

## Audit: Lymph node yield in histology resection specimens of upper gastro-intestinal cancers



Dr Manisha Ram

The College's Clinical Effectiveness Department wishes to encourage high-quality clinical audit. We therefore periodically publish interesting examples of audits that have been successfully evaluated through our clinical audit certification scheme.

### Background

Upper gastro-intestinal (GI) cancer surgery, like other specialist services, is facing rationalisation in fewer centres. Lymph node yield from surgical specimens, as compared to local and national standards, is used as a quality indicator of the histopathological assessment of the specimen and a surrogate marker for the quality of the surgery.

### Aim and objectives

The aim of this audit was to assess if the lymph node yield in surgical histology specimens for cancer from the upper GI tract (oesophagus and stomach) received in the network centre in one calendar year met local and national standards. In order to complete the audit cycle with a view to re-audit, we also examined the variables which we judged to have had a possible effect on the lymph node yield.

### Standards

The Royal College of Pathologists' standard is that the total lymph node yield from upper GI cancer histology resection specimens should be at least 15 per specimen (in 100% cases), excepting cases in which a more limited surgical resection is performed.<sup>1,2</sup>

### Method

This retrospective audit included all 64 patients who had resection operations for upper GI (oesophageal and gastric) cancer in the calendar year 1 April 2012 to 31 March 2013 at Guy's & St Thomas' NHS Foundation Trust. Of the 64 cases, 54 were resected for adenocarcinoma, five for squamous cell carcinoma, one for adenosquamous carcinoma, one each for high-grade glandular and squamous dysplasia and two for gastro-intestinal stromal tumours (GISTs). The patient with the high-grade glandular dysplasia had had a previous endoscopic mucosal resection (EMR) reported as showing at least intramucosal adenocarcinoma and the patient with high-grade squamous dysplasia had had pre-operative biopsies reported as showing high-grade squamous dysplasia.

The cases were identified from the surgical operative records. The following data were extracted from the histopathology records:

- number of lymph nodes retrieved
- number of lymph nodes positive and negative for metastases
- patient age
- type of operation
- sites of lymph nodes found
- specimen size and amount of fat included
- responsible upper GI surgeon
- responsible GI consultant histopathologist
- histopathologist who cut up the specimen
- second attempt to find more lymph nodes from the specimen
- history of neo-adjuvant therapy and histological evidence of response (Mandard tumour regression grade).

Slide review was performed only if necessary to establish the reason for which extra blocks were taken. The data collected were anonymised. The help of a King's College London statistician was enlisted for statistical analysis, with use of the SPSS (Statistical Product and Service Solutions) programme.

### Results

#### 1. Lymph node yield versus patient age

The mean number of nodes per case (total nodes/total cases) decreased from 28.7 in the age group <40 years to 15.4 in the age group >70 years. There was a negative correlation between increasing patient's age and lymph node yield (Spearman's correlation = -0.2916) and this was statistically significant ( $p = 0.0194$ ). There also appeared to be a negative correlation between the patient's age and percentage positivity of the lymph nodes, but this was not analysed statistically.

#### 2. Lymph node yield by type of operation/surgery

The various operation types included trans-hiatal oesophago-gastrectomy (THO), left thoraco-abdominal oesophago-gastrectomy (LTA), distal gastrectomy (DG), subtotal gastrectomy (STG),



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total gastrectomy (TG) and partial gastrectomy/excision of gastric mass (PG). Since there was just one case of PG, for a GIST, yielding a single negative lymph node, this case was omitted from further consideration; the operation performed for the other GIST in this series was a STG. It was seen that the mean number of lymph nodes found by operation (total number of nodes/total number of cases) was the lowest for DG specimens (13.66) and highest for TG specimens (23.3), with the oesophago-gastrectomy specimens having intermediate values (16.2 and 17.1).

### 3. Lymph node yield from the various sites

Between the various sites (para-oesophageal, lesser curve, greater curve, gastro-oesophageal junction, separately sent by surgeon and not specified), the lowest mean number of nodes was for separately sent lymph nodes (1.8). The number of lymph nodes found within this latter category will be independent of the pathologist doing the cut up, since these tend to be small specimens submitted by the surgeon, which are blocked in their entirety, and therefore this group was omitted from further analysis. In 17 cases, the lymph node site was not specified in the histology report and this group had the highest mean number of lymph nodes (17.4). Disregarding these two groups, the lowest mean number of lymph nodes found was at the gastro-oesophageal junction (5.2) and the highest at the lesser curve (11.4).

### 4. Lymph node yield versus specimen size and amount of fat included with each specimen

Spearman's test showed that the correlation between gastric lesser curve length and the number of lesser curve lymph nodes was neither strong ( $r = 0.1730$ ) nor significant ( $p = 0.2558$ ). There was a negative correlation ( $r = -0.4112$ ) between oesophageal length and the number of para-oesophageal lymph nodes and this relationship was significant ( $p = 0.0331$ ).

The most significant measurement of the lesser curve fat was judged to be the distance from the gastric serosal surface of the lesser curve to the resection margin of the lesser curve fat. Some pathologists gave only this measurement, as the depth of the lesser curve fat, and others measured the lesser curve fat in three dimensions (length x depth x thickness), in which case the middle of these three measurements by size was taken for analysis. For the greater curve fat, the greatest dimension was chosen as an approximate gauge of the amount of greater curve fat included.

There was a significant positive Spearman's coefficient of determination correlation between the maximum dimension of the greater curve fat and the total number of lymph nodes found ( $\rho = 0.322$ ,  $p = 0.007$ ), but not between the depth of the lesser curve fat and the total number of lymph nodes found. There was no correlation between the

amount of fat on the greater or lesser curves and the numbers of positive lymph nodes found.

### 5. Lymph node yield versus responsible upper GI surgeon

Fifty cases belonged to surgical team CS1, ten cases belonged to team CS2 and for the remaining four cases the histopathology request form did not bear details of the responsible operating surgeon/team. There was no significant difference in the mean number of lymph nodes per case between CS1 (18.8) and CS2 (19.9). However, the mean number of nodes per case was quite low (5.2) for the four cases in which there were no surgeon details. Of these four cases, the clinical details on two of them provided no indication as to why the lymph node yield would be expected to be low; both were elective operations for adenocarcinoma, one a DG and the other a trans-hiatal oesophagectomy. The remaining two specimens were both oesophago-gastrectomy specimens. One was for adenocarcinoma, but the patient had had a stent placed for complete dysphagia. The other patient had had a previous Nissen fundoplication for hiatus hernia, and the resection specimen showed Barrett's oesophagus with high-grade glandular dysplasia, and complete regression of the invasive component.

### 6. Lymph node yield versus responsible GI consultant histopathologist

Over the calendar year studied, seven GI consultant histopathologists reported the 64 cases, some of the consultants being at work for only part of this year, e.g. due to long-term leave or cessation of their locum contracts. The least number of cases (one) was reported by CP7 and the greatest number of cases (17) was reported by CP3. CP4 and CP6 each reported two cases. The mean number of lymph nodes found per case was lowest for CP6 (4.5) and highest for CP4 (23.5). The Kruskal-Wallis equality-of-populations rank test showed that there was no significant difference ( $p = 0.0881$ ) in the lymph node yields between the seven GI consultant histopathologists. After excluding CP4, CP6 and CP7 from the analysis (because of the small number of cases reported by each of them), the significance was reduced even further ( $p = 0.2048$ ).

### 7. Lymph node yield versus pathologist who cut up specimen

Five consultant GI histopathologists and ten trainee histopathologists performed the dissection (cut-up) of these 64 specimens. The trainees ranged from stage A (first year in histopathology), through to stage C (peri-Part 2 FRCPath exam) and in between (stage B). Thirty of these cases were indicated on the histology report as having been cut up by consultants and the remaining 34 by trainees; however, it is standard practice in this department for the GI consultant histopathologists to closely supervise the trainees, particularly if they are junior, so it is

Pathologist	Total no. cases	Total no. nodes from specimens	No. nodes positive from specimens	No. nodes negative from specimens	% positive LNs	Mean	Min-max	Range
CP1	15	266	26	240	9.8	17.7	1-33	32
CP2	15	239	55	184	23.0	15.9	5-32	27
CP3	17	340	58	282	17.1	20.0	3-35	32
CP4	2	47	27	20	57.4	23.5	13-34	21
CP5	12	254	17	237	66.9	21.2	15-31	16
CP6	2	9	3	6	33.3	4.5	4-5	1
CP7	1	7	2	5	28.6	7.0	7	NA
Total	64	1162	188	974				

likely that the cases recorded as having been cut up by junior trainees (TPA) were in fact cut up jointly between the trainee and consultant. According to the Kruskal-Wallis equality-of-populations rank test, there was no significant statistical difference between the lymph node yields of the various prosectors ( $p = 0.3178$ ).

There was no significant difference between the mean lymph node yields of the five consultant GI histopathologists as a group, versus the ten trainee histopathologists as a group ( $p = 0.995$ , two-sample Wilcoxon rank-sum/Mann-Whitney test).

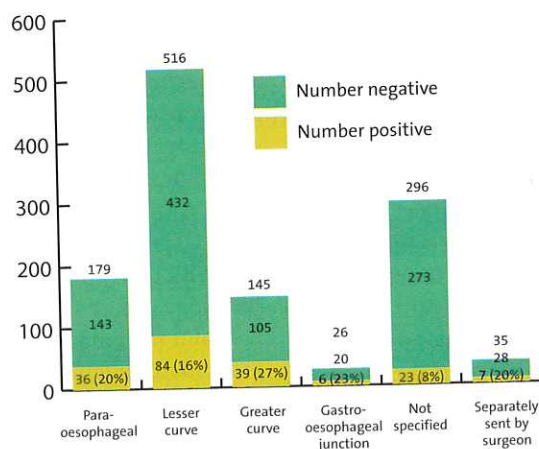
### 8. Second attempt to find more lymph nodes from the specimen (if any)

Extra blocks were taken in ten of the 64 cases, six of which were taken with the intention of increasing the lymph node yield above 15. In these six cases, a total of 35 extra lymph nodes were found (1, 4, 5, 6, 6 and 13 lymph nodes, respectively), ranging from 2 mm to 11 mm, but none contained metastases.

### 9. Lymph node yield versus history of neo-adjuvant chemotherapy (NAC) and histological evidence of response to therapy

There was a highly significant ( $p = 0.0005$ , t-test) difference in the mean lymph node count (20.4) in the 47 cases with a history of NAC, compared to the mean (12) in those 17 without.

The Mandard tumour regression grade3 of the



primary tumour is assessed and stated in the histology reports of all patients who have NAC.

There was a positive correlation between increasing Mandard score and number of lymph nodes found in each specimen (Spearman's correlation = 0.2902), and this correlation was statistically significant ( $p = 0.02$ ).

### Discussion

This was a retrospective audit of all upper GI cancer resection specimens ( $n = 64$ ) received at the Trust from April 2012 to March 2013. Two of the cases were for gastro-intestinal stromal tumours (GISTs) and the remainder for carcinomas/dysplasia. In retrospect, the GISTs should not have been included, since their biology and lymph node involvement, and therefore surgery, is entirely different to that of epithelial tumours; however, since these were only two out of 64 cases, they are unlikely to have affected the statistical outcomes significantly.

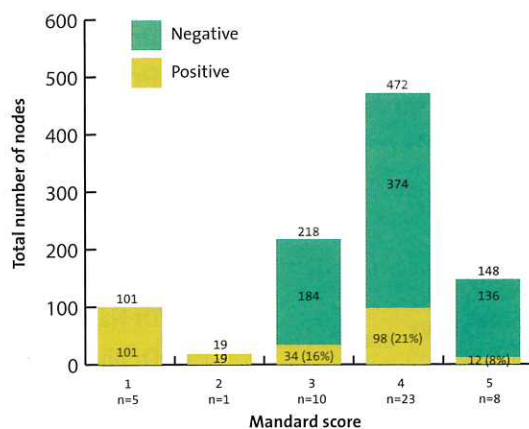
The mean number of lymph nodes dissected from the specimens was 18.2, which exceeded the RCPATH standard of 15. However the range was from three to 35, with the yield in 21 (32.8%) specimens failing to reach 15.

The expected variables that were found to correlate statistically significantly with the lymph node yield were patient age (negative correlation); type of operation; and Mandard tumour regression score (positive correlation). Surprisingly, the lymph node yield was higher in patients with a history of neo-adjuvant chemotherapy than those without. There was a negative correlation between the oesophageal length and lymph node yield. The likely explanation is that the longer oesophageal lengths relate to a THO operation, since the anastomosis is in the neck; the lymph node yields with the left thoraco-abdominal (LTA) approach are higher than with THOs as the peri-aortic lymph nodes are dissected under direct vision. The depth of the lesser curve fat resected and the greatest dimension of the greater curve fat on the specimen were analysed, in relation to the total lymph node yield and number of positive lymph nodes found. The only positive correlation was between the total

Cut-up by	Total no. cases	Total no. nodes from specimens	No. nodes positive from specimens	No. nodes negative from specimens	% positive LNs	Mean	Min-max	Range
CP1	9	158	16	142	10.1	17.6	11-32	21
CP2	13	214	29	185	13.6	16.5	5-32	27
CP3	6	149	29	120	19.5	24.8	10-34	24
CP4	1	13	0	13	0	13.0	13	NA
CP5	1	24	1	23	4.2	24.0	24	NA
TPA1	1	20	4	16	0.2	20.0	20	NA
TPA2	3	58	23	35	39.7	19.3	16-23	7
TPA3	1	33	1	32	3.0	33.0	33	NA
TPB1	3	57	11	46	19.3	19.0	7-27	20
TPB3	2	35	10	25	28.6	17.5	15-20	5
TPC1	6	72	48	24	66.7	12.0	3-34	31
TPC2	2	29	1	28	3.4	14.5	14-15	1
TPC3	7	157	0	157	0	22.4	11-35	24
TPC5	3	69	3	66	4.3	23.0	18-20	2
TPC6	6	74	12	62	16.2	12.3	1-23	22
Total	64							

lymph node yield and the amount of greater curve fat. More objective and consistent measurement of the amount of fat would be required before conclusions could be drawn from these data. There was no statistically significant difference between the operating surgeons, the responsible histopathologists or the prosectors of the specimens, in relation to lymph node yield.

Where extra blocks were taken to look for more lymph nodes, none of the additional lymph nodes found contained metastases. Similar findings have been reported in previous studies,<sup>4</sup> where a second look may yield more lymph nodes, but that these nodes do not alter patient management. More extensive surgical lymph node dissections increase the risk of post-operative lymph node leak. The practice of blocking random fat in search of more lymph nodes was expanded from June 2013, and it is proposed to repeat this audit for the June 2013 to May 2014 period, to examine the additional total lymph node yield and additional yield of positive lymph nodes.



**Dr Manisha Ram**  
 Consultant Histopathologist  
 Mid Essex Hospital Trust

**Dr Ula Mahadeva**  
 Consultant Histopathologist  
 Guy's & St Thomas' NHS Foundation Trust

**Reference**

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