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ORIGINAL REPORT

Revised TN Categorization for Colon Cancer Based on National Survival Outcomes Data

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ABSTRACT

Purpose
The sixth edition of American Joint Committee on Cancer (AJCC) Cancer Staging Manual for colon cancer subdivided stage II into IIA (T3N0) and IIB (T4N0) and stage III into IIIA (T1-2N1M0), IIIB (T3-4N1M0), and IIIC (anyTN2M0). Subsequent analyses supported revised substaging of stage III because of improved survival for T1-2N2 versus T3-4N2 and T4N1 survival was more similar to T3-4N2 than to T3N1. The AJCC Hindgut Taskforce sought population-based validation that depth of invasion and nodal status interact to affect survival.

Patients and Methods
Surveillance, Epidemiology, and End Results (SEER) population-based data from January 1992 to December 2004 for 109,953 colon cancer patients were compared with National Cancer Data Base (NCDB) data on 134,206 patients. T4N0 cancers were stratified by tumors that perforate visceral peritoneum (T4a) versus tumors that invade or are adherent to adjacent organs or structures (T4b). N1 and N2 were stratified by number of involved positive lymph nodes (N+): N1a/N1b (1 *v* 2-3), N2a/N2b (4 to 6 *v* ≥ 7). Five-year observed and relative survival data were obtained for each TN category.

Results
SEER colon cancer analyses confirm that patients with T1-2N0 cancers have better survival than T3N0, T3N0 better than T4N0, T1-2N2 better than T3-4N2, and T4bN1 similar to T4N2. Patients with T4a lesions have better survival than T4b by N category. The number of positive nodes affects survival for each T category.

Conclusion
This SEER population-based colon cancer analysis is highly consistent with rectal cancer pooled analysis and SEER rectal cancer analyses, supporting the shift of T1-2N2 lesions from IIIC to IIIA/IIIB, shifting T4bN1 from IIIB to IIIC, subdividing T4/N1/N2, and revising substaging of stages II/III. Survival outcomes by TN category for colon and rectal cancer are strikingly similar.

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INTRODUCTION

Survival and disease relapse after surgery alone or combined with adjuvant treatment for colon and rectal cancer are a function of both degree of bowel wall penetration of the primary lesion (T category of disease) and nodal status (N category of disease).[1-14] Through the fifth edition of the AJCC (American Joint Committee on Cancer) Cancer Staging Manual, however, substaging was not used to account for marked differences in survival by TN category for patients with stages II and III disease.

In the sixth edition of the AJCC Cancer Staging Manual for colon and rectal cancer, stage II was subdivided into IIA (T3N0) and IIB(T4N0), and stage III was subdivided into IIIA (T1-2N1M0), IIIB (T3-4N1M0), and IIIC (anyTN2M0), on the basis of existing outcomes for patients with IIA versus IIB disease and those with IIIA and IIIB disease.[15] The placement of all TN2 patients into stage IIIC, however, was not based on substantive data analyses, since the impact of T category of disease within N2 patients had not been evaluated in detail.

Rectal cancer pooled analyses subsequently demonstrated the independent prognostic significance of each TN and NT category in patients with resected rectal cancer.[16-23] The outcomes data supported revised substaging of stage III patients because of improved survival for T1-2N2 versus T3-4N2 cancers and survival rates for patients with T4N1 lesions that are more similar to T3-4N2 than to T3N1. A similar detailed analysis of patients with colon cancer has not been reported.

The AJCC Hindgut Taskforce (HTF) sought validation in a population-based data set before making substantive changes in the seventh edition of

Table 1. SEER Colon Cancer Analysis, Relative Survival by NT Category of Disease

NT Category	No. of Patients	5-Year Survival Rate (%)	SE (%)
N0	74,690		
Tis	2,383	95.6	1.2
T1-2	23,861	97.1	0.4
T1	10,930	97.4	0.6
T2	12,931	96.8	0.6
T3	40,338	87.5	0.4
T4	8,108	71.5	0.8
T4a	5,020	79.6	1.0
T4b	3,088	58.4	1.3
N1	25,640		
Tis	95	87.3	6.0
T1-2	3,134	87.7	1.2
T1	968	87.6	2.0
T2	2,166	87.7	1.4
T3	17,866	68.7	0.5
T4	4,545	50.5	1.0
T4a	2,771	60.6	1.4
T4b	1,774	34.9	1.5
N2	12,120		
Tis	19	83.2	14.5
T1-2	499	75.0	3.2
T1	104	68.7	7.0
T2	395	76.6	3.6
T3	8,566	47.3	0.8
T4	3,036	27.1	1.1
T4a	1,653	33.3	1.6
T4b	1,383	19.7	1.4
NX	18,312		
Tis	3,438	91.7	1.1
T1-2	9,486	87.0	0.7
T1	8,572	81.5	0.9
T2	914	79.0	1.6
T3	3,125	54.1	1.2
T4	2,263	24.1	1.1
T4a	693	45.2	2.5
T4b	1,570	14.5	1.1
N1a (1+)	12,892		
Tis	64	89.0	6.6
T1-2	1,913	90.7	1.5
T1	643	90.6	2.4
T2	1,270	90.4	1.9
T3	8,759	74.2	0.8
T4	2,156	56.2	1.5
T4a	1,311	67.6	2.0
T4b	845	38.5	2.2
N1b (2-3)	12,748		
Tis	31	73.2	12.7
T1-2	1,221	83.0	2.0
T1	325	81.0	3.8
T2	896	83.7	2.3
T3	9,107	65.3	0.8
T4	2,389	45.1	1.4
T4a	1,460	54.0	1.9
T4b	929	31.2	2.0
N2a (4-6+)	7,435		
Tis	15	82.8	17.7
T1-2	377	79.0	3.6
T1	77	68.5	8.2
T2	300	81.7	4.1
T3	5,331	53.4	1.0
T4	1,712	33.4	1.5
T4a	982	40.9	2.1
T4b	730	23.3	2.1
N2b (≥ 7)	4,685		
Tis	4	70.8	30.9
T1-2	122	62.4	6.5
T1	27	68.4	13.5
T2	95	60.3	7.3
T3	3,235	37.3	1.2
T4	1,324	18.9	1.4
T4a	671	21.8	2.2
T4b	653	15.7	1.9

NOTE. Relative survival data in 130,762 patients (invasive cancer and evaluable TN category, n = 109,953; nodal status unknown NX, n = 18,312; N0Tis, n = 2,383; N1-2Tis, n = 114).

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; NX, unknown nodal status.

the AJCC Cancer Staging Manual for colon and rectal cancer. Data were obtained for patients with both colon and rectal cancers; the rectal cancer data (35,829 evaluable patients with invasive cancer) are reported in a separate article.[24]

PATIENTS AND METHODS

SEER population-based data were obtained from January 1, 1992, to December 31, 2004, for 130,762 colon cancer patients (C18.0-18.9); 109,953 patients had invasive colon cancer and evaluable TN category of disease (T1-4N0-2), 18,312 were categorized as unknown nodal status (NX), and 2,497 were Tis or T1 polyps. Data in the 109,953 patients with invasive colon cancers and evaluable TN category of disease were compared with SEER data on 35,829 patients with invasive rectal and rectosigmoid cancer patients (C19.9 and 20.9) and National Cancer Data Base (NCDB) data on 134,206 colon cancer patients. Patients who died within 30 days of surgical resection were not included in the current analysis. The effects of different treatment approaches (surgical technique, adjuvant chemotherapy, other) were not felt pertinent to this analysis; such data were not collected or analyzed.

Tumors were stratified by SEER's "extent of disease" and "number of positive nodes" coding schemes. T4N0 cancers were stratified by "tumors that perforate visceral peritoneum" (T4a) versus "tumors that invade or are adherent to adjacent organs or structures" (T4b). N1 (metastasis in 1 to 3 regional nodes) and N2 (metastasis in 4 or more regional nodes) were stratified by number of positive lymph nodes (N+): N1a (1 N+), N1b (2 to 3 N+), N2a (4 to 6 N+), and N2b (≥ 7 N+). T1-T3 categories were defined according to prior AJCC staging (T1, tumor invades submucosa; T2, tumor invades muscularis propria; and T3, tumor invades pericolorectal tissues).

Observed and relative survival data were obtained for each TN category of disease. Observed survival is the proportion of cancer patients surviving for a specified time interval after diagnosis (similar to overall survival [OS]). Relative survival is a net survival measure representing cancer survival in the absence of other causes of death (survival corrected by age-related morbidity, similar to disease-specific survival).

Table 2. SEER Colon Cancer Analysis, Observed Survival by NT Category of Disease

NT Category	No. of Patients	5-Year Survival Rate	SE
N0	74,690		
Tis	2,383	77.4	1.0
T1-2	23,861	76.3	0.3
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T4b	3,088	45.7	1.0
N1	25,640		
Tis	95	73.8	4.9
T1-2	3,134	71.1	1.0
T1	968	73.0	1.7
T2	2,166	70.3	1.2
T3	17,866	54.9	0.4
T4	4,545	39.6	0.8
T4a	2,771	47.0	1.1
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T1-2	499	61.5	2.6
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T3	8,759	58.2	0.6
T4	2,156	43.8	1.2
T4a	1,311	52.2	1.5
T4b	845	30.6	1.8
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T3	9,107	51.7	0.6
T4	2,389	35.6	1.1
T4a	1,460	42.1	1.5
T4b	929	25.4	1.6
N2a (4-6+)	7,435		
Tis	15	71.8	15.1
T1-2	377	64.7	3.0
T1	77	57.4	6.8
T2	300	66.6	3.3
T3	5,331	42.8	0.8
T4	1,712	26.5	1.2
T4a	982	32.5	1.7
T4b	730	18.3	1.6
N2b (≥ 7)	4,685		
Tis	4	66.7	27.2
T1-2	122	51.8	5.3
T1	27	55.0	10.7
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T4a	671	17.5	1.7
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NOTE. Observed survival data in 130,762 patients (invasive cancer and evaluable TN category, 109,953; nodal status unknown [NX], 18,312; N0Tis, 2,383; N1-2Tis, 114).

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; NX, unknown nodal status.

RESULTS

Survival Outcomes by TN Category and AJCC Stage

Relative and observed 5-year survival outcomes by evaluable TN category of disease in the current SEER colon cancer analysis (109,953 patients with invasive cancers) were analyzed. As presented in Tables 1 and 2, patients with stage I colon cancers (AJCC, sixth edition) have better 5-year relative and observed survival than those with IIA cancers. For patients with T1-2N0 lesions, the 5-year relative survival was 97.1% ± 0.4% versus 87.5% ± 0.4% for T3N0 lesions, and 5-year observed survival for those with T2N0 lesions was 76.3% ± 0.3% versus 66.7% ± 0.3% for those with T3N0 lesions.

Survival outcomes for patients with AJCC stage IIA versus IIB cancers (T3N0, T4N0; AJCC, sixth edition) are also presented in Tables 1 and 2. Both 5-year relative and observed survival were higher for patients with T3N0 versus T4N0 cancers (5-year relative survival for T3N0, 87.5% ± 0.4%; for T4N0, 71.5% ± 0.8%; 5-year observed survival for T3N0, 66.7% ± 0.3%; for T4N0, 55.0% ± 0.6%). Standard errors were small because the number of patients was large (T3N0, n = 40,338; T4N0, n = 8,108).

For patients with stage III cancers, those with T1-2 lesions (confined to bowel wall) have better survival than those with T3-4 lesions by N category of disease. Similar improvements in 5-year relative and observed survival were found for patients with T1-2N1 cancers versus T3N1 and T4N1 cancers and for those with T1-2N2 lesions versus those with T3N2 and T4N2 lesions. For patients with T1-2N1 versus T3N1/T4N1 cancers, the 5-year observed survival was 71.1% ± 1.0% (T1-2N1) versus 54.9% ± 0.4% for T3N1 and 39.6% ± 0.8% for T4N1. In patients with T1-2N2 versus T3N2/T4N2 cancers, 5-year observed survival was 61.5% ± 2.6% (T1-2N2) versus 38.1% ± 0.6% for T3N2 and 21.7% ± 0.9% for T4N2. In the SEER colon cancer analysis, patients with T4N1 lesions have 5-year observed survival (39.6% ± 0.8%) similar to that of patients with T3N2 (38.1% ± 0.6%) or T4N2 (21.7% ± 0.9%) lesions.

Patients with T1-2 versus T3 lesions had improved 5-year survival for each N category; the prognostic value of a T1-2 tumor is approximately the same as a decrease of one N category of disease.

Specifically, patients with T1-2N1 cancers have 5-year observed survival (71.1% ± 1.0%) similar to that of patients with T3N0 lesions (66.7% ± 0.3%). For T1-2N2 lesions, 5-year observed survival (61.5% ± 2.6%) is similar to that of patients with T3N0 (66.7% ± 0.3%) and T4N0 (55.0% ± 0.6%) or T3N1 (54.9% ± 0.4%) lesions.

Survival Outcomes by Expanded TN Category of Disease

In view of the large number of patients in the SEER colon cancer database, 5-year relative and observed survival were calculated for each NT category of disease (Tables 1 and 2). Data were generated for

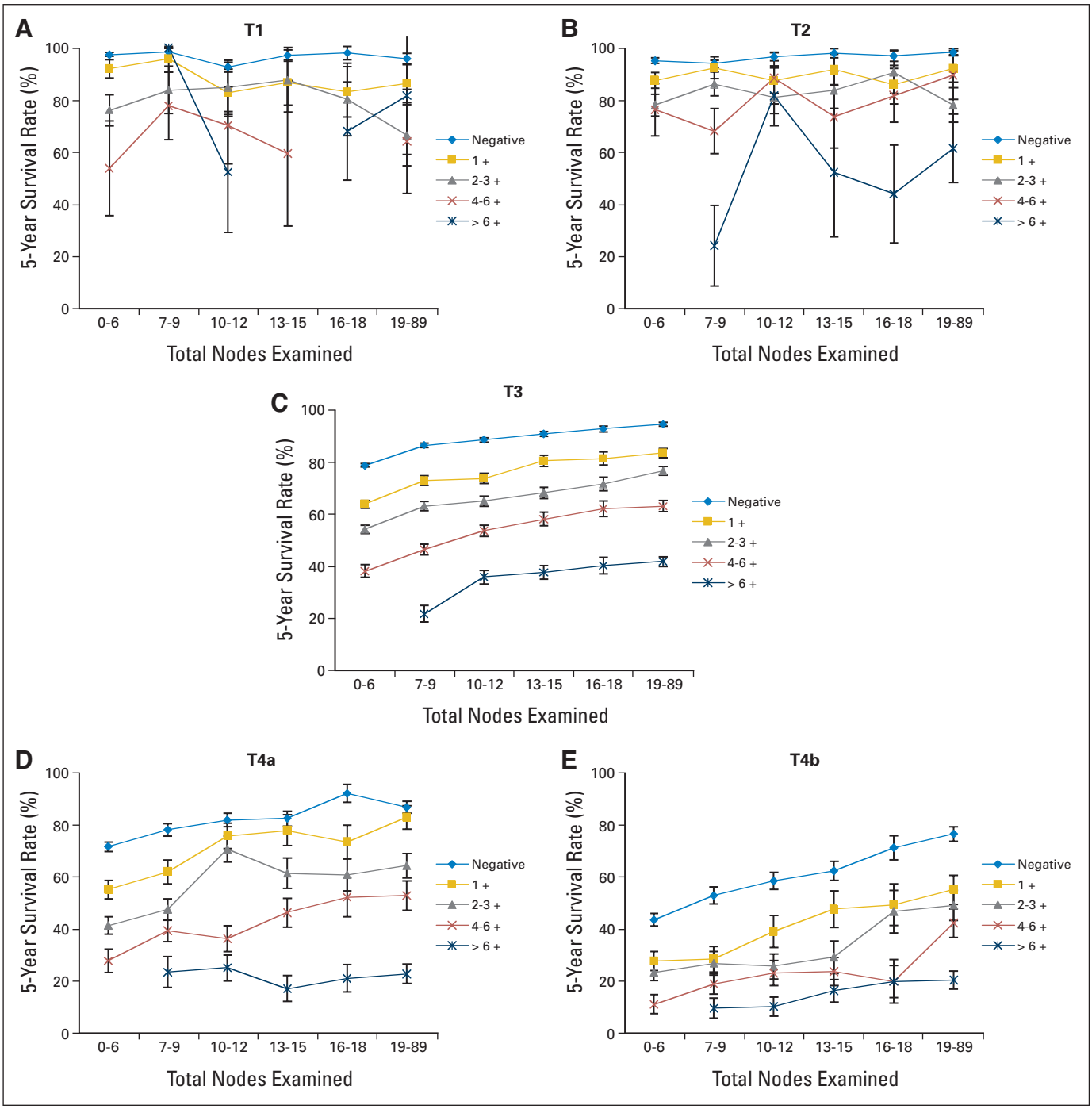

Fig 1. Interaction among T and N classifications and total nodes examined on 5-year relative survival rate in colon cancer, Surveillance, Epidemiology, and End Results (SEER) analysis. (A-E) Relative survival for pT1-4 by N1a (one positive lymph node), N1b (two to three positive lymph nodes), N2a (four to six positive lymph nodes), and N2b (≥ seven positive lymph nodes) on 109,953 patients, SEER analysis. The effect of total number of nodes examined is categorized along the abscissa. Relative survival improves for most TN categories as the number of lymph nodes examined increases. Data reprinted with permission et al.[24a]

the entire group of 130,762 patients (109,953 had invasive cancers [T1-4N0-2]; NX, 18,312; Tis or T1 polyp, 2,497), but the focus was on those with invasive cancers.

The impact of T subcategory within N category of disease was evaluated. Within both the N0 and N1 categories, patients with Tis, T1, and T2 lesions had similar 5-year relative and observed survival (relative 5-year survival for N0Tis, 95.6% ± 1.2%; N0T1, 97.4% ± 0.6%; N0T2, 96.8% ± 0.6%; N1Tis, 87.3% ± 6.0%; N1T1, 87.6% ± 2.0%; and N1T2, 87.7% ± 1.4%). For patients with N2 disease, patients with T1 and T2 lesions had similar survival (5-year relative survival for N2T1, 68.7% ± 7.0%; N2T2, 76.6% ± 3.6%), which was better than that for patients with N2T3 (47.3% ± 0.8%) or N2T4 lesions (27.1% ± 1.1%).

Patients with T4a cancers (tumor penetrates to the surface of visceral peritoneum [revised wording for AJCC seventh edition]) have better survival rates than those with T4b cancers (tumor directly invades or is adherent to other organs or structures) by N category (Tables 1 and 2). For N0T4a versus T4b lesions, relative survival was 79.6% ± 1.0% and 58.4% ± 1.3% and observed 5-year survival was 60.6% ± 0.8% and 45.7% ± 1.0%. For the N1 and N2 categories of disease, the survival differences for T4a versus T4b were also quite marked (for N1, relative survival was 60.6% ± 1.4% versus 34.9% ± 1.5% and observed survival was 47.0% ± 1.1% versus 27.9% ± 1.2%; for N2, relative survival was 33.3% ± 1.6% versus 19.7% ± 1.4% and observed survival was 26.6% ± 1.2% versus 15.8% ± 1.1%).

The number of positive nodes is prognostic for survival for most NT categories of disease (Tables 1 and 2; Fig 1). Patients with one involved regional node (N1a) have a 5% to 13% better 5-year survival than those with two to three positive nodes (N1b) by NT category of disease, with differences seen for all NT combinations. Those with four to six involved nodes (N2a) have a 5% to 19% better 5-year survival than those with seven or more positive nodes (N2b) by NT category (Tables 2 and 3), with differences seen in all NT combinations except for T1N1a versus T1N1b.

The number of nodes examined by the pathologist, in addition to the number of positive nodes, was also prognostic for survival in the current analysis. The relative survival impact of both number of positive nodes and number of nodes evaluated is shown in Figure 1. Relative survival improves as the number of nodes examined increases for most TN categories, most obvious in the large T3 category of disease (Fig 1C). Prognosis as a function of percentage of nodes examined was not evaluated.

Of the 109,953 patients with invasive cancer and evaluable TN category, 13 or more nodes were examined in 40,682 patients (37%) and seven or more were examined in 77,419 (70.4%). In the 12,101 patients with N2 category, ≥ 13 nodes were examined in 53.3% of patients and seven or more were examined in 89.7%. In contrast, of the 23,861 patients with T1-2N0 category disease, ≥ 13 nodes were examined in only 26.2% of patients and seven or more were involved in only 56.8%.

DISCUSSION

Impact of TN Category on Relapse and Survival, Implications for Staging

Through the fifth edition of the AJCC Cancer Staging Manual, substaging was not used despite marked differences in outcomes by

Table 3. SEER Colon Cancer Analysis, 5-Year Relative and Observed Survival by TN Category of Disease in Patients With Invasive Cancer and Evaluable TN Category

TN Category	No. of Patients	SEER 5-Year Relative Survival Rate (%)	SE	TNM Stage (6th edition)	Proposed TNM Stage (7th edition)*	SEER 5-Year Observed Survival Rate (%)	SE
T1N0	10,930	97.4	0.6	I	I	78.7	0.5
T2N0	12,931	96.8	0.6	I	I	74.3	0.4
T3N0	40,338	87.5	0.4	IIA	IIA	66.7	0.3
T4aN0	5,020	79.6	1.0	IIB	IIB	60.6	0.8
T4bN0	3,088	58.4	1.3	IIB	**IIC**	45.7	1.0
T1-2N1a	1,913	90.7	1.5	IIIA	IIIA	73.7	1.2
T1-2N1b	1,221	83.0	2.0	IIIA	IIIA	67.2	1.6
T1-2N2a†	377	79.0	3.6	IIIC	**IIIA/IIIB**†	64.7	3.0
T3N1a	8,759	74.2	0.8	IIIB	IIIB	58.2	0.6
T4aN1a	1,311	67.6	2.0	IIIB	IIIB	52.2	1.5
T3N1b	9,107	65.3	0.8	IIIB	IIIB	51.7	0.6
T1-2N2b	122	62.4	6.5	IIIC	**IIIB**	51.8	5.3
T4aN1b	1,460	54.0	1.9	IIIB	IIIB	42.1	1.5
T3N2a	5,331	53.4	1.0	IIIC	**IIIB**	42.8	0.8
T4aN2a‡	982	40.9	2.1	IIIC	IIIC	32.5*	1.7
T3N2b	3,235	37.3	1.2	IIIC	IIIC	30.4	0.9
T4bN1a	845	38.5	2.2	IIIB	**IIIC**	30.6	1.8
T4bN1b	929	31.2	2.0	IIIB	**IIIC**	25.4	1.6
T4bN2a	730	23.3	2.1	IIIB	IIIC	18.3	1.6
T4aN2b	671	21.8	2.2	IIIB	IIIC	17.5	1.7
T4bN2b	653	15.7	1.9	IIIC	IIIC	12.9	1.5

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.
*Proposed changes in substaging of stages II/III (bold type), based on expanded outcomes in SEER data analyses.
†Patients with T2N2a colon lesions fared better than patients with T2N2a rectal lesions; both categories placed in stage IIIB.
‡Patients with T4aN2a colon lesions fared worse than patients with T4aN2a rectal lesions; both categories placed in stage IIIC.

TN category for patients with AJCC stages II and III colorectal cancer.[1-14] In the sixth edition of the AJCC Cancer Staging Manual, stage II was subdivided into IIA (T3N0) and IIB (T4N0), and stage III was subdivided into IIIA (T1-2N1M0), IIIB (T3-4N1M0), and IIIC (any TN2M0), based on improved outcomes for patients with IIA versus IIB disease and for those with IIIA versus IIIB disease.[15,25,26] The placement of all TN2 patients into IIIC, however, was not based on in-depth outcomes analyses, since the impact of depth of bowel wall invasion (T category) in N2 patients had not been evaluated in detail.

Rectal cancer pooled analyses subsequently demonstrated the independent prognostic significance of each TN and NT category of resected rectal cancer.[16-23] Patients with T1-2N1-2 disease had a more favorable prognosis than previously thought, and those with T4N1 lesions (stage IIIB, AJCC sixth edition along with T3N1 lesions) had prognosis more akin to patients with T3-4N2 lesions (stage IIIC, AJCC sixth edition). For patients with N2 disease, data from the rectal cancer pooled analyses showed that N2 disease does not by itself confer a poor prognosis (Table 4). Substaging by T category influenced both 5-year OS (N2T1-2, 67%; N2T3, 44%; and N2T4, 37%; $P < .001$) and 5-year disease-free survival (58% *v* 36% and 30%; $P < .001$). Placement of all N2 patients within the AJCC IIIC substage in the sixth edition did not reflect the markedly different prognosis of N2 patients found in the two rectal cancer pooled analyses.[16,17] The rectal cancer pooled analyses outcomes data supported revised substaging of stage III because of improved survival for patients with T1-2N2 versus T3-4N2 lesions and survival rates for those with T4N1 lesions more similar to T3-4N2 than T3N1. In the current analysis, population-based data were used to examine those same factors in patients with colon cancer.

SEER Colon Cancer Analysis: Implications for AJCC Substaging, Seventh Edition

Data from the SEER colon cancer analysis validates data from rectal cancer pooled and SEER rectal cancer analyses. As listed in Table 4, data in the current large SEER population-based colon cancer analysis are highly consistent with the rectal cancer pooled and SEER rectal cancer analyses[16,17,24] with regard to the more favorable prognosis for patients with T1-2N1-2 lesions (IIIC, AJCC sixth edition) and less favorable prognosis for patients with T4N1 lesions (IIIB, AJCC sixth edition). Similar survival trends for patients with T1-2N1-2 and T4N1 cancers were also seen in a large NCDB analysis of 134,206 patients with invasive colon cancers (Table 4; personal communication, R. Greene, A. Stewart, April 2007). Data from the SEER colon and rectal cancer analyses, the rectal cancer pooled analyses, and the NCDB colon cancer analysis all support shifting T1-2N2 lesions from IIIC to an earlier stage of disease (IIIA/IIIB) and shifting T4N1 lesions from IIIB to IIIC (Tables 3 and 4).

SEER Outcomes: Implications for Subdividing T4, N1, and N2

SEER colon cancer outcomes data (Tables 1-4) support the substaging of T4, N1, and N2, as recommended in the SEER rectal cancer analysis.[24] Patients with T4a cancer (penetrates to the surface of visceral peritoneum; revised definition, AJCC seventh edition) have better prognosis than those with T4b cancer (directly invades or is adherent to other organs or structures) for each N category of disease (N0, N1, N2). For patients with N0T4a versus T4b lesions, there is a 15% to 20% improvement in absolute 5-year relative and overall survival, and for patients with N1T4a versus T4b and N2T4a versus T4b disease, there is a 15% to 25% improvement in 5-year relative and

Table 4. Proposed Changes in Substaging of AJCC Stages II/III Colorectal Cancer

	Rectal Cancer Pooled* 5-Year Overall Survival Rate		NCDB Colon Cancer† 5-Year Observed Survival Rate				SEER, Rectal Cancer 5-Year Observed Survival Rate			SEER, Colon Cancer 5-Year Observed Survival Rate		
TN Category	No. of Patients	%	No. of Patients	%	AJCC TNM Stage (6th edition)	Proposed TNM Stage (7th edition)	No. of Patients	%	SE (%)	No. of Patients	%	SE (%)
T1-2N0	—	—	30,159	71	I	I	9,961	77.6	0.5	23,861	76.3	0.3
T1N0	—	—	—	—	I	I	3,348	81.4	0.8	10,930	78.7	0.5
T2N0	—	—	—	—	I	I	6,613	75.7	0.6	12,931	74.3	0.3
T3N0	1,060	77	40,679	61.5	IIA	IIA	10,615	64.0	0.5	40,338	66.7	0.3
T4N0	111	65	4,604	47	IIB	T4a, IIB	818	55.7	1.9	5,020	60.6	0.8
						T4b, IIC	769	44.7	2.1	3,088	45.7	1.0
T1-2N1	355	79	3,958	67.4	IIIA	IIIA	2,008	72.1	1.2	3,134	71.1	1.0
T1-2N2	226	67	780	51.2	IIIC	**IIIA/IIIB‡**	508	56.1	2.6	499	61.5	2.6
T3N1	887	60	18,776	53.1	IIIB	IIIB	5,787	52.4	0.8	17,866	54.9	0.4
T4N1	62	35	2,600	34.1	IIIB	T4a, IIIB	480	48.2	2.5	2,771	47.0	1.1
						T4b, IIIC	423	24.3	2.5	1,774	27.9	1.2
T3N2	935	44	9,169	37.3	IIIC	**T3N2a, IIIB**	1,964	42.5	1.3	5,331	42.8	0.8
						T3N2b, IIIC	1,791	32.0	1.3	3,235	30.4	0.9
T4N2	108	37	1,986	22.4	IIIC	T4a, IIIC	397	34.3	2.7	1,653	26.6	1.2
						T4b, IIIC	308	15.6	2.5	1,383	15.8	1.1

NOTE. Proposed changes (bold type) are based on rectal cancer pooled analysis, NCDB colon cancer analysis, and SEER rectal and colon cancer analyses.
Abbreviations: AJCC, American Joint Committee on Cancer; NCDB, National Cancer Data Base; SEER, Surveillance, Epidemiology, and End Results.
*Modified from Gunderson et al.[17]
†NCDB colon series, observed survival, modified from R. Greene, A. Stewart, personal communication, April 2007.
‡IIIA, T1N2a; IIIB, T2N2a, T1-2N2b.

overall survival. Earlier analyses with much smaller data sets suggested that patients with perforated T4 lesions may have worse prognosis than those with lesions that invade or adhere to other organs or structures.[27,28] However, as shown in the large SEER colon cancer (current series) and rectal cancer data sets,[24] patients with T4 lesions that penetrate to the surface of visceral peritoneum have more favorable prognosis than patients with lesions that invade or adhere to other organs or structures.

As shown in the current analysis and prior series, both the number of positive nodes and the number of nodes examined have prognostic significance.[24-39] In the current large SEER colon cancer analysis, patients with one positive node (N1a) have a 5% to 13% better 5-year survival than those with two or three positive nodes (N1b) by T category, with improved survival for all TN categories. Patients with four to six positive nodes (N2a) have a 5% to 19% better 5-year survival than those with seven or more positive nodes (N2b) by T category, with improved survival for all TN categories except T1N1a versus T1N1b.

Limitations of the SEER colon cancer database include NX in 18,312 of the total group of 130,762 patients (14%). In addition, of the 109,953 patients with invasive colon cancer and evaluable TN category, a significant percentage did not have the preferred 10 to 14 nodes evaluated by the pathologist; 13 or more nodes were examined in 40,682 patients (37%), and seven or more nodes were evaluated in 77,419 (70.4%) patients. It is of interest that fewer nodes were examined in patients with early TN category lesions compared with patients with more extensive disease. Of the 23,861 patients with T1-2N0 lesions, $\geq$ 13 nodes were examined in 26.2% of patients and seven or more nodes were examined in 56.8% of patients, whereas for the 12,101 patients with N2 category, $\geq$ 13 nodes were examined in 53.3% of patients and seven or more nodes were examined in 89.7% of patients.

SEER Colon Cancer Analysis Supports Further Substaging of AJCC Stages II/III

Data in the current SEER colon cancer analysis combined with data in the SEER rectal cancer analysis,[24] the rectal cancer pooled analyses,[16,17] and the NCDB colon cancer analysis support revised substaging of AJCC stages II and III (Tables 3 and 4). The AJCC seventh edition HTF recommended the following changes (Table 4): (1) subdivide IIB into IIB (T4aN0) and IIC (T4bN0) on the basis of SEER colon and rectal cancer outcomes, (2) shift more favorable TN2 categories to either IIIA (T1N2a) or IIIB (T2N2a, T1-2N2b, T3N2a), and (3) shift less favorable T4N1 lesions from IIIB to IIIC (T4bN1).

Survival outcomes by TN category in the current SEER colon cancer analysis combined with those in the SEER rectal cancer analysis,[24] rectal cancer pooled analyses,[16,17] and NCDB colon cancer analysis suggest a complex biologic interaction between depth of invasion and nodal status. As listed in Tables 1-4, patients with positive nodes in some TN categories (T1-2N1, T1-2N2) have similar or better prognosis than patients with negative nodes with regard to both relapse (rectal cancer pooled analyses) and survival (SEER colon and rectal cancer analyses, rectal cancer pooled analyses, and data from NCDB). Patients with T1-2N1 lesions have better 5-year OS (rectal cancer pooled analyses), relative, and observed survival (SEER colon and rectal cancer analysis, and data from NCDB) than those with T3N0 or T4N0 cancers (Tables 1-4) and are more akin to patients with T2N0 lesions (Tables 3 and 4). Most patients with T1-2N2 lesions have 5-year survival similar to patients with T2N0, T3N0 (T1N2a), or T4aN0 (T2N2a, T1N2b) lesions. Patients with the T2N2b category of lesions have survival similar to patients with T4bN0 lesions. Since adjuvant systemic therapy is not recommended for patients with T2N0 lesions and not recommended routinely for those with T3N0 lesions, the need for such treatment in all patients with T1-2N1-2 category lesions should be evaluated in future trials.

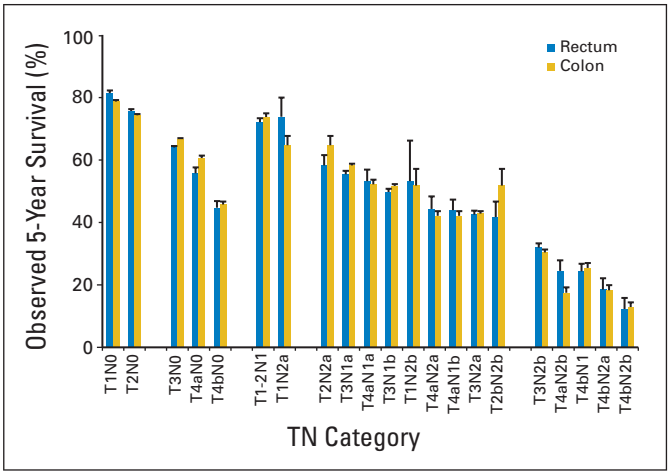

Fig 2. Observed 5-year survival by TN category. In the current Surveillance, Epidemiology, and End Results (SEER) colon cancer analysis and the previously reported SEER rectal cancer analysis,[24] 5-year survival is strikingly similar by TN category of disease for patients with rectal or colon cancers.

Survival outcomes by TN category of disease in the current SEER colon cancer analysis are strikingly similar to SEER rectal cancer outcomes (Table 4 and Fig 2). Because of the similarities in survival outcomes, the AJCC HTF made the recommendation to continue to have a common staging system for patients with colon and rectal cancers. Whether these similarities are the result of tumor biology, the impact of adjuvant treatment on survival outcomes, or other factors cannot be discerned from this and other analyses but should be evaluated.

As the AJCC HTF prepares for the next edition of the AJCC Cancer Staging Manual, prospective data will be collected with regard to peritumoral deposits, number of positive nodes, total number of nodes examined, radial margin status, and other factors.[40,41] These data, along with other information, will be used by the AJCC HTF to consider further refinements in staging, including the incorporation of molecular markers as adjuncts or modifiers to the TNM categories of disease.[42]

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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