

ORIGINAL ARTICLE

Lymph node retrieval in pancreaticoduodenectomy specimens: does educating the pathologist matter?

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Abstract

Background: Many previous studies have suggested that the number of lymph nodes retrieved should serve as a benchmark for assessing the adequacy of the resection. The aim was to retrospectively observe the impact of nodal retrieval after educating the pathologist.

Methods: Patients undergoing a pancreaticoduodenectomy (PD) between September 2005 and March 2009 were included in the study. The PDs performed between September 2005 and March 2008 were designated as Group A. The pathologists were educated regarding the importance of nodal counts in PD by the surgeon on the 1st April 2008. PDs performed between April 2008 and March 2009 were designated as Group B.

Results: Ninety-eight PDs performed by a single surgeon (D.R.J.) for peri-ampullary malignancy were evaluated. The median number of lymph nodes retrieved in Group A was 11(3–32) nodes. The median number of lymph nodes retrieved in Group B was 22 (10–29) nodes ($P < 0.001$). The lymph node ratio (positive/total nodes), median number of positive nodes retrieved, and the node positivity (node positive compared to node negative) rate did not change.

Discussion: A single intervention with the pathologists did impact the number of lymph nodes retrieved from PD specimens. However, the lymph node ratio and lymph node positivity rate remained unchanged. The pathologist is critical to nodal retrieval in PD, but the use of this lymph node number for benchmark of surgical adequacy may be simplistic.

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Introduction

Peri-ampullary malignancies include tumours of the distal bile duct, duodenum, pancreatic head and ampulla. Whenever possible, they are best treated by a pancreaticoduodenectomy (PD). Lymph node positivity (patients with any nodes positive) has an impact on the prognosis of peri-ampullary cancers, especially pancreatic cancer.^{1–4} The role of an extended lymphadenectomy on the long-term survival of patients with pancreatic cancer after a PD has been extensively debated.^{5–8} Most studies have shown no survival benefit with an extended lymphadenectomy and an increase in post-operative morbidity.⁶ The utility of a generous nodal retrieval in local control is an issue that has not been clearly documented. The lymph node ratio (LNR) is an important factor and is calculated by dividing the total number of positive nodes in node positive patients by the total number of nodes retrieved.

Recent data suggest that the ratio of positive lymph nodes to the total number of examined lymph nodes, i.e. LNR, in periampullary cancers is an independent prognostic factor.^{9–17} These data suggest that the nodal ratio, rather than the absolute number of involved nodes, may indeed be the most important prognostic factor for tumours in various sites.^{18–23} However, other studies have cited that the number of lymph nodes retrieved from a PD specimen should serve as a quality measure in the treatment of pancreatic adenocarcinoma.^{24,25} In fact, several experts in the field have suggested that there should be a minimum number of nodes to adequately stage pancreatic malignancies. Breast cancer treatment protocols use nodal retrieval as a benchmark for the adequacy of an axillary dissection.²⁶ Nevertheless, the lymph node yield (LNY) is a variable which can be impacted by several factors. These factors include anatomical factors (i.e. factors related to the individual patient), the technical aspects of the procedure (for

example, a pylorus-preserving PD compared with a standard PD), surgeon-related factors (for example, years of experience) and factors related to the pathologist (for example, how the specimen is handled).

A key objective of this study was to examine the pathologist as a factor in lymph node retrieval. The study was performed to assess the impact of the pathologist after a single intervention by the surgeon, namely verbal education on the median number of lymph nodes retrieved from PD specimens.

Methods

The records of patients who underwent PD for peri-ampullary neoplasms between September 2005 and March 2009 were reviewed. All the PDs were performed by a single surgeon at a non-university tertiary care centre (NUTCC). All patients underwent a modified extended lymphadenectomy, i.e. the vena cava was skeletonized from the gonadal vein to gonadal vein, without dissection of celiac or aortocaval lymph nodes. The records were reviewed under an institutional review board-approved protocol with respect to the number of lymph nodes retrieved, LNY, LNR and the node positivity rate. The ratio was calculated by dividing the positive node count by the total nodal count in those patients that were overall node positive. The nodal positivity rate was calculated by looking at all node positive patients compared with all patients, node positive or negative overall. The PDs performed between September 2005 and March 2008 were designated as Group A. The pathologists and pathology assistants (who gross the specimens at our institution) were educated verbally on 1 April 2008. PDs performed over the next year (April 2008 to March 2009) were designated as Group B. Briefly, the pathologists and the Physicians Assistants (PAs) – the latter gross the specimens – were gathered and briefly educated on the evolving need of nodal retrieval as a benchmark for adequate dissection in many tumour sites. The group already used the method of Verbeke with four colour inking of the specimen, as outlined below. The intervention was purely focused on nodal retrieval, and no alterations were made to handling the specimen with regards to margin assessment. The pathologists were unaware of the study until its end on 1 April 2009, allowing a comparison on lymph node yield while keeping the other factors constant. All PD specimens were inked using four colours and dissected by pathologists and pathology assistants with expertise in pancreato-biliary pathology. The peri-pancreatic and peri-gastric fat was dissected for lymph nodes. Small nodes (size ≤ 5 mm) were submitted intact, whereas larger nodes were sectioned and totally submitted. The results between Groups A and B were compared. Statistical analysis was performed using the paired *t*-test.

Results

A total of 144 PDs were performed, 98 for peri-ampullary malignancy. Sixty-three PDs were performed for peri-ampullary cancers between September 2005 and March 2008 by a single

Table 1 Distribution of the peri-ampullary cancers as per stage for Groups A (pre-education) and Group B (post-education)

Tumour stage	Number (%) of Group A	Number (%) of Group B
Tis	2 (3)	0 (0)
T1	2 (3)	1 (3)
T2	18 (29)	8 (23)
T3	29 (46)	23 (65)
T4	12 (19)	3 (9)

surgeon (Group A). Thirty-five PDs were performed for peri-ampullary cancers between April 2008 and March 2009 (Group B). The distribution of the peri-ampullary cancers by Tumor (T) stage is similar between the groups (see Table 1). T4 staged tumours consisted of duodenal and ampulla of Vater primaries. The median number of lymph nodes retrieved in Group A was 11 (range 3–32). The median number of lymph nodes retrieved in Group B was 22 (range 10–29) ($P = 0.001$). There were a higher number of nodes in retrieved node positive and node negative disease (Table 2). The distribution of pylorus preserving and a standard PD was not significant between the groups (Table 3).

There was an increase in LNY, post-intervention with pylorus preserving (PPPD) and standard PD (SPD). An increase was seen not only in the overall LNY but also in the LNY in lymph node negative (pN0) disease. Importantly, the LNR in node positive disease was not affected by the intervention. The percentage of patients with node positive disease (pN1) in the Group B was the same (66%) as those in Group A (65%) (Table 3).

Discussion

This study examines the importance of the pathologist as a factor in lymph node retrieval from PD specimens. This is the first study to show that a single intervention with the pathologist can result in an increase in nodal retrieval while keeping other factors constant. Importantly, the overall incidence of lymph node positivity and LNR in node positive patients did not change in the study period. This suggests that in spite of an increased nodal retrieval, the LNR was not affected by the number of nodes retrieved.

The behaviour of peri-ampullary cancers after a resection is influenced by many pathological factors which can include tumour size, tumour type, tumour grade, margin status, lymphovascular invasion, perineural invasion and lymph node status.^{1,2} The surgeon's aim is to minimize the risk of under-staging by performing an adequate lymph node clearance. An extended lymphadenectomy, which was postulated to avoid stage migration, has not been proven to improve long-term survival.⁷ More recently, there has been an effort to stratify lymph nodal positivity into a more discerning variable. LNR has been reported as a powerful predictor of survival in other gastrointestinal tumours, such as the colon and stomach.^{18,19,22,23} Le Voyer *et al.* reported that LNR was an important prognostic factor for colon cancer after a colec-

Table 2 Comparison of lymph node (LN) retrieval in both groups pre- and post-education

	Group A (n = 63)	Group B (n = 35)	P-value
Lymph node retrieval for malignant disease, n = 98, median (range)	11 (3–32)	22 (10–29)	<0.001
Pylorus-preserving PD	11 (4–32)	16 (12–21)	0.001
Standard PD	12 (3–23)	22 (10–38)	<0.001
LN retrieval for pN0, n = 34, median (range)	10 (3–21)	22 (10–29)	<0.001
LN retrieval for pN1, n = 64, median (range)	14 (7–32)	22 (15–27)	<0.001
LN ratio	0.19 (0.04–1)	0.17 (0.03–0.62)	0.990
Positive nodes, median (range)	3 (1–13)	4 (1–13)	0.310

PD, pancreaticoduodenectomy.

Table 3 Distribution of pathological diagnosis in both groups

	Group A	Group B
Patients with peri-ampullary cancers, n	63	35
Standard PD for peri-ampullary cancers, n (%)	44 (69%)	30 (85%)
Pylorus-preserving PD peri-ampullary cancers, n (%)	19 (31%)	5 (15%)
Patients with pN0 disease, n (%)	22 (35%)	12 (34%)
Patients with pN1 disease, n (%)	41 (65%)	23 (66%)

*Group A (pre); Group B (post).

PD, pancreaticoduodenectomy.

tomy even after adjusting for other factors as tumour stage, grade, histology and the number of positive lymph nodes.²² Similarly, LNY and LNR are increasingly being reported as prognostic factors for peri-ampullary cancers, especially pancreatic adenocarcinoma.^{18–23}

The question of whether a minimum number of nodes should be obtained to properly stage patients, has been assessed by several investigators.²⁷ Previous studies have also suggested that a 'cutoff LNY' should be established to adequately stage pancreatic cancer. This is similar to standards advocated for breast and colon cancer. The minimum number of nodes suggested vary from 10,¹¹ 12^{9,10} to 15.^{24,25} The investigators further suggest that these cutoff LNY may also serve as a tool to assess the adequacy of a surgical resection and suggest that it be regarded as a quality measure.

The LNY is dependent on many factors, as outlined above. These include the surgical procedure (PPPD versus SPD), surgeons, anatomical factors and pathologists. There is disparity in the number of nodes retrieved during a PD at different institutions. Pawlik *et al.* reported that the median number of lymph nodes evaluated at Johns Hopkins Hospital was 17,⁹ whereas in a large population-based study, Slidell *et al.* found the median LNY in the SEER dataset was 7.¹⁰ The extent of a lymph node dissection may vary from surgeon to surgeon as does the pathologists' technique in dissecting the specimen. The data presented here demonstrates that educating the pathologists resulted in an increase in LNY but without affecting the LNR. More nodes were dissected on standard PD specimens; however, an increase in LNY was seen with both SPD and PPPD post-education. The increase was seen

not only in the overall yield but also in the LNY for pN0 disease and pN1 disease, when analysed as separate groups. However, importantly, the percentage of pN1 patients in the post-education group (66%) remained the same as in the pre-education group (65%). This study clearly demonstrates that intervention resulted only in an increase in the LNY without an upstaging of the overall node status or change in the LNR.

This study demonstrates that continuous communication with the pathologists is important. The pathologists and physician assistants in this study were educated informally with these noted results. The HPB surgeon should continuously monitor their own nodal counts and communicate with the pathologists if they note variation in nodal numbers.

The patients with pN0 disease in the pre-education group would have been adequately staged if a LNY cutoff of 12, 15 or 16 nodes was assumed to be adequate. The patients in the post-education group would now be adequately staged owing to an 'adequate' LNY, however, the node positivity rate remained unchanged; in spite of the increased LNY. Moreover this did not impact the retrieval of positive nodes. The idea of 'look more to find more', which has been shown to work for margin positivity in pancreatic cancer, did not appear to affect nodal positivity in this study.

Lymph node retrieval after PD can increase significantly after a single intervention with the pathologist. However, staging, as measured by overall lymph node positivity LNR, and the number of positive nodes retrieved, were not affected by increased nodal retrieval. These data would suggest that adequate nodal staging was performed even when fewer lymph nodes were retrieved by the pathologist.

Conflicts of interest

None declared.

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