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A Data Management Approach to Quality Assurance
Using Colorectal Carcinoma Reports From Two Institutions as a Model

The following article appeared in the July 2005 issue of the American Journal of Clinical Pathology 124(1):83-88. This study reviewed data from colorectal carcinomas evaluated at the Rex Hospital pathology department and a hospital in South Carolina. The authors thank the Rex Hospital Administration and Cancer Center for a grant funding portions of the study. This article has been abridged from the original version to remove technical details concerning the hardware and software manipulation.

Abstract:
This study utilized data management software to compare pathology report data concerning regional lymph node sampling for colorectal carcinoma from two separate institutions using different dissection methods. Data were retrieved from two disparate anatomic pathology information systems for all cases of colorectal carcinoma in 2003. Initial sorting of the data included overall lymph node recovery to assess differences between the different dissection methods at the two institutions. Additional segregation of the data was used to challenge the application's capability of accurately addressing the complexity of the process.

Introduction:
The College of American Pathologists (CAP) Consensus Statement published in 1999 lists regional lymph node metastases as a Category One prognostic factor in conjunction with local extent of tumor assessed by pathologic examination[1]. The recommendations for the retrieval of a minimum number of lymph nodes in colorectal carcinoma have been variable from six to 17-20[2-7]. The CAP Working Group has recommended a minimum of at least 12 regional lymph nodes be obtained from a radical colorectal resection[8]. In the American Joint Commission on Cancer (AJCC), Cancer Staging Manual[9], a recommendation for retrieval of seven -14 lymph nodes was made with a proviso that in patients pretreated with preoperative radiation, a lower number of recovered lymph nodes may be acceptable[9]. The thoroughness of the pathologic assessment is critical in the staging process, but other factors may influence a colorectal carcinoma nodal sampling including surgical and patient factors. For example, right-sided resections are generally longer than left sided specimens and consequently yield a larger number of lymph nodes.[10,11].

The approach of the current study was to evaluate specimen data from two disparate anatomic pathology information systems, in which one institution (Institution A) used a standard manual method of dissection, whereas the other institution (Institution B) employed a fat clearance method. An automated proprietary software method bridged across the information processing from the separate anatomic pathology information systems, while maintaining patient confidentiality.

Materials and Methods

Data Management Process

Using the proprietary computer based data mining software (inREACH Corporation Data Mining Software, Anderson, SC, www.4inreach.com), colorectal carcinoma pathology reports from the two different computer systems were obtained electronically. The colorectal carcinoma cases were also manually collated for the entire calendar year 2003 by both institutions, in order to validate the automated process. The data management software identifies the source fields of the report (e.g., gross, microscopic, final diagnosis). An independent module then identifies colorectal carcinoma cases and determines the number of lymph nodes, as well as, other derivative fields (specimen type, specimen location, length of the colon portion of specimen, tumor size, nodal status and metastatic status) through pattern recognition. The software can only make decisions about the data that is present in the report, so there will always be occasional cases requiring manual review (e.g., words referring to other organs such as ovary or stomach would cause the case to be classified as indeterminate and require manual review).

Specimen Management Process

The specimens from Institution A were submitted in formalin

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and manual dissection of the pericolic adipose tissue was performed with the adipose tissue attached to the segment of colon. The dissection was completed on the same day as the specimen was received.

The specimens from Institution B were submitted fresh for fat clearance were manually evaluated to initially assess size of tumor, distance to proximal and distal margins, extent of tumor penetration and radial margin status. The fat was stripped from the bowel segment, serially sectioned at 0.5 - 1.0 cm. intervals, while maintaining an intact mesenteric fat border. The fat was placed in a separate container submerged in a formaldehyde, glacial acetic acid, ethyl alcohol, and deionized water solution (Dissect Aid, Decal Corporation) for two to three hours prior to dissection. At both sites, representative sections of grossly involved lymph nodes were taken, wheras grossly uninvolved lymph nodes were submitted in their entirety.

Statistical Methods

A two-way analysis of variance (ANOVA) was used to evaluate possible differences in the square-root transformed number of nodes across the two pathology departments (A and B) and the tumor sites. Levene's test was used to test the assumption of equal variances between groups. Square root transformations successfully normalized the distribution of nodes. The non-parametric Chi Square analysis was used to study differences among categorically distributed data. Data were validated using alternate transformations and analyses with comparable results.

Results:

The databases for Institutions A and B were searched for colorectal carcinoma cases meeting criteria of a colectomy as the specimen type and adenocarcinoma identified in the diagnosis. The search language segregated cases into the right, transverse and left colon. Cases from the transverse colon were eliminated from the study due to insufficient sample size. The data were manually confirmed prior to implementing the automated method of data processing along with ongoing QC measures.

A total of 211 specimens representing 2368 lymph nodes (mean of 11.2 lymph nodes/specimen) from the two institutions were retrieved from the database. Institution A harvested a total of 765 lymph nodes from 87 specimens (mean of 8.8 lymph nodes/specimen) and 1603 lymph nodes from 124 specimens (mean of 12.9 lymph nodes/specimen) were obtained from Institution B. Table 1 illustrates the data sorted for the two institutions for lymph node recovery. The difference in the number of lymph nodes harvested at the two institutions was statistically significant, at p<.001. Breakpoints for lymph node recovery were segregated into groups representing 0 - 10, 11-20 and greater than 20 lymph nodes per specimen. Table 2 (2 x 3 contingency table) highlights the number of cases at each institution that fell into these categories. Institution B with the fat clearance method had significantly fewer cases of < 11 lymph nodes/specimen and significantly more cases with > 20 lymph nodes/specimen (p<0.05), as analyzed with the independent samples chi square test.

Table 1: Lymph Node Recovery From Institutions A and B.

	Institution A	Institution B	P value
Total Number of Specimens Recovered	87	124	
Total Number of Lymph Nodes Harvested	765	1603	<.001
Average Number of Lymph Nodes /Specimen	8.8	12.9	

Table 2. Observed and Expected Frequencies for Number of Lymph Nodes – 2 x 3 Contingency Table.

Number of Lymph Nodes	Institution A	Institution B	Expected Frequency
< 11	53/87 (61%)	53/124 (43%)	52%
11-20	34/87 (39%)	51/124 (41%)	40%
> 20	0/87 (0%)	20/124 (16%)	8%

The data was further sorted by specimen location and whether lymph node metastases were present or absent. Table 3 presents the data from the two institutions according to specimen location (right versus left colon) and mean lengths for colon segments from the right and left sides. A statistical difference was observed between the lymph node recovery from the right colon compared to the left at Institution B (p=. 001) but not at Institution A (p=. 951). By combining the data from both institutions by specimen location, a significant difference was maintained between lymph nodes harvested from the right versus left colon (p= .032). Table 4 demonstrates the comparison of data from the two institutions by specimen location and whether the lymph nodes were either uninvolved or involved by metastatic carcinoma. At Institution A, 48 of 131 lymph nodes from 13 specimens from the right colon (mean of 10.1 lymph nodes/specimen) and 64 of 174 lymph nodes from 19 specimens from the left colon (mean of 9.2 lymph nodes/specimen) were involved by metastatic carcinoma. At Institution B, 132 of 378 lymph nodes from 26 specimens from the right colon (mean of 14.5 lymph nodes/specimen) and 96 of 307 lymph nodes from 22 specimens from the left colon (mean of 14 lymph nodes/specimen) were involved by metastatic carcinoma. Cases with metastatic carcinoma comprised 37% of the total cases at Institution A and 39% of the total cases at Institution B. Chi square analysis did not demonstrate statistical significance between cases with and without metastatic disease at each of the institutions. An analysis of variance was performed and only demonstrated statistical significance

Table 3: Lymph Node Recovery by Specimen Location (Side)			
Specimen Location	**Right Colon**	**Left Colon**	**P value**
Institution A:			
Number of Specimens Recovered:	42	45	
Number of Lymph Nodes Harvested:	374	391	.951
Mean Lymph Nodes/Specimen:	8.9	8.7	
Mean Colon Segment Length/Specimen (cm.)	21.7	17.8	
Institution B:			
Number of Specimens Recovered:	59	65	
Number of Lymph Nodes Harvested:	920	683	<.001
Mean Lymph Nodes/Specimen:	15.6	10.5	
Mean Colon Segment Length/Specimen (cm.)	25.5	21.3	
Totals from Institutions A and B			
Total Specimens Recovered	101	110	
Total Lymph Nodes Harvested	1294	1074	.032
Average Lymph Nodes/Specimen:	12.8	9.8	

(p=.004) for left colectomy specimens at Institution B between cases with and without metastases.

Discussion:

Despite the fact that there are multiple non-pathology related variables that affect lymph node number in colorectal cancer specimens, fully accurate pathologic assessment is crucial to patient outcome and treatment, and is desired by all. Sentinel lymph node mapping is not a standard of care in colorectal cancer as it is for melanoma and breast cancer. The detection of very small micrometastatic deposits in colon cancer specimen lymph nodes is very important by virtue of its N1 designation in the TNM classification system. There are different approaches to improve evaluation of the colorectal regional lymph node basin. Multiple studies have addressed different methods of fat clearance with subsequent improvement in lymph node recovery[12-18]. In addition, a method of improved histologic sectioning technique has been reported that has led to increased detection of lymph node metastases[19]. Molecular techniques have been employed for the purpose of identifying micrometastatic disease[20,21]. In this study, a fat clearing solution of formaldehyde, glacial acetic acid, ethyl alcohol and deionized water was employed at one institution and compared to the standard manual method used at the second institution. Our data supports the use of a fat clearing solution to improve lymph node dissections of colorectal cancer specimens. This particular method is valuable, since it may be incorporated into the daily workflow pattern without lengthening the turn around time for reporting of colorectal cancer cases. We recommend that to maximize the detection level, the stripped fat from the colon should be placed and kept in the clearing agent for two to three hours, divided into 0.5 - 1.0 cm. slices and

Table 4: Lymph Node Recovery by Specimen Location and Presence or Absence of Metastatic Disease				
Specimen Location	Right Colon		Left Colon	
	Present	Absent	Present	Absent
Institution A				
Number of Specimens Recovered	13	29	19	26
Number of Lymph Nodes Harvested	48/131	243	64/174	217
Average Lymph Nodes/Specimen:	10.1	8.4	9.2	8.4
Institution B				
Number of Specimens Recovered	26	33	22	43
Number of Lymph Nodes Harvested	132/378	542	96/307	376
Average Lymph Nodes/Specimen:	14.5	16.4	14.0	8.7

covered by a sufficient volume of the clearing agent.

The fat clearing method increases the yield of lymph nodes recovered from colorectal cancer specimens by facilitating the visual detection of smaller lymph nodes. The increased yield of lymph nodes appears to affect the prognosis by increasing the probability of detecting lymph node metastases[2]. In addition, the identification of small (ie < 5 mm) lymph nodes in itself is an important event in accurate staging[22,23]. Another advantage of using this type of fat clearance is that the adipose tissue may be retained in this solution overnight for re-harvesting the next day without decrement in the lymph node histology. Attention may be directed to the smallest of lymph nodes that were undetectable the previous day, if the initial lymph node harvest is considered suboptimal.

Several reports have highlighted the difference in the number of lymph nodes retrieved from the right versus left sided colectomy specimens[10,11]. The difference in the lymph node recovery is attributed to the length difference of specimens from the right versus left colon. Right-sided colectomy specimens are generally longer than left sided counterparts, which is supported from our mean colon length measurements. Our data supports a statistically significant difference in lymph nodes recovered from the right and left colon specimens, when data from both institutions were combined. However, a statistical significant difference was not recognized between right and left colectomy specimens from Institution A. At this point, we agree with a "minimum" number of recoverable lymph nodes from colorectal specimens, but would encourage continuing to separate data in the future by specimen location. Ultimately, a different "minimum" number of recoverable lymph nodes may be necessary when evaluating a specimen from the right colon versus a left colectomy specimen.

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Absolute Neutrophil Count

The absolute neutrophil count (ANC) is now reported as a subset of the white blood cell (WBC) count when a CBC with differential is ordered. If a CBC without a differential is ordered, no ANC is reported. The ANC is equal to the [WBC x (%neutrophils)] ÷100. The normal range is 2.1 to 6.3 K/ul. An ANC below the normal range is considered neutropenia. The risk of infection increases as the ANC decreases. The following is a table of the risk for infection:

Degree	K per ul*	Risk of infection
Mild	1.0 – 2.1	Low
Moderate	0.5 – 0.9	Moderate
Severe	<0.5	High

**K/ul = thousand per microliter.*

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