Original Article

An audit of lymph node retrieval and histopathology reporting of pancreaticoduodenctomy specimens undertaken at a tertiary care referral center

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Summary

Pancreaticoduodenectomy (PD) is currently the main surgical option for malignancies in the ampullary region, which includes ampulla of Vater tumours (AVT), distal bile duct tumours (DBDT), periampullary duodenal tumours (DT) and tumours of the head of the pancreas (PT). Nodal status and many other important pathological features have a significant impact on tumour prognosis and therapy. The aim of this study was to determine the total number of lymph nodes (LNs) retrieved from PD specimens, whether grouping of LNs improves the total yield and to assess the level completeness of histopathology reporting of PD specimens. Forty two PD requests and histopathology reports were assessed to determine the total number of LNs retrieved and whether the LN were grouped (G)or non-grouped (NG). The significance of difference in the number of LNs in the two groups were assessed using the Wilcoxon signed rank test. The tumours were subcategorized as AVT, DBDT, DT and PT and the reports were audited against the respective minimum data sets of the Royal College of Pathologists of United Kingdom to determine the overall completeness and the parameters poorly reported in the reports. The overall median LN yield was 14.5 and the median LN yield was 15 and 10 in G and NG respectively which was statistically significant. The completeness of the histopathology reporting was 63.6%- 77.3% in AVT (n-18), 73.9% - 95.6% in DBDT (n-5), 68.1% - 90.1% in DT (n-8), 70.8% - 83.3% in PT (n-11). The lengths of the bile duct, lesser and greater curvature of the stomach, tumour differentiation, involvement of resection margins and named blood vessels were poorly reported. In conclusion, the total LN retrieval improved by grouping according to the Union of International Cancer Control (UICC) protocol. Histopathology reporting of some of the data items requires improvement. Hence adoption of a pro forma for synoptic reporting and establishment of national guidelines on reporting and handling of specimens is recommended.

Key words: histopathology reporting, lymph nodes, ampullary tumours, pancreaticoduodenectomy

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Introduction

Pancreaticoduodenectomy (PD) is currently, the main surgical option for malignancies in the ampullary region, which includes ampulla of Vater tumours (AVT),

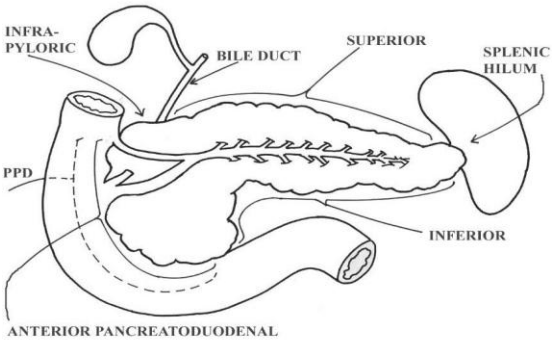

Figure 1 Regional lymph node stations in ampullary carcinoma according to UICC TNM (6). Inferior includes lymph nodes around superior mesenteric vessels; PPD = posterior pancreatoduodenal; coeliac lymph nodes and common hepatic artery nodes are not depicted in the figure; lymph nodes in the hilum of the spleen and tail of the pancreas are regional lymph nodes for tumours of the body and tail only

distal bile duct tumours (DBDT), duodenal tumours (DT) around the ampulla and tumours of the head of the pancreas (PT). The two stage PD procedure was used successfully by Kausch in 1912 and subsequently by Whipple in 1934 (1). Brunshweig then extended its use to the treatment of ductal adenocarcinoma of the head of the pancreas in 1937 (2). The one stage PD procedure in current use, involves partial gastrectomy, duodenectomy and cholecystectomy was then described as Kausch – Whipple pancreaticoduodenectomy by Allen Oldfather Whipple in 1946 (3).

PD is curative in 80% of patients with node-negative ampullary carcinomas. Once 3-year survival is reached, long-term survival can be expected(4). Nodal metastasis is considered a major prognostic factor in patients with ampulla of Vater carcinoma (5). Thus, if survival after surgery is to be improved, it would be necessary to know the extent and the pathway of spread of the cancer considering the further management of the patient.

Apart from nodal metastases, which is reflected in the staging of tumours, there are many other important pathological features which have a significant impact on tumour prognosis and therapy that need to be documented in the histopathology report. These are incorporated in the minimum data sets that have been formulated – one of which is that drawn up by the Royal College of Pathologists of United Kingdom (RCPUK) (6).

The College of Pathologists of Sri Lanka has formulated national guidelines on handling and reporting of cancers in regard to many common malignancies. However, at present, these do not include ampullary tumors or the handling of PD specimens. Hence, this audit was carried out firstly, to ascertain the adequacy of lymph nodes (LN) retrieval in PD specimens in a local setting and to determine whether the retrieval of LN according to anatomical sites, has a significant impact on the total number of LNs retrieved. Secondly, to determine the level of completeness of histopathology reporting when compared to minimum data sets laid down by the RCPUK and to identify the data items that were poorly reported.

Method

The study was conducted at the Department of Pathology, Faculty of Medicine, University of Kelaniya where PD specimens were received from Professorial unit of North Colombo Teaching Hospital which is one of the referral center for hepatobiliary and pancreatic surgeries in the country. The histopathology reports of 42 PDs performed for malignancies in the ampullary region during a five year period from 2011 – 2016 was retrieved from the files. Their corresponding request forms were also retrieved for cross reference.

The total number of LNs found in each specimen was determined and the method of identifying LNs established for each case i.e., grouped (G) when the LNs were retrieved from anatomical sites according to the Union of International Cancer Control (UICC) criteria and non- grouped(NG)when LNs were submitted without such grouping (Figure1) (6).

The handling of the specimens including LN retrieval had been carried out by a post graduate trainee under the supervision of a Consultant Pathologist. The Wilcoxon signed rank test was used to establish whether there was a statistically significant difference between these two categories ata p level of 0.1.

The histopathology reports were categorized into four subsets, AVT, DBDT, DT and PT. The data (both core data and non-core data) in the histopathology reports of each of these tumour subset was extracted by two non- pathologists (authors 1 and 2) on to the corresponding minimum data sheet that had been formulated by the RCPUK to ascertain the completeness of reporting of data items. Each of these subsets had differing number of data items (AVT 22,DBDT 23, DT22 and PT 24). The number of data items reported was divided by the total number of data items in the minimum data set to determine the completeness of reporting in each case. The frequency of a data item being reported was divided by the total number of reports and expressed as a percentage to assess the adequacy of reporting each of these data items.

Results

The overall median LN yield was 14.5 (range 1-48). In 30/42 of the specimens the LN retrieval was grouped according to UICC protocol and in 12/42 the LNs were not grouped (G- 30 and NG-12). In the G category the median number of LNs retrieved was 15 (range 5 – 48, mean 17 and standard deviation 8.34). In the NG category the median number of LNs was 10 (range 1 -31, mean 11.75 and standard deviation 12.45).Thus the difference in the total number of LNs retrieved between the two categories was of statistical significance at a p value of p=0.1 (p= 0.07). The difference between LN retrival in G and NG categories when specimens with sub-optimal harvests were excluded from both groups was not calculated as only 3/12 samples in the NG category had a LN yield of above 15 which is the minimum recommended number of LN (6).

The frequency of reporting each of data item, in each of the tumour subsets are given in Tables 1 -4. In AVTs, the reporting of the maximum tumour diameter, differentiation and resection margins were suboptimal. In DBDTs the length of the bile duct, type of tumour and involvement of a named vessel were reported less frequently. In the case of the DTs the lengths of the lesser curvature, and greater curvature of the stomach and differentiation of the tumour were poorly reported. Reporting of the length of the bile duct, differentiation of the tumour and involvement of the margins namely the anterior surface and involvement of named vessels in PTs were not satisfactory.

Table 1 Histopathology reporting in ampulla of Vater carcinoma (n=18)

Data Item	Number (%)
Specimen type	18 (100%)
Length of duodenum	16 (88.9%)
Length of lesser curve	14 (77.8%)
Length of greater curve	13 (72.2%)
Length of bile duct	15 (83.3%)
Maximum tumour diameter	3 (16.7%)
Length of gall bladder	15 (83.3%)
Size of pancreas	18 (100%)
Type of tumour	18 (100%)
Differentiation	9 (50%)
Maximum depth of tumour invasion (T)	17 (94.4%)
Tumour involvement of margins	
Transection margins	17 (94.4%)
Dissection margin	1(5.6%)
Anterior pancreatic surface	0 (0%)
Perineural invasion	18 (100%)
Total number of nodes	17 (94.4%)
Number of nodes involved	15 (83.3%)
Nx/N0/N1	15 (83.3%)
Distant metastases	17 (94.4%)
Background pathology	15 (83.3%)
Pathological staging	17 (94.4%)
Completely excised at all margins	0 (0%)

The completeness of reporting varied between 63.6% - 77.3% in AVT, 73.9% - 95.6%in DBDT 68.1% - 90.1% in DT and 70.8%- 83.3% in PT.

Discussion

The overall mean of LN yield was 14.4. However, there was a considerable increase in the identification of LNs when retrieved according to the anatomical groupings proposed by the UICC TNM classification (7). The LN yield increased from a mean of 11.8 to 17 in the NG versus the G category. The latter being more than the currently recommended minimum number which is 15(6).

In the past LNs were retrieved from PD specimens without specific knowledge of the lymphatic drainage of the pancreas and ampullary region. The system of grouping of LNs was introduced by the UICC TNM classification in 1998 (7). In 1999 the Japanese Pancreatic Society lymph node numbering system was introduced which identified 18 lymph node groups (8). The difference in the total LN yield between these two systems has however, not shown to be significant (9, 10).

The number of LNs detected in a resection specimen depends upon the anatomical differences between patients, the type of surgical excision, and the diligence of the pathologist in recovering LNs from the resection specimens. Different surgical procedures will produce specimens with different LN groups and subgroups and, therefore, different numbers of LNs (11). However, in the current study the surgical procedure was similar though the surgeons and pathologists varied which is a limitation in our study.

Based on several studies it is apparent that there is substantial variability between pathologists in the number of LNs harvested from surgical resection specimens for malignancies (12 – 16). It is also evident that the time invested in LN retrieval is the most crucial factor for the number of LNs being harvested (16).

The protocol used for handling of the PD specimens also varies from institution to institution. There are several accepted methods including sectioning along the plane of the pancreatic and common bile ducts, sectioning perpendicular to the main

Table 2 Histopathology reporting of distal bile duct carcinoma (n=5)

Data Item	Number (%)
Specimen type	5 (100%)
Length of duodenum	5 (100%)
Length of lesser curve	4 (80%)
Length of greater curve	4 (80%)
Length of bile duct	3 (60%)
Maximum tumour diameter	4 (80%)
Length of gall bladder	5 (100%)
Size of pancreas	5 (100%)
Type of tumour	3 (60%)
Differentiation	5 (100%)
Maximum depth of tumour invasion (T)	5 (100%)
Tumour involvement of margins	
Transection margins	5 (100%)
Dissection margin	4 (80%)
Anterior pancreatic surface	4 (80%)
Perineural invasion	5 (100%)
Named vessel involved	1 (20%)
Total number of nodes	5 (100%)
Number of nodes involved	5 (100%)
Nx/N0/N1	5 (100%)
Distant metastases	5 (100%)
Background pathology	5 (100%)
Pathological staging	5 (100%)
Completely excised at all margins	5 (100%)

pancreatic duct or 'breadloaf' slicing, sectioning the entire pancreatic head and duodenum perpendicular to the long axis of the duodenum ('axial sectioning') and sectioning perpendicular to the common bile duct up to the periampullary region, followed by sectioning along the plane of the ampullary duct in the immediate periampullary region (17). Currently in our institution the axial sectioning method recommended by the

RCPUK has been followed (6). This method has its advantage in that after orientation of the specimen, axial dissection serially slices the pancreatic head in an axial plane. It is easy to perform and does not include longitudinal opening of the common bile duct or pancreatic duct. It also allows key anatomical structures (e.g. ampulla, common bile duct, main pancreatic duct) to be seen in the same

slice and facilitates the identification of the tumour and its relationship to the key anatomical structures and margins.

Table 3 Histopathology reporting of duodenal carcinoma (n=8)

Data Item	Number and percentage reported
Specimen type	8 (100%)
Length of duodenum	8 (100%)
Length of lesser curve	4 (50%)
Length of greater curve	3(37.5%)
Length of bile duct	7(87.5%)
Maximum tumour diameter	8 (100%)
Length of gall bladder	8(100%)
Size of pancreas	8(100%)
Type of tumour	8 (100%)
Differentiation	4 (50%)
Maximum depth of tumour invasion (T)	8 (100%)
Tumour involvement of margins	
Transection margins	8 (100%)
Dissection margin	8 (100%)
Anterior pancreatic surface	6 (75%)
Perineural invasion	6 (75%)
Total number of nodes	7 (87.5%)
Number of nodes involved	7 (87.5%)
Nx/N0/N1	7 (87.5%)
Distant metastases (M)	6 (75%)
Background pathology	7 (87.5%)
Pathological staging	8 (100%)
Completely excised at all margins	7 (87.5%)

However, there have been several innovative methods of specimen dissection that have been devised such as the uncinate margin protocol from Toronto Canada. This protocol was initially formulated to assess the uncinate margin more adequately but also resulted in a significant increase in the LN yield. This protocol includes the amputation of the uncinate margin which is then serially sections from superior to inferior and placed in separate blocks (18).

Thus, we feel that pathologists and postgraduate trainees should gain an in depth knowledge of the anatomy and the lymphatic drainage of the ampullary region. The need for meticulous LN dissection and retrieval could be reiterated by providing illustrations of LNs sites in pro forma, guidelines and made easily available to pathologists and trainees in the grossing area.

Some of the parameter that were poorly reported in the histopathology reports of PD specimens includes the length of the bile duct, lengths of the greater and lesser curvature of the stomach,which are however deemed as non-core data items.

The differentiation or histological grading and tumour involvement of the resection margins and named vessels are however regarded as core data items and are important for the further management and prognosis of the patient. Reporting of these data items was not optimal. Involvement of a large named-vessel is a factor determining survival and prognosis appears to be related to the depth of invasion of the wall of the vein; invasion of the media or intima (but not just the adventitia) being associated with a poor prognosis. (25). The reporting of a named vessel requires the surgeons input in identifying and naming the vessels submitted. Reporting on the named vessel in DBDT and PT appears to be low mainly because the vessels were not named when the respective samples were received for grossing. Therefore, we need to update the surgeons on the value of naming the vessels that they submit.

The histological grading where present was based on the criteria of Kloppel, takes into account gland formation, nuclear changes, mitotic count and mucin production by the tumour (19). This has been found to be of prognostic significance, on univariate and/or multivariate analysis, in most studies (20, 21). Some countries recommend the use of grading the tumour according to the TNM/ AJCC system (Grade 1 – 4 depending on the percentage of gland formation)(22). The system proposed by Adsay et. al. based on the pattern of infiltration which is similar to Gleason scoring for the prostate has been

shown to have a prognostic value but is currently not widely adopted (23). No difference in the predictive value has been

Table 4 Histopathology reporting in pancreatic tumours (n=11)

Data Item	Number and percentage reported
Specimen type	11 (100%)
Length of duodenum	10 (90.9%)
Length of lesser curve	7 (63.6%)
Length of greater curve	7 (63.6%)
Length of bile duct	6 (54.5%)
Site of the tumour	11 (100%)
Maximum tumour diameter	11 (100%)
Length of gall bladder	11 (100%)
Size of pancreas	9 (81.8%)
Type of tumour	11 (100%)
Differentiation	6 (54.5%)
Maximum depth of tumour invasion (T)	10 (90.9%)
Tumour involvement of margins	
Transection margins	7(63.6%)
Dissection margin	6 (54.5%)
Anterior pancreatic surface	0 (0%)
Perineural invasion	8 (72.7%)
Named vessel involved	4 (36.4%)
Total number of nodes	11 (100%)
Number of nodes involved	11 (100%)
Nx/N0/N1	11 (100%)
Distant metastases (M)	11 (100%)
Background pathology	11 (100%)
Pathological staging	11 (100%)
Completely excised at all margins	10 (90.95)

shown between the TNM grading system and of Kloppel grading system (24). Currently in Sri Lanka we have no consensus regarding which grading system to use.

Reporting of the margins was unsatisfactory in most of the tumour subsets. Even though most reports carried a statement regarding the completeness of excision at the margins, these margins were not identified individually and the anterior surface of the pancreas was not mentioned specifically. This could partly be due to the fact that a PD specimen contains many margins which are referred to using various terms. For example the superior mesenteric artery margin has been variously referred to as the uncinate margin, medial margin, retroperitoneal inferior posterior margin, mesopancreatic margin and radial margin (26). Further confusion is caused by these margins being designated variously as transection margins, dissection margins and surfaces. Especially the anterior surface of the pancreas is not a surgical margin but invasion of this surface has been shown to be associated with local recurrence and decreased survival time (27).

There is an ongoing debate regarding adequate minimum clearance for pancreatic, common bile duct and ampullary carcinoma. While some define margin involvement when carcinoma is present at the margin (i.e. 0 mm clearance), others use the 1 mm rule adopted from margin assessment in rectal carcinoma. It has been shown in two recent studies that there is no significant difference in survival for those patients with carcinoma less than 1 mm from a margin compared to those with direct tumour involvement of a resection margin. (28). In the current context the 0 mm clearance rule was adopted.

Taking into consideration the above findings it is clear that PD specimens are possibly among some of the most difficult specimens to handle and report. Therefore it is imperative that a national policy should be adopted on handling and reporting these specimens. We recommend that such a document should contain very clear diagrams and photographs detailing the anatomy of this region, its lymphatic drainage and clear identifications and naming of the margins and surfaces that need evaluation.

With regard to reporting of these specimens introduction of minimum data set synoptic reports is a simple mechanism that is known to improve reporting of PD specimens (29). In the local setting this has proven to be very useful with regard to colorectal carcinoma reporting (30).

In conclusion we find that there are many aspects of histopathology reporting of PD specimens that need further improvement. To ensure consistency of reporting it is essential that guidelines are provided which includes detailed anatomical descriptions of the ampullary region, an accepted technique for specimen dissection and pro forma to enable synoptic reporting with diagrams, illustrations and photographs to facilitate proper understanding.

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