

Lymph Node Evaluation In Colorectal Cancer Patients in Iran

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ABSTRACT

Introduction: Colorectal cancer is the third and fourth major cause of cancer prevalence and also mortality among males and females, respectively in Iran. The number of Lymph Nodes which are remain associated after surgery, are one of the pre-notice aspects which influence on patients. This study aimed to investigate the rate of adequacy of lymph node in patients with colorectal cancer in Tehran, Iran. This study was a retrospective investigation and the studied population was the patients who had been hospitalized with colorectal cancer in Imam Khomeini Hospital, Tehran, Iran. Data on patient and tumor variables were collected from charts of 1095 patients aged, diagnosed at our hospital in 2005-2014. 877 colorectal cancer patients were evaluated for involvement of lymph nodes during study. 495 subjects (56.4%) were male with the mean age of 51.34 ± 12.23 and 382 patients (43.6%) were female with average age of 50.51 ± 13.41 . The mean number of evaluated lymph nodes in total period of the study was 8. The minimum number of involved lymph nodes in the patients was 0 and 91 cases showed such situation and maximum number of involved lymph nodes in patients was 25 that included 1.03% of the patients. with regards to importance of definition of involved lymph nodes in prognosis and chance of survival in the patients and also suggestion of national cancer institute to define at least 12 lymph nodes for determination of disease stage, it is advised that definition of involved lymph nodes conduct with higher accuracy.

Keywords: Metastasized Lymph Nodes , Surveyed Lymph Nodes , Colorectal Cancer.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide¹. It should be mentioned that a suitable evaluation of the lymph-node status of colorectal carcinoma specimens is important to comply with the suggestions of the UICC and also, to decide about the application of adjuvant therapy in patients with positive lymph nodes. In the last few years, immunohistochemical and molecular methods

have been utilized by pathologists and surgeons for the identification of micrometastases, as the tumor, spread to the locoregional lymph nodes, has been widely regarded as the principle prognostic element²⁻⁵.

A sufficient retrieval and assessment of colorectal mesenteric lymph nodes is crucial to ensure which lymph nodes do not contain metastatic disease. It is clear that failure to examine enough lymph nodes might result in a failure in identifying

the patients in whom a comparatively small fraction of the nodes is involved with cancer. Moreover, lymph node metastasis might happen in patients, irrespective of the T stage or the other pathologic factors^{6,7}.

In non-metastatic colorectal cancer, lymph node status is the strongest pathologic predictor of patient outcome. Around 68% of the patients, with no lymph node involvement, will survive 5 years, compared to only 40% of those with lymph node metastasis⁸.

The suggestions, offered by AJCC, ASCO, ACoS-CoC, CAP, and NCCN, expressed that the evaluation of eⁿ 12 LNs is adequate for staging a patient with CRC and these recommendations appeared to be able to put an end to the existing debate. However, the anecdotal evidence has indicated that such advices might not be implemented⁹. In present study, we focused on the frequency of CRC and involved lymph nodes and adequacy of lymph node dissection in patients who referred to our hospital in Tehran, Iran.

Patients and methods

Study design

This descriptive cross sectional study was performed on profiles of 1095 colorectal patients referred to radiotherapy and oncology unit of Imam Khomeini Hospital, Tehran, Iran during May 2005 to April 2014 were evaluated. From these profiles, those that lacked after surgery pathology report were excreted from study and 877 remained profiles were evaluated. The age and gender of patient and

the number of evaluated lymph nodes and the number of involved lymph nodes were recorded in this study.

The frequency of total number of colorectal patients was evaluated for each year and the frequency of numbers of evaluated lymph nodes in pathology report was evaluated for each year and the mean number of total evaluated lymph nodes in pathology report was evaluated in all years in our study. To estimate the trends in the incidence rates, these registries' data have pooled together. The ages have categorized into eight age groups (dⁿ 20 ; 21-30; 31-40; 41-50; 51-60; 61-70; 70<).

Statistical Analysis

Data have analyzed using SPSS, version 18. Chi-square test has employed to compare the scores of each of the measures and some of the parameters. A p-value of less than 0.05 has considered statistically significant.

RESULTS

877 colorectal cancer patients were evaluated for involvement of lymph nodes during 2005-2014. 495 subjects (56.4%) were men with the mean age of 51.34±12.23 and 382 patients (43.6%) were women with average age of 50.51±13.41. No significant correlation was observed between involvement rate of lymph nodes and gender (p>0.05).

The mean number of evaluated lymph nodes in total period of the study was 8. The minimum number of involved lymph nodes in the patients was 0 (10%) and 91 cases showed such situation and maximum number of involved lymph nodes in patients was 25 that included 1.03% of the patients. Diagram 1 shows the evaluated lymph nodes separately.

The mean number of involved lymph nodes in total period of the study was 7. The minimum number of involved lymph nodes in total period of study was zero that included 42.21% of cases (370 cases) and the maximum number of involved lymph nodes was 20 lymph nodes that included 0.32% (3cases) of the patients. Diagram

Table 1: the distribution of patients according to age

Percent	Number	Age (year)
1.49	13	<20
6.16	54	21-30
15.39	135	31-40
21.89	192	41-50
22.58	198	51-60
17.44	153	61-70
15.05	132	>70
100	585	Total

2 shows the rate of involved lymph nodes separately.

The minimum frequency of the patients was related to year 2007 (46 cases) and the maximum frequency was related to year 2014 (168 cases). The mean number of evaluated and involved lymph nodes is presented in table 2 for each year.

DISCUSSION

An accurate examination of lymph node status in patients with non-metastatic colorectal cancer is evidently important. Lymph node status is the best predictor of long-term outcome in patients with colorectal cancer, who do not have metastatic disease. In fact, the existence of positive lymph nodes is used to determine the need for adjuvant chemotherapy of patients with colon cancer and is associated with an improved use of adjuvant radiation and chemotherapy for patients with rectal cancer^{10, 11}. It should be mentioned that an inadequate lymph node evaluation is accompanied with a worse outcome, in terms of tumor recurrence and patient survival¹²⁻¹⁵. The basis of this relationship has not been recognized yet; however, it probably reflects an incorrect staging and the ensuing insufficient adjuvant therapy. So far, several authors have recommended that the patients, who are considered lymph node-negative on the basis of a low number of retrieved lymph nodes, should be considered at high risk of recurrence and thus, as candidates for adjuvant therapy. In fact, the retrieval of a low number of lymph nodes is usually likely to

be an indicator of a poor-quality surgical or pathologic care^{14, 15}

In the present study, 585 colorectal cancer patients were evaluated, 495 subjects (56.4%) were male and 382 patients (43.6%) were female. In this investigation, the men-to-women ratio was 1.29 to 1 and the results were consistent with the previous studies¹⁶⁻¹⁸. In this study, the majority (77%) of colorectal cancer incidences were observed in the ages higher than 40 years. This finding is in parallel with some previous studies that indicated the incidence of colorectal cancer, higher in patients older than 45 years¹⁹⁻²¹. It is worth stating that the number of affected people per year has increased during 2005-2014. The reason might be the increase in visiting the medical centers, or the increased knowledge of people about the symptoms of this disease, or the recent developments of the diagnostic facilities, or a higher incidence of this disease in comparison with the past years^{22, 23}.

The number of involved lymph nodes is one of the most important and effective factors in determining the prognosis of this disease and finding a treatment program for the patients. According to the studies by Jass and based on the guidelines of the international gut and chest surgery association, it has been proposed to evaluate, at least, 12 lymph nodes in order to be able to report the lymph nodes as negative^{23, 24}.

The mean number of evaluated lymph nodes, in this study, was 8 lymph nodes, which is lesser in comparison with the other studies such as

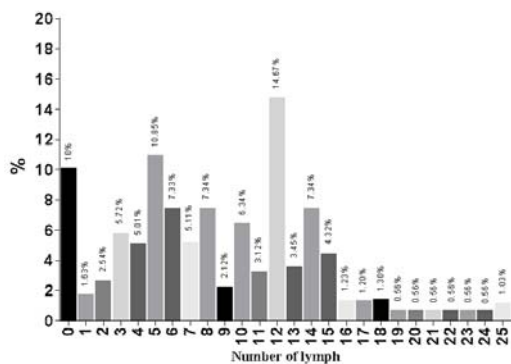


Fig. 1: The distribution of evaluated lymph nodes based on frequency

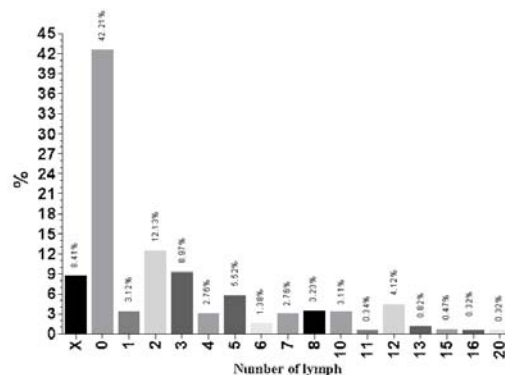


Fig. 2:

Wong *et al.*, who evaluated 11 lymph nodes on average, or Tepper *et al.*, who assessed 14 lymph nodes on average^{14, 25}. In addition, in the analysis of INT-0089, 18 lymph nodes were evaluated. The mean number in the present study was lesser than the aforementioned suggestion for evaluating, at least, 12 lymph nodes to determine the disease stage^{26, 27}. This might have been resulted from an insufficient extraction of the tissue by the surgeon or an insufficient evaluation of the sample by the pathologist that leads to an inability for correct staging of the disease and also, for determining an appropriate treatment program for these patients. It will ultimately lead to over-treatment of the patients by radiotherapy and chemotherapy, because of the inability for distinct determination of the negativity of involved lymph-nodes.

In this study, in 578 cases (65.9%), less than 12 lymph nodes were evaluated, among which 234 subjects (26.7% of the total subjects) had zero involved lymph nodes and 74 cases (8.43% of the total subjects) had unknown numbers of involved lymph nodes (i.e., X lymph nodes). This means that in total, 37.1% of the entire studied cases, or in other words, 56.2% of the cases with less than 12 evaluated lymph nodes, did not possess a complete staging. Consequently, since it was unknown whether they have involved lymph nodes or not, they experienced over-treatment with radiotherapy and chemotherapy. Such a situation would cause

financial expenses and other side effects on patients.

Although the remained 271 cases, with the evaluated lymph nodes of less than 12, did not have a complete staging, because of the presence of involved lymph nodes and also, the likelihood of involvement of more lymph nodes, they went under additional treatments with a higher certainty.

In the remained 318 cases, among the subjects in which the number of involved lymph nodes was equal or higher than 12, it was possible to correctly categorize the disease and define the lymph nodes' involvement positive or negative, and to appropriately make an accurate decision about the necessity of additional treatments, including chemotherapy or radiotherapy.

In an evaluation, conducted by international gut and chest surgery protection institute on 844 patients, the depth of tumor and the number of positive lymph nodes were indicated as the two effective factors on the prognosis of the patients. The results of their study showed that the patients with positive lymph nodes, at the ratio of 1 to 4, had a better prognosis compared to the patients with a higher ratio of involved lymph nodes²².

A widespread analysis was performed on the results of the lymph nodes' samples among the

Table 2: shows the number of patients based on gender, the evaluated and involved lymph nodes for each year

Year of diagnosis	Mean of Involved lymph nodes /Evaluated lymph nodes	Male Number (%)	Female Number (%)	Total Number (%)
2005	3 / 10	18 (62.07)	11 (37.93)	29 (4.96)
2006	8-Mar	14 (48.28)	15 (51.72)	29 (4.96)
2007	7-Apr	16(76.19)	5 (23.81)	21 (3.59)
2008	7-Feb	25 (62.5)	15 (37.5)	40 (6.84)
2009	8-Mar	21 (51.22)	20 (48.78)	41 (7.01)
2010	7-Feb	33 (50)	33 (50)	66 (11.28)
2011	8-Mar	38 (58.46)	27 (41.54)	65 (11.11)
2012	7-Feb	56 (62.22)	34 (37.78)	90 (15.38)
2013	10-Mar	52 (52.53)	47 (47.47)	99 (16.92)
2014	8-Mar	57 (54.39)	48 (45.61)	105 (17.95)

patients, participated in an inter-group evaluation of INT-0089. The analyses were conducted separately on the positive lymph node group (2,768 patients) and the negative lymph node group (698 patients). The mean number of reported lymph nodes in searchable patients was 11 (the range was from 1 to 87). These results demonstrated that the survival rate, independent of the disease, showed a significant decrease with a higher number of involved lymph nodes. The survival rate increased after controlling the number of involved lymph nodes, and even in the patients with negative lymph nodes, the survival rate was normally increased and the chance of cancer was significantly also increased²⁵.

CONCLUSION

With regard to the importance of defining involved lymph nodes in the prognosis, and based on the chance of survival in patients and according to the suggestion of the national cancer institute for defining, at least, 12 lymph nodes for the determination of the disease stage, it is advised to provide the definition of involved lymph nodes with a higher accuracy. It should be also declared that this study was subjected to a number of limitations, such as the lack of stage determination, life-span determination, and survival of patients after treatment. Thus, it is strongly suggested to conduct further studies on these limitations and appraise them.

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