Targeting Lymph Node Retrieval and Assessment in Stage II Colon Cancer: A Quality Outcome Community-Based Cancer Center Study

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Abstract

Purpose: Adequate lymph node evaluation is required for the proper staging of colon cancer. The current recommended number of lymph nodes that should be retrieved and assessed is 12.

Methods: The multidisciplinary Gastrointestinal Tumor Board at the Derrick L. Davis Forsyth Regional Cancer Center reviewed and recommended that a minimum of 12 lymph nodes be examined in all cases of colon cancer to ensure proper staging. This recommendation occurred at the end of the first quarter of 2005. To ensure this new standard was being followed, an outcomes study looking at the number of lymph nodes evaluated in stage II colon cancer was initiated. All patients with stage II colon cancer diagnosed between 2004 and 2006 were reviewed.

Results: There was a statistically significant improvement in the number of stage II colon cancer patients with 12 or more lymph nodes evaluated. Before the Gastrointestinal Tumor Board's recommendation, 49% (40 out of 82 patients) had 12 or more lymph nodes sampled. The median number of lymph nodes evaluated was 11. After the Gastrointestinal Tumor Board's recommendation, 79% (70 out of 88 patients) had 12 or more lymph nodes sampled. The median number of lymph nodes was 16.

Conclusion: Multidisciplinary tumor boards can impact the quality of care of patients as demonstrated in this study. Although we do not yet have survival data on these patients, based on the previous literature referenced in this article, we would expect to see an improvement in survival rates in patients with 12 or more nodes retrieved and assessed.

Introduction

In 2007, an estimated 112,340 Americans were diagnosed with colon cancer, and an estimated 52,180 deaths occurred.¹ Prognosis is related to stage at diagnosis. Surgery alone provides cures for the majority of patients with stage II disease (T3N0, T4N0). Chemotherapy in the adjuvant setting has not been routinely recommended. For stage III patients (T1 to T4, N1 to N2), surgical cure rates are approximately 50%. Adjuvant chemotherapy reduces relapse rates by about one third in this setting and is commonly recommended.²

Accurate staging is critical for improving the outcomes of patients with colon cancer. The College of American Pathologists, the American Joint Committee on Cancer, the National Cancer Institute, the International Union Against Cancer, and the National Comprehensive Cancer Network recommend a minimum of 12 lymph nodes be examined to accurately identify stage II colon cancers.³⁻⁷ Inadequate evaluation of lymph nodes may have serious implications. Some patients with stage II colon cancer may be understaged due to inadequate lymph node evaluation and may not be given the opportunity to benefit from adjuvant chemotherapy. Inadequate lymph node sampling may result in higher local recurrence due to failure to remove involved lymph nodes, though literature support to confirm this is lacking. Finally, inadequate lymph node evaluation might be a marker for poor surgical quality or pathologic examination.

Despite the importance and implications of adequate lymph node evaluation, most colon cancer patients do not have 12 or

more lymph nodes examined. The National Cancer Database analysis of lymph node evaluation in patients with stage II (T3N0) colon cancer diagnosed from 1985 through 1991 showed that only approximately 40% of 35,787 patients had 12 or more lymph nodes evaluated.⁸ In 2005, Baxter et al⁹ reported on 116,995 adults with colorectal cancer from the Surveillance, Epidemiology, and End Results database from 1988 to 2001. Only 37% had 12 or more lymph nodes analyzed. Finally, a study of 1,789 stage II colon cancers from the Ontario Cancer Registry between the years 1997 to 2000 showed that 73% of cases were based on the assessment of less than 12 lymph nodes.¹⁰

Furthermore, many studies have shown poorer prognosis with inadequate lymph node sampling. An analysis of the Intergroup trial INT 0089 demonstrated that the 5-year survival rate improved from 73% to 87% in patients with stage II colon cancer when more than 20 lymph nodes were recovered (rather than 1 to 10 lymph nodes).¹¹ In the report of 35,787 cases of stage II colon cancer from the National Cancer Database, patients in whom one or two lymph nodes were examined had a 5-year survival rate of 64% compared with an 86% rate in patients in whom greater than 25 nodes were examined.⁸ A review of the Surveillance, Epidemiology, and End Results database reported in 2006 showed a 5-year survival rate of 78% when more than 15 lymph nodes were evaluated compared with 70% for eight to 14 lymph nodes and 66% for one to seven lymph nodes in stage II colon cancer.¹² Chang et al¹³ reviewed 17 clinical studies from nine countries. In 16 of 17 studies, there was an associa-

tion between increased numbers of lymph nodes evaluated and longer survival in stage II colon cancer patients.

As a part of a GI cancer quality initiative, the multidisciplinary Gastrointestinal Tumor Board at the Derrick L. Davis Forsyth Regional Cancer Center reviewed the available literature at the end of first quarter of 2005. The multidisciplinary group consists of pathologists, radiologists, surgeons, radiation oncologists, and medical oncologists. It was recommended that a minimum of 12 or more lymph nodes be the goal for every patient with colon cancer. Furthermore, an outcome study to look at our efforts was to be undertaken. We chose to focus this study on stage II colon cancer cases because guidelines specifically recommended examination of a minimum of 12 lymph nodes to clearly establish stage II (T3 to T4, N0) colon cancer. Proper staging of these patients has a great impact on their prognosis and the use of adjuvant chemotherapy. This article summarizes our findings, highlighting the important role of multidisciplinary tumor boards in quality improvement.

Methods

This study was comprised of patients with stage II (T3N0, T4N0) colon cancer aged 34 to 97 years who were diagnosed at FRCC between January 1, 2004, and December 31, 2006. We selected this timeframe to compare nodes retrieved and assessed before and after our discussion of the importance of lymph node sampling during our multidisciplinary Gastrointestinal Tumor Board at the end of the first quarter of 2005. Patients from 2004 and 2005 were identified through the FRCC cancer registry database and included analytic stage II colon patients cases reported during the above timeframe. Since 2006 cases were not complete in this database at the time of the study, the registrars reviewed their pathology reports in the suspense system for surgical cases that met the stage criteria of the study. To finalize our list of eligible patients, we only included patients with an adenocarcinoma histology, and we excluded one patient where the number of lymph nodes was unknown. In addition to the number of nodes examined, the patient's age, sex, and location of disease were collected. For 2004 and 2005, this data came from the cancer registry. For 2006, a review of the patient's chart was performed to collect these additional data.

To ensure the quality of our cancer registry database, cases are identified through several different means. On a daily basis, registrars review all pathology reports to screen for reportable cases. They also review the history and physical reports from *Radiation Oncology* daily. In addition, quarterly International Classification of Diseases, 9th Revision, Clinical Modification (ICD9) lists from our hospital's admitting system are reviewed, which allows us to capture up to six levels of diagnoses.

Resection Types

The location of the disease for the stage II colon patient cases was separated into three areas: (1) the right colon, which included the hepatic flexure, ascending colon, cecum and appen-

dix, (2) the transverse colon, and (3) the left colon, which included the descending colon, sigmoid colon, and splenic flexure.

Statistical Analysis

For analysis of the lymph node retrieval from 2004 to 2006, the SAS/STAT statistical software (SAS system, version 9.1; SAS Institute, Cary, North Carolina) was used. A Pearson χ^2 was performed on all categorical data. A Mann-Whitney *U* test was used on the number of nodes due to the lack of normality of the data. Significance levels of $P < .05$ for both tests were used. For the analysis of the interaction between the number of lymph nodes and age, sex, and location of disease, Factorial Anova statistics were employed.

Results

Data was collected on a total of 170 cases of stage II colon cancer reported from FRCC's cancer registry system from January 2004 through December 2006. Group A (2004 to first quarter 2005) represented patient cases reported before the Gastrointestinal Tumor Board's recommendation (82 total patient cases). The median age was 71 years with 50% males and 50% females. The location of the colon cancer was 56.1% right colon, 4.9% transverse colon, 37.8% left colon, and 1.2% not specified. Group B (second quarter 2005 to 2006) represented patient cases reported after the tumor board recommendation (88 total patient cases). The median age was 73 with 40.9% males and 59.1% females. The location of the colon cancer was 46.6% right colon, 12.5% transverse colon, and 40.9% left colon (Fig 1).

The distribution of recovered lymph nodes (0 to 6, 7 to 11, 12+) in Groups A and B is graphically displayed in Figure 2. There was a statistically significant improvement in the number of patients with 12 or more lymph nodes evaluated (Pearson χ^2 statistic 10.05; $P < .0001$). The mean number of lymph nodes was 12.1 in Group A and 15.6 in Group B, which was also statistically significant ($P < .0001$ using the Mann-Whitney *U* test). Table 1 presents the data table for the distribution of recovered lymph nodes (0 to 11, 12+) in Groups A and B. We performed a separate analysis of the interaction between age, sex, and location of colon cancer and the number of lymph nodes recovered. There was no statistical significance that could be found (Table 2).

Discussion

FRCC's multidisciplinary Gastrointestinal Tumor Board was created in 2004. Multidisciplinary tumor boards can have many functions. The role of this Tumor Board was set forth by the recommendations of the Health Care Advisory Board and others.^{14,15} This tumor board meets twice monthly. Prospective cases are discussed, literature is reviewed, research efforts are overviewed, and outcome measures are studied. The first outcomes study undertaken was assessing the adequacy of lymph node examination in stage II colon cancer. The Tumor Board reviewed the available literature and made a recommendation

Figure 1. Percent of stage II colon cancer cases by cancer location at D.L. Davis Forsyth Regional Cancer Center from 2004 to 2006. Group A cases include 2004-1Q05 and Group B cases include 2Q05-2006.

that a minimum of 12 lymph nodes should be retrieved and examined in all cases of colon cancer. Surgeons and pathologists were targeted as these disciplines have a direct bearing on the outcome.

With focused attention to this quality metric, the multidisciplinary Gastrointestinal Tumor Board at FRCC was able to spearhead adherence such that 12 or more lymph nodes were reviewed and examined in 79% of the stage II colon cancer cases. Through the Tumor Board's effort, we were able to statistically improve the median number of lymph nodes examined as well as the percentage of patients with 12 or more lymph nodes examined. Before the board's recommendation in April 2005, 49% of stage II colon cancer cases had 12 or more lymph nodes retrieved and assessed. After the recommendation, 79% had adequate lymph node sampling.

The Tumor Board investigated which discipline impacted this outcome; surgery or pathology. Ideal bowel resections, margins,

Figure 2. Number of nodes examined in stage II colon cancer cases at D.L. Davis Forsyth Regional Cancer Center from 2004 to 2006. Group A cases include 2004-1Q05 and Group B cases include 2Q05-2006.

Table 1. Distribution of Recovered Lymph Nodes (0 to 11, 12+) in Groups A and B

Nodes Examined	Group A, 2004-1Q05	Group B, 2Q05-2006
0-11 nodes	42	18
12+ nodes	40	70
Number of nodes		
Mean	12.1	15.6
Standard deviation	7	5.4
Median	11	16
Total cases	82	88

and lymphadenectomy have been described by a National Cancer Institute panel of experts.⁵ The extent of the bowel resection is defined by removing the blood and lymphatic supply at the origin of the feeding arterial vessel. Although debatable, 5 cm of normal bowel on either side of the primary tumor is considered adequate for minimizing local recurrences. The lymph nodes at the origin of the feeding arterial vessel should be removed if possible and tagged. All suspicious lymph nodes outside the field of resection should be removed or have a biopsy. As mentioned previously, a minimum of 12 lymph nodes should be removed. Multiple surgeons perform colon cancer surgery at FRCC. When asked if the Tumor Board's recommendation lead to a change in their surgical approach, the answer was no. In reviewing the data, it did not appear that any one surgeon had a different rate of obtaining 12 or more lymph nodes.

Pathologists, on the other hand, admit to a change in their practice. After the Tumor Board's recommendation, there was a concerted effort to dissect out more lymph nodes and to make every effort to obtain a minimum of 12 lymph nodes. Pathologic detection of lymph nodes in fat-laden specimens can be difficult. As many as 70% of lymph nodes are less than 0.5 cm in diameter, and these may be the only lymph nodes involved.¹⁶ Despite this difficulty, several single institution studies have demonstrated higher rates of lymph node retrieval when employing standardized methods of evaluation.^{17,18} The pathologist's role is determining whether the number of lymph nodes examined was dramatically reported in a recent correspondence in the *Journal of Clinical Oncology*. This report was about a

Table 2. Variables and Their Impact on Lymph Node Recovery*

Variable	F Value	P
Age	1.56	.0587
Sex	2.81	.1001
Location	2.55	.0884
Age and location	1.03	.4596
Age and sex	1.61	.0767
Sex and location	1.66	.1999

* Both groups (A and B) are combined in these data.

single high-volume surgeon operating at two hospitals with two different pathology groups. In 76 cases at one hospital, the median number of lymph nodes was 10, and in 54 cases at another hospital, the median number of lymph nodes was 18. The authors believed the difference to be driven by the pathologic care at the two hospitals.¹⁹

Despite good surgical and pathologic care, other factors may impact lymph node recovery. Some studies suggest that age and left-sided location may decrease lymph node recovery. The strength of this association is not known.^{8,10} We did a separate analysis on our data looking at whether age, sex, or location of disease had any impact on the number of nodes retrieved, and we did not see a statistical significance.

As previously mentioned, this study demonstrates that multidisciplinary tumor boards can impact the quality of care of

patients. Although we do not have survival data on this patient population yet, a future study is planned to review that data. Based on the literature referenced in this document, we expect to see an improvement in survival rates for those patients with 12 or more nodes retrieved and assessed that will improve the quality of care of our stage II colon cancer patients.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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