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Tumor size predicts long-term survival in colon cancer: an analysis of the National Cancer Data Base

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Abstract

BACKGROUND: American Joint Committee on Cancer uses tumor size for "T" staging of many solid tumors for its effect on prognosis. However, tumor size has not been incorporated in tumor (T), nodal status (N), metastasis (M) staging for colon cancer. Hence, the National Cancer Data Base was used to determine whether tumor size correlates with TNM staging and survival.

METHODS: For the 300,386 patients, tumor size was divided into S_1 (0 to 2 cm), S_2 (>2 to 4 cm), S_3 (>4 to 6 cm), and S_4 (>6 cm). Statistical comparison was done for TNM stage, grade, and nodal status with tumor size. Kaplan–Meier survival analysis was done for each "S" stage.

RESULTS: Of the 300,386 patients, 13% were classified as S_1, 39% S_2, 30% S_3 and 18% as S_4. Right colon was the most common site (48%). Tumor size positively correlated with grade, T stage, and nodal stage. Tumor size was inversely associated with survival.

CONCLUSION: Tumor size is positively correlated with important prognostic factors and negatively impacted survival.

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The first edition of the Cancer Staging Manual of the American Joint Commission on Cancer (AJCC) was published in 1977.[1] Since then, including the 7th edition of the AJCC Cancer Staging Manual published in 2012, the prognostic significance of the tumor size is reflected by its major role in determining the T stage of many solid tumors including breast, lung, renal, and thyroid cancers. In breast cancer, increasing tumor size is associated with increased axillary node metastasis and decreased overall survival.[2] Likewise, tumor size greater than or equal to 4 cm has been shown to increase risk of mortality in non–small cell lung cancer[3] and to be a predictor of metastatic potential in renal cell carcinoma.[4] Despite the value of tumor size as a prognostic indicator in many other solid tumors, tumor size has not been incorporated into the tumor (T), nodal status (N), metastasis (M) staging system for colon cancer.

The AJCC TNM staging system for colon cancer bases the T (tumor) stage on depth of tumor invasion through the different layers of the bowel rather than tumor size. The AJCC consensus statement released in January 2000 listed 8 separate studies showing no association between tumor size and patient outcome.[5] However, all these studies were limited because of a small patient sample size ranging from 98 to 463 patients. Additional consideration was paid to the 1980s landmark analyses of the National Surgical Adjuvant Breast and Bowel Project data by Wolmark et al reiterating previous studies showing no association between tumor size and lymph node positivity, specifically in Dukes C tumors. These studies, although composed of prospective, randomized data, were also limited by small sample size, with one analysis comparing a cohort of only 47 and 362 patients.[6,7] Another important 1980s analysis, a retrospective study of 391 colon cancer cases at MD Anderson by Miller et al,[8] was one of the few at the time to examine survival, and found no association with tumor size. Rather than considering tumor size in isolation, it could be considered in connection with other known prognostic variables for staging and treatment decisions, as suggested by Wolmark et al and Miller et al.[7,8] On that basis, Saha et al[9] sought to further examine the role of tumor size in a larger retrospective analysis of 681patients undergoing conventional surgery or sentinel node mapping in addition to conventional surgery and demonstrated that increasing tumor size correlated with higher nodal positivity, higher T stage, and decreased 5-year overall survival. Similarly, in a recent study by Kornprat et al,[10] tumor size was significantly associated with progression-free and cancer-specific survival in a cohort of 359 colon cancer patients. Thus, whether tumor size may hold value as a prognostic indicator in colon cancer remains somewhat uncertain.

Despite advances in surgical and oncologic treatment, up to 25% of patients with stage I and II colon cancer will develop a recurrence after a potentially curative surgical resection. This suggests that there are potential prognostic factors that are not incorporated into the current staging system. Because prior studies used by the AJCC to determine TNM staging in colon cancer may have been underpowered for tumor size, we have analyzed data from 300,386 colon cancer patients within the National Cancer Data Base (NCDB) to evaluate the potential role of tumor size as a prognostic indicator.

Methods

Population

Data were collected from the NCDB for 994,627 patients with colon cancer between 1998 and 2010. The NCDB is a nationwide oncologic outcome database that encompasses approximately 70% of all new invasive cancers diagnosed in the United States. Only patients diagnosed with invasive adenocarcinoma (8,140/3) by International Classification of Diseases, ninth revision, coding system and with surgery of primary tumor were included. Patients were excluded from analysis if they had incomplete data for age, sex, tumor grade, nodal status, or TNM stage and for incomplete follow-up. All patients analyzed had complete data for TNM staging, tumor grade, tumor size, nodal status, and survival. After exclusion criteria were implemented, data from a total of 300,386 patients were analyzed. Patients were divided into 4 quartiles based on tumor size: S_1 (0 to 2 cm), S_2 (>2 to 4 cm), S_3 (>4 to 6 cm), and S_4 (>6 cm). The division of tumor size into variables was somewhat empiric and was chosen for its relative simplicity. We then compared tumor size in each quartile with T stage, nodal status, survival and tumor grade.

Statistical analysis

Demographics and clinical characteristics were analyzed using *t* test for continuous variable and chi-square test for categorical variables. Using univariate analysis, the 4 quartiles of tumor size were compared with TNM stage, tumor grade, nodal status, and T stage. The measure of linear association was measured using Mantel–Haenszel linear-by-linear association chi-square test and the correlation for the ordinal variable was obtained using gamma statistics. Survival analysis was done using the Kaplan–Meier method to evaluate the role of different tumor size on survival. Covariates were adjusted for tumor grade, nodal status, patient age, and sex using a regression model (Cox proportional hazard). The final model was built by using a step-up method by sequentially adding clinically relevant variables including tumor size. Variables with a *P* value less than .05 were included in the final model. A *P* value less than .05 was considered statistically significant for all analysis. All statistical analysis was done on SAS 9.3, SAS Institute, Inc., Cary, NC.

Results

In total, 300,386 patients with invasive adenocarcinoma of the colon were included in the study. The median age of the patients included in the study was 72 years. There was a slight female predominance at 52% of the study population. The data also revealed that the majority of patients were