Emergency surgery for colorectal cancer does not result in nodal understaging compared with elective surgery

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Background: It has been suggested that inadequate lymph node harvest may result in pathologically understaged or indeterminate staging of patients with colorectal cancer (CRC). We compared the adequacy of nodal staging in patients undergoing emergency surgery compared with elective surgery for CRC.

Methods: Using a prospectively collected CRC surgery database at a tertiary care centre, we performed a cohort study. The mean number of lymph nodes harvested and the proportion of patients who had inadequate staging (< 12 nodes harvested) were compared between emergency and elective surgery cohorts. Our analysis was adjusted for tumour site, type of resection, surgical training and pathologic stage.

Results: A total of 1279 of 1356 (94%) enrolled patients had nodal data available for analysis; 161 (13%) patients had emergency surgery and 1118 (87%) had elective surgery. The mean number of nodes removed was higher in the emergency surgery group (mean difference +2.8, 95% confidence interval [CI] 0.6–5.1, $p = 0.012$). The proportion of patients with inadequate nodal staging did not differ between groups (emergent 16%, elective 17%, $p = 0.79$). The odds of adequate nodal staging, adjusting for site, type of resection, training and stage was no different between groups (OR 0.80, 95% CI 0.47–1.35, $p = 0.41$).

Conclusion: The evidence does not support the common belief that emergency surgery is more commonly understaged in CRC. Our data suggest emergency surgery resulted in a significant increase in the average number of nodes harvested, with no difference in inadequate nodal staging.

Contexte : Il semble qu'une méthode erronée de prélèvement de lymphonœuds pourrait expliquer pourquoi le stade d'évolution du cancer colorectal (CCR) est sous-évalué ou qu'il est impossible de le déterminer chez certains patients. On a comparé la méthode de détermination de l'atteinte des lymphonœuds chez des patients atteints d'un CCR devant subir une chirurgie d'urgence à celle utilisée chez des patients devant subir une chirurgie non urgente.

Méthodes : En utilisant une base de données prospectives sur des chirurgies du côlon pratiquées dans un établissement de soins tertiaires, on a comparé le nombre moyen de prélèvements de lymphonœuds et la proportion de patients pour lesquels le stade d'évolution était erroné (prélèvement de < 12 lymphonœuds) entre la cohorte de patients ayant subi une chirurgie d'urgence et celle ayant subi une chirurgie non urgente. Les résultats de notre analyse ont été ajustés en fonction du siège des tumeurs, du type de résection, de la formation chirurgicale et du stade pathologique.

Résultats : Pour 1279 (94 %) des 1356 patients recrutés, on disposait des données sur les lymphonœuds; 161 patients (13 %) avaient subi une chirurgie d'urgence et 1118 (87 %), une chirurgie non urgente. Le nombre moyen de lymphonœuds prélevés était plus élevé pour le groupe de patients ayant subi une chirurgie d'urgence (écart moyen +2,8, intervalle de confiance [IC] à 95 % 0,6–5,1, $p = 0,012$). Mais la proportion de patients pour lesquels le stade d'évolution de la maladie était erroné ne différait pas entre les groupes (intervention d'urgence 16 %, intervention non urgente 17 %, $p = 0,79$). La probabilité que le stade d'évolution soit exact, l'ajustement en fonction du siège des tumeurs, du type de résection, de la formation chirurgicale et du stade d'évolution ne différaient pas entre les groupes (RR 0,80, IC à 95 % 0,47–1,35, $p = 0,41$).

Conclusion : Les résultats de notre étude ne confirment pas la croyance répandue selon laquelle le stade d'évolution du CCR est plus souvent sous-évalué chez les patients ayant subi une chirurgie d'urgence. En effet, nos données semblent indiquer que les chirurgies d'urgence étaient associées à un nombre plus élevé de lymphonœuds prélevés, mais qu'il n'y avait aucune différence pour ce qui est des erreurs de détermination du degré d'atteinte des lymphonœuds.

Colorectal cancer (CRC) is the fourth most common cancer in Canada and accounts for the second most cancer-related deaths. An estimated 23 300 Canadians received diagnoses of CRC in 2012, with 9200 succumbing to the disease.[1] The accepted management of CRC is complete resection, surgical dissection of the associated lymph node basin and removal of any contiguous organs involved. The common occurrence of CRC and the emphasis of early surgical intervention indicates that management of this disease is, and will remain, a significant part of general surgical practice.

Adjuvant chemotherapy has shown clear improvement in survival and lower recurrence rates in node-positive or stage III disease.[2] Adjuvant chemotherapy with fluorouracil plus leucovorin or capecitabine-based regimes is now the standard of care for treatment of stage III disease.[3,4] Although some advocate for adjuvant therapy in stage II disease, the evidence is less clear.[5] A significant improvement in survival with adjuvant chemotherapy in stage II disease has been elusive, although there may be some benefit in high-risk populations.[6]

Pathological examination of the resected specimen is an essential step in determining node positivity, cancer stage, indication for the use of adjuvant chemotherapy and patient prognosis. The greater the number of nodes examined, the more confidence can be placed in the reported nodal status of the patient.[7] The American Joint Commission on Cancer and the College of American Pathologists recommend examination of a minimum of 12 lymph nodes to accurately diagnose stage II disease.[8] This has now become a measure of surgical resection adequacy in stage I–III CRC.

Patients presenting with obstructing or perforated cancers requiring emergent surgery represent a high-risk population with poor outcomes compared to those with nonemergently resected cancers. The cause for decreased survival in this high-risk population has been poorly evaluated in the literature.[9] It has been suggested that owing to technical difficulty or instability of the patient, inadequate lymph node harvest may occur, resulting in pathologically understaged or indeterminate staging of the patient. Consequently these patients may not receive the survival benefits of adjuvant chemotherapy, or they may be subjected to unnecessary side effects of chemotherapeutic drugs.[10,11]

The objective of our study was to compare the adequacy of nodal staging in patients undergoing emergency surgery with those undergoing elective surgery for CRC in a high volume tertiary referral Canadian hospital.

Methods

Database

Patient information was entered prospectively into a database from January 2008 to December 2013. Patient information, surgical information, neoadjuvant and adjuvant therapy, pathology information, tumour-node-metastasis (TNM) classification and staging were entered manually. Surgical nature (elective v. emergent) was determined from the operative notes and International Classification of Diseases (ICD)-10 codes during individual patient data entry. The indication for emergent surgery was not included in the original data set. Quarterly quality assessment data runs and random chart audits were completed to assure accuracy of the data set. We obtained information on pathologic staging and lymph node count from the synoptic pathology reports.

Exposure and outcomes

The primary exposure was the nature of surgery (emergency v. elective surgery). The primary outcome was adequacy of lymph node harvest, with 12 or more nodes considered adequate. In addition, we compared the mean number of nodes harvested between groups.

We explored several factors to determine if they modified the effect of nature of surgery on nodal harvest. These included surgeon subspecialty training (colorectal, surgical oncology, general surgery), tumour site (right, transverse, left, rectum, multiple), type of resection (right hemicolectomy, left hemicolectomy, sigmoid resection, segmental resection, abdominoperineal resection (APR), Hartmann, low anterior resection, subtotal colectomy) and pathologic stage. Owing to location and the expected difference in use between elective and emergent surgery, we grouped low anterior resections, APR and Hartmann procedure together for analysis.

Statistical analysis

We performed all statistical analyses using STATA software version 12.0 (Statacorp).

The crude association between nature of surgery and adequacy of lymph node harvest was determined using a Pearson χ^2 test. The difference in means was calculated using analysis of variance between groups. We completed a Mantel–Haenszel analysis to assess the effect of surgeon training, tumour site, type of resection and pathologic stage on the adequacy of lymph node harvest between groups.

We then performed logistic regression analysis to assess the association between adequacy of lymph node harvest and nature of surgery, adjusting for surgeon training, tumour site, type of surgery and pathologic stage. Significance testing was completed using the likelihood ratio test.

Results

Of the 1356 patients enrolled in the database, 1279 patients (94%) had complete pathologic information and were

included in this study. Of these, 12.6% required an emergency operation. Patient characteristics can be found in Table 1. Overall, the most common tumour sites were right-sided (29.4%), left-sided or sigmoid (28.9%) or rectal (30.5%). The surgeons' subspecialties included colorectal training (35.0%), surgical oncology (9.8%) and general surgery (54.9%).

The mean number of nodes harvested and proportion of adequate lymph node sampling can be found in Table 2. The emergency group on average had more lymph nodes sampled than the elective group (mean difference +2.8, 95% confidence interval [CI] 0.6–5.1, p = 0.012). There was no difference in the proportion of adequate harvests between the emergency and elective groups (risk ratio 1.01, 95% CI 0.94–1.09, p = 0.79). Furthermore, no trends were identified in the inadequate node harvest data set. The proportion of cases with fewer than 5 nodes and 5–9 nodes harvested were comparable in both emergent and elective groups.

We completed stratified analyses to assess the effect of surgeon training, tumour site, type of resection, pathologic stage and age on the association between adequacy of lymph node harvest and surgical nature (Table 3).

The Mantel–Haenszel analysis revealed that the association between adequacy of lymph node harvest and surgical nature was not influenced by surgical training (test of homogeneity, p = 0.31), tumour site (p = 0.31) type of resection (p = 0.96), pathologic stage (p = 0.45) or age (p = 0.46; Table 4).

A logistic analysis was completed assessing the association between lymph node adequacy and surgical nature, adjusting for surgeon training, tumour site, type of resection, pathologic stage and age. We found no evidence of an association between surgical nature and lymph node harvest, after adjusted analysis. The odds ratio of an adequate resection in the emergency group compared with the elective group was 0.77 (95% CI 0.45–1.31, p = 0.35; Table 4).

Table 1. Characteristics of study participants

Characteristic	Group; no. (%)		
	Total	Elective surgery	Emergency surgery
Nature of surgery	1342 (100)	1181 (87.4)	161 (12.6)
Age, yr			
< 50	91 (7.1)	75 (6.7)	16 (9.9)
50–59	204 (16.0)	190 (17.0)	14 (8.7)
60–69	343 (26.8)	297 (26.6)	46 (28.6)
70–79	373 (29.2)	334 (29.9)	39 (24.2)
≥ 80	268 (21.0)	222 (19.9)	46 (28.6)
Tumour site			
Right colon	376 (29.3)	325 (29.1)	51 (31.7)
Transverse colon	123 (9.6)	95 (8.5)	29 (17.4)
Left or sigmoid colon	370 (28.9)	307 (27.5)	63 (39.1)
Rectum	390 (30.5)	378 (33.8)	12 (7.5)
Multiple	10 (0.8)	6 (0.5)	4 (2.5)
Other	10 (0.8)	7 (0.6)	3 (1.9)
Surgery type			
Right colectomy	433 (33.9)	367 (32.8)	66 (41.0)
Left colectomy	138 (10.8)	124 (11.1)	14 (8.7)
LAR	406 (31.7)	384 (34.4)	22 (13.7)
APR	129 (10.1)	128 (11.5)	1 (0.6)
Hartmann	31 (2.4)	14 (1.3)	17 (10.6)
Subtotal colectomy	76 (5.9)	45 (4.0)	31 (19.3)
Segmental colectomy	40 (3.1)	30 (2.7)	10 (6.2)
Other	13 (1.0)	13 (1.2)	0 (0)
Surgeon training			
Colorectal	448 (35.0)	417 (37.3)	31 (19.3)
Surgical oncology	125 (9.8)	109 (9.8)	16 (9.9)
General surgery	702 (54.9)	589 (52.7)	113 (70.2)
Other	4 (0.3)	3 (0.3)	1 (0.6)
Pathologic stage			
Stage 0	50 (3.9)	50 (4.5)	0 (0)
Stage I	226 (17.7)	224 (20.0)	2 (1.2)
Stage II	402 (31.4)	354 (31.7)	48 (29.8)
Stage III	465 (36.4)	404 (36.1)	61 (37.9)
Stage IV	135 (10.6)	85 (7.6)	50 (31.1)
Unknown	1 (0.1)	1 (0.1)	0 (0)

APR = abdominoperineal resection; LAR = low anterior resection.

Discussion

Our results showed that there was no evidence of a difference in the adequacy of lymph node harvest between elective and emergency surgery. This was true, even after adjusting for age, tumour site, type of resection, surgeon training and pathologic stage.

Strengths and limitations

This study used information from a prospectively collected database of patients with CRC. We had complete nodal information on more than 90% of patients who were included in the study. The accuracy of the pathology reports have been assured and maintained with routine audits. In addition, we had complete information on age, type of resection, tumour site, full pathologic staging and surgeon training. This allowed us to analyze the independent effects of the nature of surgery after adjusting for these potential confounders.

Table 2. Mean number of lymph nodes removed and proportion of adequate lymph node harvest, by surgical nature

Factor	Group; mean (SD) or no. [%]		p value
	Elective surgery	Emergency surgery	
No. of nodes	19.1 (13.3)	22.0 (13.8)	0.012
Adequacy of lymph node harvest			0.79
Adequate, ≥ 12 nodes	928 [83.0]	135 [83.9]	
Inadequate, < 12 nodes	190 [17.0]	26 [16.1]	

SD = standard deviation.

Limitations of the study may include misclassification of the nature of surgery. We extracted the nature of surgery from operative notes. We were unable to further validate the nature of surgery. In addition, the database did not capture the indication for surgery in the emergency group. It is possible that operating for bleeding, obstruction or perforation could affect the adequacy of the lymph node harvest differently. The database included patients who were treated at an academic institution by surgeons with varying levels of training. The results of this study may not translate to the community hospital experience, where training may be similar but volumes and case complexity may be variable. An additional limitation is that adequacy of lymph node harvest can be affected by the reporting pathologist.[12] Our database did not distinguish among reporting pathologists, and adequacy of nodal harvest by pathologist was not available.

Table 3. Stratified analysis of adequacy of lymph node harvest, by surgical nature

Factor	Group; no. (% inadequate)		*p* value
	Elective surgery	Emergency surgery	
Surgeon training			
Colorectal	417 (17.3)	31 (9.7)	0.28
Surgical oncology	109 (18.4)	16 (6.3)	0.23
General surgery	589 (16.5)	113 (19.5)	0.44
Other	3 (33.3)	1 (0.0)	0.51
Tumour site			
Right colon	325 (7.4)	51 (9.8)	0.55
Transverse colon	95 (9.5)	28 (3.6)	0.32
Left or sigmoid colon	307 (20.5)	63 (22.2)	0.76
Rectum	378 (24.3)	12 (25.0)	0.96
Multiple	6 (0.0)	4 (0.0)	N/A
Other	7 (28.6)	3 (100.0)	0.038
Surgery type			
Right colectomy	367 (7.4)	66 (9.1)	0.63
Left colectomy	124 (18.6)	14 (14.3)	0.70
LAR/APR/Hartmann	539 (20.8)	40 (27.5)	0.32
Subtotal colectomy	45 (8.9)	31 (9.7)	0.91
Segmental colectomy*	30 (36.7)	10 (40.0)	0.85
Other	13 (100.0)	0 (0.0)	N/A
Pathalogic stage			
Stage 0	50 (36.0)	0	N/A
Stage I	224 (23.6)	2 (50.0)	0.39
Stage II	354 (15.0)	48 (16.7)	0.76
Stage III	404 (11.6)	61 (6.6)	0.24
Stage IV	85 (21.2)	50 (26.0)	0.52
Unknown	1 (100.0)	0	N/A
Age, yr			
< 50	75 (12.0)	16 (12.5)	0.96
50–59	190 (16.8)	14 (28.6)	0.27
60–69	297 (17.2)	46 (8.7)	0.15
70–79	334 (20.4)	39 (23.1)	0.69
≥ 80	222 (13.5)	46 (15.2)	0.76

APR = abdominoperineal resection; LAR = low anterior resection; N/A = not applicable.
*Nonformal resection (e.g., cecectomy, segment of sigmoid).

Strengths and limitations in comparison to previous publications

A previous study by Lewis and colleagues[13] examined 296 patients operated for colon cancer, 15% of whom had an emergency operation. Comparing the results from our study and theirs, we found a similar proportion of patients requiring emergency surgery (15% v. 12.6%). The study by Lewis and colleagues did not include patients with rectal cancers. In addition, there was a smaller proportion of inadequate harvest in the elective group in their study compared with ours (11.9% v. 17.0%), but there was no difference in the proportion of inadequate harvest in the emergency group (14.0% v. 16.1%). Univariate analysis in the study by Lewis and colleagues found no association between nature of surgery and adequacy of lymph node harvest ($p = 0.70$). They did not attempt to adjust for the effects of surgeon training, tumour site, resection type or pathologic stage.

Previous studies have found that specialty training may result in differences in adequacy of node harvest.[14,15] In addition, tumour site has previously been found to affect adequacy of nodal harvest.[16,17] Our study stratified and then adjusted for these 2 factors as well as resection type and pathologic stage. Even after adjusting for these important factors, we found no difference in the adequacy of nodal harvest.

Table 4. Mantel–Haenszel and logistic regression analysis

Type of analysis	OR (95% CI)	Significance testing	Test of homogeneity
Mantel–Haenszel odds			
Adjusted for training	1.06 (0.68–1.68)	$p = 0.77$	$p = 0.31$
Adjusted for site	0.87 (0.54–1.41)	$p = 0.57$	$p = 0.31$
Adjusted for type of resection	0.82 (0.50–1.31)	$p = 0.40$	$p = 0.96$
Adjusted for pathologic stage	0.99 (0.61–1.63)	$p = 0.99$	$p = 0.45$
Adjusted for age group	1.01 (0.64–1.58)	$p = 0.97$	$p = 0.46$
Logistic regression			
Adjusted for training, site, type of resection, stage and age group	0.77 (0.45–1.31)	$p = 0.35$	N/A

CI = confidence interval; N/A = not applicable; OR = odds ratio.

Population-based studies have identified age as a statistically significant variable affecting adequacy of lymph node resection.[18,19] Baxter and colleagues[18] studied more than 100 000 patients with invasive colon and rectal cancer. Our results show a similar trend with decreasing rates of adequate lymph node resection with increasing age. The rates of adequate resection are improved compared with these previous findings of Baxter and colleagues in patients younger than 50 (12% v. 45%) and older than 71 years of age (16.9% v. 65%).[18] Our stratified analysis assessing the effect of age on adequacy of lymph node resection was not significant when comparing the emergent and elective groups.

Conclusion

Patients undergoing emergency surgery had no difference in the adequacy of nodal staging compared with their elective counterparts. The commonly held belief that inadequate staging occurs more frequently in the emergency group was not supported by our patient population and analysis.

Competing interests: None declared.

Contributors: All authors designed the study. M. Brackstone acquired the data, which S. Patel and S. Patel analyzed. S. Patel and S. Patel wrote the article, which all authors reviewed and approved for publication.

References

1. Canadian Cancer Society, Steering Committee on Cancer Statistics. Canadian Cancer Statistics 2012. Toronto (ON): Canadian Cancer Society; 2012.
2. NIH consensus conference. Adjuvant therapy for patients with colon and rectal cancer. *JAMA* 1990;264:1444-50.
3. Macdonald JS. Adjuvant therapy of colon cancer. *CA Cancer J Clin* 1999;49:202-19.
4. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjunvant treatment for stage II colon cancer. *N Engl J Med* 2005;352: 2696-704.
5. André T, Boni C, Navarro M, et al. Improved overall survival with oxaliplatin, flurouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial. *J Clin Oncol* 2009;27:3109-16.
6. Benson AB III, Schrag D, Somerfield MR, et al. American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer. *J Clin Oncol* 2004;22:3408-19.
7. Swanson RS, Compton CC, Stewart AK, et al. The prognosis of T3N0 colon cancer is dependent on the number of lymph nodes examined. *Ann Surg Oncol* 2003;10:65-71.
8. NCCN Clinical practice guidelines in Oncology: Colon Cancer. Available: www.nccn.org (accessed 2013 March 10).
9. Carraro PG, Segala M, Cesana BM, et al. Obstruction colonic cancer: failure and survival patterns over a ten-year follow-up after one-stage curative surgery. *Dis Colon Rectum* 2001;44:243-50.
10. Gill S, Loprinzi CL, Sargent DJ, et al. Pooled analysis of flurouracil-based adjuvant therapy for stage II and III colon cancer: Who benefits and by how much? *J Clin Oncol* 2004;22:1797-806.
11. Serpell JW, McDermott FT, Katrivessis H, et al. Obstructing carcinomas of the colon. *Br J Surg* 1989;76:965-9.
12. Evans MD, Barton K, Rees A, et al. The impact of surgeon and pathologist on lymph node retrieval in colorectal cancer and its impact on survival for patients with Dukes' stage B disease. *Colorectal Dis* 2008;10:157-64.
13. Lewis A, Akopian G, Carillo S, et al. Lymph node harvest in emergent versus elective colon resections. *Am Surg* 2012;78:1049-53.
14. Barbas A, Turley R, Mantyh C, et al. Advanced fellowship training is associated with improved lymph node retrieval in colon cancer resection. *J Surg Res* 2011;170:e41-6.
15. Nicholl MB, Wright BE, Conway WC, et al. Does specialized surgical training increase lymph node yield in colon cancer? *Am Surg* 2009;75:887-91.
16. Bilimoria KY, Palis B, Stewart AK, et al. Impact of tumor location on nodal evaluation for colon cancer. *Dis Colon Rectum* 2008;51: 154-61.
17. Bernhoff R, Holm T, Sjovall A, et al. Increased lymph node harvest in patients operated on for right-sided colon cancer: a population-based study. *Colorectal Dis* 2012;14:691-6.
18. Baxter NN, Virnig DJ, Rothenberger DA, et al. Lymph node evaluation in colon cancer patients: a population-based study. *J Natl Cancer Inst* 2005;97:219-25.
19. Bilimoria KY, Stewart AK, Palis BE, et al. Adequacy and importance of lymph node evaluation for colon cancer in the elderly. *J Am Coll Surg* 2008;206:247-54.