

# The Impact of Surgeons: Pathologists Dialog on Lymph Node Evaluation of Colorectal Cancer Patients

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**ABSTRACT:** **Background:** Lymph node (LN) retrieval and assessment is essential for accurate staging and treatment planning in colorectal cancer (CRC). According to U.S. National Cancer Institute recommendations, the minimal number of LNs needed for accurately staging of node-negative CRC is 12. Awareness and implementation of the guidelines has been shown to improve after assigning an opinion leader who has a special interest in CRC.

**Objectives:** To evaluate the impact of dialogue between surgeons and pathologists in LN evaluation.

**Methods:** Consecutively treated CRC patients at the Department of Surgery B at Rambam Medical Center from January 1, 2000 through July 30, 2005 were identified from hospital discharge files. Demographic, surgical, and pathological data were extracted. Patients were divided into two groups. Group I patients underwent surgery before the initiation of a structured surgical oncology service (January 1, 2000 to October 30, 2004). Group II patients underwent surgery after the initiation of the service (November 1, 2004 to July 30, 2005).

**Results:** The study comprised 212 patients (Group I: n=170; Group II: n=42). The median number of LNs examined was 9 in Group I and 14 in Group II ( $P = 0.003$ ). Only 35% of patients in Group I received adequate LN evaluation compared to 79% in Group II ( $P = 0.0001$ ). Patients with left-sided or rectal cancer were less likely to receive adequate LN evaluation than patients with right-sided cancers.

**Conclusions:** A durable improvement in LN evaluation was realized through a multi-pronged change initiative aimed at both surgeons and pathologists.

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**KEY WORDS:** colon cancer, rectal cancer, colorectal cancer (CRC), lymph node evaluation, accurate staging

**C**olorectal cancer (CRC) is the second leading cause of cancer death in the United States. Approximately 80% of patients diagnosed with CRC are operable at presentation [1], and surgical resection remains the definitive treatment for CRC. Lymph node (LN) retrieval and assessment is critically important for accurate staging and treatment planning. Several

studies have shown improved survival rates when increasing the number of LNs extracted and examined [2,3]. The improvement is probably due in part to more accurate staging, allowing increased utilization of adjuvant therapy [1].

Multiple factors influence adequate lymph node recovery. These include surgical resection techniques, evaluation techniques of the pathology, and patient factors such as obesity and age [4]. As such, much debate has been centered on the significant role of both the pathologist and the surgeon on patient survival [5]. The surgeon must provide the pathologist with an adequate specimen in which the ideal resection includes the tumor, its blood supply, and lymphatic drainage at the origin of the feeding vessel [6], and the pathologist should analyze the specimen in search of the largest number of LNs. Identifying tumors is not always a simple task since metastatic LNs in the mesentery are frequently < 5 mm in size [7]. Furthermore, there are various LN extraction techniques that may affect the number of nodes retrieved [8].

Many efforts have been made in recent years to determine the adequate number of LNs that should be examined to predict node negativity [9]. From these investigations, evidence-based guidelines from the College of American Pathologists (CAP) have suggested 12 nodes minimum [3]. However, there is a clear gap between the guidelines and clinical practice. For example, in the United States, only 37–50% of CRC patients have 12 or more nodes examined [10]. Thus, increasing knowledge, awareness, and implementation of the guidelines is vital and has been shown to improve by assigning an opinion leader who has special interest in CRC [11]. In our single center study, we set up a multi-pronged change initiative aimed at both surgeons and pathologists, which included assigning an oncology surgeon to act as an opinion leader to emphasize communication between the doctors in these two specializations. The aim of the study was to evaluate the impact of this dialogue initiative between surgeons and pathologists on lymph node evaluation, while keeping the surgical and pathology techniques unchanged.

## PATIENTS AND METHODS

Retrospectively consecutive patients with CRC who underwent surgical resection at the Department of Surgery B, Rambam

Medical Center from January 1, 2000 through July 30, 2005, were identified from hospital discharge files. Demographics as well as surgical and pathological data were extracted, including patient age, gender, type of colorectal resection, and number of lymph node assessed.

Colorectal specimens were subdivided into right colon resections (includes right colon to transverse colon), left colon (includes mid transverse to sigmoid), sigmoid colon, and rectal (low anterior and abdominal perineal) resections.

Pathologic examination of the resection specimen included palpable identifying and harvesting of all regional lymph nodes for microscopic assessment. The number of lymph nodes assessed was retrieved from the diagnosis section in the pathology report. At the time of pathologic grossing of the specimen, identification of pericolic lymph nodes could be inaccurate; therefore, the number of lymph nodes stated in the macroscopic description component of the pathology report was disregarded.

The structured surgical oncology service was initiated in the Department of Surgery B on September 2004 and a surgical oncologist was assigned as an opinion leader to promote communication between the surgeons and pathologists regarding awareness and implementation of the guidelines of CAP for LN assessment in CRC.

Patients were divided into two groups. Group I included patients who underwent surgery before the initiation of the structured surgical oncology service (January 1, 2000 to October 30, 2004). Group II was comprised of patients who underwent surgery after the initiation of the service (November 1, 2004 to July 30, 2005). The surgical and pathology techniques was unchanged during the study, the only change in Group II was if fewer than 12 lymph nodes were found, reexamining the specimen for additional lymph nodes without visual enhancement techniques such as fat clearance technique.

#### STATISTICAL ANALYSIS

Statistical analysis was performed using descriptive analyses that were based on comparisons of median lymph node counts per group of patients. The *t*-test was used to compare the two groups and the ANOVA test was used to compare lymph node retrieval based on type of surgery. A *P* < 0.05 was considered significant.

#### RESULTS

This study involved 212 patients. Group I included 170 patients (80%) prior to initiating the oncology service and the assignment of an opinion leader. Group II comprised 42 patients (20%) who were evaluated after the initiation of the service. In both groups the ratio of female to male patients was almost 1:1. There was also no difference between the two groups in the number of urgent and elective surgeries [Table 1].

When considering the pathology results, there was a significant improvement in Group II with a median ( $\pm$  standard error) of  $14 \pm 1$  lymph nodes examined compared to  $9 \pm 0.7$  lymph nodes observed in Group I (*P* = 0.003). Furthermore, only 35% of patients (n=33) in Group I received an adequate lymph node evaluation. This result is in dramatic contrast to the 79% of patients (n=60) in Group II who had an adequate evaluation of their lymph nodes (*P* = 0.0001). As a consequence, the percentage of patients receiving adequate staging was improved from 58% in Group I to 86% in Group II [Table 2]. After dividing the groups into subgroups, it was found that patients with left-sided or rectal cancer were less likely to receive adequate lymph node evaluation than patients with right-sided cancers, but it was not statistically significant (*P* < 0.06) [Table 3].

#### DISCUSSION

Many studies in recent years have emphasized the importance of a multidisciplinary approach to CRC patients [12]. In particular, there has been some discussion on the significant roles

**Table 1.** Demographic and surgical data

	Total 212	Group I 170 (80%)	Group II 42 (20%)	<i>P</i> value
Male	110 (52%)	88 (52%)	22 (52%)	0.8
Female	102 (48%)	82 (48%)	20 (48%)	0.8
Elective surgery	159 (75%)	128 (75%)	32 (76%)	0.5
Urgent surgery	53 (25%)	42 (25%)	10 (24%)	0.5

**Table 2.** Pathology data

	Total	Group I	Group II	<i>P</i> value
LNs examined	$11 \pm 0.75$	$9 \pm 0.7$	$14 \pm 1$	0.003
Adequate LN retrieval	93 (44%)	60 (35%)	33 (79%)	0.0001
Adequate staging	135 (64%)	99 (58%)	36 (86%)	0.001

All data are shown as median  $\pm$  standard error

LN = lymph node

**Table 3.** Lymph node retrieval based on type of surgery

	Total (n=210)		Group I (n=168)		Group II (n=42)	
	N	LN*	N	LN*	N	LN*
Right hemicolectomy	72	$11 \pm 0.3$	62	$10 \pm 0.3$	10	$13 \pm 0.7$
Left hemicolectomy	20	$8 \pm 0.5$	16	$8 \pm 0.6$	4	$13 \pm 1$
Sub-total colectomy	36	$15 \pm 0.4$	27	$14 \pm 0.5$	9	$19 \pm 0.7$
Sigmoidectomy	40	$8 \pm 0.4$	37	$8 \pm 0.4$	3	$14 \pm 1.2$
Anterior resection	31	$12 \pm 0.4$	16	$8 \pm 0.6$	15	$14 \pm 0.5$
APR	11	$4 \pm 0.6$	10	$3 \pm 0.7$	1	22

N = number of patients, LN = lymph nodes retrieved,  
APR = abdominoperineal resection

\*median  $\pm$  standard error of number of lymph nodes

of the pathologist and surgeon on patient survival [5]. The present investigation was undertaken to evaluate the impact of a dialogue initiative between surgeons and pathologists in evaluating the number and adequate evaluation of LNs that had been surgically resected. Specifically, an oncology surgeon was assigned as an opinion leader to promote communication between the surgeons and pathologists in our department. The results showed a significant improvement in the number of LNs assessed after the establishment of the dialogue initiative (Group II). This positive effect of the surgeon-pathologist dialogue subsequently had the effect of improving the number of examined LNs and the percentage of patients receiving adequate staging. The findings were not influenced by gender or whether the surgery was elective or urgent.

Improving the number of LNs examined has been shown to increase survival in CRC patients [13]. It follows that survival is also influenced by the LN status at the time of diagnosis. For example, a long-term study found 75–80% of CRC patients with stage I or II at diagnosis had a 5 year survival, versus only 45% for patients who presented with stage III at diagnosis [8,14]. Those patients with more advanced disease only had treatment with surgery. Adjuvant chemotherapy has been shown to significantly improve 5 year survival by one-third (up to 65%) in LN-positive patients [8].

Both surgical and pathologic barriers influence the number of LNs assessed. The surgeon must provide the pathologist with an adequate specimen. The ideal resection includes the tumor, its blood supply, and LNs at the origin of the feeding vessel. The pathologist's analysis should concentrate on searching for the most LNs in the specimen. Identifying LNs in the mesentery could be a difficult task since metastatic LNs are frequently < 5 mm in size [10]. A number of techniques can be used to achieve adequate retrieval of LNs. These include fat clearance, LN revealing solution, an increased number of pathology assistants, and the use of a pathology template [8]. In fact, 47 retrieved LNs have been reported in a standard colon resection after use of the fat clearing technique [15]. Other studies have also reported a clinical significance of the fat clearance technique for rectal adenocarcinoma [16]. Teamwork between the surgeons and pathologists is therefore essential in producing a sufficient number of lymph nodes to examine.

Nevertheless, this study did not aim to change the surgical or pathological techniques used in our department, but rather to see the impact of increased communication between these two specializations. Several studies and surveys have been conducted over the years to assess the level of awareness and implementation of the guidelines regarding LN retrieval, and whether it can be used as a colon cancer quality measure [1,11].

There is a clear gap between guidelines and clinical practice. In the United States only 37–50% of CRC patients have 12 or more nodes examined [16]. Awareness is the first step toward implementation of the guidelines. Many pathologists are not

aware of the existence of guidelines for the recommended number of LNs to assess in CRC. A significant number of specialists who are aware that at least 12 nodes should be examined have indicated that workload pressure and time involved in retrieving a larger number of LNs is a major concern [11]. Recognizing such barriers, and working on diminishing or removing them, facilitates the transition from knowledge to clinical practice, thus shrinking gaps in practice.

Bianco et al. [17] demonstrated the importance of the number of LNs harvested at surgery in patients with CRC as a surrogate marker of quality assurance for hospitals for "minimum best" standard of care. Assigning an opinion leader who has a special interest in CRC has been shown to improve knowledge, awareness, and implementation of the guidelines [15]. This finding has been supported by the present study, where the number of LNs resected had significantly increased after assigning such an opinion leader.

Our study has several limitations. First, the study was retrospective and included a small sample size of rectal cancer cases. Second, we had no information regarding neoadjuvant chemoradiation for rectal cancer, surgical and pathologic factors such as the adequacy and length of the resected specimen, and use of specialized pathology techniques for better node retrieval.

## CONCLUSIONS

The number of LNs retrieved and assessed is an important prognostic variable for outcome in patients with CRC. It is of such significance that it is being considered as a quality measure in CRC. Therefore, efforts should concentrate on increasing the number of LNs analyzed. Our study has demonstrated that simple low cost actions such as feedback and assigning an opinion leader improve the number of LNs examined.

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## Capsule

### Efficacy, safety, and tolerability of secukinumab in patients with active ankylosing spondylitis

Secukinumab, an anti-interleukin-17A monoclonal antibody, improved the signs and symptoms of ankylosing spondylitis (AS) in two phase 3 studies (MEASURE 1 and MEASURE 2). Pavelka et al.) presented 52 week results from the MEASURE 3 study assessing the efficacy and safety of secukinumab 300 mg and 150 mg subcutaneous maintenance dosing, following an intravenous loading regimen. The primary efficacy endpoint was met; the ASAS20 response rate was significantly greater at week 16 in the IV-300 mg (60.5%;  $P<0.01$ ) and IV-150 mg (58.1%;  $P<0.05$ ) groups versus placebo (36.8%). All secondary endpoints were met at week 16, except partial remission

in the IV-150 mg group, according to the Assessment of SpondyloArthritis international Society criteria. Improvements achieved with secukinumab in all clinical endpoints at week 16 were also sustained at week 52. Infections, including candidiasis, were more common with secukinumab than with placebo during the placebo-controlled period. During the entire treatment period, pooled incidence rates of *Candida* infections and grade 3-4 neutropenia were 1.8% for both of these adverse events in secukinumab-treated patients.

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## Capsule

### Impact of moving from a widespread to multisite pain definition on other fibromyalgia symptoms

Dean and colleagues tried to investigate whether associations between pain and the additional symptoms associated with fibromyalgia are different in persons with chronic widespread pain (CWP) compared to multisite pain (MSP), with or without joint areas. Six studies were used: There were 34,818 participants across the study populations (adults age range 42-56 years, male 43-51% [excluding WHEST], and CWP prevalence 12-17%). Among those reporting MSP, the proportion reporting CWP ranged between 62% and 76%. Among those reporting the symptoms associated with fibromyalgia, there was an increased likelihood of reporting pain, the magnitude of which was similar regardless of the definition used. For example, within WHEST, reporting moderate/severe fatigue (Chalder

fatigue scale 4-11) was associated with a  $\geq$  fivefold increase in likelihood of reporting pain, CWP OR 5.2 (95% confidence interval [95%CI] 3.9-6.9, MSP-positive joints OR 6.5 (95%CI) 5.0-8.6, and MSP-negative joints OR 6.5 (95%CI 4.7-9.0). This large-scale study demonstrates that regardless of the pain definition used, the magnitude of association between pain and other associated symptoms of fibromyalgia is similar. This finding supports the continued collection of data when classifying fibromyalgia, but highlights the fact that levels of pain may not follow the definition outlined within the 1990 American College of Rheumatology criteria.

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“Mystery creates wonder and wonder is the basis of man’s desire to understand”

Neil Armstrong, (1930-2012), American astronaut, engineer, and the first person to walk on the moon