e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(6); 187-195

Original Research Article

Tumour Positivity Rate in Heidelberg Triangle Operation for Periampullary Carcinoma

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Received: 10-05-2026 / Revised: 23-05-2026 / Accepted: 22-06-2026

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Conflict of interest: Nil

Abstract:

Background: The Heidelberg triangle operation has emerged as an important surgical approach for achieving radical clearance of periarterial, neural, and lymphatic tissue in periampullary malignancies. However, data regarding the frequency and clinical significance of tumour positivity within the Heidelberg triangle specimen remain limited, particularly in patients with periampullary carcinoma.

Aim: To determine the tumour positivity rate in the Heidelberg triangle specimen and evaluate its association with preoperative, operative, histopathological, nodal, and postoperative variables in patients undergoing triangle operation for periampullary carcinoma.

Methodology: This prospective observational study was conducted in the Department of Surgical Gastroenterology, IGIMS, Patna, from February 2024 to April 2026. Fifty consecutive patients with periampullary carcinoma who underwent triangle operation were included. Demographic, clinical, operative, pathological, nodal, and postoperative data were analyzed. Comparisons between triangle tissue-positive and triangle tissue-negative groups were performed using the Mann–Whitney U test and Fisher's exact test, with $p<0.05$ considered statistically significant.

Results: The mean age of the patients was 54.0 ± 12.0 years, and 62.0% were male. Heidelberg triangle tissue positivity was identified in 4 of 50 patients, yielding a positivity rate of 8.0% (95% CI: 2.2%–19.2%). Triangle-positive patients had significantly higher CA 19-9 levels (950.0 ± 500.0 vs. 381.8 ± 520.7 U/mL; p=0.037), longer operative time (427.5 ± 15.0 vs. 379.6 ± 47.0 minutes; p=0.027), increased perineural invasion (75.0% vs. 8.7%; p=0.007), higher positive lymph node count (4.00 ± 2.94 vs. 0.41 ± 1.24; p=0.002), greater nodal positivity (75.0% vs. 17.4%; p=0.029), and universal triangle lymph node positivity (100.0% vs. 0.0%; p<0.001).

Conclusion: Tumour positivity within the Heidelberg triangle specimen was uncommon but strongly associated with aggressive locoregional disease characteristics, including elevated CA 19-9, perineural invasion, and increased nodal burden. Separate assessment of Heidelberg triangle tissue may provide valuable prognostic information and improve pathological staging in periampullary carcinoma.

Keywords: Periampullary carcinoma; Heidelberg triangle; Triangle operation; Tumour positivity; Perineural invasion; Lymph node metastasis; CA 19-9; Pancreaticoduodenectomy.

DOI: 10.25258/ijpqa.17.6.31

Introduction

Periampullary carcinoma are a varied group of malignant tumors located within 2cm of the major duodenal papilla, consisting of ampullary carcinoma, distal common bile duct carcinoma, periampullary duodenal carcinoma and selected tumours of the pancreatic head. While these tumours arise from

nearby structures, they have significant differences in their biological behavior, dissemination, histopathology, treatment and long-term prognosis. Periampullary malignancies represent an important fraction of hepato pancreatobiliary cancers and often manifest with symptoms of biliary obstruction which can include jaundice, pruritus, dark urine, pale stools and weight loss. The wide use of diagnostic imaging, endoscopic procedures, and pathological evaluation have allowed for earlier detection, but for most patients with localized disease surgical resection is the only potentially curative therapy [1].

Surgical resection of respectable periampullary carcinoma is best achieved by pancreatoduodenectomy (Whipple procedure). With the advances in anesthetic management, critical support, surgical skills and post-surgical care over the last few decades, the morbidity and mortality rates associated with surgery have significantly diminished. Even with these developments, recurrence still occurs in a high percentage of cases and a number of bad pathological features, such as lymph node metastasis, lymph vascular invasion, perineural invasion, positive resection margins and occult locoregional spread [2], remain associated with long-term survival. In recent years, modern pancreatic surgery has increasingly focused on the gross removal of the tumour, as well as careful and exact oncological clearance of all possible routes of tumour spread.

The most difficult part of pancreatoduodenectomy is the complete clearance of the posterior portion of the portal/superior mesenteric artery (SMA) space. It is a complex network of lymphatic channels, neural plexuses, small vascular structures and fibrofatty tissues which can contain microscopic tumour deposits [3]. Multiple pathological investigations have shown that there are often areas of residual disease within this region, which are responsible for positive margins and local or regional recurrence after surgery [4]. Consequently, there is greater interest in recognizing the anatomical and oncological importance of the area of the tissue plane from the posterior pancreatic head and uncinate process to the SMA and mesenteric root.

The term mesopancreas was coined to refer to this anatomically important tissue compartment. There is still some controversy over whether the mesopancreas is a true embryological mesentery, but its clinical significance is agreed. The mesopancreatic area is rich in lymphatic, neural and connective tissue pathways for the spread of tumour from the primary lesion. A number of studies have identified the uncinate process margin and SMA-side tissue as frequent spots for microscopic residual disease after the typical pancreatoduodenectomy procedure. Awareness of these findings has resulted in more radical and artery-oriented surgical procedures with the aim of better oncologic results. These have included superior mesenteric artery-first approaches, total mesopancreatic excision and more recently the Heidelberg TRIANGLE operation [5].

The Heidelberg TRIANGLE operation was invented at the Heidelberg University, Heidelberg, Germany, Pancreatic Center, as a standardized artery-sparing radicalization procedure designed to achieve optimal local tumour clearance whilst sparing important vascular structures. The anatomical compartment between the superior mesenteric artery, the axis of the celiac and common hepatic arteries, and the portal vein-superior mesenteric vein confluence is completely dissected to create a triangular operative field called the Heidelberg triangle. This area includes lymphatic channels, neural plexuses, fibrofatty connective tissues and possible areas of occult tumour spread that might not be completely removed during the traditional pancreatoduodenectomy. The pathological diagnosis can be properly done by systematically removing the triangle tissue and individually collecting it for examination and by detecting micro focally contaminated tumour that would not be detected otherwise [6].

Pathological assessment of the Heidelberg triangle specimen has been increasingly investigated as the presence of tumour within this compartment may be a reflection of aggressive biological behavior. Tumour positivity can be defined as: metastatic lymph nodes; direct infiltration of the fibrofatty tissue by tumour; perineural infiltration; lymph vascular invasion; isolated tumour deposits. The identification of this involvement is significant for staging, prognosis, planning of adjuvant treatment and evaluation of surgical radicality. In addition, a separate analysis of triangle tissue can offer valuable insights into the mechanisms of local tumour extension and pattern of recurrence in periampullary malignancies [7].

The literature available on the Heidelberg TRIANGLE operation has largely concentrated on the treatment of pancreatic ductal adenocarcinoma (PDAC) in patients with borderline respectable or inoperable (locally advanced) disease after neoadjuvant treatment [8]. However, there are limited data supporting its use in periampullary carcinoma. Periampullary tumours are far more likely to have good prognosis, but a subset has a high rate of posterior extension, neural invasion or regional nodal metastasis which occur in the same compartment as the triangle dissection. Thus, analysis of the positivity rate of the tumour within the Heidelberg triangle tissue in patients with periampullary carcinoma could improve the understanding of the spread of the disease and the oncological value of this surgery [9].

In this context the present study was conducted in the Department of Surgical Gastroenterology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna and aimed to evaluate the tumour positivity rate amongst the patients undergoing triangle operation for periampullary carcinoma of the pancreas

with the output specimens of the triangle being retrieved separately in the form of the Heidelberg triangle. The study also proposes to compare the parameters of positivity of the triangles with the clinicopathological parameters and postoperative results, which will add to the evidence on the importance of Heidelberg triangle dissection for oncological clearance and surgical management of periampullary malignancies.

Methodology

Study Design: This study was designed as a prospective observational study to evaluate the tumour positivity rate in the Heidelberg triangle specimen among patients undergoing triangle operation for periampullary carcinoma and to assess its association with clinicopathological characteristics and postoperative outcomes.

Study Area: The study was conducted in the Department of Surgical Gastroenterology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India.

Study Duration: The study was carried out over a period of 27 months from February 2024 to April 2026.

Sample Size: A total of 50 consecutive eligible patients were included in the study during the study period.

Study Population: The study population comprised all patients diagnosed with periampullary carcinoma who underwent Heidelberg triangle operation in the Department of Surgical Gastroenterology, IGIMS, Patna, during the study period and fulfilled the eligibility criteria.

Inclusion Criteria

- All patients with periampullary carcinoma undergo Heidelberg triangle operation.
- Patients are willing to participate in the study and provide written informed consent.

Exclusion Criteria

- Patients undergo triangle operation for duodenal masses other than periampullary carcinoma.
- Patients undergoing triangle operation for cystic lesions of the pancreas.
- Patients undergoing triangle operation for pancreatic head or pancreatic body carcinoma outside the intended periampullary carcinoma study group.
- Patients are unwilling to participate in the study or unable to provide informed consent.

Preoperative Evaluation: All enrolled patients underwent a comprehensive preoperative assessment. A detailed clinical history was obtained, including presenting symptoms, duration of illness, associated comorbidities, and previous medical or surgical interventions. Thorough physical examination was performed in all cases. Routine laboratory investigations included complete blood count, liver function tests, renal function tests, coagulation profile, serum electrolytes, and blood glucose levels.

Radiological assessment included contrast-enhanced computed tomography (CECT) of the abdomen and/or magnetic resonance imaging (MRI) whenever indicated for evaluation of tumour extent, vascular involvement, and respectability. Side-view endoscopy with biopsy was performed wherever feasible to obtain tissue diagnosis. Serum carbohydrate antigen 19-9 (CA 19-9) levels and other relevant investigations were obtained according to clinical requirements.

Operative Procedure: All eligible patients underwent Heidelberg triangle operation as per the standard institutional protocol. The procedure involved radical clearance of the soft tissue compartment bounded by the portal vein-superior mesenteric vein axis, the celiac axis-common hepatic artery, and the superior mesenteric artery, collectively forming the Heidelberg triangle. The dissection included removal of lymphatic tissue, neural plexuses, and fibrofatty tissue within this anatomical space while preserving the major arterial structures.

The triangle specimen was retrieved separately from the main surgical specimen and submitted independently for histopathological examination. Operative details including surgical approach, operative duration, estimated blood loss, and intraoperative events were recorded prospectively.

Data Collection: Data were collected using a structured proforma and included demographic, clinical, operative, histopathological, and postoperative variables.

Demographic Variables

- Age
- Sex
- Associated comorbidities

Preoperative Variables

- Imaging findings
- Tumour size
- Tumour location
- Serum CA 19-9 level

Intraoperative Variables

- Surgical approach
- Operative time
- Estimated blood loss
- Intraoperative complications or events

Histopathological Variables

- Histological tumour type
- Tumour grade

- Resection margin status
- Lymph vascular invasion
- Perineural invasion
- Total lymph node yield
- Number of positive lymph nodes
- Tumour positivity in the Heidelberg triangle specimen

Postoperative Variables

- Postoperative complications
- Length of hospital stay
- Postoperative morbidity

Histopathological Assessment: All resected specimens, including the separately retrieved Heidelberg triangle tissue, were examined by experienced gastrointestinal pathologists. Histopathological assessment included evaluation of tumour subtype, degree of differentiation, margin status, lymph vascular invasion, perineural invasion, and lymph node involvement.

Particular attention was given to the Heidelberg triangle specimen to determine the presence or absence of malignant cells. Tumour positivity was defined as identification of tumour deposits, metastatic lymph nodes, direct tumour infiltration, or malignant cells within the separately submitted triangle tissue. The tumour positivity rate was calculated as the proportion of patients demonstrating malignant involvement of the Heidelberg triangle specimen.

Outcome Measures

Primary Outcome

- Tumour positivity rate in the Heidelberg triangle specimen.

Secondary Outcomes

- Association of tumour positivity with clinicopathological characteristics.
- Correlation of triangle positivity with lymph node status, margin status, lymph vascular invasion, and perineural invasion.
- Association of triangle positivity with postoperative morbidity and short-term surgical outcomes.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution. Categorical variables were expressed as frequencies and percentages.

Comparisons between tumour-positive and tumour-negative groups were performed using the Chi-square test or Fisher's exact test for categorical variables. Continuous variables were compared using Student's t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed variables.

The tumour positivity rate was calculated as a proportion along with its 95% confidence interval (CI). Statistical significance was assessed using two-tailed tests, and a p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Prior approval for the study was obtained from the Institutional Ethics Committee of Indira Gandhi Institute of Medical Sciences (IGIMS), Patna. Written informed consent was obtained from all participants before enrolment. Participation was voluntary, and patients were free to withdraw from the study at any stage without affecting their treatment. Confidentiality of patient information was maintained throughout the study, and all data were used solely for academic and research purposes in accordance with ethical guidelines and the principles of the Declaration of Helsinki".

Result

Table 1 Overall Demographic Profile and Triangle Tissue Positivity Rate a total of 50 patients undergoing triangle operation for periampullary carcinoma were included in this prospective observational study. The average age was 54.0 ± 12.0 years, ranging between 26 and 74 years, with most of the cases being observed in the middle aged and elderly population. Male predominance was seen with males making up 62.0% of the study population. Overall, the tissue positivity rate was 8.0% (95% CI: 2.2%–19.2%) with Heidelberg triangle tissue positivity identified in 4 patients. This discovery indicates that the Heidelberg triangle was rarely involved in the current series and was the main result of the study.

Table 1: Overall Demographic Profile and Triangle Tissue Positivity Rate

Variable	Value
Study design	Prospective observational study
Sample size	50
Mean age (years)	54.0 ± 12.0
Age range (years)	26–74
Male sex	31 (62.0%)
Triangle tissue positivity	4 (8.0%)
95% confidence interval of positivity	2.2% to 19.2%
Statistical interpretation of positivity rate	Not applicable (single-cohort descriptive proportion)

Table 2 shows the differences between the two groups regarding demographic and preoperative variables, which were not significant (p>0.05). Serum CA 19-9 level, however, was significantly elevated in triangle-positive patients compared with triangle-negative patients (950.0 ± 500.0 U/mL vs 381.8 ± 520.7 U/mL; p=0.037). This discovery suggests that high levels of tumour markers could be linked to involvement of the Heidelberg triangle and a more aggressive or advanced disease. CA 19-9 was the only variable that was significantly associated with triangle tissue positivity among all the preoperative variables investigated.

Table 2 Comparison of Demographic and Preoperative Variables by Triangle Tissue Positivity				
Variable	**Triangle Negative (n=46)**	**Triangle Positive (n=4)**	**p value**	**Inference**
Age (years), mean ± SD	53.7 ± 12.1	57.5 ± 11.5	0.667	Not significant
Male sex	29/46 (63.0%)	2/4 (50.0%)	0.629	Not significant
Jaundice	39/46 (84.8%)	4/4 (100.0%)	1	Not significant
Pain abdomen	21/46 (45.7%)	1/4 (25.0%)	0.621	Not significant
Fever	18/46 (39.1%)	0/4 (0.0%)	0.283	Not significant
Preoperative biliary drainage	29/46 (63.0%)	2/4 (50.0%)	0.629	Not significant
CA 19-9 (U/mL), mean ± SD	381.8 ± 520.7	950.0 ± 500.0	0.037	**Not Significant**

Table 3 Comparison of Operative Variables by Triangle Tissue Positivity Among the operative variables assessed, operative duration was significantly longer in triangle-positive patients than in triangle-negative patients (427.5 ± 15.0 minutes vs. 379.6 ± 47.0 minutes; p=0.027). This implies that surgery of cases involving Heidelberg triangle involvement could be more complicated and extensive. Other factors, such as the location of the tumour, blood loss, postoperative hospital stay and requirement for vascular repair, did not differ significantly between the two groups. The difference in the blood loss and duration of hospitalization were not statistically significant, suggesting that operative time was the most significant operative variable associated with triangle positivity.

Table 3: Comparison of Operative Variables by Triangle Tissue Positivity				
Variable	**Triangle Negative (n=46)**	**Triangle Positive (n=4)**	**p value**	**Inference**
Ampullary intraoperative growth site	32/46 (69.6%)	4/4 (100.0%)	0.566	Not significant
Distal CBD intraoperative growth site	14/46 (30.4%)	0/4 (0.0%)	0.566	Not significant
Operative time (min), mean ± SD	379.6 ± 47.0	427.5 ± 15.0	0.027	Significant
Blood loss (mL), mean ± SD	615.2 ± 219.8	637.5 ± 275.0	1	Not significant
Postoperative stay (days), mean ± SD	10.3 ± 4.2	13.2 ± 4.6	0.194	Not significant
Vascular repair performed	1/46 (2.2%)	0/4 (0.0%)	1	Not significant

Table 4 shows the comparison of histopathological factors according to triangle tissue positivity, with significant association between triangle tissue positivity and periampullary tissue involvement of pancreatic head and perineural invasion. There was a significant difference in the occurrence of periampullary pancreatic head tissue in the tumour between half of the triangle-positive patients and none of the triangle-negative patients (p=0.007). Perineural invasion was also more frequently seen in triangle positive cases (75.0%) as compared to triangle negative cases (8.7%) (p=0.007). The larger tumour size, higher tumour grade, LVI and neuroendocrine histology were more common in triangle-positive patients, however these findings were not statistically significant. The current results indicate that Heidelberg triangle positivity is highly correlated with aggressive pathological features, especially neural invasion and pancreatic head tumour involvement.

Table 4: Comparison of Histopathological Factors by Triangle Tissue Positivity				
Variable	**Triangle Negative (n=46)**	**Triangle Positive (n=4)**	**p value**	**Inference**
Tumour site: Periampullary pancreatic head tissue	0/46 (0.0%)	2/4 (50.0%)	0.007	**Significant**
Tumour size >4 cm	2/46 (4.3%)	1/4 (25.0%)	0.326	Not significant
Grade 3 tumour	2/46 (4.3%)	1/4 (25.0%)	0.251	Not significant
Perineural invasion present	4/46 (8.7%)	3/4 (75.0%)	0.007	**Significant**

Lymph vascular invasion present	20/46 (43.5%)	3/4 (75.0%)	0.322	Not significant
Neuroendocrine tumour	0/46 (0.0%)	1/4 (25.0%)	0.08	Not significant

Table 5 Comparison of Nodal Variables by Triangle Tissue Positivity Nodal analysis revealed some of the strongest associations with Heidelberg triangle tissue positivity. The mean number of positive lymph nodes was significantly higher in triangle-positive patients compared to triangle-negative patients (4.00 ± 2.94 vs. 0.41 ± 1.24, p=0.002), suggesting a significantly more severe lymph node burden. Also, the triangle-positives had significantly more metastatic lymph nodes (75.0% vs. 17.4%, p=0.029). Most important, at least one positive triangle lymph node was found in all triangle-positive patients and in none of the triangle-negative patients (p<0.001). The results were very supportive of the correlation of Heidelberg triangle positivity with advanced local lymph node involvement.

Table 5 Comparison of Nodal Variables by Triangle Tissue Positivity

Variable	Triangle Negative (n=46)	Triangle Positive (n=4)	p value	Inference
Tumour size (cm), mean ± SD	2.57 ± 0.99	3.38 ± 1.70	0.208	Not significant
Total lymph node yield, mean ± SD	19.5 ± 8.5	16.0 ± 8.2	0.485	Not significant
Positive lymph node count, mean ± SD	0.41 ± 1.24	4.00 ± 2.94	0.002	**Significant**
Triangle lymph node yield, mean ± SD	3.3 ± 2.6	1.8 ± 1.0	0.254	Not significant
Any positive lymph node	8/46 (17.4%)	3/4 (75.0%)	0.029	**Significant**
Any positive triangle node	0/46 (0.0%)	4/4 (100.0%)	<0.001	**Significant**

Table 6 explores the predictive value of some clinicopathological variables for the diagnosis of Heidelberg triangle. With CA 19-9 ≥200 U/mL, sensitivity and negative predictive value were 100%, indicating that triangle positivity would be improbable at lower levels of the marker. The presence of periampullary pancreatic head tissue involvement had a perfect specificity and positive predictive value (100%), thus suggesting a very strong association with the presence of the tissue. The perineural invasion had a good predictive profile with high sensitivity (75.0%), specificity (91.3%) and negative predictive value (97.7%) and so did the positive lymph nodes status also. Overall, the predictive value of a negative test was very high for the majority of variables indicating the low prevalence of triangle positivity. Perineural invasion, nodal metastasis, and periampullary pancreatic head tissue positivity were the most useful of the evaluated factors regarding Heidelberg triangle tissue positivity.

Table 6: Exploratory Predictive Values for Triangle Tissue Positivity

Variable Used as Test	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV
CA 19-9 ≥200 U/mL	4	16	0	30	100.00%	65.20%	20.00%	100.00%
Periampullary pancreatic head tissue	2	0	2	46	50.00%	100.00%	100.00%	95.80%
Tumour size >4 cm	1	2	3	44	25.00%	95.70%	33.30%	93.60%
Grade 3 tumour	1	2	3	44	25.00%	95.70%	33.30%	93.60%
Perineural invasion present	3	4	1	42	75.00%	91.30%	42.90%	97.70%
Lymph vascular invasion present	3	20	1	26	75.00%	56.50%	13.00%	96.30%
Any positive lymph node	3	8	1	38	75.00%	82.60%	27.30%	97.40%
Any delayed gastric emptying	3	10	1	36	75.00%	78.30%	23.10%	97.30%

Discussion

This prospective observational study involved 50 patients who had a triangle operation of periampullary carcinoma, and the tumour positivity rate of the Heidelberg triangle specimen was analyzed. The positivity rate of the overall Heidelberg triangle was 8.0% while only 4 patients had tumour involvement in the separately retrieved tissue of the triangle. The positivity rate was relatively low, but patients with a positive Heidelberg triangle had significantly more CA 19-9, longer operations, higher perineural invasion and significantly higher nodal disease burden, reflecting that Heidelberg triangle positivity is a reflection of biologically more aggressive locoregional disease than a pathological finding. Similar findings have been noted in surgeries that assess the mesopancreatic and the Heidelberg triangle compartments in the case of pancreatic and periampullary malignancies" (Klotz et al., 2023; Maharjan et al., 2024) [10].

The demographic characteristics of the present study were similar to those previously reported. The mean age was 54.0 ± 12.0 years and 62.0% were males. A mean age of 56.38 ± 14.79 years and a male preva-

lence of around 55% was reported by Maharjan et al., which is very similar to that in our study [11]. In contrast, neither age nor sex was significantly associated with Heidelberg triangle positivity, as in our study. These observations indicate that the demographic parameters may play a role in the occurrence of the disease, but the risk of tumour dissemination into the periarterial triangle compartment cannot be determined by these parameters.

Preoperative factors that were significantly associated with triangle positivity were CA 125 and CA 19-9.Of the pre-operative factors, CA 19-9 was most important for triangle positivity. Patients with triangle positivity had a significantly higher mean CA 19-9 level compared with patients with triangle negativity (950.0 ± 500.0 U/mL, 381.8 ± 520.7 U/mL, respectively; p=0.037). Moreover, CA 19-9 ≥200 U/mL has 100% sensitivity and 100% negative predictive value in the diagnosis of triangle positivity. Ballehaninna and Chamberlain also noted that significantly higher CA 19-9 levels are associated with high tumour burden, nodal metastases and poor prognosis in pancreatic and periampullary cancers [12]. The present findings indicate that if CA 19-9 is significantly elevated, surgeons should be more suspicious of the possibility of occult locoregional extension, despite its potential to be affected by biliary obstruction.

Additionally, meaningful relationships were observed between the operatives and Heidelberg triangle positivity. Patients with triangle positivity had a significantly longer mean operative time (427.5 ± 15.0 minutes) compared to the patients with triangle negativity (379.6 ± 47.0 minutes; p=0.027). Hang et al. noted that the soft tissue clearance and periarterial dissection of TRIANGLE pancreaticoduodenectomy were significantly longer than for standard pancreaticoduodenectomy because of this [13]. Klotz et al. were also able to demonstrate that TRIANGLE resections were more likely to be associated with increased operability yet were also performed with superior oncological clearance. Blood loss and length of postoperative hospital stay, however, were not significantly different between the groups in this study, indicating that positivity of the pathological triangle is more likely to affect technical difficulty and not immediate postoperative outcomes of surgery.

Histopathological analysis showed there were strong correlations between Heidelberg triangle positivity and aggressive tumour biology. The incidence of PNI in triangle-positive patients (75.0%) was significantly higher than that of triangle-negative patients (8.7%) (p=0.007). Similarly, periampullary pancreatic head tissue involvement was seen in 50.0% of triangle-positive patients compared to 0.0% of patients who were triangle-negative (p=0.007). The same has been observed by Adham and Singhirunnusorn who noted that the mesopancreas and perineural tissue around the superior mesenteric artery were very important routes of tumour spread and local recurrence [14]. These findings suggest the Heidelberg triangle is a significant route in neural and lymphatic spread.

In the current study, the most significant correlations were found with the nodal. The triangle-positive group had a significantly higher mean number of positive lymph nodes (4.00 ± 2.94) as compared to the triangle-negative group (0.41 ± 1.24; p=0.002). Likewise, 75.0% of the triangle-positive patients had nodal positivity while 17.4% of the triangle-negative patients did (p=0.029). Most importantly, all triangle-positive had at least one triangle lymph node involved while none of the triangle-negative had positive triangle nodes (p<0.001). Maharjan et al. reported that 33.9% of patients with Heidelberg triangle dissection had positive triangle/apical lymph nodes, which is significantly higher than our 8.0% of patients [15]. The difference might arise from the differences in tumour spectrum, since our study was mainly based on periampullary carcinomas, while many of the published TRIANGLE studies were based on the more aggressive spread of perineural and nodal infiltration of pancreatic ductal adenocarcinoma.

The predictive value analysis additionally indicated the clinical importance of certain pathological factors. Perineural invasion had a sensitivity of 75.0%, specificity of 91.3% and a negative predictive value of 97.7% for triangle positivity, while positive lymph nodes had a sensitivity of 75.0% and specificity of 82.6% for triangle positivity. The findings confirm those from Klotz et al. who showed that the resection of TRIANGLE enables better evaluation of the periarterial lymphatic and neural tissue, and more precise detection of local-regional tumour spread. High negative predictive values in our study indicate that the absence of these pathological characteristics of involvement with Heidelberg triangle suggests less likelihood of involvement [16].

There was no significant difference among the postoperative outcomes based on triangle status. The association with delayed gastric emptying was only marginally significant (p=0.052); it was more prevalent in triangle-positive patients than in triangle-negative patients (75.0% vs. 21.7%). However, delayed gastric emptying rates of 10.8% were reported after TRIANGLE pancreaticoduodenectomy, suggesting that gastrointestinal dysfunction after a pancreaticoduodenectomy may be dependent on the extent of surgery and disease biology. Likewise, a higher risk for surgical site infection was observed but was not statistically significant in triangle-positive patients. These results suggest a higher oncological than postoperative prognostic value of Heidelberg triangle positivity [17].

The overall positivity rate of 8.0% in the present study is also lower as compared to 33.9% reported by Maharjan et al. and lower than reported in TRIANGLE series that focused on pancreatic ductal adenocarcinoma [18]. Despite that, the biological importance of positivity seems to be the same in various studies. Compared to our cohort, patients with triangles had significantly higher CA 19-9 levels, more perineural invasion, higher nodal burden, and 100% triangle nodal metastasis. Hence, Heidelberg triangle positivity defines a separate and distinct group with aggressive locoregional disease features, though rare.

To summarize, the findings of the present study clearly illustrate that positivity for tumour in the Heidelberg triangle specimen is rare but of clinical significance in periampullary carcinoma. The Heidelberg triangle involvement is associated with high CA 19-9, longer duration of surgery, perineural invasion and positive lymph nodes as well as a greater number of lymph nodes involved, supporting the concept that the triangle involvement is a marker of advanced locoregional tumour spread. These findings confirm the significance of retrieving and pathologically evaluating the Heidelberg triangle specimen separately during the periampullary cancer surgery and support further the importance of the Heidelberg triangle as an oncologically relevant anatomical compartment.

Conclusion

In the present prospective observational study, it was shown that the incidence of Heidelberg triangle tissue positivity in patients with periampullary carcinoma was relatively low with an incidence of 8.0% in patients who underwent the triangle operation. Even though triangle positivity occurred at a low rate, there were strong correlations with poor tumor prognosis such as significantly higher CA 19-9 levels before surgery, longer operation times, more perineural invasion, more positive lymph nodes, more total lymph nodes positivity, and total triangle node positivity. Demographic characteristics, presenting symptoms, tumour size, tumour grade, blood loss and most postoperative complications did not exhibit any significant association with triangle positivity. These results suggest that Heidelberg triangle involvement is more of an indicator of the aggressive locoregional tumour biology than of a demographic or perioperative effect. Pathological evaluation of the Heidelberg triangle specimen can offer important staging and prognostic data in that it allows for identification of a subset of patients with greater neural disease burden and/or nodal disease burden that may benefit from more intensive adjuvant therapy regimens and closer follow-up. The prognostic significance and therapeutic implications of Heidelberg triangle positivity in periampullary carcinoma needs further to be clarified with larger multicentric studies with long-term survival analysis.

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