [5] Sasieni, P. and Adams, J. (2001) Changing Rates of Adenocarcinoma and Adenosquamous Carcinoma of the Cervix in England. *The Lancet*, **357**, 1490-1493. [https://doi.org/10.1016/s0140-6736\(00\)04646-8](https://doi.org/10.1016/s0140-6736(00)04646-8)
- [6] Adegoke, O., Kulasingam, S. and Virnig, B. (2012) Cervical Cancer Trends in the United States: A 35-Year Population-Based Analysis. *Journal of Women's Health*, **21**, 1031-1037. <https://doi.org/10.1089/jwh.2011.3385>
- [7] Noh, J.M., Park, W., Kim, Y.S., Kim, J., Kim, H.J., Kim, J., et al. (2014) Comparison of Clinical Outcomes of Adenocarcinoma and Adenosquamous Carcinoma in Uterine Cervical Cancer Patients Receiving Surgical Resection Followed by Radiotherapy: A Multicenter Retrospective Study (KROG 13-10). *Gynecologic Oncology*, **132**, 618-623. <https://doi.org/10.1016/j.ygyno.2014.01.043>
- [8] Yamazaki, H., Todo, Y., Okamoto, K., Yamashiro, K. and Kato, H. (2015) Pretreatment Risk Factors for Parametrial Involvement in FIGO Stage IB1 Cervical Cancer. *Journal of Gynecologic Oncology*, **26**, 255-261. <https://doi.org/10.3802/jgo.2015.26.4.255>
- [9] Nougaret, S., Reinhold, C., Alsharif, S.S., Addley, H., Arceneau, J., Molinari, N., et al. (2015) Endometrial Cancer: Combined MR Volumetry and Diffusion-Weighted Imaging for Assessment of Myometrial and Lymphovascular Invasion and Tumor Grade. *Radiology*, **276**, 797-808. <https://doi.org/10.1148/radiol.15141212>
- [10] Chen, X., Chen, G., Xu, G., Ren, J., Li, Z., Pu, H., et al. (2018) Tumor Size at Magnetic Resonance Imaging Association with Lymph Node Metastasis and Lymphovascular Space Invasion in Resectable Cervical Cancer: A Multicenter Evaluation of Surgical Specimens. *International Journal of Gynecologic Cancer*, **28**, 1545-1552. <https://doi.org/10.1097/igc.0000000000001327>
- [11] 冯晓艳, 贾淑敏. 早期宫颈癌患者术后 5 年生存情况及预后影响因素研究[J]. 实用癌症杂志, 2023, 1(38): 36-38.
- [12] Ren, J., Li, Y., Yang, J., Zhao, J., Xiang, Y., Xia, C., et al. (2022) MRI-Based Radiomics Analysis Improves Preoperative Diagnostic Performance for the Depth of Stromal Invasion in Patients with Early Stage Cervical Cancer. *Insights into Imaging*, **13**, Article No. 17. <https://doi.org/10.1186/s13244-022-01156-0>
- [13] 何路路, 辜佳婷, 罗喜平. IA2~IIB 期宫颈癌临床病理特征及盆腔淋巴结转移的危险因素[J]. 广东医学, 2021, 6(42): 666-670.

- [14] Margolis, B., Cagle-Colon, K., Chen, L., Tergas, A.I., Boyd, L. and Wright, J.D. (2020) Prognostic Significance of Lymphovascular Space Invasion for Stage IA1 and IA2 Cervical Cancer. *International Journal of Gynecological Cancer*, **30**, 735-743. <https://doi.org/10.1136/ijgc-2019-000849>
- [15] Pagnini, C.A., Della Palma, P. and De Laurentiis, G. (1980) Malignancy Grading in Squamous Carcinoma of Uterine Cervix Treated by Surgery. *British Journal of Cancer*, **41**, 415-421. <https://doi.org/10.1038/bjc.1980.65>
- [16] Delgado, G., Bundy, B., Zaino, R., Sevin, B., Creasman, W.T. and Major, F. (1990) Prospective Surgical-Pathological Study of Disease-Free Interval in Patients with Stage IB Squamous Cell Carcinoma of the Cervix: A Gynecologic Oncology Group Study. *Gynecologic Oncology*, **38**, 352-357. [https://doi.org/10.1016/0090-8258\(90\)90072-s](https://doi.org/10.1016/0090-8258(90)90072-s)
- [17] Ten Eikelder, M.L.G., Hinten, F., Smits, A., Van der Aa, M.A., Bekkers, R.L.M., Int'Hout, J., *et al.* (2022) Does the New FIGO 2018 Staging System Allow Better Prognostic Differentiation in Early Stage Cervical Cancer? A Dutch Nationwide Cohort Study. *Cancers*, **14**, Article No. 3140. <https://doi.org/10.3390/cancers14133140>
- [18] Ishikawa, M., Kasamatsu, T., Tsuda, H., Fukunaga, M., Sakamoto, A., Kaku, T., *et al.* (2018) Prognostic Factors and Optimal Therapy for Stages I-II Neuroendocrine Carcinomas of the Uterine Cervix: A Multi-Center Retrospective Study. *Gynecologic Oncology*, **148**, 139-146. <https://doi.org/10.1016/j.ygyno.2017.10.027>
- [19] Liu, Y., Zhao, L., Li, M., Li, M., Wang, J. and Wei, L. (2015) The Number of Positive Pelvic Lymph Nodes and Multiple Groups of Pelvic Lymph Node Metastasis Influence Prognosis in Stage IA-IIB Cervical Squamous Cell Carcinoma. *Chinese Medical Journal*, **128**, 2084-2089. <https://doi.org/10.4103/0366-6999.161372>
- [20] Obrzut, B., Semczuk, A., Naróg, M., Obrzut, M. and Król, P. (2017) Prognostic Parameters for Patients with Cervical Cancer FIGO Stages IA2-IIB: A Long-Term Follow-Up. *Oncology*, **93**, 106-114. <https://doi.org/10.1159/000471766>
- [21] Weyl, A., Illac, C., Lusque, A., Leray, H., Vaysse, C., Martinez, A., *et al.* (2020) Prognostic Value of Lymphovascular Space Invasion in Early-Stage Cervical Cancer. *International Journal of Gynecological Cancer*, **30**, 1493-1499. <https://doi.org/10.1136/ijgc-2020-001274>
- [22] Mohamud, A., Høgdall, C. and Schnack, T. (2022) Prognostic Value of the 2018 FIGO Staging System for Cervical Cancer. *Gynecologic Oncology*, **165**, 506-513. <https://doi.org/10.1016/j.ygyno.2022.02.017>
- [23] Figge, D.C. and Tamimi, H.K. (1981) Patterns of Recurrence of Carcinoma Following Radical Hysterectomy. *American Journal of Obstetrics and Gynecology*, **140**, 213-220. [https://doi.org/10.1016/0002-9378\(81\)90110-1](https://doi.org/10.1016/0002-9378(81)90110-1)
- [24] Sykes, P., Allen, D., Cohen, C., Scurry, J. and Yeo, D. (2003) Does the Density of Lymphatic Vascular Space Invasion Affect the Prognosis of Stage IB and IIA Node Negative Carcinoma of the Cervix? *International Journal of Gynecological Cancer*, **13**, 313-316. <https://doi.org/10.1136/ijgc-00009577-200305000-00009>
- [25] Chernofsky, M.R., Felix, J.C., Muderspach, L.I., Morrow, C.P., Ye, W., Groshen, S.G., *et al.* (2006) Influence of Quantity of Lymph Vascular Space Invasion on Time to Recurrence in Women with Early-Stage Squamous Cancer of the Cervix. *Gynecologic Oncology*, **100**, 288-293. <https://doi.org/10.1016/j.ygyno.2005.08.019>
- [26] Praiss, A.M., Allison, D., Tessier-Cloutier, B., Flynn, J., Iasonos, A., Hoang, L., *et al.* (2023) Extensive versus Focal Lymphovascular Invasion in Squamous Cell Carcinoma of the Cervix: A Comprehensive International, Multicenter, Retrospective Clinicopathologic Study. *Gynecologic Oncology*, **176**, 147-154. <https://doi.org/10.1016/j.ygyno.2023.07.011>
- [27] Olthof, E.P., van der Aa, M.A., Adam, J.A., Stalpers, L.J.A., Wenzel, H.H.B., van der Velden, J., *et al.* (2021) The Role of Lymph Nodes in Cervical Cancer: Incidence and Identification of Lymph Node Metastases—A Literature Review. *International Journal of Clinical Oncology*, **26**, 1600-1610. <https://doi.org/10.1007/s10147-021-01980-2>
- [28] Uno, T., Ito, H., Isobe, K., Kaneyasu, Y., Tanaka, N., Mitsushashi, A., *et al.* (2005) Postoperative Pelvic Radiotherapy for Cervical Cancer Patients with Positive Parametrial Invasion. *Gynecologic Oncology*, **96**, 335-340. <https://doi.org/10.1016/j.ygyno.2004.09.061>
- [29] Grigsby, P.W., Heydon, K., Mutch, D.G., Kim, R.Y. and Eifel, P. (2001) Long-Term Follow-Up of RTOG 92-10: Cervical Cancer with Positive Para-Aortic Lymph Nodes. *International Journal of Radiation Oncology, Biology, Physics*, **51**, 982-987. [https://doi.org/10.1016/s0360-3016\(01\)01723-0](https://doi.org/10.1016/s0360-3016(01)01723-0)
- [30] Guani, B., Gaillard, T., Teo-Fortin, L., Balaya, V., Feki, A., Paoletti, X., *et al.* (2022) Estimation Risk of Lymph Nodal Invasion in Patients with Early-Stage Cervical Cancer: Cervical Cancer Application. *Frontiers in Oncology*, **12**, Article 935628. <https://doi.org/10.3389/fonc.2022.935628>
- [31] Olthof, E.P., Mom, C.H., Snijders, M.L.H., Wenzel, H.H.B., van der Velden, J. and van der Aa, M.A. (2022) The Prognostic Value of the Number of Positive Lymph Nodes and the Lymph Node Ratio in Early-Stage Cervical Cancer. *Acta Obstetrica et Gynecologica Scandinavica*, **101**, 550-557. <https://doi.org/10.1111/aogs.14316>
- [32] Macedo, F., Sequeira, H., Ladeira, K., Bonito, N., Viana, C. and Martins, S. (2021) Metastatic Lymph Node Ratio as a Better Prognostic Tool than the TNM System in Colorectal Cancer. *Future Oncology*, **17**, 1519-1532. <https://doi.org/10.2217/fon-2020-0993>
- [33] Zheng, Y., Lu, Z., Shi, X., Tan, T., Xing, C., Xu, J., *et al.* (2022) Lymph Node Ratio Is a Superior Predictor in Surgically

- Treated Early-Onset Pancreatic Cancer. *Frontiers in Oncology*, **12**, Article 975846. <https://doi.org/10.3389/fonc.2022.975846>
- [34] Hao, W., Zhao, J., Guo, F., Gu, P., Zhang, J., Huang, D., *et al.* (2023) Value of Lymph Node Ratio as a Prognostic Factor of Recurrence in Medullary Thyroid Cancer. *PeerJ*, **11**, e15025. <https://doi.org/10.7717/peerj.15025>
- [35] Kim, S.I., Kim, T.H., Lee, M., Kim, H.S., Chung, H.H., Lee, T.S., *et al.* (2021) Lymph Node Ratio Is a Strong Prognostic Factor in Patients with Early-Stage Cervical Cancer Undergoing Minimally Invasive Radical Hysterectomy. *Yonsei Medical Journal*, **62**, 231-239. <https://doi.org/10.3349/ymj.2021.62.3.231>
- [36] Widschwendter, P., Janni, W., Scholz, C., De Gregorio, A., De Gregorio, N. and Friedl, T.W.P. (2019) Prognostic Factors for and Pattern of Lymph-Node Involvement in Patients with Operable Cervical Cancer. *Archives of Gynecology and Obstetrics*, **300**, 1709-1718. <https://doi.org/10.1007/s00404-019-05341-3>
- [37] Chandacham, A., Charoenkwan, K., Siriaunkgul, S., *et al.* (2005) Extent of Lymphovascular Space Invasion and Risk of Pelvic Lymph Node Metastases in Stage IB1 Cervical Cancer. *Journal of the Medical Association of Thailand*, **88**, 31-36.
- [38] Roman, L.D., Felix, J.C., Muderspach, L.I., Varkey, T., Burnett, A.F., Qian, D., *et al.* (1998) Influence of Quantity of Lymph-Vascular Space Invasion on the Risk of Nodal Metastases in Women with Early-Stage Squamous Cancer of the Cervix. *Gynecologic Oncology*, **68**, 220-225. <https://doi.org/10.1006/gyno.1998.4943>
- [39] 郑金锋, 马淑芳, 耿明. p16 和 p15 及 PCNA 在子宫颈癌组织中的表达及临床病理意义[J]. 中华肿瘤防治杂志, 2007, 14(4): 291-293.
- [40] 李伟英, 范长玲, 张敏, 等. p16 蛋白在宫颈癌中的表达及其与患者临床特征和预后的关系[J]. 癌症进展, 2019, 17(10): 1222-1224.
- [41] Yao, H., Lan, J., Li, C., Shi, H., Brosseau, J., Wang, H., *et al.* (2019) Inhibiting PD-L1 Palmitoylation Enhances T-Cell Immune Responses against Tumours. *Nature Biomedical Engineering*, **3**, 306-317. <https://doi.org/10.1038/s41551-019-0375-6>
- [42] Huang, W., Liu, J., Xu, K., Chen, H. and Bian, C. (2022) PD-1/PD-L1 Inhibitors for Advanced or Metastatic Cervical Cancer: From Bench to Bed. *Frontiers in Oncology*, **12**, Article 849352. <https://doi.org/10.3389/fonc.2022.849352>
- [43] Kazemi, M.H., Sadri, M., Najafi, A., Rahimi, A., Baghernejadan, Z., Khorramdelazad, H., *et al.* (2022) Tumor-Infiltrating Lymphocytes for Treatment of Solid Tumors: It Takes Two to Tango? *Frontiers in Immunology*, **13**, Article 1018962. <https://doi.org/10.3389/fimmu.2022.1018962>
- [44] Ni, H., Zhang, H., Li, L., Huang, H., Guo, H., Zhang, L., *et al.* (2022) T Cell-Intrinsic STING Signaling Promotes Regulatory T Cell Induction and Immunosuppression by Upregulating FOXP3 Transcription in Cervical Cancer. *Journal for ImmunoTherapy of Cancer*, **10**, e005151. <https://doi.org/10.1136/jitc-2022-005151>