

New Predictors for Periapillary Resectability

Siddig Abdelazeem Hassan Alam-Al Huda¹, Abdulmagid Mohammed Musaad^{2,3}, Nassir Alhaboob Arabi^{4,5}

¹Department of GI Surgery, Ibn Sina Specialized Hospital, Khartoum, Sudan, ²Department of GI Surgery, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan, ³Department of GI Surgery, Ibn Sina Specialized Hospital, Khartoum, Sudan, ⁴Department of Surgery, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan, ⁵Department of GI Surgery, Ibn Sina specialized Hospital, Khartoum, Sudan

ABSTRACT

Background: Periapillary tumor involves ampullary, pancreatic, biliary and duodenal mucosa, and pancreaticoduodenectomy considered the curative option. Hence, imaging evaluation to describe the lesion is important. Furthermore, certain specific features could help in pre-operative prediction of resectability for periampullary cancers. The aim of this study is to find out any specific perioperative predictor of resectability on periampullary cancers. **Patients and Methods:** This is an observational cross-sectional hospital-based study done in tertiary hospital, a total of 79 patients were included in the study. Variables such as age, gender, symptoms (back pain, jaundice, etc.), investigations (bilirubin, alkaline phosphatase, etc.), and imaging (Triphasic computed tomography [CT], magnetic resonance cholangiopancreatography, endoscopic ultrasonography, etc.) were studied and the data collected and analyzed using SPSS 20. **Results:** Male was slightly predominant and male to female ratio was 1:0.9. The mean age was 50 years (SD ±6.54). Triphasic CT abdomen pancreatic protocol was the most effective modality of investigation. High bilirubin (>10 mg/dl) and back pain were statistically significant among patients with unresectable tumor. **Conclusions:** Back pain and high bilirubin could be helpful in pre-operative prediction of operability of periampullary cancers.

Key words: Pancreaticoduodenectomy, Periapillary cancer, Resectability

INTRODUCTION

The periampullary tumors (usually carcinomas) can arise from ampulla, terminal common bile duct (CBD), pancreatic duct, and adjacent duodenal mucosa and by definition these include tumors that are located within 1.0 cm of the papilla.^[1,2] The presenting symptoms of periampullary cancers include jaundice, pruritus, anorexia, nausea, vomiting, weight loss, abdominal pain, and diarrhea.^[3] In the absence of specific clinical symptoms, early diagnosis is delayed, and vague symptoms back like pain often leads to misdiagnosis.^[4]

Hyperbilirubinemia (conjugated type) and elevated alkaline phosphatase (ALP) may be present due to biliary obstruction,

and tumor marker is neither sensitive nor specific enough to serve as reliable screening tool for this carcinoma. Abdominal ultrasound is the first-line radiological investigation in obstructive jaundice as it is accessible and cost effective, but its sensitivity is low both in the diagnosis and staging.^[5] Magnetic resonance imaging, magnetic resonance cholangiopancreatography (MRCP), positron emission tomography (PET), PET-computed tomography (CT) scan, multidetector, pancreatic protocol CT scan, and endoscopic ultrasonography (EUS) are used to evaluate the periampullary tumors and assess for their resectability. Treatment options depend on the stage of the disease.^[6] In operable fit patient, the treatment of choice is excision by pancreaticoduodenectomy.^[1,7-9]

Address for correspondence:

Nassir Alhaboob Arabi, Ibn Sina Hospital, P. O. Box 12217 Alamarat, Khartoum, Sudan.

© 2020 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

PATIENTS AND METHODS

This is an observational cross-sectional, hospital-based study, conducted in Ibn Sina hospital in the period from December 2017 to December 2019, it included 79 patients who were diagnosed with periampullary cancer, and planned for pancreaticoduodenectomy during the study period. It included clinical parameters such as jaundice, pale stool, weight loss, epigastric pain, back pain, palpable mass or gallbladder, serum levels of hemoglobin, bilirubin, tumor markers and albumin, and recent onset diabetes, in addition to radiological parameters such as abdominal ultrasonography esophagegastroduodenoscopy, MRCP, pancreatic protocol CT scan, and EUS.

Convenience non-randomized sampling technique was used; statistical analyses were performed using statistical software (SPSS version 20). Frequencies and proportions were used to describe patient demographics. Non normally distributed variables such as age were described with mean, and non-parametric tests for differences. Tests for differences in proportions were performed using Chi-square or Fisher exact tests, and risk presented as an odds ratio with 95% confidence intervals where appropriate. Correlation was done with the Spearman rho, assuming a nonparametric distribution. All tests were two-tailed and statistical significant was considered as $P < 0.05$.

RESULTS

There were 79 patients, 51.9% ($n = 41$) were males and 48.1% ($n = 38$) were females, male to female ratio was 1:0.92. The majority of patients were in the age group of 40–60 years with mean age of 50 years (SD ± 6.54). Nearly 94% of the patients presented with the ordinary symptoms of obstructive jaundice (Jaundice, pale stools, dark urine, and itching). The majority of the patients had loss of weight (75%) and appetite (68%). Epigastric pain was present in 19 patients (24.1%) while abdominal discomfort was the presenting complains in three patients (3.8%) and vomiting in one patient (1.2%).

All patients with back pain were inoperable and had palliative management and 25% of the patients with palpable epigastric mass underwent palliative management, in addition to high bilirubin (more than 10 mg/dl) was statistically correlated with palliative surgery [Table 1]. Those 19 patients with epigastric pain, six patients (31.57%) had palliative management.

Triphasic CT abdomen with pancreatic protocol was the most modality of investigation used for pre-operative prediction (74.7%). In 46 patients (78%), triphasic CT abdomen with pancreatic protocol was used alone and in 25 patients (42.3%) [Table 2]. The majority of cancers were located at the pancreatic head 59.5% ($n = 47$), followed by

Table 1: Demonstrates the correlation between high bilirubin and palliative surgery

Bypass/Bilirubin correlation	Bypass	Bilirubin more than 10 mg/dl
Bypass		
Pearson correlation	1	-0.249*
Sig. (two-tailed)		0.027
<i>n</i>	79	79
Bilirubin more than 10 mg/dl		
Pearson correlation	-0.249	1
Sig. (two-tailed)	0.027*	
<i>n</i>	79	79

*Correlation is significant at the 0.05 level (two-tailed)

ampulla 21.5% ($n = 17$), distal CBD 12.7% ($n = 10$), and the duodenum 6.3% ($n = 5$). There were 25 patients who had regional lymphadenopathy, 21.5% of patients ($n = 17$) had vascular involvement.

DISCUSSION

Periampullary cancers represent 0.2% of all gastrointestinal tumors.^[10] The majority of periampullary tumors present with biliary obstruction due to the tumor location, often this obstruction will lead to features such as abdominal discomfort, jaundice, nausea, and pruritus.^[11] Many patients may require either endoscopic measures to relieve the obstruction, either temporarily in resectable tumors or permanently those unresectable.^[12] Surgical resection (for operable tumors) gives the best chance for cure. Management depends on the pre-operative operability measures.

Periampullary cancer is rising in our local population. Its incidence increases with age and has a high mortality and morbidity rate. Nuzzo reported that the mean age was 67.4 years^[13] while Kim *et al.* found the average age to be 61.5 years.^[14] On the other hand, Mersin *et al.* reported the median age as 53 years^[15] and also Temel reported, the mean age was 63.7 years and all results are nearly equal to our study which was 50 years.^[16]

Periampullary cancer is considered more common in men, Kim *et al.* reported male/female ratio was 1.5 and Temel reported that male/female ratio was found to be 1.2, and in our study the male was little prominent.^[14,16]

All patients with back pain (100%) have had palliative surgery, this should raise attention for the importance of back pain as a predictive factor in operability. To the best of our knowledge, we did not find a study using back pain as single independent predictive factor in operability of periampullary cancer.

Table 2: Demonstrate the relationship between triphasic computed tomography abdomen with pancreatic protocol and definitive management

		Whipple	Triphasic computed tomography abdomen with pancreatic protocol
Whipple	Pearson correlation	1	0.237
	Sig. (two-tailed)		0.035
	<i>n</i>	79	79
Triphasic computed tomography abdomen with pancreatic protocol	Pearson correlation	0.237	1
	Sig. (two-tailed)	0.035*	
	<i>n</i>	79	79

*Correlation is significant at the 0.05 level (two-tailed)

Kau *et al.* stated that CA 19-9 was a significant prognostic factor in both resectable and unresectable periaampullary cancers, carcinoembryonic antigen (CEA) was significant only in the resectable group,^[17] but in our study, both Ca19-9 and CEA showed no predictive significance.

On the other hand, bilirubin level more than 10 mg/dl is associated with increased rate of palliative surgery. A study by Samaali *et al.* reported that serum level ALP was identified as an independent factor of unresectability in malignant obstructive jaundice.^[18] ALP is statistically not significant in predicting periaampullary cancer operability. CT scanning remains the initial investigation of choice in the diagnosis and staging of periaampullary tumors,^[5] but EUS might be superior for overall detection of lesions, especially those smaller than 2 cm.^[19] Although CT remains the investigation of choice, it is essential that EUS is performed by experienced operators and used when the clinical suspicion is high and CT fails to demonstrate a mass. Abdominal ultrasonography, MRCP, OGD, EUS, and CT scan when used in combined can give excellent pre-operative prediction results even in cases of anatomical variation.^[20] This could increase the number of early lesions detection and improve the overall prognosis which is similar to our study.

CONCLUSION

Back pain could help in prediction of unresectability of periaampullary cancers, and bilirubin level more than 10 mg/dl is significant for pre-operative unresectability of periaampullary cancers. Triphasic CT Abdomen, MRCP, EUS, ABD US, and OGD provide excellent preoperative prediction of operability of periaampullary cancer.

REFERENCES

- Cuschieri A, Hanna G. Essential Surgical Practice: Higher Surgical Training in General Surgery. Boca Raton: CRC Press; 2015.
- Chandrasegaram MD, Gill AJ, Samra J, Price T, Chen J, Fawcett J, *et al.* Ampullary cancer of intestinal origin and duodenal cancer-a logical clinical and therapeutic subgroup in periaampullary cancer. *World J Gastrointest Oncol* 2017;9:407-15.
- Martin J. Ampullary Carcinoma: Epidemiology, Clinical Manifestations, Diagnosis and Staging, UpToDate; 2019.
- Faisal M, Fathy H, Abu-Elela ST, Shams ME. Prediction of resectability and surgical outcome of periaampullary tumors. *Res Rev* 2018;7:14-21.
- Myatra S, Divatia J, Jibhkate B, Barreto G, Shrikhande S. Preoperative assessment and optimization in periaampullary and pancreatic cancer. *Indian J Cancer* 2011;48:86.
- Edge SB, Byrd DR, Carducci MA, Compton CC, Fritz A, Greene F. *AJCC Cancer Staging Manual*. New York: Springer; 2010.
- Kang SP, Saif MW. Ampullary and periaampullary tumors: Translational efforts to meet a challenge in diagnosis and treatment. Highlights from the "2011 ASCO gastrointestinal cancers symposium". San Francisco, CA, USA. January 20-22, 2011. *JOP* 2011;12:123-5.
- Hoskin P, Neal AJ, Hoskin PJ. *Clinical Oncology: Basic Principles and Practice*. Boca Raton: CRC Press; 2009.
- Poston GJ, Beauchamp D, Ruers T. *Textbook of Surgical Oncology*. Boca Raton: CRC Press; 2007.
- Al-Jumayli M, Batool A, Middiniti A, Saeed A, Sun W, Al-Rajabi R, *et al.* Clinical outcome of ampullary carcinoma: Single cancer center experience. *J Oncol* 2019;2019:3293509.
- Latenstein AE, Dijksterhuis WP, Mackay TM, Beijer S, van Eijck CH, de Hingh I, *et al.* Cachexia, dietetic consultation, and survival in patients with pancreatic and periaampullary cancer: A multicenter cohort study. *Cancer Med* 2020;1-11.
- Lee RC, Kanhere H, Trochsler M, Broadbridge V, Maddern G, Price TJ. Pancreatic, periaampullary and biliary cancer with liver metastases: Should we consider resection in selected cases? *World J Gastrointest Oncol* 2018;10:211-20.
- Nuzzo G, Clemente G, Cadeddu F, Giovannini I. Palliation of unresectable periaampullary neoplasms. surgical versus non-surgical approach. *Hepatogastroenterology* 2004; 51:1282-5.
- Kim CG, Jo S, Kim JS. Impact of surgical volume on nationwide hospital mortality after pancreaticoduodenectomy. *World J Gastroenterol* 2012;18:4175-81.
- Mersin HH, Yıldırım E, İrkin F, Berberoğlu U, Gülben K. Pancreaticoduodenectomy experience in a low density center. *Ulus Cerrahi Derg* 2010;20:18-23.
- Şeren TD, Topgül K, Koca B, Erzurumlu K. Factors affecting

- survival in patients who underwent pancreaticoduodenectomy for periampullary cancers. *Ulus Cerrahi Derg* 2015;31:72-7.
17. Kau SY, Shyr YM, Su CH, Wu CW, Lui WY. Diagnostic and prognostic values of CA 19-9 and CEA in periampullary cancers. *J Am Coll Surg* 1999;188:415-20.
 18. Samaali I, Bouasker I, Khézami H, Sbai A, Dougaz MW, Jarraya H, *et al.* Alkaline phosphatase is a predictive factor of unresectability in ampullary and periampullary tumors. *Tunis Med* 2017;95:297-303.
 19. Saad A-TO, Gianpiero G, Andrew SJ, Ong SL, Robert DA, Stephen MM. The difference between EUS and CT scan in diagnosing and staging peri ampullary tumours: An evidence-based approach. *J Gastroenterol Hepatol Res* 2015;4:1830-7.
 20. Arabi NA, Abdoun AA, Ali MO, Elhaj SK, Mohd SA. Pancreaticoduodenectomy in a patient with intestinal malrotation and distal cholangiocarcinoma: A case report and review of the literature. *J Med Case Rep* 2020;14:153.

How to cite this article: Alam-Al Huda SAH, Musaad AM, Arabi NA. New Predictors for Periampullary Resectability. *J Clin Res Oncol* 2020;3(2):1-4.