综 述

进展期胃癌D2根治术淋巴结不符合研究进展

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[摘要] 淋巴结不符合是指标本送检的各组淋巴结中，未检测到多个淋巴结组，这种情况的出现使相当一部分患者预后不良。虽然目前D2淋巴结根治术已成为进展期胃癌的标准术式并被纳入指南，但术后仍会出现淋巴结检出率下降。因此，充分的D2解剖仍然是外科医师的研究重点和难点。本文就进展期胃癌D2根治术淋巴结不符合的研究进展进行综述。

[关键词] 进展期胃癌；D2淋巴结根治术；淋巴结不符合

Research progress on lymph node noncompliance in D2 radical resection of advanced gastric cancer

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[**Abstract**] Lymph node noncompliance is an indicator. If multiple lymph node stations are not detected in each group of lymph nodes submitted for inspection, the specimen is regarded as lymph node noncompliance. Under the background that the incidence of advanced gastric cancer has been increasing year by year, more and more surgeons have begun to pay attention to the surgical effect of radical gastric cancer surgery and the prognostic quality of life of patients. A large number of domestic and foreign experimental studies have shown that the sequence of lymph node metastasis of gastric cancer is roughly from the lesser curvature of the stomach to the lymph nodes around the abdominal aorta. In addition, during the process of lymph node metastasis, there may be lymph nodes that do not appear in the specified location, or due to the factors such as the patient's advanced age, different surgical procedures, thick abdominal fat, deep tumor invasion, and more intraoperative bleeding, the D2 lymph node may be used for gastric cancer. During the resection operation and postoperative pathological sorting, certain errors occurred. Although radical resection of D2 lymph nodes has become a standard surgical approach for the treatment of advanced gastric cancer, a variety of congenital anatomical factors or human error factors will still cause a decrease in the detection rate of postoperative lymph nodes. Therefore, adequate D2 anatomy is still a research focus and difficulty for surgeons. This article discusses the research progress of lymph node noncompliance in D2 radical resection of advanced gastric cancer.

[**Key words**] advanced gastric cancer; D2 radical lymphadenectomy; lymph node noncompliance

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胃癌是一种临床常见的恶性肿瘤，确诊时多已处于晚期[1]。据统计，全球每年新增胃癌病例超过102万例，且病死率很高，仅2018年就有78.5万例患者死亡[2]。尽管在过去几十年中胃癌总体发病率有所下降，但进展期胃癌发病率仍呈现逐年升高的趋势[3]。由于非手术治疗不能很好地解决患者预后及生存质量的问题[4-5]，因此手术切除是进展期胃癌的主流治疗方法，目前胃癌根治术与D2淋巴结清扫术已成为多个国家认同的标准诊疗方案[6]。研究显示，胃癌淋巴结转移顺序大体按照由胃小弯侧向腹主动脉周围淋巴结靠拢[7]，但肿瘤压迫或淋巴管解剖发育异常等因素可造成正常淋巴引流方向发生改变，从而导致术中淋巴结清扫缺失及术后检出率下降[8]。日本学者根据第15版《胃癌处理规约》提出了“淋巴结不符合”的概念，即从胃癌D2淋巴结清扫术后标本中解剖各组淋巴结并送检，但无法检测出超过2组淋巴结，或每站淋巴结的检出率差异明显，甚至可能不包含任何淋巴结，在此基础上允许缺失1组淋巴结。当缺失超过1组淋巴结时，则这类偏差可视为淋巴结不符合[9]。本文就进展期胃癌D2根治术淋巴结不符合的研究进展进行综述。

1　胃癌淋巴结不符合的研究现状

在荷兰的全国随机性研究及长期随访中，淋巴结不符合被用于确定D2淋巴结清扫术治疗胃癌的可行性[10-11]。韩国COACT1001试验(腹腔镜辅助与开放D2根治术治疗晚期胃癌的多中心随机二阶段临床试验)将淋巴结不符合作为主要参考对象，证实腹腔镜胃部分切除治疗进展期胃癌较开放手术更具优势，且术后淋巴结检出率更高[12-15]。有部分学者观察腹腔镜胃癌手术患者发现，腹腔镜下远端胃切除术组与腹腔镜下全胃切除术组淋巴结不符合程度差异显著，且肿瘤直径>60 mm是第5组淋巴结不符合的术前危险因素[16]。Nam等[17]的多中心前瞻性随机对照试验发现，腹腔镜手术组与开放手术组淋巴结不符合率差异无统计学意义，但对于晚期胃癌，两组淋巴结不符合率差异明显(52% *vs*. 25%，*P*=0.043)。由此可见，淋巴结不符合是目前进展期胃癌仍需探索的一个重要方面。

2　淋巴结不符合的发生机制

目前，D2根治术已成为胃癌的标准术式，但术后病理有时发现一个或多个指示性淋巴结组未能按规定切除，从而导致淋巴结检出率下降[13]。在胃旁引流正常的淋巴结中，各组的淋巴结数目差别较大，这种生物变异可能是术前淋巴结检测量低和淋巴结不符合发生的重要原因[18]。

2.1　淋巴结跳跃性转移　有研究发现，胃癌患者可能出现一些异常的淋巴结转移模式，淋巴结转移途中会绕过淋巴管，表明淋巴结转移不再按照由胃小弯侧向腹主动脉周围转移的模式，从而出现术中清扫的规定站点缺失，这种现象被称为淋巴结跳跃性转移[19]。Zhao等[20]对接受治疗性胃切除术的871例淋巴结转移患者的阳性淋巴结进行研究，比较不同组间的临床病理特征，发现淋巴结跳跃性转移发生率在晚期胃癌患者中较高(4.2%)，且年龄、胃下部癌直径≤5 cm、浸润超过黏膜下层和淋巴管浸润可能是淋巴结跳跃性转移的危险因素。此外，国外已有大量研究证实，胃癌淋巴结切除术后出现跳跃转移的常见位置为第7、8、9、11组[21-22]。这种特殊的转移模式和复杂的淋巴引流可能限制了淋巴结清扫在胃癌患者中的临床应用，从而导致D2淋巴结清扫过程中出现部分淋巴结缺失的情况。

2.2　病理标本处理　淋巴结应由外科医师在手术室标记或从标本中分离出来。病理学家应积极参与单独淋巴结组的识别过程，不同病理学家在收获的淋巴结数量和质量方面有所不同[23]。Liu等[24]发现，胃癌淋巴结不符合的发生与标本处理有关，尤其在晚期胃癌患者术后病理分拣中更有可能出现淋巴结不符合。Lin等[25]对淋巴结不符合的危险因素进行分析，发现体重指数(BMI)高的患者由于腹部脂肪较多，在术后淋巴结分拣过程中可能存在一定的人为误差，从而导致淋巴结检出率降低。此外，D2淋巴结切除术患者的方案偏差结果证实，不同的外科医师在手术操作方面的差异不显著，但外科医师本人检索淋巴结后可明显减少不符合情况的发生，从而认为淋巴结不符合可能与病理标本处理质量不佳有关[26]。因此，病理标本的加工和处理过程可能影响淋巴结不符合的发生。

3　影响进展期胃癌淋巴结不符合的因素

目前，影响进展期胃癌淋巴结不符合的因素尚未明确。国内学者对1745例行腹腔镜D2根治术患者的临床数据进行分析，发现淋巴结不符合是腹腔镜胃癌根治术患者预后不良的独立危险因素；年龄≥65岁、BMI ≥25、腹腔镜全胃切除是淋巴结不符合的危险因素，特别是在第6、8a和12a组淋巴结[27]。国外Dhar等[28]探讨了BMI对胃癌手术中淋巴结清扫程度的影响，发现超重患者清扫淋巴结数目和检出率降低，尤其是引流胃癌的区域淋巴结位于脂肪组织中，使其完全切除受到阻碍。为了进一步深入研究导致淋巴结不符合的因素，有学者对胃癌

根治性胃切除术患者的临床病理资料进行整理分析，发现胃切除程度(全胃切除/远侧胃切除)、原发性肿瘤部位、腹腔手术史、BMI和开放性胃切除术是术前淋巴结不符合的独立预测因素，而高龄、高度肿瘤浸润和大量淋巴结转移是术后淋巴结不符合的独立危险因素[29]。有研究发现，临床分期和术前淋巴结检测情况与淋巴结不符合程度明显相关，其中术前淋巴结检测数量增加有助于主刀医师在术中精确定位，从而降低淋巴结不符合率[30]。综上，在进展期胃癌患者中BMI和术前淋巴结检测数量与淋巴结不符合密切相关。

4 进展期胃癌淋巴结不符合对预后的影响

de Steur等[15]对D1与D2淋巴结切除术患者进行对比分析，发现未充分切除淋巴结组(即不符合规定)的患者占81.6%；当排除不符合性和D1污染的病例后，D2组患者的长期生存率明显高于D1组；淋巴结符合的进展期胃癌D2淋巴结根治术后患者的总体存活率明显高于不符合者[25]。意大利的一项临床试验发现，行D2淋巴结清扫术的胃癌患者病死率与切除术后淋巴结不符合率有关，且行D2根治术的淋巴结阳性患者中淋巴结符合者生存获益较高[31]。

在治疗方面，Chen等[29]发现，化疗可能是改善淋巴结不符合患者预后的补救治疗，术后化疗可消除术中残留的无法检测到的肿瘤组织和细胞，从而提高患者的生存质量。Peeters等[32]对比胃癌患者的预后数据发现，在接受手术的患者中，淋巴结不符合可显著影响预后生存情况。国外大量研究证实，化疗可提高进展期胃癌淋巴结不符合患者的生存率，分析其原因为，早期胃癌患者发生淋巴结转移的风险较低，而进展期胃癌患者发生淋巴结转移的风险较高[33-34]。因此，在进展期胃癌患者中，D2淋巴结清扫时应充分清除所有可能部位的淋巴结，以有效阻止转移。若出现淋巴结不符合的情况，化疗可能为改善患者的预后提供帮助。

5 新技术在胃癌淋巴结不符合患者中的应用

5.1 达芬奇机器人 腹腔镜胃切除术尤其是D2淋巴结切除术受到常规淋巴结清扫复杂性的限制。机器人手术是腹腔镜手术的延伸。与腹腔镜和开放手术相比，机器人可提高手术灵活性，增强视觉效果，减少疲劳以及外科医师的生理震颤[35-36]，可更好地识别解剖平面，甚至在大多数危险区域进行更安全的解剖，特别是一些关键的淋巴结组。

5.1.1 影响因素 肥胖和出血可能会限制腹腔镜手术的表现，Lee等[37]对接受机器人远端次全胃切除术和D2淋巴结切除术(robotic distal subtotal gastrectomy with D2 lymphadenectomy，RDGD2)或腹腔镜远端次全胃切除术和D2淋巴结切除术(laparoscopic distal subtotal gastrectomy with D2 lymphadenectomy，LDGD2)胃癌患者的临床数据进行分析，发现在行D2淋巴结切除术时，机器人手术对高BMI的患者的益处较BMI正常患者更明显，特别是在失血较多的情况下和D2淋巴结切除术的质量方面。机器人手术可作为传统腹腔镜手术治疗高BMI胃癌患者的有效替代方法。由于高BMI患者的过量脂肪会影响手术区域的充分暴露和生理黏附，导致很难在主要血管周围进行精确的淋巴结切除[38-40]。此外，在腹腔镜远端胃切除术和D2淋巴结切除术中，失血会模糊手术部位，从而造成淋巴结切除站点缺失[41]。

5.1.2 手术切除方式 不同的手术方式可能会影响患者的预后及生存。Lu等[36]比较了机器人远端胃切除术(RDG)和腹腔镜远端胃切除术(LDG)的淋巴结不符合发生情况，发现RDG组的淋巴结不符合率明显低于LDG组(24.8% *vs.* 40.1%)；进一步分层分析发现，RDG组和LDG组胃周区域的淋巴结不符合率接近(7.9% *vs.* 8.1%)，而RDG组胃外组的不符合率明显低于LDG组(7.7% *vs.* 16.9%)；此外，RDG组第7、9、11p、12a组淋巴结的剥离率明显高于LDG组。综上，机器人手术可改善胃癌患者术中的淋巴结清扫情况，有利于改善患者预后。

5.2 吲哚菁绿示踪荧光成像技术(the introduction of the indocyanine green，ICG) 胃癌淋巴结切除过程中的荧光成像可通过更好的可视化解剖平面指导手术操作，ICG指导下的微创治疗已逐渐成为临床探索的新方向[42]。外科医师广泛报道了在结直肠和肝胆肿瘤手术中血管和淋巴结构可视化方面的经验。Roh等[43]发现，ICG在腹腔镜设备中的成功应用有助于实现更好的组织穿透，并能更精准地发现肥厚脂肪组织中的淋巴结。黄昌明等[44]研究发现，ICG示踪组腹腔镜远端胃切除患者的淋巴结不符合率仅为23.9%，而腹腔镜全胃切除患者的淋巴结不符合率为41.4%，均明显低于既往研究报道。因此，ICG在腹腔镜胃癌根治手术中的应用有助于降低淋巴结不符合率，可实现改善患者预后的目的。Chen等[45]比较了ICG组与非ICG组的淋巴结检出量和淋巴结不符合率，发现ICG组检出的淋巴结总数明显多于非ICG组；对于接受远端胃切除术的患者，ICG组与非ICG组的淋巴结不符合率相当(8.4% *vs.* 11.7%)；对于接受全胃切除术的患者，ICG组淋巴结不符合率明显低于非ICG组(22.4% *vs.* 39.5%)，同一淋巴结组特别是第4sa、7、11d和12a组的淋巴结剥离率明显高于非ICG组，表明术中ICG示踪可

降低淋巴结不符合率。由此可见，吲哚菁绿可明显改善D2淋巴结切除术的手术质量，减少淋巴结不符合的发生，从而减少术后并发症。

6 总结与展望

在胃癌的正常淋巴结引流中，各组的淋巴结数目差别较大，甚至一个特定的淋巴结组可能不含任何淋巴结。行D2淋巴结清扫的进展期胃癌患者淋巴结不符合率较高，但早期胃癌患者淋巴结不符合率较低，这可能与早期淋巴结转移较少有关。淋巴结不符合的发生机制可能与淋巴结跳跃性转移及病理标本的分拣处理有关，导致术后病理回报可发现一个或多个指示性淋巴结组未能按规定切除，从而导致淋巴结检出率下降。BMI、术前淋巴结检测数量及腹部手术史是淋巴结不符合发生的危险因素。为了提高患者的生存率，对于进展期胃癌，建议开展ICG技术引导腹腔镜或逐步普及机器人辅助胃癌根治术。对外科医师进行系统培训时，应强调术前淋巴结检测数量的重要性，确保D2淋巴结解剖合规，并分析淋巴结不符合的情况，以进一步提高患者的生存质量。

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