Colon and Rectum

(Sarcomas, lymphomas, and carcinoid tumors of the large intestine are not included)



SUMMARY OF CHANGES

- In the sixth edition, Stage II was subdivided into IIA and IIB on the basis of whether the primary tumor was T3N0 or T4N0, respectively, and Stage III was subdivided into IIIA (T1-2N1M0), IIIB (T3-4N1M0), or IIIC (any TN2M0). In the seventh edition, further substaging of Stage II and III has been accomplished, based on survival and relapse data that was not available for the prior edition
- Expanded data sets have shown differential prognosis within T4 lesions based on extent of disease. Accordingly T4 lesions are subdivided as T4a (Tumor penetrates the surface of the visceral peritoneum) and as T4b. (Tumor directly invades or is histologically adherent to other organs or structures)
- The potential importance of satellite tumor deposits is now defined by the new site-specific factor Tumor Deposits (TD) that describes their texture and number. T1-2 lesions that lack regional lymph node metastasis but have tumor deposit(s) will be classified in addition as N1c
- The number of nodes involved with metastasis influences prognosis within both N1 and N2 groups. Accordingly N1 will be subdivided as N1a (metastasis in 1 regional node) and N1b (metastasis in 2–3 nodes), and N2 will be subdivided as N2a (metastasis in 4–6 nodes) and N2b (metastasis in 7 or more nodes)
- Stage Group II is subdivided into IIA (T3N0), IIB (T4aN0) and IIC (T4bN0)
- Stage Group III:
 - A category of N1 lesions, T4bN1, that was formerly classified as IIIB was found to have outcomes more akin to IIIC and has been reclassified from IIIB to IIIC
 - Similarly, several categories of N2 lesions formerly classified as IIIC have outcomes more akin to other stage groups; therefore, T1N2a has been reclassified as IIIA and T1N2b, T2N2a-b, and T3N2a have all been reclassified as IIIB
- M1 has been subdivided into M1a for single metastatic site vs. M1b for multiple metastatic sites

ICD-0-3 TOPOGRAPHY CODES

- C18.0 Cecum
- C18.2 Ascending colon
- C18.3 Hepatic flexure of colon
- C18.4 Transverse colon
- C18.5 Splenic flexure of colon
- C18.6 Descending colon
- C18.7 Sigmoid colon
- C18.8 Overlapping lesion of colon
- C18.9 Colon, NOS
- C19.9 Rectosigmoid junction
- C20.9 Rectum, NOS

ICD-0-3 HISTOLOGY CODE RANGES

8000-8152, 8154-8231, 8243-8245, 8247-8248, 8250-8576, 8940-8950, 8980-8981

ANATOMY

The divisions of the colon and rectum are as follows (Figures 14.1 and 14.2, respectively):

Cecum Ascending colon Hepatic flexure Transverse colon Splenic flexure Descending colon Sigmoid colon Rectosigmoid junction Rectum

Primary Site. The large intestine (colorectum) extends from the terminal ileum to the anal canal. Excluding the rectum and vermiform appendix, the colon is divided into four parts: the right or ascending colon, the middle or transverse colon, the left or descending colon, and the sigmoid colon. The sigmoid colon is continuous with the rectum which terminates at the anal canal.

The cecum is a large, blind pouch that arises from the proximal segment of the right colon. It measures 6–9 cm in length and is covered with a visceral peritoneum (serosa). The ascending colon measures 15–20 cm in length. The posterior surface of the ascending (and descending) colon lacks peritoneum and thus is in direct contact with the retroperitoneum. In contrast, the anterior and lateral surfaces of the ascending (and descending) colon have serosa and are intraperitoneal. The hepatic flexure connects the ascending colon with the transverse colon, passing just inferior to the liver and anterior to the duodenum.

The transverse colon is entirely intraperitoneal, supported on a mesentery that is attached to the pancreas. Anteriorly, its serosa is continuous with the gastrocolic ligament. The splenic flexure connects the transverse colon to the descending colon, passing inferior to the spleen and anterior to the tail of the pancreas. As noted above, the posterior aspect of the descending colon lacks serosa and is in direct contact with the retroperitoneum, whereas the lateral and anterior surfaces have serosa and are intraperitoneal. The descending colon measures 10–15 cm in length. The colon becomes completely intraperitoneal once again at the sigmoid colon, where the mesentery develops at the medial border of the left posterior major psoas muscle and extends to the rectum. The transition from sigmoid colon to rectum is marked by the fusion of the taenia of the sigmoid colon to the circumferential longitudinal muscle of the rectum. This occurs roughly 12–15 cm from the dentate line.

Approximately 12 cm in length, the rectum extends from the fusion of the taenia to the puborectalis ring. The rectum is covered by peritoneum in front and on both sides in its upper third and only on the anterior wall in its middle third. The peritoneum is reflected laterally from the rectum to form the perirectal fossa and, anteriorly, the uterine or rectovesical fold. There is no peritoneal covering in the lower third, which is often known as the rectal ampulla.

The anal canal, which measures 3–5 cm in length, extends from the superior border of the puborectalis sling to the anal verge. The superior border of the puborectalis sling is the proximal portion of the palpable anorectal ring on digital rectal examination and is approximately 1–2 cm proximal to the dentate line. **Regional Lymph Nodes.** Regional nodes are located (1) along the course of the major vessels supplying the colon and rectum, (2) along the vascular arcades of the marginal artery, and (3) adjacent to the colon – that is, located along the mesocolic border of the colon. Specifically, the regional lymph nodes are the pericolic and perirectal nodes and those found along the ileocolic, right colic, middle colic, left colic, inferior mesenteric artery, superior rectal (hemorrhoidal), and internal iliac arteries (Figure 14.3).

In the assessment of pN, the number of lymph nodes sampled should be recorded. The number of nodes examined from an operative specimen has been reported to be associated with improved survival, possibly because of increased accuracy in staging. It is important to obtain at least 10–14 lymph nodes in radical colon and rectum resections in patients without neoadjuvant therapy, but in cases in which tumor is resected for palliation or in patients who have received preoperative radiation, fewer lymph nodes may be removed or present. In all cases, however, it is essential that the total number of regional lymph nodes recovered from the resection specimen be described since that number is prognostically important. A pN0 determination is assigned when these nodes are histologically negative, even though fewer than the recommended number of nodes has been analyzed. However, when fewer than the number of nodes recommended by the College of American Pathologists (CAP) have been found, it is important that the pathologist report the degree of diligence of their efforts to find lymph nodes in the specimen.

The regional lymph nodes for each segment of the large bowel are designated as follows:

Segment	Regional Lymph Nodes
Cecum	Pericolic, anterior cecal, posterior cecal, ileocolic, right colic
Ascending colon	Pericolic, ileocolic, right colic, middle colic
Hepatic flexure	Pericolic, middle colic, right colic
Transverse colon	Pericolic, middle colic
Splenic flexure	Pericolic, middle colic, left colic, inferior mesenteric
Descending colon	Pericolic, left colic, inferior mesenteric, sigmoid
Sigmoid colon	Pericolic, inferior mesenteric, superior rectal (hemorrhoidal), sigmoidal, sigmoid mesenteric
Rectosigmoid	Pericolic, perirectal, left colic, sigmoid mesenteric, sigmoidal, inferior mesenteric, superior rectal (hemorrhoidal), middle rectal (hemorrhoidal)
Rectum	Perirectal, sigmoid mesenteric, inferior mesenteric, lateral sacral, presacral, internal iliac, sacral promontory, superior rectal (hemorrhoidal), middle rectal (hemorrhoidal), inferior rectal (hemorrhoidal)

Metastatic Sites. Although carcinomas of the colon and rectum can metastasize to almost any organ, the liver and lungs are most commonly affected. Seeding of other segments of the colon, small intestine, or peritoneum also can occur.

Tumor Deposits. Discrete foci of tumor found in the pericolic or perirectal fat or in adjacent mesentery (mesocolic fat) away from the leading edge of the tumor and showing no evidence of residual lymph node tissue but within the lymph drainage area of the primary carcinoma are considered to be peritumoral deposits or satellite nodules, and their number should be recorded in the site-specific Prognostic Markers on the staging form as Tumor Deposits (TD) (Figure 14.4). Such tumor deposits may represent discontinuous spread, venous invasion with extravascular spread (V1/2), or a totally replaced lymph node (N1/2). If tumor deposits are observed in lesions that would otherwise be classified as T1 or T2, then the primary tumor classification is not changed, but the nodule is recorded in the TD category and as a N1c positive node.

PROGNOSTIC FEATURES

Seven new prognostic factors that are clinically significant are included for collection, in addition to the prior notation of serum CEA levels. The new site-specific factors include: tumor deposits (TD, the number of satellite tumor deposits discontinuous from the leading edge of the carcinoma and that lack evidence of residual lymph node); a tumor regression grade that enables the pathologic response to neoadjuvant therapy to be graded, the circumferential resection margin (CRM, measured in mm from the edge of tumor to the nearest dissected margin of the surgical resection); microsatellite instability (MSI), an important but controversial prognostic factor especially for colon cancer; and perineural invasion (PN, histologic evidence of invasion of regional nerves) that may have a similar prognosis as lymphovascular invasion. KRAS mutation status will also be collected since recent analyses indicate that mutation in KRAS is associated with lack of response to treatment with monoclonal antibodies directed against the epidermal growth factor receptor (EGFR) in patients with metastatic colorectal carcinoma. The 18q LOH assay has been validated, and there is work to qualify this as a prognostic marker that would suggest the need for adjuvant therapy in stage II colon cancer.

Tumor Regression Grade. The pathologic response to preoperative adjuvant treatment should be recorded according to the CAP guidelines for recording the tumor regression grade (see CAP Protocol for the examination of Specimens from Patients with Carcinomas of the Colon and Rectum) because neoadjuvant chemoradiation in rectal cancer is often associated with significant tumor response and down-staging. Although the data are not definitive, complete eradication of the tumor, as detected by pathologic examination of the resected specimen, may be associated with a better prognosis and, conversely, failure of the tumor to respond to neoadjuvant treatment appears to be an adverse prognostic factor. Therefore, specimens from patients receiving neoadjuvant chemoradiation should be thoroughly examined at the primary tumor site, in regional nodes and for peritumoral satellite nodules or deposits in the remainder of the specimen. The degree of tumor response may correlate with prognosis. Those patients with minimal or no residual disease after therapy may have a better prognosis than gross residual disease. Whereas a number of different grading systems for tumor regression have been advocated, a four-point tumor regression grade will be used to assess response that is similar to that of Ryan et al. except that the complete absence of viable tumor will be recorded as a Grade 0.

Circumferential Resection Margins. It is essential that accurate pathologic evaluation of the CRM adjacent to the deepest point of tumor invasion be performed. The CRM is the surgically dissected nonperitonealized surface of the specimen. It corresponds to any aspect of the colorectum that is not covered by a serosal layer of mesothelial cells and must be dissected from the retroperitoneum or subperitoneum in order to remove the viscus. In contradistinction, serosalized surfaces of the colorectum are not dissected; they are naturally occurring anatomic structures and are not pathologic surgical margins. The circumferential surface of surgical resection specimens of ascending colon, descending colon, or upper rectum is only partially peritonealized, and the demarcation between the peritonealized surface and the nonperitonealized surface (corresponding to the CRM) of such specimens is not always easily appreciated on pathologic examination. Therefore, the surgeon is encouraged to mark the peritoneal reflection and/or the area of deepest tumor penetration adjacent to a nonperitonealized surface with a clip or suture so that the pathologist may accurately identify and evaluate the CRM.

For mid and distal rectal cancers (subperitoneal location), the entire surface of the resection specimen corresponds to a CRM (anterior, posterior, medial, lateral). For proximal rectal or retroperitoneal colon cancers (ascending, descending, possibly cecum), surgically dissected margins will include those that lie in a retroperitoneal or subperitoneal location as described above (Figure 14.5). For segments of the colon that are entirely covered by a visceral peritoneum (transverse, sigmoid, possibly cecum), the only specimen margin that is surgically dissected is the mesenteric margin, unless the cancer is adherent to or invading an adjacent organ or structure. Therefore, for cancers of the cecum, transverse or sigmoid colon that extends to the cut edge of the mesentery, assignment of a positive CRM is appropriate.

For rectal cancer, the quality of the surgical technique is likely a key factor in the success of surgical outcomes relative to local recurrence and possibly long-term survival. Numerous nonrandomized studies have demonstrated that total mesorectal excision (TME) with adequate surgical clearance around the penetrating edge of the tumor decreases the rate of local relapse. The TME technique entails precise sharp dissection within the areolar plane of loose connective tissue outside (lateral to) the visceral mesorectal fascia in order to remove the rectum. With this approach, all mesorectal soft tissues encasing the rectum, which includes the mesentery and all regional nodes, are removed intact. Thus, the circumferential surface (CRM) of TME resection specimens is the mesorectal or Waldeyer's fascia. Rectal resection performed by less precise techniques may be associated with incomplete excision of the mesorectum. It is critical that the analysis of the surgical specimen follows the CAP guidelines that refer to examination of the TME specimen. In addition, it is essential that the distance between the closest leading edge of the tumor and the CRM (known as the surgical clearance) be measured pathologically and recorded in mm in the CRM field on the staging form. A margin of greater than 1 mm is required with TME to be considered a negative margin because surgical clearance of 1 mm or less is associated with a significantly increased risk of local recurrence and should be classified as positive (Figure 14.5).

Residual Tumor (R). The completeness of resection is largely dependent on the status of the CRM, although the designation is global and would include the transverse margins and other disease observed but not removed at surgery. The resection (R) codes should be given for each procedure:

- R0—Complete tumor resection with all margins histologically negative
- R1—Incomplete tumor resection with microscopic surgical resection margin involvement (margins grossly uninvolved)
- R2—Incomplete tumor resection with gross residual tumor that was not resected (primary tumor, regional nodes, macroscopic margin involvement)

Isolated Tumor Cells and Molecular Node Involvement. As technology progresses and sentinel node biopsy or other procedures may become feasible in colon and rectal surgery, the issue of interpretation of very small amounts of detected tumor in regional lymph nodes will continue to be classified as pN0, and the universal terminology for these isolated tumor cells (ITC) will follow the terminology referenced in Chap. 1. The prognostic significance of ITCs, defined as single malignant cells or a few tumor cells in microclusters, identified in regional lymph nodes that otherwise would be considered to be negative is still unclear. Therefore, ITC identified the collection of data on ITC that may be generated by pathologists who use special immunohistochemical stains or molecular analysis procedures to identify ITC in nodes that might otherwise be considered negative for metastasis by standard hematoxylin and eosin (H&E). It should be noted that isolated tumor cells identified on H&E stains alone are also classified as ITC and are annotated in the same fashion as ITC seen on immunohistochemical stains (i.e., pN0(i+); "i" = "isolated tumor cells").

KRAS. Analysis of multiple recent clinical trials has shown that the presence of a mutation in either codon 12 or 13 of KRAS (abnormal or "mutated" KRAS) is strongly associated with a lack of response to treatment with anti-EGFR antibodies in patients with metastatic colorectal carcinoma. It is recommended that patients with advanced colorectal carcinoma be tested for the presence of mutations in KRAS if treatment will include an anti-EGFR antibody. Where the status of KRAS is known, it should be recorded as a site-specific factor as either Normal (Wild Type) or Abnormal (Mutated).

Anatomic Boundary. The boundary between the rectum and anal canal most often has been equated with the dentate line, which is identified pathologically. However, with advances in sphincterpreservation surgery, defining the boundary between the rectum and the anus as the anorectal ring, which corresponds to the proximal border of the puborectalis muscle palpable on digital rectal examination, is more appropriate.

TNM Stage of Disease. Since publication of the sixth edition, new prognostic data with regard to survival and disease relapse justifies further substaging of both Stages II and III by anatomic criteria. Differential prognosis has been shown for patients with T4 lesions based on the extent of disease in SEER analyses for both rectal cancer and colon cancer. Accordingly, for the seventh edition of AJCC, T4 lesions have been subdivided as T4a (tumor penetrates to the surface of the visceral peritoneum) and T4b (tumor directly invades or is adherent to other organs or structures). In addition, the number of nodes involved by metastasis has been shown to influence prognosis within both N1 and N2 groups, in separate analyses of SEER. For the SEER analyses, both relative and observed survival are listed by TN category of disease (relative survival is survival corrected by age-related comorbidity; see Chap. 2 for more information). Also the total number of nodes examined has an important impact on survival in colon and rectal cancer. The impact of increased nodes examined in the resected specimen is clearly associated with better outcome in colon cancer for all combinations of T and N whereas the association holds in T1–T3 lesions in rectal cancer but appears to be less important in T4a and T4b lesions, perhaps because of the greater use of preoperative radiation or concurrent chemoradiation of the smaller number of patients in the rectal carcinoma subgroups.

Stage Group II has been further subdivided into IIA (T3N0), IIB (T4aN0), and IIC (T4bN0), based on differential survival prognosis. These differences are shown in the SEER analyses for both rectal cancer and colon cancer.

Within Stage III, a number of changes have been made based on differential prognosis found in the rectal cancer pooled analyses, the SEER rectal and colon cancer analyses, and the NCDB colon cancer analysis. A category of N1 tumors has prognosis more akin to IIIC (T4bN1) and has been shifted from Stage IIIB to IIIC. In addition, several categories of N2 tumors have prognosis more akin to IIIA (the T1N2a group) or IIIB (the T1N2b, T2N2a-b, and T3N2a groups) and have been shifted out of Stage IIIC accordingly.

Independent Prognostic Factors and Molecular Markers. In addition to the TNM, independent prognostic factors that are generally used in patient management and are well supported in the literature include residual disease, histologic type, histologic grade, serum carcinoembryonic antigen and cytokine levels, extramural venous invasion, and submucosal vascular invasion by carcinomas arising in adenomas. Small cell carcinomas, signet ring cell carcinomas, and undifferentiated carcinomas have a less favorable outcome than other histologic types. In contrast, medullary carcinoma is more favorable prognostically. Submucosal vascular invasion by carcinomas arising in adenomas is associated with a greater risk of regional lymph node involvement. Lymphatic, venous, and perineural invasion also have been shown to have a less favorable outcome. A number of these independent prognostic factors are currently being evaluated in nomograms that also include TNM stage of disease.

In the future, the intratumoral expression of specific molecules, e.g., Deleted in Colorectal Cancer (DCC) or 18q loss of heterozygosity (LOH), p27^{Kip1}, DNA microsatellite instability, KRAS mutation, or thymidylate synthase, may be proven to be associated either with prognosis or response to therapy that is independent of TNM stage group or histologic grade. Currently, these molecular markers are not part of the staging system, but it is recommended that they be recorded if available and especially if studied within the context of a clinical trial. Furthermore, it is now clear that there is interaction

between the T and N designations that is likely to rely on the expression of specific molecules within the cancer. Thus, by the time of the next edition of TNM staging it may be possible to add molecular profiling information to the TNM information to enhance the precision of predicting prognosis or even response to therapy. Finally, it is important to consider that other factors such as age, gender, race/ethnicity are important factors that affect response to therapy and disease outcome. Although these factors are not included in the TNM Summary or Working Stages at this time, several groups are studying the interaction of these clinicopathological factors with TNM and other prognostic factors in various nomograms such as those at http://www.nomograms.org. In order to determine the optimal way to integrate these various clinical, pathologic, and molecular factors with TNM, collection of the appropriate information prior to the next edition must be carried out.

DEFINITIONS OF TNM

The same classification is used for both clinical and pathologic staging.

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*Note: Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

***Note*: Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (i.e., respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).

****Note*: Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classifications should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN site-specific factor should be used for perineural invasion.

Regional Lymph Nodes (N)			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in 1–3 regional lymph nodes		
Nla	Metastasis in one regional lymph node (Figure 14.10		

Nlb	Metastasis in 2–3 regional lymph nodes (Figure 14.10)
Nlc	Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in four or more regional lymph nodes
N2a	Metastasis in 4–6 regional lymph nodes (Figure 14.11A)
N2b	Metastasis in seven or more regional lymph nodes (Figure 14.11A, B)

Note: A satellite peritumoral nodule in the pericolorectal adipose tissue of a primary carcinoma without histologic evidence of residual lymph node in the nodule may represent discontinuous spread, venous invasion with extravascular spread (V1/2), or a totally replaced lymph node (N1/2). Replaced nodes should be counted separately as positive nodes in the N category, whereas discontinuous spread or venous invasion should be classified and counted in the Site-Specific Factor category Tumor Deposits (TD).

Distant Metastasis (M)

MO	No distant metastasis
M1	Distant metastasis
Mla	Metastasis confined to one organ or site (e.g., liver, lung, ovary, nonregional node) (Figure 14.12)
M1b	Metastases in more than one organ/site or the peritoneum

ANATOMIC STAGE/PROGNOSTIC GROUPS					
Stage	Т	Ν	М	Dukes*	MAC*
0	Tis	N0	MO	-	-
Ι	T1	N0	MO	А	А
	T2	N0	MO	А	B1
IIA	Т3	N0	MO	В	B2
IIB	T4a	N0	MO	В	B2
IIC	T4b	N0	MO	В	B3
IIIA	T1-T2	N1/N1c	MO	С	C1
	T1	N2a	MO	С	C1
IIIB	T3–T4a	N1/N1c	MO	С	C2
	T2-T3	N2a	MO	С	C1/C2
	T1-T2	N2b	MO	С	C1
IIIC	T4a	N2a	MO	С	C2
	T3–T4a	N2b	MO	С	C2
	T4b	N1-N2	MO	С	C3
IVA	Any T	Any N	Mla	-	-
IVB	Any T	Any N	Mlb	-	-

Note: cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (e.g., ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).

*Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.



FIGURE 14.1. Anatomic subsites of the colon.



FIGURE 14.2. Anatomic subsites of the rectum.



FIGURE 14.3. The regional lymph nodes of the colon and rectum are colored by anatomic location, e.g., dark brown – right colon and cecum; blue – hepatic flexure to mid transverse colon; red – splenic flexure, left colon and sigmoid colon.



FIGURE 14.4. Tumor deposit. Discrete foci of tumor found in the pericolic or perirectal fat or in adjacent mesentery (mesocolic fat) away from the leading edge of the tumor and showing no evidence of residual lymph node tissue but within the lymph drainage area of the primary carcinoma are considered to be peritumoral deposits or satellite nodules, and their number should be recorded in the site-specific Prognostic Markers on the staging form as Tumor Deposits (TD).



FIGURE 14.5. Circumferential resection margin. T4a (left side) has perforated the visceral peritoneum. In contrast, T3; R2 (right side) shows macroscopic involvement of the circumferential resection margin of a non-peritonealized surface of the colorectum by tumor with gross disease remaining after surgical excision.



FIGURE 14.6. T1 tumor invades submucosal.



FIGURE 14.7. T2 tumor invades muscularis propria.



FIGURE 14.8. T3 tumor invades through the muscularis propria into pericolorectal tissues.



FIGURE 14.9. (A) T4a tumor penetrates to the surface of the visceral peritoneum. The tumor perforates (penetrates) visceral peritoneum, as illustrated here. (B) T4a tumor perforates visceral peritoneum (shown with gross bowel perforation through the tumor). (C) T4b tumor directly invades or is adherent to other organs or structures, as illustrated here with extension into an adjacent loop of small bowel. (D) T4b tumor directly invades or is adherent to other organs or structures (such as the sacrum shown here).



FIGURE 14.10. N1a is defined as metastasis in one regional lymph node. N1b is defined as metastasis in 2 to 3 regional lymph nodes.



FIGURE 14.11. (A) N2a is defined as metastasis in 4 to 6 regional lymph nodes. N2b is defined as metastasis in seven or more regional lymph nodes. (B) N2b showing nodal masses in more than 7 regional lymph nodes.



FIGURE 14.12. M1a disease is defined as distant metastasis confined to one organ or site (e.g., liver, lung, ovary, nonregional node). In this case, involvement is outside the regional nodes of the primary tumor.

PROGNOSTIC FACTORS (SITE-SPECIFIC FACTORS) (Recommended for Collection)			
Required for staging	equired for staging None		
Clinically significant	Preoperative or pretreatment carcinoembryonic antigen (CEA) (ng/ml) Tumor deposits (TD) Circumferential resection margin (CRM) Perineural invasion (PN) Microsatellite instability (MSI) Tumor regression grade (with neoadjuvant therapy) KRAS gene analysis		