

乳腺癌患者腋窝淋巴结转移评估和诊疗策略研究进展

罗文培, 蒋乾坤, 杨露*

重庆医科大学附属第二医院乳腺甲状腺外科, 重庆

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摘要

乳腺癌外科治疗理念在转变, 在适合患者情况的前提下应避免更多的侵入性操作。有一些研究证实了前哨淋巴结活检(Sentinel lymph node biopsy, SLNB)结果为阳性的患者豁免腋窝淋巴结清扫(Axillary lymph node dissection, ALND)的安全性, 本研究的目的是系统地回顾文献, 分析乳腺癌患者腋窝淋巴结转移(Axillary lymph node metastasis, ALNM)的评估和诊疗现状, 并对其前沿进展作一综述。

关键词

乳腺癌, 腋窝淋巴结, 前哨淋巴结, 淋巴结清扫

Research Progress on Evaluation and Treatment Strategy of Axillary Lymph Node Metastasis in Breast Cancer Patients

Wenpei Luo, Qiankun Jiang, Lu Yang*

Department of Breast and Thyroid Surgery, The Second Affiliated Hospital of Chongqing Medical University, Chongqing

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Abstract

The concept of surgical treatment of breast cancer is changing, and more invasive procedures should be avoided under the premise of appropriate patient conditions. Several studies have con-

*通讯作者。

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firm the safety of exempting Axillary lymph node dissection (ALND) in patients with positive Sentinel node biopsy (SLNB) results. The purpose of this study was to systematically review the literature and analyze the current status of evaluation, diagnosis and treatment of Axillary lymph node metastasis (ALNM) in patients with breast cancer. The advances in this field are also summarized.

Keywords

Breast Cancer, Axillary Lymph Node, Sentinel Lymph Node, Lymph Node Dissection

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1. 引言

乳腺癌是最常见的恶性肿瘤，也是妇女癌症相关死亡的主要病因之一[1]。由于化疗、靶向治疗、内分泌治疗、放疗及免疫治疗等系统治疗的规范，乳腺癌患者的生存率不断提高。大约 90% 的乳腺癌患者在初次诊断后存活至少 5 年[2]。广泛的早期筛查和女性对乳腺癌预防意识的提高，使得新确诊的乳腺癌患者往往处于一个肿瘤体积较小的阶段。有调查显示，肿瘤大小 ≤ 2 cm (T1) 的患者占新诊断患者的 80% [3]。所以随着乳腺癌的精准诊疗逐步发展，精准的保乳、保腋已经成为趋势，SLNB 应运而生，然而 SLN 阳性的患者是否需要进一步的清扫，逐渐变得有争议。在什么条件下能够豁免清扫，甚至豁免 SLNB，如何准确评估 ALN 状态，是目前研究的关注点。

2. ALND 与 SLNB 的现状

ALN 的状态是影响乳腺癌患者生存和预后密切的因素，随着新辅助治疗 (Neoadjuvant systemic treatment, NST) 的有效性不断提高，新辅后的病理完全缓解率升高，获得病理完全缓解的患者提高了生存率[4] [5]。尽管如此，到目前为止，ALND 仍然是初始淋巴结阳性患者接受 NST 后的标准手术方法，这也得到了许多国家 (芬兰、瑞典、罗马尼亚) 和国际指南 (西班牙医学肿瘤学会，德国 S3 指南) 的认可[6]。当然 ALND 的目的包括了尽量清除肿瘤转移的淋巴结，得到更加准确的分期，为后续的辅助治疗提供一些依据。但目前乳腺癌外科治疗理念在由既往的“最大可耐受”向“最小有效”转变，保乳术和 SLNB 的应用佐证了这一点[7] [8]。在过去的几十年里，只要临床适应症允许，手术逐渐从根治性乳房切除术加 ALND 转变为更微创化的手术方式。ALND 和 SLNB 都会引起淋巴水肿的发生，降低生活质量。ALND 后发生淋巴水肿的风险明显高于 SLNB。特别是在乳腺癌复发时，因为有时在进行手术或放疗后，可能会在淋巴管中形成疤痕，进行腋窝手术更会增加淋巴水肿的风险[9]。合并严重疾病的老年患者也应尽量避免 ALND，因为对老年患者来说，腋窝治疗对生活质量的限制，可能引起不可预测的附带问题[10] [11]。保留腋窝淋巴组织能够极大地减少相关术后的并发症，提高患者的生活质量。所以 SLNB 能迅速应用于临床实践，因而我们更要关注和完善它的使用。

乳腺癌 SLN 是指乳腺肿瘤细胞最先转移的第一枚或第一站淋巴结[12] [25]。SLN 的转移状况能够为评估腋窝其他淋巴结的转移提供一些参考，也能够为完善乳腺癌的淋巴结分期提供一些依据，为术后辅助治疗提供一些证据[13]。但在 SLNB 早期经验的粗略概述中，假阴性率为 6.2% [14]，假阴性活检结果

的患者有可能面临疾病进行性发展的风险。此外,假阴性结果可能会影响系统治疗的决定。这需要权衡承担假阴性淋巴结结果的潜在风险与生活质量降低(淋巴水肿和其他 ALND 术后的并发症所引起)的利弊[10]。SLNB 通常在原发肿瘤手术切除时进行,其准确率为 93.5%~97.5% [15] [16] [17] [18],若想术前就对 ALNM 进行评估,这种侵入性手术就会造成额外的手术疤痕、术前注射痛等[19] [20],但是术前对 ALN 受累情况的了解有助于乳腺癌患者的个性化治疗[21]。SLNB 被引入作为 ALND 的替代方案,其具有分期能力[22]。T1 乳腺癌 ALNM 的发生率为 10%至 26% [23],SLNB 漏诊的风险为 1%至 4% [24],假阴性率为 10%,但原发肿瘤部位的差异会导致假阴性率的显著变化[18] [26]。SLNB 需要核医学专家和病理检查辅助,这是一个耗时且复杂的过程[3]。同时其并发症发病率虽然低于 ALND,但该手术并非没有并发症。据报道,注射蓝色染料后出现荨麻疹或瘙痒症,甚至短暂性低血压等[27],随着 SLNB 的使用增加,不良反应的总数可能增加[28]。

3. 豁免 ALND 的相关临床研究

3.1. ACOSOG Z0011 临床研究

美国外科医师学会肿瘤学组(American College of Surgeons Oncology Group, ACOSOG) Z0011 临床研究(NCT Trial ID: 00003855)是一项前瞻性、随机、多中心试验。ACOSOG Z0011 试验表明在 SLN 阳性的一些情况下,ALND 没有优势,意味着对腋窝进行更广泛的手术并不能改善结果[29]。在 ACASOG Z0011 试验中只有 7%的参与者患有浸润性小叶癌(ILC, Invasive lobular carcinoma),而 ILC 是浸润性乳腺癌中第二常见的组织学类型,占有浸润性乳腺癌的 5%~15% [30]。但 Wang 等人证实了与 ACASOG Z0011 试验的一致性[31]。

3.2. AMAROS 试验

AMAROS 试验的目的是评估腋窝放疗与 ALND 在局部控制上,是否有可比性,同时评估谁的副作用更少[32]。根据随访结果提示,临床淋巴结阴性但 SLN 阳性的患者可以放弃 ALND,接受腋窝放疗[33]。

4. ALN 状态的影像学评估

影像学评估有腋窝超声检查(Axillary ultrasound, AUS), PET/CT 和增强 MRI 等。有 Meta 分析提示, AUS 检测 ALNM 的敏感性和特异性分别为 61%和 82% [34]。增强 MRI 和 PET/CT 的实施成本较高,这两种检查的成本效益值得怀疑[3]。

5. 美国 SEER 数据库的应用

美国 SEER 数据库是临床常用的公共数据库之一,它收录了大量的临床肿瘤回顾性研究资料,数据获取便捷并且公开免费。通过使用从 SEER 数据库收集的,可基于大型人群队列研究筛选出的与淋巴结状态相关的临床病理特征,并将其用于建立预测模型,可生成临床事件的数字概率。目前已有研究基于该数据库建立预测模型[35]。

6. 总结

目前大量研究显示乳腺癌患者进行 SLNB 或 ALND 在无病生存率和总生存率方面无显著统计学差异。即代表在 SLN 阳性的一些情况下,ALND 可被豁免。但 SLNB 其也存在假阴性率、并发症等问题。预测模型能筛查出一些标准来数字化评估 ALNM 的概率,规范化的术前评估可能会影响原发性乳腺癌淋巴结转移的未来治疗模式。

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