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Colorectal Surgical Specimen Lymph Node Harvest: Improvement of Lymph Node Yield with a Pathology Assistant

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Abstract
Introduction Adequate lymph node harvest from colorectal cancer specimens has become a standard of care, influencing both staging and survival. To improve lymph node harvests at our hospital, a pathology assistant was trained to meticulously harvest lymph nodes from colorectal cancer specimens. An analysis of trends in lymph node harvests over time is presented.
Methods The number of harvested lymph nodes from 391 consecutive colorectal cancer pathology reports was retrospectively reviewed from a single community hospital over 8 years (1999–2006). This spanned 4 years prior to the training of the pathology assistant and 4 years after.
Results From 1999–2002, the mean number of harvested lymph nodes varied from 12.2 to 14.4. The percentage of specimens achieving 12 lymph nodes was 50–67%. From 2003–2006, the mean number of harvested lymph nodes increased to 18.4–20.7, while the percentage of specimens achieving 12 lymph nodes was 83–87%. Both of these improvements achieved statistical significance with p values of <0.00001.
Conclusions Over time, lymph node harvests at our hospital dramatically improved. The training of a pathology assistant to harvest the lymph nodes from colorectal cancer specimens dramatically affected lymph node harvests and can be a crucial component of pathologic analysis of these specimens.

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Introduction

Lymph node harvests in surgically removed colorectal cancer specimens have become increasingly important. Many authors have demonstrated that the number of harvested and pathologically examined lymph nodes affects staging[1–4] and potentially survival.[3–8] Some authors have also noted that the total number of negative lymph nodes and/or the ratio of positive to negative nodes is an independent prognostic factor in colorectal cancer survival.[9,10] Although there is some controversy about the survival benefit,[11] achieving an adequate lymph node assessment (usually defined as at least 12) has become a standard of care for colorectal cancer.[12,13] As the importance of adequate lymph node harvest and

pathologic assessment has become clearer, institutions involved in cancer care have sought to improve lymph node harvests. However, very little has been published regarding specific factors, procedures, or techniques which improve lymph node harvests. The question as to whether the key to adequate lymph node assessment is dependent on the surgical removal of a large enough mesentery or a meticulous enough pathologic dissection has been debated both in the literature and other forums.[14–16] Undoubtedly, as this issue has gained increasing awareness, both surgeons and pathologists have made extra efforts to insure adequate staging of their colorectal cancer patients.

We were interested in the trend in lymph node harvests at our institution over time during the last 8 years as lymph node harvest importance has become better understood. We hypothesized that our lymph node harvests have improved over time with the increasing national attention on this issue. We also hypothesized that the hiring and training of a pathology assistant (Mr. Bowles) to harvest lymph nodes from colorectal cancer specimens had resulted in a positive impact on the lymph node yield at our institution.

McKay-Dee Hospital Center, owned by Intermountain Healthcare, is a 317 bed community hospital which provides comprehensive medical and surgical care. Located in Ogden, UT (2006 population 78,000),[17] it serves patients primarily in Weber, Morgan and northern Davis Counties (2006 populations 213,000, 8,100 and 276,000 respectively)[17] in northern Utah. However, it serves as a tertiary referral center and draws patients from a vast geographic area including all of northern Utah, north of Salt Lake City, as well as southwestern Wyoming and southeastern Idaho. It has an American College of Surgeons Committee on Cancer accredited cancer care program.

Methods

Three hundred ninety-one consecutive surgically removed colorectal adenocarcinoma pathology reports were retrospectively reviewed from Jan. 1999 to Dec. 2006—a total of 8 years. We excluded local transanal rectal cancer excisions. The primary data we looked at were the number of lymph nodes examined and reported for each cancer. The study was approved by the Intermountain Healthcare Institutional Review Board. Comparison of mean numbers of lymph nodes reported from year to year was done using the Students T test statistic. Comparison of percentages of specimens achieving at least 12 lymph nodes from year to year was done using the Chi-square statistic. Statistical significance was assumed at the $p<0.05$ level.

In terms of procedures for pathologic processing of these specimens, colorectal resection specimens for malignancy are transported to the McKay-Dee Pathology Department by operating room personnel. Some are sent prior to fixation for intraoperative consultation to grossly assess margin adequacy or to confirm that an early lesion or polyp site is included in the specimen. Intraoperative consultation is performed by the responsible pathologist. The pathology assistant (PA) then assumes responsibility for these specimens as well as the other resection specimens that are not sent for intraoperative consultation and are received in formalin.

The PA is supervised by three pathologists, each of whom is responsible for essentially identical numbers and types of specimens. Certified as a histology technician, he had approximately 20 years of experience in surgical pathology gross examination including a children's hospital and a community hospital prior to starting his employment at McKay-Dee Hospital Center.

The pathology assistant (PA) spent the first 2 years of his employment working under the supervision of the pathologists, while the pathologists maintained complete responsibility for colorectal carcinoma specimens. Training in gross examination and lymph node retrieval, again under the direct supervision of the pathologists, occurred in the third year. In subsequent years, the PA assumed primary responsibility for retrieval of lymph nodes, following the approach detailed below.

The PA documents and dictates the size of the specimen and the size and the location of the tumor. Distance to margins, (proximal, distal, and circumferential radial margin) is documented prior to the shrinkage that occurs due to formalin fixation. Any unusual or irregular gross findings are reviewed with the pathologist. If serosal changes, raising the possibility of peritoneal invasion by tumor are noted, these areas are marked with ink. The PA then removes the mesocolic adipose tissue from the entire specimen, with the exception of the tissue at the level of the tumor. Approximately 1 cm of tissue is left in contiguity with the tumor, and it is examined at the time of submission of the bowel segment and tumor sections by the pathologist. In addition, removal of adipose tissue of low anterior and rectosigmoid specimens stops at the level of the peritoneal reflection.

The removed adipose tissue is placed in at least twice as much *Dissect Aid™ as there is tissue and left in this solution for a minimum of 4 h, but more often overnight (Dissect Aid is a special fixative for easier, quicker lymph node recovery. It turns lymph nodes white in the surrounding tissue mass making them simple to find. Since Dissect Aid fixes and dehydrates simultaneously, it will also firm up fatty tissues making them easier to handle. Paraffin infiltration is quick and complete. Routine H & E and special stains, including immunoperoxidase, all work well with tissues fixed in Dissect Aid.).[18] The removed adipose tissue with lymph nodes is then sectioned at approximately 3 mm intervals to retrieve the lymph nodes. The lymph nodes are

white against a yellow-tan translucent background of altered adipose tissue (see Fig. 1). Unless there is grossly apparent tumor involving multiple lymph nodes, all lymph nodes are submitted with documentation of numbers per tissue cassettes and how it was handled (e.g., "A3: one lymph node, bisected; A4: four lymph nodes; A5: one lymph node, serially sectioned") in order to maintain an accurate total node count. Lymph nodes are not separated into anatomical locations (e.g., proximal, tumor, distal), unless the surgeon has indicated a special interest by providing orientation of nodes (e.g., "stitch marks *Decal Chemical Corporation, Tallman, NY, USA highest lymph node"). The pathologist is responsible for submitting the sections of the bowel segment and tumor and also maintaining an accurate total node count. Dissect Aid was used by pathologists prior to the PA's assuming responsibility for node retrieval. These procedures are all consistent with published national standards.[19]

Results

The most important results are displayed in Table 1. For each year 1999–2006, the total number of colorectal cancer specimens is given, followed by the average number of lymph nodes and the percentage of specimens that had greater than 11 lymph nodes in each succeeding column. The differences are remarkable. Average lymph node harvest for the years 1999–2002 were all between 12.2 and 14.4. The percentage of specimens achieving 12 lymph nodes during these years varied from 50% to 67%. From 2003–2006, the average number of lymph nodes examined per specimen increased to 18.4 to 20.7. The percentage of specimens reaching 12 lymph nodes during those years was 83–87%. Comparing 1999–2002 with 2003–2006, the difference in the average lymph node harvest reached a p value of <0.00001 (T test). Comparing the percentage of specimens with at least 12 lymph nodes between 1999–2002 and 2003–2006, the difference reaches a p value of <0.00001 (Chi-square). The division in the table noted by "Training of a PA" denotes that time period where Mr. Bowles took over responsibility for dissecting our colorectal cancer specimens in 2003.

Table 1 Lymph Node Harvests and Percentage of Specimens Achieving 12 Lymph Nodes for each Year

Year	No. of specimens	Mean no. of LN[a]	Percent specimens> 11 LN[b]
1999	18	13.3	67
2000	48	12.2	50
2001	53	14.3	55
2002	49	14.4	67
Training of PA			
2003	40	20.7	83
2004	50	20.6	84
2005	75	18.4	87
2006	58	20.0	86

The division marked by "Training of PA" indicates the time frame where the PA took over responsibility for all specimen lymph node processing, i.e., at the beginning of 2003

LN lymph nodes

[a] $p<0.00001$ years 1999–2002 compared to years 2003–2006

[b] $p<0.00001$ years 1999–2002 compared to years 2003–2006

Figure 1 Colonic mesenteric lymph nodes fixed with Dissect Aid. The lymph nodes are the lighter areas within the specimens.

It is thought that it might be more difficult to harvest 12 lymph nodes in rectal specimens.[3,14,15] This could be due to a smaller mesentery and due to the effect of neoadjuvant radiation therapy which has become much more common in the treatment of rectal cancers. Although this review does not include data on which specimens had neoadjuvant therapy, some comparisons can be made. For the first 4 years, 1999–2002, there were a total of 36 non-stage IV rectal cancers (21% of all specimens). The average number of lymph nodes assessed in these specimens each year was 12.3, 13.0, 10.6, and 12.4 respectively—virtually identical to the averages for all specimens, for those years. Additionally, 42% of the rectal specimens achieved 12 nodes, only a little lower than the colon specimens. For the years 2003–2006, the average number of lymph nodes for

the 38 rectal specimens (17% of total) was 29.0, 17.8, 24.0, and 18.3, respectively (One rectal specimen was excluded from this analysis because it was a re-resection at the site of an anastomotic recurrence.). For these years, the percentage of rectal specimens with at least 12 lymph nodes was 82%. Thus, for the second 4-year period, lymph node harvests of rectal specimens were nearly as high as the colon specimens, as they were in the preceding 4 years, and the percentage achieving 12 nodes was statistically identical.

Subset analysis of the 2006 specimens was done, the results being illustrative. For the colon specimens in 2006, the average lymph node harvest is 22.4 with a range of 8–37, while the rectal specimens averaged 18.3 with a range of 5–34. A two-tailed Student's *T* test of these two means gives a *p* value of 0.07, which does not achieve statistical significance but may be meaningful. Based on that, we cannot say with certainty that rectal lymph node harvests are the same as the colon lymph node harvests and may be slightly lower on average. However, we believe that achieving the 12 node standard in rectal specimens is usually achievable. In 2006, the percentage of colon specimens achieving at least 12 nodes was 91%, and the percentage of rectal specimens achieving at least 12 nodes was 83% (excluding the one specimen which was a re-resection). Chi-square *p* value on achieving 12 nodes between the colon and rectal specimens in 2006 is 0.67.

We looked at harvests from stage IV specimens and from laparoscopic specimens as well. The numbers of these cases were small, but there was no apparent significant difference in lymph node harvests in these specimens compared to the other specimens during the same time frames.

Discussion

Obtaining adequate lymph node harvests from surgical colorectal adenocarcinoma specimens is clearly multifactorial. Surgeons need to resect enough mesentery for adequate lymph node assessment, and pathologists need to carefully dissect the resected mesentery to obtain as many lymph nodes as possible for analysis. This is a time and labor-intensive process. In addition to fastidious dissection, other techniques can reveal more lymph nodes for harvest, including the use of Dissect Aid as noted in the "Methods" section. The Dissect Aid is particularly helpful in retrieving small lymph nodes that can be missed even by an experienced dissector. Although we think that Dissect Aid or similar solutions maximizes node retrieval, it is important to note that it was in use prior to delegating the responsibility for node retrieval to the PA, and thus is not likely to be related to the improvement in node retrieval. Although we made no cost analysis of using Dissect Aid and our pathology assistant to harvest lymph nodes, we believe the cost is offset by the freeing of our pathologists' time from this tedious duty to do other things, and we clearly believe that the cost is more than justified by the more complete lymph node retrieval and staging data.

It is interesting to compare our data with nationally published data. An abstract, presented at the American Society of Clinical Oncology in 2007, looked at lymph node harvest data from NCCN institutions in 2005–2006 as well as SEER data from 2002. Although these two databases are vastly different in terms of time frame and hospital setting, the data are remarkably consistent with our own. They noted that 45% of stage I–III colorectal cancer specimens in the SEER database in 2002 achieved 12 lymph nodes, whereas the NCCN data from 2005 to 2006 showed 89% compliance with the 12 lymph node guideline.[20]

A large analysis of over 2,400 colorectal specimens over a 45-year period demonstrated that specimens with a larger number of lymph nodes analyzed had a much higher probability of finding positive nodes.[21] In our data, the average number of lymph nodes in specimens with negative nodes was 16.8 as opposed to 18.1 lymph nodes in specimens with positive nodes. Although suggestive that node positive specimens had a higher number of lymph nodes analyzed, it did not reach statistical significance ($p=0.165$; *T* test.) The same author emphasizes the importance of looking at all recoverable nodes including those that may be only 1–2 mm in size, a practice which we enthusiastically support.

We believe the substantial improvement in lymph node harvest in colorectal cancer specimens over the last 8 years at our institution is largely attributable to the training of a pathology assistant to fastidiously dissect colorectal mesentery and carefully search for nodes. The PA has greater time to devote to this task than pathologists and works in an environment with fewer distractions. Since the pathology assistant performs this task more frequently than any single pathologist, it is likely that ongoing proficiency exceeds that of any single pathologist. Another advantage is that a more uniform sampling for specimen examination occurs, since one person does most of the specimens instead of three pathologists with varying interests and amounts of time to devote to this task. We also believe that the importance placed on adequate lymph node harvests has had some influence on surgical technique with larger mesenteric resections, but the effect of this is admittedly more difficult to quantify.

Our data demonstrate that close attention to pathologic standards which are data-driven can clearly improve the quality of pathological analysis and consequently improve patient care. We were pleased to see the rapid and impressive improvement in our results following efforts to meet the nationwide standard of pathologic care for colorectal cancer specimens. Intermountain Healthcare, which owns

and operates 20 hospitals in Utah and Idaho, has made the 12-lymph node standard a system-wide Quality Assurance goal for 2008. We anticipate that many health care organizations and professional societies will do the same.[22]

Conclusion

A retrospective review of 391 consecutive colorectal adenocarcinoma pathology reports at a single community hospital was undertaken to follow the trend in lymph node harvests over an 8-year period. This time frame coincided with increased national recognition of the importance of adequate lymph node harvests for colorectal cancer staging. During this time, a pathology assistant was hired and trained to meticulously dissect colorectal mesentery and prepare as many lymph nodes as possible for pathologic analysis.

A highly statistically significant improvement in lymph node harvests was seen after this pathology assistant began processing all colorectal cancer specimens. This improvement has been sustained over a 4-year time frame. Fastidious dissection of colorectal mesentery clearly improves lymph node yields in colorectal cancer specimens. As medical institutions and national organizations focus on lymph node harvests as a Quality Assurance standard, factors that clearly improve lymph node harvests are becoming increasingly important. An appropriately trained and motivated pathology assistant is among the best of measures to ensure adequate lymph node assessment and accurate colorectal cancer staging.

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