The Relationship between Size of Adenocarcinoma of Colon and Lymph Node Involvement

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ABSTRACT

Background and Objectives: Involvement of lymph nodes is an important prognostic factor in the most cancers, including colorectal cancer. In the recent years, invasion to blood and lymphatic vessels has been shown to predict involvement of lymph nodes and the number of involved nodes has been less studied issue. The aim of this study was determination of the relationship between the size of colorectal adenocarcinoma and lymph node involvement.

Materials & Methods: In this cross-sectional study, 116 patients were enrolled with colorectal cancer from Rasoul-e-Akram and Mehr Hospitals in 2002-2008. Data analysis was performed by SPSS-15 software. Results were expressed as frequency, percent, and mean ±SD. We used Chi², student t-test and correlation tests for statistical analysis.

Results: 54.3% of patients were male and 45.7% were female. Mean age of them was 59.4± 12.9 years. Mean of tumor size (longest diameter) was 5.4± 2.2 (range: 1.5 to 12) cm. Mean number of involved lymph nodes was 4.9± 3.5(range: 1-14). There was no correlation between number of lymph node involvement and tumor size. There was no correlation between lymph node involvement and tumor and age group, sex, location and depth of tumor. Poorly differentiated tumor significantly correlated to lymph node involvement (P=0.001).

Conclusion: There is no correlation between tumor size and number of involved lymph node in colorectal cancer. However, poor histopathologic grade is associated with lymph node involvement.

Keywords: Adenocarcinoma, Colon, Tumor Burden, Lymphatic Metastases
Introduction

The prognostic significance of tumor size and lymph node status has served as the basis for staging system in the majority of solid tumor (TNM) (1, 2). The relationship between tumor size and prognosis has been perceived to indicate that the smaller the tumor the greater the likelihood of prolonged control with operative extirpation (3). Moreover, a direct relationship between tumor size and regional lymph node metastases has been assumed in numerous solid tumors (4-7), and the data available in breast cancer have been utilized to illustrate an association between these two variables (3), although results contradicting such a relationship have appeared (8). The various staging schemes available for colorectal cancer are exceptional in that tumor penetration rather than tumor size is utilized as a predictive index of prognosis. The inherent implication in these colorectal classifications is that tumor size is predictive of neither prognosis nor regional lymph node status suggesting a unique biological situation (3). In an effort to explore the relationship between tumor size and regional lymph node status, the national surgical adjuvant project for breast and bowel cancer (NSABP) was carried out and analysis obtained from an initial cohort of 924 patients with colorectal cancer. The result indicated that tumor size was unrelated to regional lymph node status. Moreover, the relationship between tumor size and number of the positive nodes was not addressed (3).

Involvement of lymph node is a relevant prognostic parameter, which determines the duration of survival in patients with colonic and rectal adenocarcinoma (9). Presence of involved lymph nodes necessitates adjuvant chemotherapy after surgery (10, 11). In the recent years, invasion the blood and lymphatic vessels has been shown to predict involvement of lymph node (12). However, the issue that the size of tumor can be used for prediction of lymph node was less studied. The number of involved lymph nodes is an important factor in determination of patient’s survival (12-14). Thus, finding a relationship between tumor size and number of involved lymph nodes will help us to predict the number of metastatic lymph nodes (and thereby survival of patients) based on tumor size.

If such relationship is confirmed in other studies, we can use tumor size as a major prognostic marker in predicting lymph node involvement and risk stratification in particularly stage IIA rectal cancers.

Our aim in this study was to determine the relationship between size of adenocarcinoma of colon and lymph node involvement and number of involved nodes.

Materials and Methods

In this cross-sectional study, 116 consecutive patients were enrolled with colorectal cancer in Rasoul-e-Akram and Mehr hospitals in 2002-2008. After identifying the patients, we collected our data (demographic and pathologic data) from the samples by means of a checklist. All pathologic examinations were done by one pathologist.

Statistical analysis

We used SPSS-15 software for data and chi2, student t-test and person correlation for statistical analysis to compare frequencies, comparison of means and to assess correlations, respectively.

Results

Male to female ratio was approximately 1.2:1. 54.3% of patients were male and
45.7% were female. Age of patients ranged from 27 and 87 years and mean age of them was 59.4±12.9 years. 57.9% of patients were above 50 years old and only two patients (1.7%) were under 30 years. Frequencies of location of tumor in Rt. colon, Lt. colon, sigmoid and rectum were 35.3%, 8.6%, 15.5%and 40.5%, respectively. 56.9% of tumors were well differentiated, 25% were moderately differentiated, and 18.1% were poorly differentiated. Tumor size ranged from 1.5 to 12 cm and mean of tumor size (maximum diameter) was 5.4±2.2 cm.

Reactive lymph nodes were seen in all patients. Lymph nodes were involved by tumor in 56 patients (48.3%). Mean number of involved lymph nodes was 4.9±3.5 (range: 1-14).

Tumor stages were in a scale from I to IV; the most common stage was stage II A with frequency of 33.6%.

There was not any significant difference between two groups of patients with involved lymph nodes and those without involved lymph nodes as regards age, tumor size, and depth of tumor (T). Furthermore, there was no relation between number of lymph node involvement and tumor size. Mean number of involved lymph nodes in patients with tumor size 5cm was not different from patients with tumor size>=5cm (4.53± 3.4 vs 5.32± 3.7). There was no correlation between lymph node involvement and age group, sex and location of tumor.

Grade of tumor significantly correlated to lymph node involvement (P=0.001). These results are summarized in Table1.

### Table 1: Comparison of characteristics of patients with colorectal cancer with involved lymph nodes and those without involved lymph nodes

<table>
<thead>
<tr>
<th>LN involvement</th>
<th>Neg.</th>
<th>Pos.</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>27(42.9%)</td>
<td>36(57.1%)</td>
<td>&gt;0.05</td>
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<tr>
<td>Female</td>
<td>29(54.7%)</td>
<td>24(45.3%)</td>
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<tr>
<td><strong>Location of tumor</strong></td>
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<tr>
<td>Rt. colon</td>
<td>18(43.9%)</td>
<td>23(56.1%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lt. colon</td>
<td>6(60.0%)</td>
<td>4(40.0%)</td>
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</tr>
<tr>
<td>Sigmoid</td>
<td>11(61.1%)</td>
<td>7(38.9%)</td>
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<tr>
<td>Rectum</td>
<td>21(44.7%)</td>
<td>26(55.3%)</td>
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<tr>
<td><strong>Tumor depth (T)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>T2</td>
<td>12(70.6%)</td>
<td>5(29.4%)</td>
<td>&gt;0.05</td>
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<tr>
<td>T3</td>
<td>34(45.3%)</td>
<td>41(54.7%)</td>
<td></td>
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<tr>
<td>T4</td>
<td>10(43.5%)</td>
<td>13(56.5%)</td>
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<tr>
<td><strong>Age group</strong></td>
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<tr>
<td>&lt;30yr</td>
<td>0(0.0%)</td>
<td>2(100.0%)</td>
<td>&gt;0.05</td>
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<tr>
<td>30-50yr</td>
<td>11(42.3%)</td>
<td>15(57.7%)</td>
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<tr>
<td>&gt;50yr</td>
<td>45(51.1%)</td>
<td>43(48.9%)</td>
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<tr>
<td><strong>Grade(differentiation)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Well</td>
<td>40(60.6%)</td>
<td>26(39.4%)</td>
<td>&gt;0.001</td>
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<tr>
<td>Moderate</td>
<td>13(44.8%)</td>
<td>16(55.2%)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>3(14.3%)</td>
<td>18(85.7%)</td>
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<tr>
<td><strong>Tumor size</strong></td>
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<tr>
<td>&lt;=5cm</td>
<td>36(53.7%)</td>
<td>31(46.3%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>&gt;5cm</td>
<td>20(40.8%)</td>
<td>29(59.2%)</td>
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<tr>
<td><strong>Mean age (yr)</strong></td>
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<tr>
<td>60.6±11.6</td>
<td>58.2±13.9</td>
<td>&gt;0.05</td>
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<tr>
<td><strong>Mean tumor size</strong></td>
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<tr>
<td>5.07±2.3</td>
<td>5.7±2.04</td>
<td>&gt;0.05</td>
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<tr>
<td><strong>Mean depth of tumor (T)</strong></td>
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<tr>
<td>2.96±0.63</td>
<td>3.2±0.6</td>
<td>&gt;0.05</td>
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</table>
Discussion

Tumor staging systems characterize the extent of neoplastic dissemination. Each tumor class is defined by a number of features invariably based upon specific morphological properties of the particular tumor.

In order to classification scheme to be clinically useful, each defined category must serve as a marker for a specific tumor subset with discrete biological features, as well as unique natural history characteristics and prognosis.

Patient prognosis is the function of clinical and histopathological stage of colon cancer at diagnosis. In addition to the well-established significance of standard pathological features such as depth of bowel wall penetration (T), the number of regional lymph nodes involved (N), and presence of extracolonic metastases (M), several other factors have been proven to be of importance. These include number of harvested and processed lymph node, histologic grade, and evidence of lymphvascular as well as perineural invasion. The most of previous studies have evaluated the relationship between factors such as tumor histological grade and lymph vascular invasion and lymph node involvement (15-17). However, studies assessing relationship between tumor size and number of involved lymph node are lacking.

Bjelovic et al. (1998) in the survey in the institute of digestive disease, clinical center of Serbia, evaluated a correlation between the macroscopic (size and consistency) and microscopic characteristics of the regional lymph node (type of involvement in tumor tissue, state of the capsule, adherence of the lymph nodes, etc) in patient with colorectal carcinoma.

In this prospective study, 46 patients with rectal and sigmoid adenocarcinoma were studied through randomized selection. From the resected specimens, a total of lymph nodes were identified (average 15.66 per patient), with the precise location determine according to Enker and Philipshken.

The macroscopic characteristics of each lymph node were identified. Within the group of "small" lymph nodes, 17.18% were malignant. Additionally, of all the malignant lymph nodes, 46.23% were less than 5 mm in diameter. Although the malignant lymph nodes were diffusely involved within the tumor tissue, 19.50% were focally involved within the tumor tissue, of which 48.38% were "small" lymph nodes, which are commonly non-palpable. These authors concluded that size and consistency of the lymph nodes were not dependable parameter for appraisal of lymph node involvement in tumor tissue, the state of the lymph node capsule, and the interrelation among the lymph nodes. As in the case of the primary tumor local tumor aggression in the lymph nodes is conditional by the grade of differentiation, i.e. histologic immaturity, rather than by tumor size (9).

In our study, there was no correlation between number of lymph node involvement and tumor size. The mean number of involved lymph nodes in patients with tumor size <5cm was not different form patient with tumor size >5cm. Other studies reported that no correlation was found between lymph node involvement and tumor size, but numbers of involved lymph nodes were not considered. Wolmark et al. (2006) in a study explored the relationship between tumor size and regional lymph node involvement in patients with Dukes' B and C colorectal cancer in the randomized prospective clinical trials.

Overall, 670 patients with colon cancer, and 236 patients with carcinoma of the rectum were available for analysis. The result indicated that there was no correlation between
the longest diameter of the primary tumor
and the status of regional lymph nodes for
either colon or rectal cancer. Moreover, this
lack of association was evident throughout
the distribution. These findings underscore
the unique biological behavior of colorectal
cancer and emphasize the function of the
current generation of randomized pros-
pective trials in providing natural history infor-
mation (18).

The lack of correlation between tumor size
and regional lymph node involvement has
received sporadic attention for many years.
In 1938, Gilchrist and David (19) pro-
claimed that the size of a tumor was of little
value in determining the presence or the ab-
sence of lymph node metastases and in 1940
Coller et al. (20) described 52 rectal lesions
and concluded that there was no relationship
between the size of the lesion and the pres-
ence of regional metastases. These authors
specifically noted that the incidence of me-
tastases was the same for the smallest and
largest lesions. A relationship was noted
between tumor configuration and regional
node involvement with sessile tumors demon-
strating the highest percentage and “exca-
vating” tumors the lowest. Coller and col-
leagues (21) not only reaffirmed that their
initial conclusions related to tumor size but
also suggested that the incidence of meta-
stasis was actually higher in tumors of small
surface area. Reports by Steams and deddish
(22) and Spratt and Ackerman (23) revealed
that the size of a rectal cancer bore no rela-
tion to the penetration of the bowel and fre-
cuency of lymph node involvement. The latter report analyzed 226 consecutive pa-
tients with carcinoma of the colon or rectum
who underwent tumor resection. In a subse-
quent analysis in 1962, (24), reaffirmed that
tumor morphology was an important predic-
tive index in that pedunculated cancers were
far less likely to be associated with lymph
node metastasis than were ulcerated lesions
of similar size. There is a considerable inter-
est in chance of lymph metastases from visi-
ble cancer <2 cm was statistically the same
as larger lesion and small-ulcerated cancer
were the most infiltrating of all.

In another study, miller et al. analyzed the
relationship of tumor size to regional and
system metastasis and to survival according
to stage of disease. Colon cancers (391
cases) that were treated surgically at M.D.
Anderson Hospital from 1955 to 1975 were
reviewed. Staging of disease was based on
the astler-coller modification of Dukes' stag-
ing classification. The mean diameters
(cm±s.e.m.) of Dukes' B1, B2, C2 and D
tumor were 4.47±0.34 (n = 46), 6.61±.029 (n
= 147), 5.39±0.23 (n= 71) and 5.78±0.24
(n= 120), respectively. The mean diameter
of Dukes' B2 tumor was significantly greater
than C2 (P<0.001) and D (P<0.05) tumors.
Within stage B and C, there was no relation-
ship between the size of the primary tumor
and the 5-year adjusted survival. These
finding suggest that colon carcinoma me-
tastasis and survival are independent of tu-
mor size. Because tumor burden dose nit
account for distant disease, specific tumor
cell phenotypes and biological processes are
probably more important in determining
metastatic disease (24).

In our study, histopathologic grade of tumor
is significantly correlated to lymph node in-
volvement. This is similar to Miller study
(11).

In the statistical analysis, there was no sig-
nificant correlation between lymph node in-
volvement and location of tumor or depth to
tumor (T). Depth of tumor penetration in
colon wall has been reported to be associ-
ated with lymph node involvement; Wol-
mark et al., examined the interrelationship
of depth of penetration, tumor size, and the
number of positive nodes in Dukes C colo-
rectal cancer. The result indicated that depth of tumor penetration was related to both tumor size and the number of positive regional lymph nodes. Tumors with positive nodes, which failed to penetrate the muscularis propria (C1), were smaller, and were associated with fewer positive nodes as compared to tumors penetrating all coats of the bowel (C2). Although tumor penetration was related to tumor size and the number of positive nodes within the C1 and C2 patient subsets. The data underscore the biological significance of depth of tumor penetration and militate against tumor size as a prognostic discriminate in patients with colorectal cancer. The finding represents a contradiction to the prevailing biological concept related to the behavior of solid tumors as reflected in the TNM classification scheme (3).

Conclusion

This study indicates that there is no correlation between tumor size and number of involved lymph node in colorectal cancer. However, Histopathologic grade is associated with lymph node involvement.

Acknowledgment

The authors declare that there is no conflict of interests.

References

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