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Original Research Article

Postoperative morbidity following Whipple's procedure for periampullary carcinoma: a retrospective study spanning 5 years

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ABSTRACT

Background: The morbidity rates for Whipple's procedure has remained high even as mortality rates were coming down. This study was intended to assess postoperative morbidity rates in a tertiary care centre and to compare it with other centres.
Methods: Data was collected from various registers and medical records for this retrospective cohort study. All Whipple's procedures for 5 years were included in the study. Statistical analysis was done using R statistical software and the results were tabulated.
Results: There were 48 patients and half of them developed morbidity. Surgical site infection was the most common complication (18.8%) followed by pulmonary complications (12.5%) and bile leak (6.25%). Half of the patients having pulmonary complications died while nobody with surgical site infection or bile leak died.
Conclusions: In this study the morbidity rates were comparable to other centres. Hypoalbuminemia is a significant predictor of morbidity. Surgical site infection was the most common morbidity. Pulmonary complications were the most common cause for death. Morbidity rate is comparable to other centres and Whipple's procedure is a safe surgery in the tertiary centre where the study was conducted.

Keywords: Morbidity, Pancreatoduodenectomy, Periampullary carcinoma, Whipple's procedure

INTRODUCTION

Pancreatoduodenectomy, also called the Whipple's operation, is a common operation in major centres worldwide.[1] It is done mostly for periampullary cancers and very rarely for benign diseases. The first operation of pancreatoduodenectomy was done as an improvisation, in 1935, after finding that it was not stomach malignancy for which the abdomen was opened but was a pancreatic cancer. Dr Whipple who did the operation took out the head portion of the pancreas, the duodenum, the pylorus, a portion of the bile duct and a portion of the jejunum. Tumours occurring in the region around the ampulla of Vater are called periampullary carcinoma. Adenocarcinomas of the head of pancreas constitute a vast majority of them. Other tumours are carcinomas of distal bile duct, the ampulla of Vater and adjoining portion of duodenum. The way of presentation is similar in all periampullary carcinomas. Most of the cases present at old age. In many cases the prognosis is very poor. Whipple's procedure is considered to be the only potentially curative option for periampullary carcinoma.[2] Over the years the operation and its morbidity have been subject to much research. Starting from the initial days postoperative mortality rate has come down but morbidity rate still remains high.[3,4] Centres doing more than 10 cases of Whipple's procedure per year are classified as high volume centres.[5] These high volume centres have less morbidity compared to low volume ones.

The number of pancreatoduodenectomy has been increasing over the years in Government Medical College, Thrissur in comparison to other referral centres across the state of Kerala. This study was aimed at assessing the perioperative morbidity rates and pattern of morbidity. The study was also intended to compare the results with those of high volume centres. All these can ultimately benefit patients.

METHODS

This study was a retrospective one done in the department of General Surgery at the Government Medical College, Thrissur, Kerala, India. Approval was obtained from the Ethics committee of the institution. The Declaration of Helsinki was fully observed. The data collected was kept confidential throughout the study.

The purpose of the study was to ascertain the rate of morbidity and the different types of morbidity in patients undergoing pancreatoduodenectomies for periampullary carcinoma. It was also intended to assess whether the Whipple's procedure was a safe operation for patients depending upon the institution. Study period was Five years from January 2012 to December 2016.

Inclusion criteria

All patients who underwent Whipple's procedure for periampullary carcinoma from January 2012 to December 2016 at the Department of General Surgery, Government Medical College, Thrissur.

Exclusion criteria

Benign lesions as provided in the histopathology registers maintained at the department of Pathology, Government Medical College, Thrissur.

Study population

All patients who underwent Whipple's procedure for periampullary carcinoma from January 2012 to December 2016 at the Department of General Surgery, Government Medical College, Thrissur.

Methodology

Data pertaining to the operation was drawn out from the registers maintained at the department of General Surgery. Registers maintained at the department of Pathology was used to pick out data regarding histopathology of operated specimens. Any further information was collected from medical records stored in the Medical Records Library of the institution. Data so collected was entered into a pretested data collection chart specifically designed for the study. This data was later entered into excel. Data collection errors were carefully avoided. Patient details regarding any complications, readmissions and death were noted up to a period of 30 days following surgery and followed up with histopathological reports. Other variables studied with respect to morbidity were age of patients, sex of patients, tumour differentiation, tumour size and lymph node status.

Statistical analysis

Analysis was done in R statistical software. The quantitative data was summarized as mean and standard deviation or median and interquartile range. The qualitative data was analyzed using pie charts, bar diagrams and other appropriate methods. The results were tabulated and discussed in detail after compilation and analysis of the data.

RESULTS

Altogether 48 cases were included in the study. The age range was 33-75 years with a median of 61 years. There were 31(64.6%) males and 17(35.4) females. The predominant presenting symptom was jaundice in 25(52.1%) cases. The other presenting symptoms were abdominal pain in 18(37.5%), vomiting in 3(6.25%) and fever in 2(4.17%) cases (Figure 1).

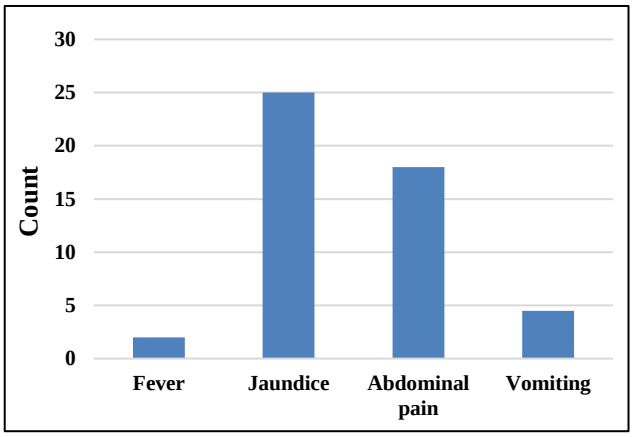

Figure 1: Presenting symptoms.

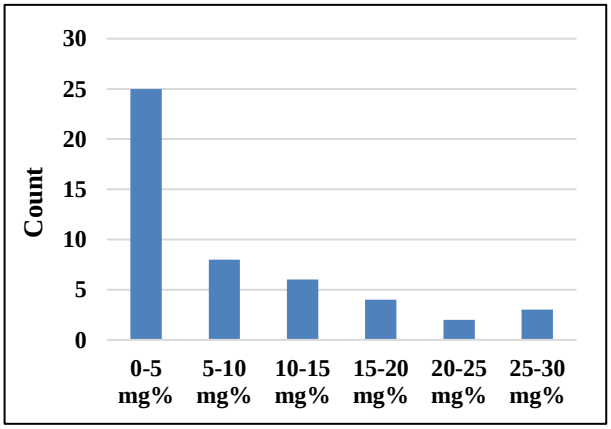

Figure 2: Serum Bilirubin Level.

Only 14 patients had pre-existing comorbidities. In 2(4.17%) patients the case records did not carry any information

regarding comorbidities. The mean serum bilirubin value was 4.8(IQR: 1.08-11.8) mg% (Figure 2). The median value of serum albumin was 3.37(±0.56) gm%. The tumour size at pathological examination was less than 3 cm in 43(89.6%) cases and more than 3 cm in the remaining. Lymph node positivity for malignancy at histopathological examination was present only in 6(12.5%) patients. Well differentiated tumours were seen in 29(60.4%) cases, moderately differentiated ones were seen in 9(18.75%) and poorly differentiated ones in 10(20.8%).

Half of the patients developed morbidity. The median age in which morbidity occurred was 62 years. There were 17 females in the study and 7(41.2%) of them developed some form of postoperative morbidity while out of the 31 males 17(54.8.2%) developed morbidity (Table 1). Surgical site infection accounted for morbidity in 9(37.5%) while pulmonary complications was the next frequent morbidity occurring in 6(25%). The frequency of other complications were bile leak 3(6.25%), myocardial infarction 2(4.17%), bile sepsis 1(2.08%), pancreatic leak 1(2.08%), liver failure 1(2.08%) and subarachnoid haemorrhage 1(2.08%). These results were statistically significant with p-value of <0.005. Mortality among those who developed morbidity stood at 8(33.3%). This was also statistically significant (p-value of 0.004) (Table 1). A mean serum bilirubin of 7.2(IQR: 2.25-14.5) mg% was noticed in those who became morbid, but this was not statistically significant. However, a median serum albumin of 3.09 gm% was associated significantly (p-value <0.001) with morbidity.

Table 1: Comparison of various factors affecting morbidity.

Variables		Total cases=48	Cases with no morbidity=24	Cases with morbidity=24	p overall
Sex	Female	17 (35.4%)	10 (41.7%)	7 (29.2%)	0.546
	Male	31 (64.6%)	14 (58.3%)	17 (70.8%)	
Mortality	Yes	40 (83.3%)	24 (100%)	16 (66.7%)	0.004
	No	8 (16.7%)	0 (0.00%)	8 (33.3%)	
Serum bilirubin		4.80 (1.08;11.8)	3.00 (0.90;9.55)	7.20 (2.25;14.5)	0.204
Serum albumin		3.37 (0.56)	3.65 (0.36)	3.09 (0.60)	<0.001
Symptom	Fever	2 (4.17%)	1 (4.17%)	1 (4.17%)	0.287
	Jaundice	25 (52.1%)	12 (50.0%)	13 (54.2%)	
	Pain	18 (37.5%)	11 (45.8%)	7 (29.2%)	
	Vomiting	3 (6.25%)	0 (0.00%)	3 (12.5%)	
Tumour size	<3 cm	43 (89.6%)	24 (100%)	19 (79.2%)	0.050
	>3 cm	5 (10.4%)	0 (0.00%)	5 (20.8%)	
Lymph node	Negative	42 (87.5%)	24 (100%)	18 (75.0%)	0.022
	Positive	6 (12.5%)	0 (0.00%)	6 (25.0%)	
Differentiation	Moderate	9 (18.8%)	2 (8.33%)	7 (29.2%)	0.037
	Poor	10 (20.8%)	3 (12.5%)	7 (29.2%)	
	Well	29 (60.4%)	19 (79.2%)	10 (41.7%)	

While 19(44%) patients with tumour size less than 3cm developed morbidity (p-value of 0.05), all 5(100%) patients with tumour size more than 3 cm developed one or other form of morbidity. This was statistically significant (p-value of 0.05). Similar results were obtained for patients with lymph node positivity compared with those without lymph node positivity. All patients with positive lymph nodes developed morbidity (p-value of 0.022). Among those who developed morbidity, 18(75%) were negative for lymph nodes (p-value of 0.022). Regarding tumour differentiation the proportion of those who turned morbid varied significantly (p-value of 0.037) according to whether it was poorly differentiated or moderately differentiated or well differentiated. Only 10(34%) patients with well differentiated tumours developed morbidity but 7(70%) of those with poorly differentiated ones became morbid. Only 8(33.3%) patients who developed morbidity died. Pulmonary complications was the leading cause of death after Whipple's procedure 3(12.5%) (Table 2). These results were statistically significant with p-value of 0.004.

DISCUSSION

This study was done to assess morbidity following Whipple's procedure in patients with periampullary carcinoma in a tertiary care centre which caters to a large segment of population in central Kerala. The operation, after being done for the first time in 1935, is the only curative option for periampullary cancers.[2,6] During the 1960s and 1970s the morbidity and mortality rates were so high that Whipple's procedure was nearly considered for abandonment.7 However it stood the test of time. Meanwhile, over the years Kerala has seen an increase in

number of patients of periampullary cancer treated by pancreatoduodenectomy. Added on to that is the fact that tropical pancreatitis is a disease which is highly prevalent in Kerala and is one which is evidently associated with pancreatic cancer.[8,9] During the study period all Whipple's procedure performed was for periampullary carcinoma, mainly carcinoma of head of pancreas. The age range of patients studied was 33-75 years with the mean age being 61. Across the globe, mortality rates following pancreatoduodenectomy are falling but morbidity rates have remained high. The overall morbidity rate in a study by Iacono et al, in 1997 was 45.8%.[10] But in the same year another study by Stephens et al, revealed a lower morbidity rate of 29%.[11] However, in 1999 Povoski et al, in their study found that 47% of patients who underwent pancreatoduodenectomy developed morbidity.[12] The year 1999 had yet another study by Bottger et al, in which it was revealed that surgical complications happened in 25% and general complications in 18.5%.[7] The rate of complications in the postoperative period was 41.5%.[13] The rate of serious complications was 27% in a study in 2011 by Greenblatt et al.[14] In our study the morbidity rate was 50% which is comparable to other centres.

Table 2: Causes of death in pancreatoduodenectomy.

Variables		Total cases=48	Cases with no morbidity=24	Cases with morbidity=24	p overall
Mortality	No	40 (83.3%)	24 (100%)	16 (66.7%)	0.004
	Yes	8 (16.7%)	0 (0.00%)	8 (33.3%)	
Cause of death	Pulmonary	3 (6.25%)	0 (0.00%)	3 (12.5%)	0.004
	Bile sepsis	1 (2.08%)	0 (0.00%)	1 (4.17%)	
	Liver failure	1 (2.08%)	0 (0.00%)	1 (4.17%)	
	MI	1 (2.08%)	0 (0.00%)	1 (4.17%)	
	No mortality	40 (83.3%)	24 (100%)	16 (66.7%)	
	Pancreatic leak	1 (2.08%)	0 (0.00%)	1 (4.17%)	
	SAH	1 (2.08%)	0 (0.00%)	1 (4.17%)	

Various types of morbidities occur to patients undergoing Whipple's procedure. In the study by Povoski et al, 14% of the complications turned out to be wound infection and 12% intraabdominal abscess.[12] Infection rates are similar in our study. Surgical site infection came as 18.8%. However biliary leak occurred only in 6.25% of cases. Grobmyer et al, in their study in 2007 obtained only 11% infection rate and a pancreatic anastomotic leak of 12%.[15] The rate of pancreatic leak was 10.6% in a study by Fathy et al.[6] Pancreatic leak is a severe complication and is associated with high morbidity and mortality rates.[16] In the study conducted by us pancreatic leak occurred only in 2.08% of cases. Sepsis and surgical site infection were the most common complications in the postoperative period in Whipple's procedure.[14] In the same study respiratory complications constituted 9.5%. The same in our study was 12.5%, which is comparable.

Hypoalbuminemia is a significant predictor of morbidity.[14] This is true in our study also as the median value of serum albumin was 3.09 gm% which is statistically significant in causing morbidity. All patients with tumour size more than 3 cm became morbid while only 44% of patients with tumour size less than 3 cm did so. However, there were only 5 patients with tumour size more than 3 cm compared to 43 patients with tumour size less than 3 cm. This reflects the care taken in sticking to clear indications for Whipple's procedure. Similar results were noticed in the case of lymph node positivity and tumour differentiation. While all 6 patients with lymph node positivity developed morbidity only 18(42.9%) out of 42 who had no pathologically involved nodes developed morbidity. The proportion of patients becoming morbid among those with well differentiated tumour was 34%. The same was 77% and 70% respectively for those with moderately differentiated and poorly differentiated tumours.

Among the various morbidities pulmonary complications contributed to majority of the deaths. Half of the patients who developed pulmonary complications died. However, the most common complication of surgical site infection and a frequent complication of bile leak did not lead to death. In a study conducted in 2017 Nagale et al, has reported a very high mortality owing to pneumonia.[17]

In the current study, details were extracted from patient records and histopathology records. Being a retrospective study there were no omission of cases. The limitation was that the number of pancreatoduodenectomies fell marginally short of being characterized as high-volume. In all, there were 48 patients in this study. Over the years the definition of high volume centre for pancreatoduodenectomies have changed. In 1999 Birkmeyer et al, had called a centre as a high volume centre if it had carried out 5 such operations in a year.[18] Ho et al, redefined it in 2003 as 10 or more cases per year.[5] At Government Medical College in Thrissur, where

the study was conducted the number of cases came upto 10 per year. In a 6 year study conducted by Rosemurgy et al, found that patients are better served by surgeons who perform pancreatoduodenectomy frequently.[19]

CONCLUSION

Pancreatoduodenectomy was studied with regards to morbidity in a hospital which is depended upon by a large population. The morbidity rate is comparable to that of other centres. Pulmonary complications are the most frequent morbidity leading to death. Hypoalbuminemia is a significant predictor of postoperative morbidity. Whipple's procedure is a safe operation in the tertiary care centre where the study was conducted. This would ultimately benefit people of central Kerala who depend on this institution for their health needs.

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