How many lymph nodes to stage colorectal carcinoma?

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Abstract
This study aimed to establish the number of cassettes that should be filled with lymph nodes to stage a colorectal carcinoma as Duke's stage C. The records from the Oxford Colorectal Cancer database of all patients diagnosed with Duke's stage C cancer from late 1988 to early 1993 were reviewed. Each slide of lymph nodes was examined to determine how many slides needed to be looked at to find the first positive lymph node. The resected specimens were not fat cleared but dissected manually in a routine fashion. One hundred and eight slides were retrieved. The mean total lymph node harvest was 8.44 for each patient. Ninety eight patients (90.7%) had positive lymph nodes on the first slide with an average of 3.42 lymph nodes on each slide, of which a mean of 1.82 were positive. For nine patients, two slides were required to make a diagnosis of lymph node involvement, and for one patient the first three slides needed inspection to establish Duke's stage C. In conclusion, using a routine technique to obtain lymph nodes from colorectal cancer specimens 99% of Duke's stage C colorectal carcinoma can be found by filling two cassettes with lymph nodes.

Keywords: lymph nodes; colorectal cancer; tissue cassettes

Since Cuthbert Dukes introduced his staging system for rectal cancer in 1932 the presence of lymph node metastases in colorectal cancer has been recognised as prognostically significant. Patients with a single lymph node metastasis have reduced overall survival compared with patients with similar tumours and no node involvement. The presence of lymph node metastases also helps to decide whether adjuvant radiotherapy and/or chemotherapy should be offered to the patient. The development of the TNM staging system acknowledges that the number of involved lymph nodes is important prognostically and several time consuming methods for the identification of lymph nodes in pathological specimens have been described. However, for the non-specialist colorectal histopathologist with little time to carry out these special techniques a routine method of dissection and lymph node harvesting is usually practised. There are few data to suggest the optimum number of lymph nodes, other than as many as possible, that should be harvested to find the maximum yield of Duke's stage C tumours.

Methods
We took all the Duke's stage C patient records from the Oxford Colorectal Cancer database from late 1988 to early 1993 and studied all the slides of lymph nodes. The resected specimens were not fat cleared but dissected in a routine fashion by a number of general histopathologists. Slides with just the apical lymph node in rectal specimens were not included in the study. The slides containing lymph nodes were then looked at by three observers to determine how many slides needed to be looked at to find the first positive lymph node. The first slide was the first one filled with lymph nodes by the dissector, the second the next one filled, etc. Metastases to pericolic adipose tissue outside of lymph nodes were counted as lymph node metastases only if they were >3 mm in diameter as advised by Hermanek. The pathology report was not used for determination of the number of lymph nodes recovered nor the number of lymph nodes with metastases. This information was determined purely by examination of the slides.

Results
One hundred and eleven patients were diagnosed with Duke's stage C colorectal carcinoma on the database and we retrieved the slides of 108 of these patients, providing 911 lymph nodes. Ninety eight patients (90.7% (95% confidence interval 79.24 to 100%)) had lymph nodes containing adenocarcinoma metastasis on the first slide with an average of 3.42 lymph nodes (range 1–9) on each slide of which 1.82 were positive. The mean total lymph node harvest was 8.24 for each patient. Nine patients (8.33% (CI 3.12 to 13.54%)) had two slides reviewed to establish lymph node involvement with a mean of 7.33 lymph nodes (range 1–8) on the first two slides; the mean total lymph node harvest was 9.33 for each patient.

For one patient, three slides were needed to stage a Duke's C and these contained 19 lymph nodes.

Discussion
In this retrospective analysis we found that when using a routine technique to obtain lymph nodes from colorectal cancer specimens, 99% (95% CI 98 to 100%) of Duke's stage C tumours can be found by filling two cassettes with lymph nodes. However, we cannot know how many patients classified as Duke's stage B actually had small lymph nodes.
nodes containing metastases. Using a modification of the clearing method first described by Gilchrist and David in 1938, Morikawa and colleagues found a mean lymph node harvest for each patient of 74.3 by finding smaller ones. Andreola and colleagues found that in patients staged as Dukes’s C 174 of 960 lymph nodes were positive. This is fewer than our figure of 503 of 911 (55%). However, using a fat clearance or manual dissection technique, metastatic involvement has been shown in 50–78% of lymph nodes < 5 mm in diameter. Goldstein and colleagues showed that there was a profound increase in the percentage of patients with at least one lymph node metastasis when 12 to 20 lymph nodes were recovered from each specimen compared to specimens in which fewer lymph nodes were found.

Therefore, until further information is found regarding the number of lymph nodes needed to be found to stage colorectal cancer, to establish a prognosis, and to help plan adjuvant treatment, we advocate that as many lymph nodes as possible should be found as advised in the new Royal College of Surgeons guidelines for the management of colorectal cancer.