Adequacy of Lymph Node Harvesting in Colorectal Cancer Management

Improving Standards, Ensuring Quality

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ABSTRACT

Objective: *The aim of this study was to determine the adequacy of nodal sampling in resection specimens for colorectal carcinoma in a Jamaican population.*

Methods: *The pathology records of all patients who underwent operation for colorectal carcinoma at the University Hospital of the West Indies (UHWI) during the five-year period, 2003−2007, were reviewed. Pertinent clinical and pathologic data were obtained and analysed.*

Results: *One hundred and ninety-one patients were identified with M:F ratio of 1.1:1 and a mean age of 66 years. There were 119 (63%) left-sided lesions and 70 (37%) right-sided lesions. Stage T3N0 lesions were the most common and accounted for 41.1% of cases. The predominant histologic type was adenocarcinoma (99.5%) with the majority being moderately differentiated. The mean number of nodes sampled in node-negative cases was 13.8 ± 9.75 nodes for right-sided lesions and 10.64 ± 7.25 nodes for left-sided lesions (*p = *0.05, CI 95%). The adequacy of nodal sampling was acceptable in cases of N0 right-sided carcinomas but was unsatisfactory in cases of N0 left-sided carcinomas. More importantly, however, in two cases from the right and 10 cases from the left, two or fewer nodes were harvested.*

Conclusion: *This review suggests the need for re-examination of the adequacy of surgical resection and/or nodal sampling technique for colorectal cancer resection specimens, given the importance of nodal status in determining the need for adjuvant therapy. Less than adequate node sampling should not be accepted by the reporting pathologist or attending surgeon as this has important prognostic implications.*

Keywords: Colorectal cancer, lymph nodes, quality assurance

Adecuación de la Recolección de Ganglios Linfáticos en el Tratamiento del Cáncer Colorrectal: Perfeccionamiento de los Estándares y Aseguramiento de la Calidad

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RESUMEN

Objetivos: *El objetivo de este estudio fue determinar la adecuación del muestreo nodular en la resección de especimenes para el carcinoma colorectal en una población jamaicana.*

Métodos: *Las historias clínicas de las patologías de todos los pacientes sometidos a operación por carcinoma colorectal en el Hospital Universitario de West Indies (UHWI), fueron revisadas por un período de 5 años (2003-2007). Se obtuvieron y analizaron los datos clínicos y patológicos pertinentes.*

Resultados: *Se identificaron ciento noventa y un pacientes en una proporción H:M de 1.1:1 y una edad promedio de 66 años. Había 119 (63%) lesiones del lado izquierdo y 70 (37%) con lesiones del lado derecho. Las lesiones de etapa T3N0 fueron las más comunes y daban cuenta del 41.1% de los casos. El tipo histológico predominante fue el adenocarcinoma (99.5%), con diferenciación moderada en su mayor parte. El número promedio de linfonodos muestreados en los casos de nodos negativos fue 13.8+/-9.75 nodos en las lesiones del lado derecho y 10.64+/-7.25 nodos en las lesiones del lado izquierdo (*p = *0.05, CI 95%). La adecuación del muestreo nodular fue aceptable en los casos de los carcinomas N0 del lado derecho, pero insatisfactoria en los casos de carcinomas N0 del lado izquierdo.*

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Sin embargo, aún más importante, en dos casos de la derecha, y 10 casos de la izquierda, se recolectaron dos o pocos nodos.

Conclusión: *Esta revisión sugiere la necesidad de re-examinar la adecuación de la resección quirúrgica y/o la técnica del muestreo nodular para los especimenes de la resección del cáncer colorrectal, dada la importancia del estado nodular a la hora de determinar la necesidad de la terapia adyuvante. Cualquier muestreo nodular que sea menor que el adecuad, no debe ser aceptado por el patólogo que reporta, o el cirujano a cargo del caso, ya que este caso tiene implicaciones importantes en relación con la prognosis.*

Palabras claves: Cáncer colorrectal, ganglios linfáticos, aseguramiento de la calidad

West Indian Med J 2012; 61 (2): 135

INTRODUCTION

Quality assurance (QA) is increasingly being recognized as an important part of professional activity in medicine. Many specialty associations have major initiatives directed at audit and quality assurance. In pathology, there are elaborate programmes developed by national associations in the United Kingdom [UK] (Royal College of Pathologists), Australia (Royal College of Pathologists of Australasia) and the United States of America [USA] (American College of Pathologists), some of which cover all aspects of the activity of a clinical department, from specimen handling and turnaround time for reports, to assessment of accuracy in specialized areas such as hormone receptors and frozen sections. In spite of this, the specialty of pathology has run into trouble in several countries (1).

Pathologists are accustomed to collaborating with surgeons and internists in a form of audit/QA that is active in most tertiary hospitals. Mortality/morbidity rounds usually involve the clinical presentation and the management being discussed in detail, and the final answer being presented by the pathologists. It is not as common for the clinical departments to be integrated into audit and collaborating with the pathology departments' QA and efforts to raise standards.

In Jamaica, colorectal carcinoma is the third most common malignancy affecting men and women (2) and a leading cause of cancer related morbidity and mortality. Recent research has demonstrated that the adequacy of nodal sampling and examination is an independent prognostic factor in patient survival (3). Moreover, nodal examination has an important role in the determination of the need for adjuvant therapy in patients with colorectal carcinoma. The outcome of surgery and the prognosis in colorectal cancer as well as the need for adjuvant chemotherapy is therefore critically dependent on the pathology findings. The gastroenterologists, surgeons and pathologists all have a need and interest in ensuring that standards in reporting histology are met and maintained.

The current guidelines of the American Joint Committee on Cancer (AJCC) suggest that a minimum of 12 lymph nodes should be retrieved in a colorectal resection for adequate staging (4). The number of nodes sampled is a function of how carefully the specimen was searched for nodes in the Pathology department, and how many nodes were taken in the resection by the surgeon. There is therefore a dual responsibility and an important target for audit/QA.

The use of synoptic reporting by "check list" cues the pathologist to assess and record specific prognostic parameters. It is thus one means of ensuring that lymph nodes are consistently examined and recorded in the report. Approximately five years ago, an audit was performed in our Pathology department to assess the proportion of reports that complied with the recommended "synoptic" report format compared to those which were still "narrative". We presented the results internally to the Department and reported the results and the rationale for the change, at the Jamaican Association of Clinical Pathologists annual meeting in 2005. We plan a repeat to assess the change, but this is an area where demand from the clinicians would be helpful.

This study examines the performance of the Pathology department in the critical area of lymph node involvement and number of nodes sampled in a five-year review of colon cancer pathology reports. No prior research on this topic has been done in the Jamaican population.

SUBJECTS AND METHODS

The University Hospital of the West Indies (UHWI) is a tertiary care academic institution. The surgical histopathology records of all patients who underwent surgery at this hospital for colon and rectal cancer from January 2003 to December 2007 were reviewed. Clinical and pathologic data were extracted including age, gender, location of primary carcinoma, histologic diagnosis, grade and stage. In adherence with ethical guidelines, there was no disclosure of patient identity. For the purpose of this study, lesions which occurred proximal to the splenic flexure were designated as right-sided carcinomas because they are usually treated with right or extended-right hemicolectomy. Lesions at and distal to this location were designated as left-sided.

Based on the pathologic description, the tumour, node, metastasis (TNM) stage of each lesion was derived based on AJCC guidelines. The number of lymph nodes examined per case was retrieved from the pathology report. For each pN

stage on the right and left sides, (a) the number of cases, with (b) the range, (c) mean, (d) modal and (e) median numbers of nodes examined as well as (f) the standard deviation were ascertained. Patients were excluded from analysis if the location of the tumour was not stated or if they had synchronous carcinomas located in both the right and left colon. Unpaired *t*-tests were performed for pN0 and pN1 cases, on each side, to assess the statistical significance of any observed difference in mean number of nodes examined. Also, Fisher's exact test was done to determine the significance of any observed difference in likelihood of node positivity for right- and left-sided tumours.

RESULTS

One hundred and ninety-seven carcinomas were identified in 191 patients. Ninety-nine of them males and 92 females with a male:female ratio of 1.1:1. The patients' ages ranged from 24−101 years with a mean of 66.17 ± 14.19 years. The incidence was highest in the seventh and eighth decades of life with both age groups accounting for 50% of the total cases. One hundred and twenty-seven tumours (64%) were located distal to the splenic flexure and 70 (36%) were proximal to that landmark. Two patients had synchronous carcinomas (a total of five carcinomas) both proximal and distal to the splenic flexure and these patients were excluded from further analysis. The rectum and sigmoid (as a group) were the most frequent locations with 57% of tumours arising there. The next most common single site was the caecum which bore 23% of the tumours, followed by the descending colon (7%), transverse (7%) and ascending colon (6%). One hundred and eighty-eight (99.5%) of the tumours were adenocarcinomas, and one (0.5%) was an adenosquamous carcinoma. Tumours were well, moderately and poorly differentiated in 22%, 70% and 6% of lesions, respectively. The degree of differentiation was not reported for four tumours. T3N0 was the most common stage overall (41.1%) and accounted for 45.7% of right-sided lesions and 38.6% of left-sided lesions. Node-positive carcinomas were diagnosed in 25 (35.7%) and 51 (40.3%) of right-sided and left-sided lesions, respectively. These cases with positive nodes were not analysed further.

The total number of cases with negative nodes (N0) on the right side was 45. The number of nodes sampled ranged from 0 to 65 with a mean of 13.8 ± 9.75, with a median of 12 and a mode of 10 (Table 1). With respect to the left colon, in node-negative cases (n = 69), the number of nodes sampled ranged from 0−37 with a mean of 10.64 ± 7.25, a median of 10 and a mode of 5 (Table 2). Unpaired *t*-test confirmed this difference in means to be statistically significant: $p = 0.05$, 95% CI. Twelve or more lymph nodes were sampled in 57.1% of cases of right-sided lesions and in 42.5% of cases of left-sided lesions. Among the cases where the sampling was inadequate, two or fewer nodes comprised the extreme. There were a total of two cases from the right and 10 from the left side which met this criterion. In a total of six cases, two from the right and four from the left side, the reports indicated that no nodes were examined. While these may best be classified as Nx or unknown, for the purposes of discussion, these were included with the N0 cases as the implications for prognosis and management are the same.

DISCUSSION

The College of American Pathologists endorses the following definitions of QA: Quality assurance in pathology and laboratory medicine is the practice of assessing performance in all steps of the laboratory testing cycle including pre-analytic, analytic and post-analytic phases to promote excellent outcomes in medical care. One aspect of promoting consistent excellence in outcome in the care of patients with colorectal cancer is accepting the current guidelines of the AJCC which suggest that a minimum of 12 lymph nodes

Table 1: Nodal status and the mean, median and modal number of nodes examined for right-sided carcinomas

Nodal Status	Number of cases	Range of number of nodes examined	Mean number of nodes	Median	Mode
N0	45	0−65	13.8 ± 9.75	12	10
N1	14	4−30	13.5 ± 8.69	11	16
N2	11	5−29	12.82 ± 7.14	13	14

Table 2: Nodal status and the mean, median and modal number of nodes examined for left-sided carcinomas

Nodal Status	Number of cases	Range of number of nodes examined	Mean number of nodes	Median	Mode
N0	69	0−37	10.64 ± 7.25	10	5
N1	38	3−37	10.84 ± 8.19	9	3
N2	12	7−23	14.00 ± 5.34	13	11

should be retrieved in a colorectal resection for adequate staging (4). This has been universally accepted and Chen and Bilchik suggest that harvesting of 15 nodes or more improved survival, independent of stage, patient demographics or tumour characteristic (5). While there is evidence that depth of invasion, degree of differentiation, involvement of blood vessels or lymphatics and distance from the margins may all affect outcome, it is lymph node status that is paramount in importance and consistency in prognosis in colorectal carcinoma (3−8).

The reliability of this particular parameter is dependent on the number of nodes sampled. The number of nodes sampled is a function of how carefully the specimen was searched for nodes in the Pathology department, and how many nodes were taken in the resection by the surgeon. A large number of harvested nodes, not only improves the accuracy of staging, but is also indicative of the adequacy of the surgical resection of the mesenteric pedicle and therefore impacts prognosis. This is therefore a dual responsibility and an important target for audit/QA. In a meta-analysis of 17 studies from nine countries, Chang *et al* found that 16/17 studies showed increased survival of stage II patients with increased numbers of lymph nodes and suggested that the number of lymph nodes examined may be a measure of the quality of care (9).

Lymph node status in colorectal carcinoma also determines the utility of adjuvant therapy. Therefore, accurate designation of tumour stage is the single most important role of the pathologist examining the specimen. The assignment of the responsibility of macroscopic assessment and thus lymph node sampling to training pathologists solely represents an undue limitation in quality. We believe this duty should not be relegated to residents in their first or second years of training without adequate supervision and specific training.

In the present study, the disease demographics of being predominantly in the elderly with a mean age of 66.17 ± 14.19 years (range 24–101 years) is consistent with previous published demographic data by McFarlane *et al* from Jamaica (10). T3N0 was the most frequent stage for lesions in all anatomic subsites (41.1%). Using the AJCC guidelines (11), patients who have less than 12 nodes sampled are potentially under-staged and thus potentially inadequately treated. Given the frequency of T3N0 in our population and the significance of pN in these tumours (6), the importance of the accuracy of the designation of N0 is underscored. While the authors advocate complete lymph node dissection as the ideal, it is vital for quality improvement to evaluate what has obtained in practice and how it compares to minimum requirements.

Functionally, it is well recognized that more lymph nodes are retrieved from right and extended right hemicolectomies than from left hemicolectomies, anterior and abdomino-perineal resections (12, 13). Wong *et al* (14) wrote in their case series from Hawaii, during the period 1990−2002, that mean numbers of 22.9 and 19.9 nodes were examined for lesions of the ascending and transverse colon respectively while mean numbers of 20.4, 15.2 and 16.3 were examined for the descending and sigmoid colon and rectosigmoid. The results of the present study are consistent with this finding. All cases tolled, the number of lymph nodes examined was greater than 12 in 57.1% of cases of right-sided and 42.5% of left-sided cases. This difference in mean number of nodes sampled for pN0 right-sided lesions and for pN0 left-sided lesions was statistically significant indicating that there is a substantive difference in nodal examination for right-sided pN0 tumours when compared to similar lesions on the left. Despite this, it is worrisome that for pN0 cases, the authority of this designation may be questionable and 60% of the patients treated at a tertiary care academic institution are potentially under-staged. Prospective studies of survival as well as the use of adjuvant therapy in our population without consideration of the number of nodes sampled would thus be flawed.

In pN2 cases, the mean was 14 with a median of 13 and mode of 11. These figures indicate generally adequate sampling for pN2 patients. This finding of node-positive cases yielding more nodes than node-negative cases is not unique to our study (13, 14).

Other centres have found lymph node harvest to be inadequate (13, 15−18). In a 20-year retrospective study (1985–2004) in Barbados, the mean number of nodes sampled for all specimens was 6.32 (18). Similarly, another retrospective study (1988–2001) done using the SEER (Surveillance Epidemiology and End Results) database found that only 37% of patients had 12 or more nodes sampled with an overall median of nine and the inadequacy was worse for older patients and left-sided lesions (19). A consecutive cohort done in Canada (1997–2000) revealed that only 22.4% of patients had a mean of 8.3 nodes sampled per case (12) and a study of the National Cancer Database of 1296 hospitals in the USA found that more than 60% of institutions failed to achieve the requisite benchmark of 12 nodes (20).

The description of node sampling as “inadequate” is understandable if the examination misses the mark by one or two nodes. It is particularly alarming, however, when a pathology report on a colon cancer specimen is signed out with less than two nodes (and several with 0 nodes) without a detailed commentary about the concern of the pathologist on the lack of nodes in the specimen. Similarly, there is no record in the department that those reports generated a concerned response from the clinical team. There is clearly a dual responsibility.

Overall nodal sampling at our institution could and should be improved, especially for left-sided lesions. In a country with limited financial resources, submission of the entire pericolic fat as recommended (4) is impractical and fat dissolution remains unaffordable. Critically, therefore, the quality of training and preparation of the pathology residents for lymph node sampling must be examined and the

provision of skilled supervision mandated. Staff pathologists should insist on the minimum acceptable lymph node count to facilitate an acceptable standard of lymph node sampling and a specific comment should be made on the report where this count is inadequate. It is also imperative that the attending surgeon not only ensures the adequacy of the resection but also of the report being provided by the pathologist. If these surgical procedures are being performed by residents-in-training and do not conform to the usual resection as dictated by the lymphovascular drainage of the tumour occupying bowel, lymph node examination may remain unsatisfactory.

Thus, given the importance of nodal status in determining prognosis and the need for adjuvant therapy, the responsibility of QA is a collective one, involving both the surgical and pathology teams and there is need for re-examination of the adequacy of surgical resection and nodal sampling techniques in our institution, particularly for node negative cases and left-sided tumours.

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