

Lymph Node Metastasis in Colorectal Cancer

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KEYWORDS

- Colon cancer • Metastatic lymph node • Staging • Tumor deposit
- Micrometastasis • Lymph node ratio • Rectal cancer • Neoadjuvant treatment effect

KEY POINTS

- Pathologic lymph node staging remains crucial for colon cancer prognosis. Per American Joint Committee on Cancer (AJCC) 7th and 8th editions, it is important to obtain at least 12 lymph nodes in resections intended for cure.
- Although the definition of tumor deposits has evolved over the years, interpretation challenges and interobserver variability still exist.
- Lymph nodes with isolated tumor cells are designated as N0; micrometastases are designated as N1. Additional use of special/ancillary techniques is not recommended for detection.
- Although not included in AJCC TNM staging, many studies have shown that lymph node ratio provides useful prognostic stratification in addition to the number of positive lymph nodes.
- The evaluation of lymph nodes after neoadjuvant treatment in rectal cancer can be challenging; finding of viable tumor cells is essential to classify a lymph node as positive.

INTRODUCTION

Surgical resection remains the most effective therapy for colon cancer. Pathologic findings in surgical resection specimens are the best predictor of prognosis. As in any organ system, cancer staging, the assessment of primary tumor (T), lymph node metastasis (N), and distant metastasis (M) is an important task for pathologists and treating clinicians. The College of American Pathologists (CAP) cancer protocol recommends using the American Joint Committee on Cancer (AJCC) TNM staging system and the International Union Against Cancer, but does not preclude the use of other staging systems. In this review, the authors focus on lymph node (LN)

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metastasis in colorectal cancer using the AJCC staging criteria,¹⁻⁴ CAP cancer protocol,⁵ as well as the literature. Several key or controversial topics including LN staging, tumor deposit (TD), micrometastasis, LN ratio, and neoadjuvant treatment effect in rectal cancer are discussed. Updates from the AJCC 8th edition are included.

CONTENT

American Joint Committee on Cancer Lymph Node Staging

The LN is the most common site of metastasis. Tumor spreads to LN via the lymphatic vessels usually in order of proximity to the primary site. LN (N category) staging includes information on whether the cancer has spread to regional LNs and how many LNs are involved. The regional LNs are designated based on the anatomic subsite of the large intestine.^{4,5} These regional LNs are located along the course of the major vessels supplying the large intestine. LN outside the regional drainage area of the primary tumor should be characterized as distant metastasis (M category). Although colonic and rectal cancer can metastasize to almost any organ, the liver and lungs are the most common distant organ metastatic sites.

Required number of total lymph nodes

To accurately evaluate the LN metastasis, as many LNs as possible should be assessed to determine the N stage. Both the total number of regional LNs removed and the number of positive LN involved are prognostically important and thus should be reported. Studies have shown that the total number of LN removed correlates with survival, likely because of optimal mesenteric resection by the surgeon and increased accuracy in staging.^{6,7} In colorectal cancer resections that are intended for cure, AJCC 7th and 8th editions state it is important to obtain and examine at least 12 LNs. The prior 6th edition suggested a range of 7 to 14 LNs that should be obtained. Even if less than the suggested number of LNs is identified, actual N stage rather than Nx should be provided.

There are many factors that can impact LN recovery, including patient age, gender, body habitus; immune response; tumor site, size, and length of colon resected; the experience of surgeon; and the diligence and experience of pathology grossing personnel.⁸ In addition, the new classification of TD leads to a reduction in the total number of LNs identified because of reclassification of some LN as TD.⁹ CAP cancer protocol suggests that if fewer than 12 LNs are found, reexamining the specimen for additional LN, with or without enhancement techniques, should be considered.

Some studies aimed at increasing LN yield and stage accuracy have been reported, but no major changes have been made recently in standard grossing protocols. Fat clearing can help in some cases, but is not the standard of care. Recently, Lisovsky and colleagues¹⁰ reported that emphasis on the number of LNs examined from primary nodal basin (<5 cm away from the tumor edge) and a “second look” protocol (a second search performed in cases that were N0 after the first search) improve nodal staging. Another group concluded that the method of methylene blue intra-arterial staining (methylene blue injection into an artery in the resected colorectal specimen) significantly improved staging accuracy by finding more small-diameter LNs.¹¹ Additional evidence is necessary before any changes are made in the standard protocols.

American Joint Committee on Cancer N staging definition

Table 1 illustrates colon cancer AJCC N staging comparison among 6th, 7th, and 8th editions.

Compared with the 6th edition, the 7th edition further subdivides N1 into N1a, N1b, and N1c; and N2 into N2a and N2b. N1c is a newly introduced category

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