Pancreaticoduodenectomy: Impact of Volume on Outcomes at a Tertiary Care Center—Our Experience in Single Institute of Nepal

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Abstract

Background Pancreaticoduodenectomy is a complex high-risk surgical procedure usually done for malignant disease carrying significant postoperative morbidity and mortality. An audit and analysis of rate of postoperative morbidity and mortality and the impact of case volume can provide information about the lacunae in patient care and methods to improve it for safe and early discharge of patients. This study was conducted to find out demographic profile, the rate of perioperative morbidities, mortality, and impact of case volume on patients undergoing pancreaticoduodenectomy for malignant disease which may serve as a guide to uplift the patient care in our center.

Methods Retrospective analysis of prospectively collected data of patients undergoing pancreaticoduodenectomy from 2015 to 2019 was performed. A total of 62 patients were included in the study. Patient’s clinic-demographic details and intraoperative and postoperative events were recorded. The rate of various postoperative morbidities and mortality and year-wise trend of these factors were analyzed.

Results Most of the patients were in the sixth decade of life (38.7%) with male preponderance (61.3%). Pancreatic cancer was most commonly seen followed by cholangiocarcinoma (46.8%). SSI (32.3%), intraabdominal collection (25.8%), anastomotic leak (14.5%), pancreatic fistula (22.6%), and postpancreatectomy hemorrhage (8.1%) were the major postoperative events. Mortality was found in 12.9% patients.

Conclusion There has been a decrease in rate of all these postoperative adverse events and improvement in the intraoperative blood loss and surgical duration with advancing years and increasing number of cases.

Keywords Pancreaticoduodenectomy · Postoperative outcome · Whipples operation

Introduction

Pancreatic cancer remains one of the cancers with the poorest prognosis, with an overall 5-year survival rate of about 5%, without much difference between high-income and low-income and middle-income countries [1]. Pancreaticoduodenectomy (PD) is a complex, high-risk surgical procedure usually performed for malignancy of the pancreatic head or periampullary region [2].

For the first time, Allen O Whipple described pancreaticoduodenectomy in 1935 when he modified the procedure that was performed before by Alessandro Codivilla in Italy and Walter Keusch in Germany [3]. The prevalence of this disease increases with age in the population. Patients aged 20–29 years old have an annual incidence of 0.1 cases of pancreatic cancer per 100,000 population, while patients older than 80 have an annual incidence of 87.2 cases per 100,000 population. The causes of pancreatic cancer are unknown, but we consider risk factors like smoking and tobacco usage, alcohol and coffee consumption, history of diabetes, or chronic pancreatitis [4]. At the time of diagnosis, only 20% of patients are a candidate for pancreaticoduodenectomy. Even after a successful pancreatic resection, the...
prognosis is very poor with a 5-year survival of approximately 4–30% and a median survival of 18–29 months [5]. This procedure is associated with significant postoperative morbidity, rates of which range from 30 to 60%. Major postoperative complications include pancreatic leak or fistula, intra-abdominal abscess, bile leak, postoperative hemorrhage requiring blood transfusion or re-exploration, delayed gastric emptying, and complications related to the surgical site such as infection and wound dehiscence [6]. Various studies have demonstrated that high-volume tertiary centers have significantly lower (<5%) in-hospital mortality rates for pancreaticoduodenectomy than the low-volume centers (>10%) [2]. We set out to conduct this systematic research to link our evidence regarding the volume of cases and outcome at a tertiary care center in an underdeveloped country and to implement the data to improve our practice in managing such patients and analyze the impact of turning our department from a medium to a high-volume care provider of PD.

Material and Methods

Patients who underwent pancreaticoduodenectomy for malignancy in our institute in the past 5 years (2015–2019) were included in our study. Patients who underwent pancreaticoduodenectomy for benign and trauma cases were excluded. Sixty-two patients who fulfilled inclusion criteria were retrospectively analyzed in our study.

Study Procedure

Data were collected retrospectively from a prospectively maintained database in the medical record of our institute who underwent pancreaticoduodenectomy for periampullary carcinoma and pancreatic cancer. Patients’ demographic details, symptoms, baseline preoperative parameters, surgical parameters, and intraoperative and postoperative events were recorded and analyzed. All the surgical procedures were performed by the same senior surgeon with his team. The rate of complication was recorded, and year-wise trend of various intraoperative parameters as well as postoperative adverse events was recorded and analyzed.

Statistical Analysis

All statistical analysis was done using SPSS version 19. Continuous variables like age, blood investigation, blood loss, and duration of stay were presented as means and standard deviation or median and interquartile range according to distribution of variables assessed using the Shapiro–Wilk test. Descriptive variables were analyzed and recorded as frequency.
Results

This study includes a total of 62 patients who underwent pancreaticoduodenectomy for malignant disease from 2015 to 2019 in accordance with the inclusion and exclusion criteria.

Table 1 shows basic demographic details and symptoms of the patients at presentation. In this study, the age of the study population ranged from 33 to 89 years with mean age of $58.56 \pm 12.54$ years. Among a total of 62 patients, 61.3% were male and 38.7% were female. A total of 30.6% of the population was found to be smokers. Diabetes and hypertension were seen in 17.7% and 6.5% of patients respectively while comorbidity was absent in the remaining 75.8%. Of the total 62 patients, jaundice was the most common symptom (80.7%), pain abdomen was present in 38.7%, clay-colored stool in 41.9%, weight loss in 67.7%, and pruritus in 61.3%, and upper gastrointestinal bleed was observed in 6.5% of patients. The mean duration of hospital stay was $15.35 \pm 8.91$ days.

Figure 1 illustrates the age distribution, and Table 2 depicts the histopathological diagnosis of the study participants.

Table 3 demonstrates the baseline preoperative parameters of the study participants. The mean hemoglobin is $10.27 \pm 1.83$ g/dL, total count is $12,550 \pm 5616.94$ cells/mm$^3$, platelet count is $318,500 \pm 135,946.43$ cells/mm$^3$, PT is $18.42 \pm 3.19$ s and INR is $1.38 \pm 0.26$. Similarly, the mean total protein of the study participants is $5.36 \pm 1.35$ g/dL, serum albumin is $2.73 \pm 0.66$ g/dL, direct bilirubin is $4.86 \pm 3.53$ mg/dL, ALP is $461.45 \pm 291.61$ (IU/L), urea is $21.72 \pm 14.56$ mg/dL, creatinine is $0.597 \pm 0.32$ mg/dL, and CA 19–9 is $33.72 \pm 66.96$ U/mL. The mean intraoperative blood loss was $321.77 \pm 105.43$ mL, and the mean operative duration was $5.23 \pm 0.87$ h.

Table 4 Rate of postoperative adverse events in study participants

| Complications (n) | Frequency (%) |
|-------------------|--------------|
| No complications  | 29.03%       |
| POPF              | 22.6%        |
| SSI               | 32.3%        |
| Chest infection   | 38.7%        |
| PPH               | 8.1%         |
| Anastomotic leak  | 14.5%        |
| Intra-abdominal collection | 25.8% |
| AKI               | 12.9%        |
| Re-intubation     | 17.7%        |
| Mortality         | 12.9%        |
| Readmission       | 25.8%        |

Table 3 Baseline laboratory parameters of study participants

| Variables               | Mean ± SD | Median (IQR) |
|-------------------------|-----------|--------------|
| **Laboratory findings** |           |              |
| Hemoglobin (g/dL)       | 10.27 ± 1.83 | 10.750 (8.925–11.575) |
| Total leukocyte count (cells/mm$^3$) | 12,250.00 ± 5616.94 | 11,000 (7875–16,700) |
| Platelets (cells/mm$^3$) | 318,500.00 ± 135,946.43 | 280,500 (237,750–459,000) |
| PT (s)                  | 18.42 ± 3.19  | 18 (16–19)   |
| INR                     | 1.38 ± 0.26   | 1.360 (1.220–1.490) |
| Total protein (g/dL)    | 5.36 ± 1.35   | 5.2 (4.4–6.7) |
| Serum albumin (g/dL)    | 2.73 ± 0.66   | 2.7 (2.175–3.250) |
| Total serum bilirubin (mg/dL) | 6.979 ± 1.49 | 7.050 (3.225–10.375) |
| Direct serum bilirubin (mg/dL) | 4.86 ± 3.53 | 4.150 (1.800–7.825) |
| ALP (IU/L)              | 461.45 ± 291.61 | 327 (236.25–728) |
| RBS (mg/dL)             | 120.43 ± 52.32 | 106.50 (86.25–131.50) |
| Serum Creatinine (mg/dL) | 21.72 ± 14.56 | 13 (12–31) |
| CA 19–9 (U/ml)          | 33.72 ± 66.96 | 19 (18.50–24) |
| **Intraoperative**      |           |              |
| Blood loss (ml)         | 321.77 ± 105.435 | 300 (250–400) |
| Operative duration (hours) | 5.226 ± 0.867 | 5 (4.5–6) |
| **Preoperative ERCP (%)** | 6.5% |              |
Table 4 demonstrates the overall rate of all the postoperative morbidities with around one-third of the study population (29%) with no complications. Postoperative pancreatic fistula in 22.6% of the patients, surgical site infection in 32.3% of the patients, chest infection in 38.7% of the patients, post-pancreatectomy hemorrhage in 8.1% of the patients, anastomotic leak in 14.5% of the study participants, intra-abdominal collection in 25.8% of the participants, and acute kidney injury in 12.9% of the patients. Similarly, 17.7% of patients underwent re-intubation, and 25.8% of the patients underwent readmission. Total mortality observed was 12.9%.

Table 5 illustrates the year-wise trend of various postoperative adverse events of the study participants. A total of 9 patients underwent pancreaticoduodenectomy in the year 2015 of which every patient developed one or more of the complications like two patients developed an anastomotic leak, 4 patients suffered from surgical site infection, 4 patients suffered from a chest infection, one patient developed post-pancreatectomy hemorrhage, 5 patients developed postoperative pancreatic fistula, 5 patients developed intraabdominal collection, 2 patients developed acute kidney injury, 2 patients underwent re-intubation, and 5 patients underwent readmission. Two patients died in 2015.

Similarly, a total of 11 patients underwent pancreaticoduodenectomy in the year 2016 among which two patients developed an anastomotic leak, 7 patients suffered from surgical site infection, 7 patients developed chest infection, 2 patients had post-pancreatectomy hemorrhage, 3 patients developed postoperative pancreatic fistula, 4 patients developed intraabdominal collection, 2 patients developed acute kidney injury, 4 patients underwent re-intubation, and 4 patients underwent readmission. Three patients died in 2016.

Similarly, a total of 12 patients underwent pancreaticoduodenectomy in the year 2017 of which 3 patients did not develop any complications, 3 patients developed an anastomotic leak, 3 patients suffered from surgical site infection, 5 patients suffered from a chest infection, one patient

| Complications (n)                          | 2015 (n = 9) | 2016 (n = 11) | 2017 (n = 12) | 2018 (n = 15) | 2019 (n = 15) |
|-------------------------------------------|-------------|--------------|--------------|--------------|--------------|
| No complications (n = 18)                 | 0           | 0            | 3            | 8            | 7            |
| Anastomotic leak (n = 9)                  | 2           | 2            | 3            | 1            | 1            |
| SSI (n = 20)                              | 4           | 7            | 3            | 2            | 4            |
| Chest infection (n = 24)                  | 4           | 7            | 5            | 4            | 4            |
| PPH (n = 5)                               | 1           | 2            | 1            | 1            | 0            |
| POPF (n = 14)                             | 5           | 3            | 3            | 1            | 2            |
| Intra-abdominal collection (n = 16)       | 5           | 4            | 3            | 2            | 2            |
| AKI (n = 8)                               | 2           | 2            | 1            | 1            | 2            |
| Re-intubation (n = 11)                    | 2           | 4            | 2            | 2            | 1            |
| Mortality (n = 8)                         | 2           | 3            | 1            | 1            | 1            |
| Readmission (n = 16)                      | 5           | 4            | 3            | 2            | 2            |

Fig. 2 Year-wise trend of post-operative complication
developed post-pancreatectomy hemorrhage, 3 patients developed postoperative pancreatic fistula, 3 patients developed intraabdominal collection, 1 patient developed acute kidney injury, 2 patients underwent re-intubation, and 3 patients underwent readmission. One patient died in 2017.

A total of 15 patients underwent pancreaticoduodenectomy in the year 2018 of which 8 patients did not develop any complications, 1 patient developed an anastomotic leak, 2 patients suffered from surgical site infection, 4 patients suffered from a chest infection, one patient developed post-pancreatectomy hemorrhage, one patient developed postoperative pancreatic fistula, 2 patients developed intraabdominal collection, one patient developed acute kidney injury, 2 patients underwent re-intubation, and 2 patients underwent readmission. One patient died in 2018.

Likewise, a total of 15 patients underwent pancreaticoduodenectomy in the year 2019 of which 7 patients did not develop any complications, 1 patient developed an anastomotic leak, 4 patients suffered from surgical site infection, 4 patients suffered from a chest infection, no patient developed post-pancreatectomy hemorrhage, 2 patients developed postoperative pancreatic fistula, 2 patients developed intraabdominal collection, 2 patients developed acute kidney injury, 1 patient underwent re-intubation, and 2 patients underwent readmission. One patient died in 2019.

Figures 2, 3, and 4 give a pictorial demonstration of the decreasing trend of various postoperative adverse events as a line diagram.

Table 6 shows the association of three parameters: blood loss during the surgery, duration of surgery, and hospital
stay in terms of mean and standard deviation with the yearly trend from 2015 to 2019. Though the mean difference between considered parameters is not statistically significant in respect to consequent years from 2015 to 2019, data do suggest 2015 as the year with the least favorable outcome with highest blood loss, duration of surgery, and hospital stay.

### Discussion

Pancreatectoduodenectomy is a complex surgery that is done for various benign and malignant causes, and it is associated with numerous intraoperative as well as postoperative difficulties and adverse events [7]. In this study, we set out to conduct a retrospective analysis of baseline characteristics and various postoperative adverse events in patients who underwent surgery for malignant disease in our center. The incidence of periampullary carcinoma increases with age, and most of the patients in our study were in their sixth decade of life which is similar to other previous studies [8]. Male preponderance for the malignant disease has been observed.

The majority of the study participants presented features of obstructive jaundice which is classical and consistent with all previous studies. Many of the patients (38.6%) also presented with pain abdomen which may be attributable to cholangitis or associated pancreatitis (8). Pain abdomen may also arise because of the tumor itself or the infiltration of the tumor to the retroperitoneal nerves and nerves surrounding the pancreas [9]. Few patients (6.5%) also presented with features of upper gastrointestinal bleeding in the form of hematemesis or melena. This may be due to coagulopathy caused by obstructive jaundice leading to decreased absorption of fat-soluble vitamins especially vitamin K which is required for the formation of factors II, VII, IX, and X.

In our study, 17.7% patients presented with diabetes mellitus. This may be attributed to the presence of new-onset diabetes mellitus or chronic pancreatitis in patients with pancreatic cancer [9]. However, the majority of patients had no comorbidities at all. The majority of study participants were diagnosed to have pancreatic cancer (46.8%) followed by cholangiocarcinoma (30.6%) and ampullary cancer (16.1%). Only a few patients had duodenal cancer (6.5%).

Majority of the patients developed chest infection postoperatively (38.7% vs 28%) which is higher in comparison to other studies [10]. The observed higher pulmonary complication may be due to the old age and poor pulmonary reserve of majority of patients who underwent surgery. Poor pain control is due to lack of modern analgesic support such as patient-controlled analgesia in a resource-limited setup like ours, and also, epidural analgesia is given only for 2–3 days postoperatively which may have caused a lack of adequate participation of patients for chest physiotherapy and incentive spirometry leading to chest infections. In a similar study conducted in a resource-limited setup by Karim et al., high rates of pulmonary complications were observed due to inadequate pain control and chest physiotherapy [6]. With regard to these causes, various steps were taken which have led to a static rate of chest infection in our setup and makes us hopeful to reduce it further.

Surgical site infection is a common complication following pancreatectoduodenectomy causing increased hospital stay [11], re-admission, and increased cost of treatment [12]. In our study, a majority of patients developed postoperative surgical site infection. This may be attributed to the poor nutritional status of the patient due to underlying malignant disease, intraoperative blood transfusion, and preoperative biliary stenting which are known to cause an increased incidence of surgical site infection [13, 14]. Precautions against these factors have led to a decreasing trend of surgical site infection in our institute.

The overall rate of postoperative pancreatic fistula (22%) in our setup was found to be similar to other studies (10 to 29%) [15]. There is a decrease in the rates of pancreatic fistula following pancreatectoduodenectomy in our setup. This may be attributed to the improvement in surgical skill and technique of the operating surgeon with an increase in the volume of cases and experience.

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### Table 6  Association between different parameters and mean difference in the years from 2015 to 2019

| Parameters                  | 2015         | 2016         | 2017         | 2018         | 2019         | p-value   |
|-----------------------------|--------------|--------------|--------------|--------------|--------------|-----------|
| Blood loss (ml)             | Mean ± SD    | 344.4 ± 186.2| 354.5 ± 133.1| 295.8 ± 72.2 | 313.3 ± 61.4 | 313.3 ± 78.9| 0.846     |
|                            | Median (IQR) | 300 (225–400)| 350 (250–400)| 300 (250–375)| 300 (250–350)| 300 (250–400)|           |
| Duration of surgery (h)    | Mean ± SD    | 5.8 ± 1.2    | 5.5 ± 0.9    | 4.8 ± 0.7    | 5.0 ± 0.6    | 5.2 ± 0.7  | 0.099     |
|                            | Median (IQR) | 5.5 (5–6.75) | 5 (5–6.5)    | 4.5 (4.5–5.375)| 5 (4.5–5)   | 5 (4.5–6)   |           |
| Duration of hospital stay (day) | Mean ± SD | 17.0 ± 10.5  | 15.3 ± 9.2   | 13.5 ± 8.8   | 14.8 ± 7.9   | 16.4 ± 9.6  | 0.895     |
|                            | Median (IQR) | 20 (6–26.50) | 13 (10–25)   | 14 (5.5–20.75)| 15 (10–19)  | 19 (7–25)   |           |

Bold signifies statistical significance at p < 0.05
*Kruskal–Wallis test*
Postpancreatectomy hemorrhage is one of the most dreaded complications following pancreaticoduodenectomy. It is associated with mortality as high as 30% with a decreasing trend after the introduction of minimally invasive procedures such as endoscopy and angiographic embolization. The rate of post-pancreatic hemorrhage is similar to other studies [16], and there has been a further decrease in the incidence of post-pancreatectomy hemorrhage.

Anastomotic leak following pancreaticoduodenectomy is another dreaded complication. The patient may develop a biliary leak and pancreatic leak leading to biliary peritonitis or pancreatic fistula. The rate of anastomotic leakage in our setup is similar to other studies [17]. There has been a decrease in the trend of anastomotic leakage with advancing years and number of cases; this may be attributed to the improved surgical technique and use of prophylactic octreotide postoperatively in our patients.

Almost all the cases have been admitted in ICU following pancreaticoduodenectomy in our setup. This is due to the unavailability of monitoring facilities and a trend of ICU admission following major surgeries for monitoring in our setup.

The rate of mortality following pancreaticoduodenectomy is similar to other studies in our setup in the past 5 years [18]. There has been a decrease in mortality in recent years with only single mortality in 2019. The various causes for mortality include post-pancreatectomy hemorrhage, intra-abdominal collection, sepsis, anastomotic leak, myocardial infarction, etc. The reduction in mortality is due to early recognition and prompt intervention with intensive care done in our setup following high-risk complications.

There has been a significant reduction in hospital stay with advancing years in our hospital. The duration of hospital stay in our setup is similar to other studies [19]. The observed reduction in length of stay is due to increased operative skills, decreased rate of complication, early detection, and treatment of various complications, and decreased readmission rates as well.

The study highlights the improvement in perioperative outcome following pancreaticoduodenectomy with respect to various intraoperative factors such as duration of surgery, decreased blood loss, decreased incidence of various postoperative adverse events, and reduced length of hospital stay. This sheds light on the fact that with an increase in number of cases, there is an improvement in the perioperative outcome of patients following pancreaticoduodenectomy in our hospital. This study may serve as a source of various changes that can be made to improve the outcomes in a limited setup like ours. All the cases in this study that underwent pancreaticoduodenectomy were resectable. The effect of stage on post-operative outcome was not assessed which can be considered as a limitation of this study.

Pancreaticoduodenectomy is a complex surgery demanding meticulous surgical skills and good postoperative care for early detection and management of postoperative adverse events. There is an improvement of surgical skills which is evident by the decreased intraoperative blood loss and decreased duration of surgery in our setup. Also, the decreased rate of various postoperative adverse events in our study points to the fact that with an increase in volume and experience of pancreaticoduodenectomy, a picture of a better outcome with reduced morbidity and mortality can be expected in a resource-limited setup, and we are not far behind the developed countries in this regard.

Author Contribution Sunit Agrawal—data collection, analysis, result and discussion. Bhawani Khanal—data collection and framing manuscript. Ujjwal Das—data analysis, result and discussion. Suresh Prasad Sah—data analysis and discussion. Rakesh Kumar Gupta—discussion and proof reading.

Data Availability Hospital record section.

Code Availability Not applicable

Declarations

Ethics Approval The ethical approval was obtained from the institutional review committee (IRC) of our institute. The reference number is IRC/1991/020.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Competing Interests The authors declare no competing interests.

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