An Evaluation of the American Joint Committee (pTNM) Staging Method for Cancer of the Colon and Rectum

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This study, using prospective data, compares the survival of 1011 patients who had a colorectal cancer resected at Concord Hospital between 1971 and 1983. The results are expressed both in terms of Australian clinicopathologic (CP) staging and the modified pTNM method proposed by the American Joint Committee for Cancer Staging and End Results reporting. The aim of the study was to determine which of the two staging methods gave the better guide to prognosis. The results indicate that pTNM does not add to information beyond that given by CP staging. We conclude that the pTNM classification is only partially able to separate patients into different survival groups; it is complicated and difficult to memorize, and does not give useful prognostic information beyond that provided by the simpler CP system. [Key words: Clinicopathologic staging; pTNM staging; Colorectal cancer; Survival]

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THE TNM CLASSIFICATION SYSTEM proposed by the Union International Contre le Cancer (UICC) is now the most widely used staging system for categorizing the anatomic extent of tumor spread.[1] Since it was described initially by Pierre Denoix[2] in 1954, it has been modified and applied to stage cancers at most gastrointestinal sites,[3] and is considered to be a reliable, reproducible indicator of prognosis. This method was designed to classify tumors by stage at the time of diagnosis in terms of T (extent of the primary tumor), N (condition of regional lymph nodes) and M (presence or absence of distant metastases).[1] An essential feature of the system has been that the description of the tumor is applied to patients who have not been treated previously, and that the extent of the disease may be determined on clinical examination only. Each case is assigned the highest category of T, N, and M that describes the extent of the disease at the time of diagnosis.

The Task Force on the Colon and Rectum of the American Joint Committee (AJC) for Cancer Staging and End Results Reporting was established to unify the staging of colorectal cancer (CRC) based on the principle of TNM defined by the UICC.[4] For sites such as the colon and rectum, it was argued that a classification based solely on clinical examination was of little practical use because of the inaccessibility of the large bowel. The pTNM (postsurgical treatment - pathologic staging) method was therefore proposed as a modification of the TNM system, and incorporates the clinical definition as well as all histologic information, including that from resected specimens of CRC. In this alternative method, there are five stages that have been described; the system has been reviewed in several publications.[5-8] The method has yet to be evaluated prospectively.

The aim of this study was to evaluate pTNM in terms of its ability to predict survival, using prospective data from the Colorectal Cancer Project at Concord Hospital. A comparison was also made between the Concord Clinicopathological Staging System[9] and pTNM staging to determine which of the two gave the better guide to prognosis.

A tumor staging system whose purpose is to aid in prognosis should be capable of separating patients into categories which have significantly different survival, and the survival time should diminish with each successive advance in stage. The effectiveness of the pTNM and the Concord Clinicopathological (CP) Staging Systems may be compared using these two criteria. A further basis for comparison is the extent to which either staging system can encompass the information provided by the other. For example, if a group of CP Stage A patients is also staged according to pTNM, and if there are progressive and significant differences in survival between the subgroups thus formed, it can be seen that the pTNM system is providing a finer degree of discrimination than the CP system. Conversely, if there are no differences in survival between the subgroups, then pTNM is incapable of supplementing information given by CP.

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Patients and Methods

The Colorectal Cancer Project at Concord Hospital is a continuing, mulidisciplinary, computerized study of all patients with a histologic diagnosis of adenocarcinoma of the colon or rectum who have had a bowel resection or excision of the rectum. The project commenced in 1971 as a collaborative study between the Department of Anatomical Pathology and the Department of Surgery at the University of Sydney. More than 90 percent of the operative specimens have been dissected by one pathologist (RN) who staged, reported, and coded the histology of every case.

The method of classifying patients using the CP Staging System at Concord Hospital has been described previously,[9,10] and is summarized in Table 1. In general principle, this system is similar to that described by Turnbull *et al.*.[11] The method utilizes Stage D to identify patients considered incurable at the time of surgery. This category includes all patients with histologic evidence of tumor in a line of resection or in whom metastatic tumor is shown either clinically, by additional investigations, or at surgery (often confirmed histologically) to be outside the limits of the resected specimen. Because of the detailed method of data collection and coding in the Concord operative series,[9] it has been possible to stage the tumors by both pTNM (Table 2) and CP methods.

All data were stored, retrieved, and analyzed on a Cyber (72-170) computer using version 9.0 of the Statistical Package for the Social Sciences[12] (SPSS). Life-table survival analyses were computed using the method of Berkson and Gage.[13] Survival was measured from the time of resection of the tumor until death from any cause. Censored cases were those in which the patient was alive at the most recent followup. Immediate postoperative deaths were not excluded from analysis for reasons suggested by Ederer and his colleagues.[14] Differences in observed survival experience between groups were tested for statistical significance using a nonparametric technique developed by Lee and Desu[15] based on the Gehan method,[16] using a generalized Wilcoxon test. A probability level of $P \leq 0.05$ was accepted as statistically significant. Because the age and sex composition of the groups compared were not significantly different, no corrections were made for non-cancer deaths.

TABLE 1. Staging System

Stage	Spread
A*	Not beyond muscularis propria; no lymph node metastases; no tumor in lines of resection; no distant metastases.
B	Beyond muscularis propria and/or free mesothelial surface involved; no lymph node metastases; no tumor in lines of resection; no distant metastases.
C	Lymph node metastases present irrespective of depth of direct penetration through bowel wall. No tumor in lines of resection; no distant metastases.
D	Tumor in a line of resection (histologic) and/or distant metastases.

*Tumors confined to the mucosa (no penetration of muscularis mucosa) are excluded in this analysis.

Results

Between 1971 and 1983, 1020 patients had resections for CRC at Concord Hospital. Nine patients who had a tumor of pTNM Stage 0 were excluded from the study. No patient was lost to followup and of the 1011 patients available for study, 438 had died at the time of analysis. There were 715 men (average age, 68.7 years, SD 23.3) and 296 women (average age, 70 years, SD 11.3). The predominance of men reflects the population of this veterans' hospital.

Table 3 shows the cross-tabulation of patients classified in terms of CP and pTNM staging systems. Both methods of staging consistently identified early and advanced stage tumors. All pTNM, Stage Ia cases qualified as CP Stage A; and all Stage IV cases qualified as CP Stage D. Stage Ib (pTNM method) included only a portion of CP Stage A; the majority (85 percent) fell into CP Stage B. Of the 53 Stage II patients (pTNM method), 26 fulfilled the criteria for CP Stage D, while 35 of the 337 Stage III patients (pTNM method), also were CP Stage D.

Survival diminished stage by stage in the CP system (Fig. 1), with statistically significant differences obtained between every pair of stages except Stages A and B (Table 4). In the pTNM system, survival diminished stage by stage (Fig. 2) except that Stage III showed better survival than Stage II, though the difference was not statistically significant (Table 5).

The differences in survival of patients staged according to pTNM for each CP stage are shown in Table 6, while the survival of patients staged according to the CP method for each pTNM stage is shown in Table 7.

TABLE 2. pTNM (AJC) Staging System

Stage	Spread
0*	Carcinoma *in situ*.
Ia	Tumor confined to mucosa or submucosa; no lymph node or distant metastases.
Ib	Tumor limited to wall of colon or rectum but not beyond—viz, invasion into M. propria or subserosa (colon and proximal rectum) and into M. propria but not beyond (distal rectum): no lymph node or distant metastases.
II	Tumor involves all layers of bowel wall with invasion of immediately adjacent structures; no lymph node or distant metastases.
III	Any degree of bowel wall invasion with lymph node metastases.
IV	Any invasion of bowel wall with or without lymph node metastases but with evidence of distant metastases.

*Cases excluded for purpose of this analysis.

TABLE 3. Cross Tabulation of CP Stage by pTNM Stage (Number of Patients)

CP Stage	pTNM Stage					
	Ia	Ib	II	III	IV	Total
A	46	59	—	—	—	105
B	—	342	27	—	—	369
C	—	—	—	302	—	302
D	—	—	26	35	174	235
TOTAL	46	401	53	337	174	1011

TABLE 4. Differences in Survival According to CP Stage

Stage	Stage Compared	Median Survival (Months)	Chi-Square	Significance (*P* Values)
A		131		
	B		2.35	0.09
	C		27.25	<0.0001
	D		102.46	<0.0001
B		72		
	C		33.30	<0.0001
	D		177.46	<0.0001
C		34		
	D	12	78.85	<0.0001

Discussion

This study, using prospective data from one center, demonstrates that the pTNM classification is capable of categorizing patients into different survival groups. The results also confirm the prognostic importance of the depth of direct spread of tumor through the bowel wall, lymph node status, and the presence or absence of distant metastases. However, these pathology variables have been shown already to be important in other forms of clinicopathologic staging.[9,11,17]

In the CP staging method used at Concord Hospital, lesions confined to the mucosa are documented as a separate entity (Sub-stage A_1).[9] Although some may argue that these lesions may not represent the initial phase in the evolution of CRC, in practice, we believe that it is important to identify such patients to allow us to regroup our data for purposes of comparison with other staging methods. In the pTNM classification, stage 0 lesions refer to *in situ* carcinoma in which no submucosal invasion can be demonstrated. However, because of the difficulties in precise definition and the small number of cases involved, Stage 0 lesions were excluded from the analysis.

In the pTNM method, Stage Ia includes patients with carcinoma confined to the mucosa, and those with demonstrable submucosal invasion. It is inappropriate to place these two groups of patients in the same category, since it has been shown that direct spread that is limited to the submucosa carries a small but definite risk of associated lymph node metastases.[18,19] These patients, therefore, need to be distinguished as a separate group.

The separation of survival curves for Stages Ia and Ib tumors using the pTNM classification occurs because Stage Ib includes patients in whom the tumor has spread into the muscularis propria, but does not clearly distinguish between partial and complete penetration of the muscular wall. Furthermore, Stage Ib (pTNM method) presumably may include patients where there is involvement of a free mesothelial surface by tumor. The pTNM classification does not make this distinction clear, and such cases were arbitrarily placed in Stage Ib. These patients are known to have a poor survival.[9]

The pTNM system failed to separate patients in Stages II and III into groups having significantly different sur-

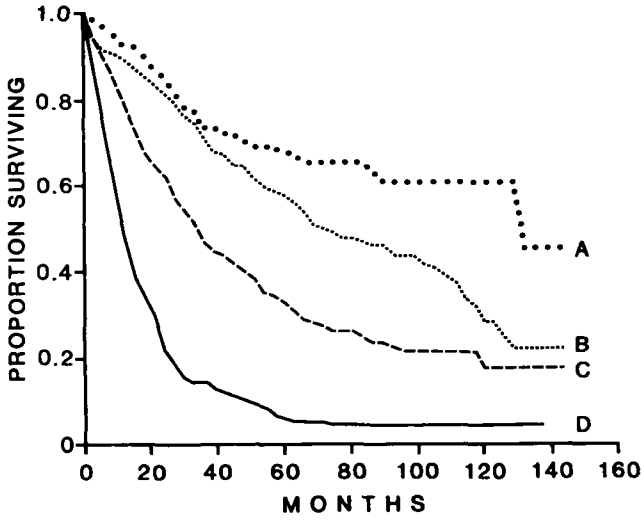

FIG. 1. Survival by CP stage.

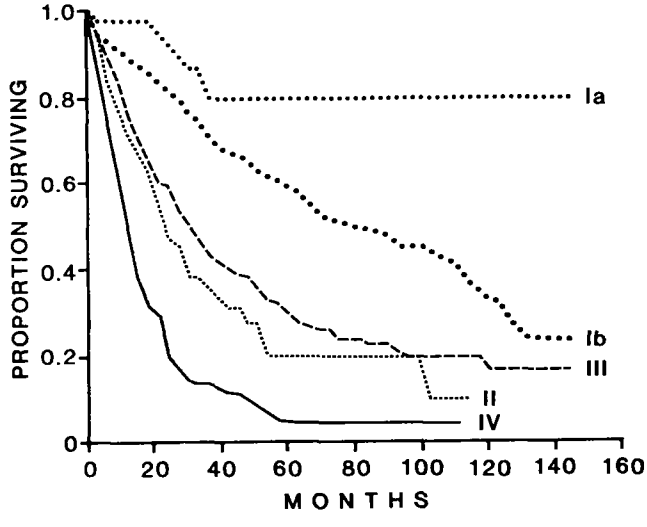

FIG. 2. Survival by pTNM stage.

TABLE 5. Differences in Survival According to pTNM Stage

Stage	Stage Compared	Median Survival (Months)	Chi-Squared	Significance (*P* Values)
Ia		141		
	Ib		5.91	0.01
	II		24.73	<0.0001
	III		25.72	<0.0001
	IV		60.25	<0.0001
Ib		81		
	II		27.27	<0.0001
	III		52.77	<0.0001
	IV		169.29	<0.01
II		23		
	III		1.26	0.26
	IV		13.39	0.0003
III		31		
	IV	12	60.94	0.0001

TABLE 6. Differences in Survival Between pTNM Stages Standardized for the Same CP Stage

CP Stage	pTNM Stage Compared	Median Survival (Months)	Chi-Squared	Significance
A (N = 105)	Ia (N = 46)	141		
			4.78	0.029
	Ib (N = 59)	89		
B (N = 369)	Ib (N = 342)	76		
			2.58	0.10
	II (N = 27)	47		
C (N = 302)	III (N = 302)	34	—	—
D (N = 235)	II (N = 26)	17		
	III (N = 35)	11	1.52	0.46
	IV (N = 174)	12		

TABLE 7. Differences in Survival Between CP Stages Standardized for the Same pTNM Stage

pTNM Stage	CP Stage Compared	Median Survival (Months)	Chi-Squared	Significance
Ia (N = 46)	—	—	—	—
Ib (N = 401)	A (N = 59)	89		
			0.001	0.96
	B (N = 342)	76		
II (N = 53)	B (N = 27)	47		
			9.12	0.002
	D (N = 26)	17		
III (N = 337)	C (N = 302)	34		
			18.41	<0.0001
	D (N = 35)	11		
IV (N = 174)	—	—	—	—

vival (Table 5). Moreover, Stage III patients appeared to have a better survival than those in Stage II (Fig. 2). This may be explained. Patients in whom residual tumor was identified histologically in a line of surgical resection (Table 3) were included in Stage II. Presumably the prognostic significance of inadequate clearance of the tumor outweighs the effect of lymph node metastases (Stage III patients). This requires clarification, because there appears to be no provision made for cases which can be shown pathologically to have had an incomplete surgical clearance. Such patients perhaps would best be included in Stage IV.

When different pTNM stages were compared for the same CP stage (Table 6), the only significant difference demonstrated was the difference in survival within CP Stage A (between Stages Ia and Ib). This suggests that CP staging is a robust system which essentially provides better discrimination than the pTNM method. However, when CP Stages were compared with the same pTNM Stage (Table 7), significant differences in survival were obtained for pTNM Stage II (between CP Stages B and C) and for pTNM Stage III (between CP Stages C and D). This confirms that pTNM does not provide additional information beyond CP staging.

Conclusions

A comparison of the pTNM and CP methods was possible in this study because, in the Concord series, data were collected in such a way as to allow each case to be staged according to either method. Although the pTNM system appears comprehensive, its benefits are few, and it lacks precision. Our assessment of the pTNM system is that: 1) The separation between Stages II and III is inadequate and in reverse order, *i.e.*, Stage II appears to have a worse prognosis than Stage III. This suggests that these stages do not differentiate groups with significantly different survival; 2) The pTNM system does not give information beyond that provided by the simpler CP system; and 3) the pTNM system is complex and cumbersome to apply in a clinical situation.

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Announcements

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