

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 lacunas 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. Patients clinic-demographic details, intraoperative and postoperative events were recorded. Rate of various postoperative morbidities and mortality and year wise trend of these factors were analyzed.

Results

Most of the patients were in 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%), 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.

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 countries 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 tertiary care center in underdeveloped country and to implement the data to improvise 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.

Materials 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. 62 patients who fulfilled inclusion criteria were retrospectively analysed in our study.

Study procedure:

Data were collected retrospectively from a prospectively maintained database in the medical record of our institue who underwent pancreaticoduodenectomy for perampullary carcinoma and pancreatic cancer. Patients' demographic details, symptoms, baseline preoperative parameters, surgical parameters, intraoperative and postoperative events were recorded and analyzed. All the surgical procedures were performed by a 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 for all normally distributed variables. 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, age of the study population ranged from 33 years to 89 years with mean age of 58.56 ± 12.54 years. Amongst a total of 62 patients, 61.3% were male and 38.7% were female. 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%, pruritus in 61.3% and upper gastrointestinal bleed was observed in 6.5% of patients. The mean duration of hospital stay was 15.35 ± 8.91 days.

Table 3 demonstrates the baseline preoperative parameters of study participants. The mean hemoglobin is 10.27 ± 1.83 g/dL, total count is 12550 ± 5616.94 cells/mm³, platelet count is 318500 ± 135946.43 cells/mm³, PT is 18.41 ± 3.19 sec and INR is 1.38 ± 0.26 . Similarly, the mean total protein of the study participants is 5.36 ± 1.35 g/dL, serum albumin is 2.73 ± 0.66 g/dL, total serum bilirubin is 6.979 ± 4.19 mg/dL, direct bilirubin is 4.86 ± 3.53 mg/dL, ALP is 461.45 ± 291.61 (IU/L), urea is 21.72 ± 14.56 mg/dL, creatinine is 0.597 ± 0.32 mg/dL and CA 19-9 is 33.72 ± 66.96 U/mL. The mean intraoperative blood loss was 321.77 ± 105.43 mL and the mean operative duration was 5.23 ± 0.87 hours.

Table 4 demonstrates the overall rate of all the postoperative morbidities with around one-third of the study population (29%) with no any complications. Postoperative pancreatic fistula in 22.6% of patients, surgical site infection in 32.3% of patients, chest infection in 38.7% of patients, post-pancreatectomy hemorrhage in 8.1 % of patients, anastomotic leak in 14.5% study participants, intra-abdominal collection in 25.8% participants, and acute kidney injury in 12.9% patients. Similarly, 17.7% of patients underwent re-intubation, and 25.8% 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 amongst 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 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, 1 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.

Table 1: Demographic profile and symptoms.

Variables	Frequency (%)
Age (mean ± SD)	58.56 ± 12.54 years
Sex	
Male	61.3%
Female	38.7%
Smoker	30.6%
Co-morbidities	
Diabetes	17.7%
Hypertension	6.5%
COPD	0%
None	75.8%
Symptoms	
Pain abdomen	38.7%
Jaundice	80.6%
Clay coloured stool	41.9%
Weight loss	67.7%
Pruritus	61.3%
UGI bleed	6.5%
Duration of hospital stay (mean ± SD)	15.35 ± 8.91 days

Table 2: Histopathological diagnosis of study participants.

Diagnosis	Frequency (%)
Cholangiocarcinoma	30.6%
Pancreatic head cancer	46.8%
Ampullary	16.1%
Duodenal cancer	6.5 %

Table 3: Baseline laboratory parameters of study participants.

Variables	Mean ± SD
Laboratory findings:	
Hemoglobin (g/dl)	10.27 ± 1.83
Total count (cells/mm3)	12250.00 ± 5616.94
Platelets (cells/mm3)	318500.00 ± 135946.43
PT (seconds)	18.41± 3.19
INR	1.38 ± 0.26
Total protein (g/dl)	5.36±1.35
Serum Albumin (g/dl)	2.73±0.66
Serum bilirubin (mg/dl)	
Total	6.979 ± 4.19
Direct	4.86±3.53
ALP (IU/L)	461.45± 291.61
RBS (mg/dl)	120.43 ± 52.32
Serum Urea (mg/dl)	21.72± 14.56
Serum Creatinine (mg/dl)	0.597 ± 0.32
CA 19-9 (U/ml)	33.72± 66.96
Preoperative ERCP (%)	6.5%
Intraoperative	
Blood loss: (Mean ± SD)	321.774 ± 105.43 ml
Operative duration: (Mean ± SD)	5.23 ± 0.87 hours

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 5: Trend of postoperative outcomes from 2015-2019

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

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

Parameters	2015 (Mean±SD)	2016 (Mean±SD)	2017 (Mean±SD)	2018 (Mean±SD)	2019 (Mean±SD)	p-value
Blood loss (ml)	344.4±186.2	354.5±133.1	295.8±72.2	313.3±61.4	313.3±78.9	0.679
Duration of surgery (Hours)	5.8±1.2	5.5±0.9	4.8±0.7	5.0±0.6	5.2±0.7	0.067
Duration of Hospital Stay (Day)	17.0±10.5	15.3±9.2	13.5±8.8	14.8±7.9	16.4±9.6	0.909

Discussion

Pancreaticoduodenectomy 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 malena. 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 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 regards to these causes, various steps were taken which has 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 pancreaticoduodenectomy 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, 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 pancreaticoduodenectomy 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.

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 five 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 strength of our study is that we have an adequate sample size with respect to our scenario with adequate power of the study. This 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 and cost of treatment. This sheds light on the fact that with an increase in experience and number of cases in our hospital 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.

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.

Declarations

Funding : Not applicable

Conflicts of interest/Competing interests : None declared.

Availability of data and material : Hospital record section.

Code availability:Not applicable

Authors' contributions

Sunit Agrawal- Data collection, analysis, result and discussion.

Bhawani Khanal- Data collection and framing manuscript

Ujjwal Das- Data analysis, result asnd discussion

Suresh Prasad Sah- Data analysis and discussion

Rakesh Kumar Gupta- Discussion and proof reading

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

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Figures

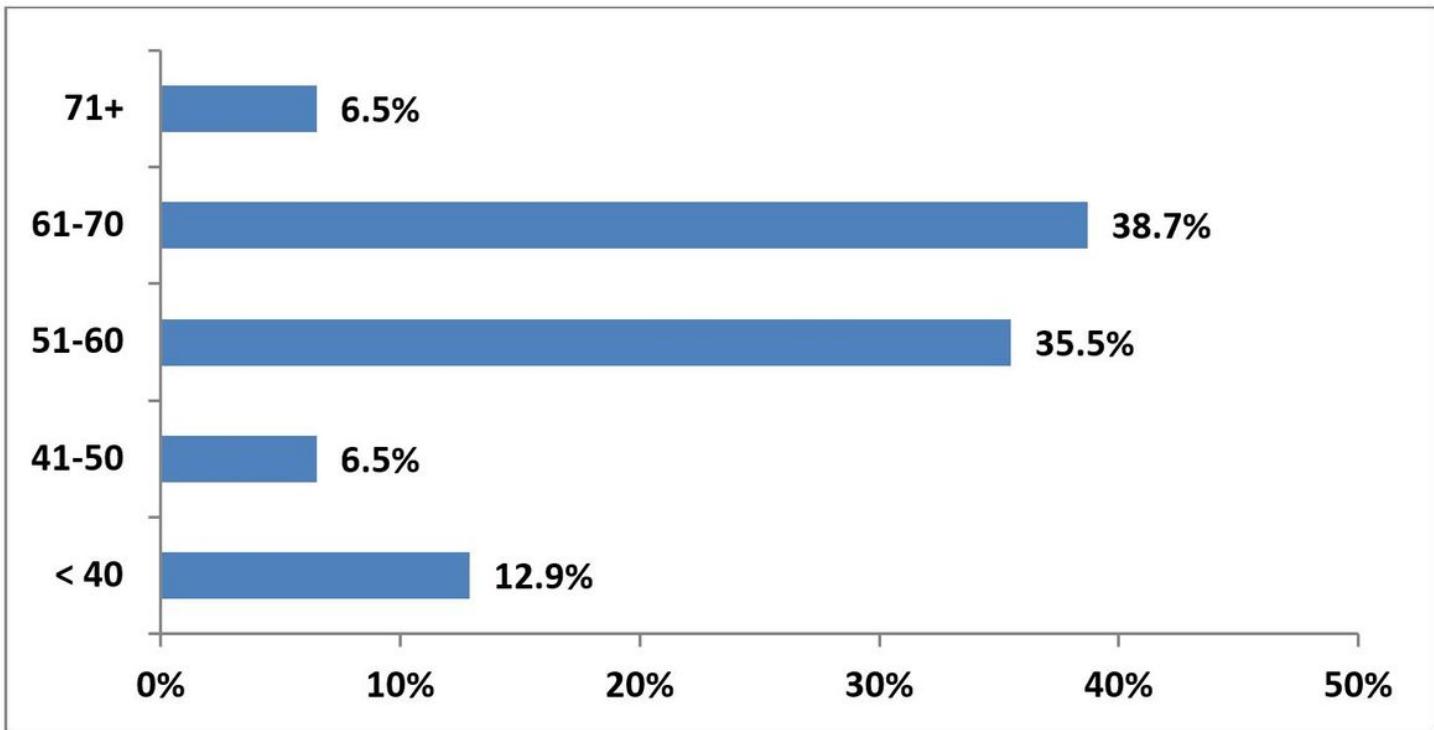


Figure 1

Distribution of patient's age group

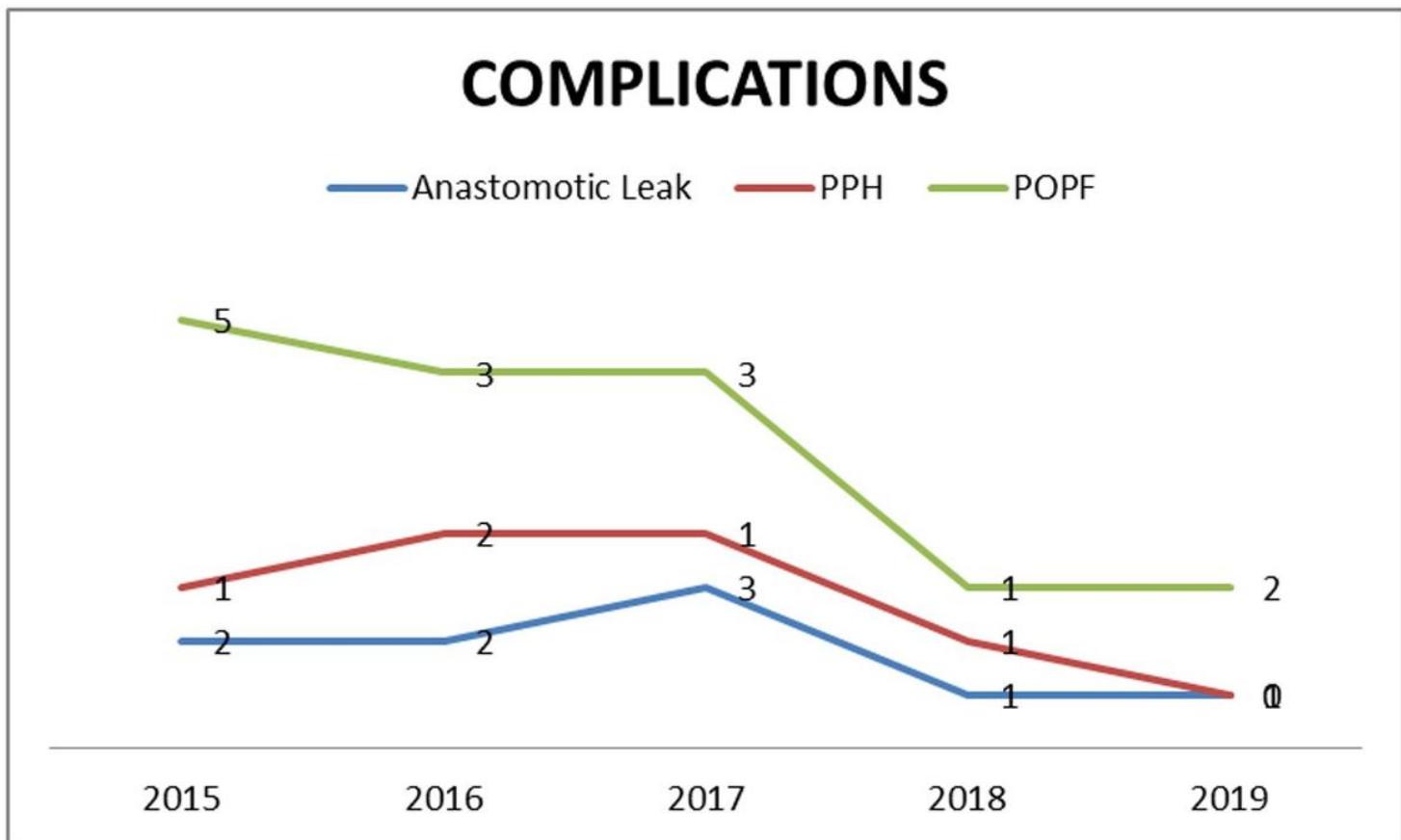


Figure 2

Year-wise trend of postoperative complications

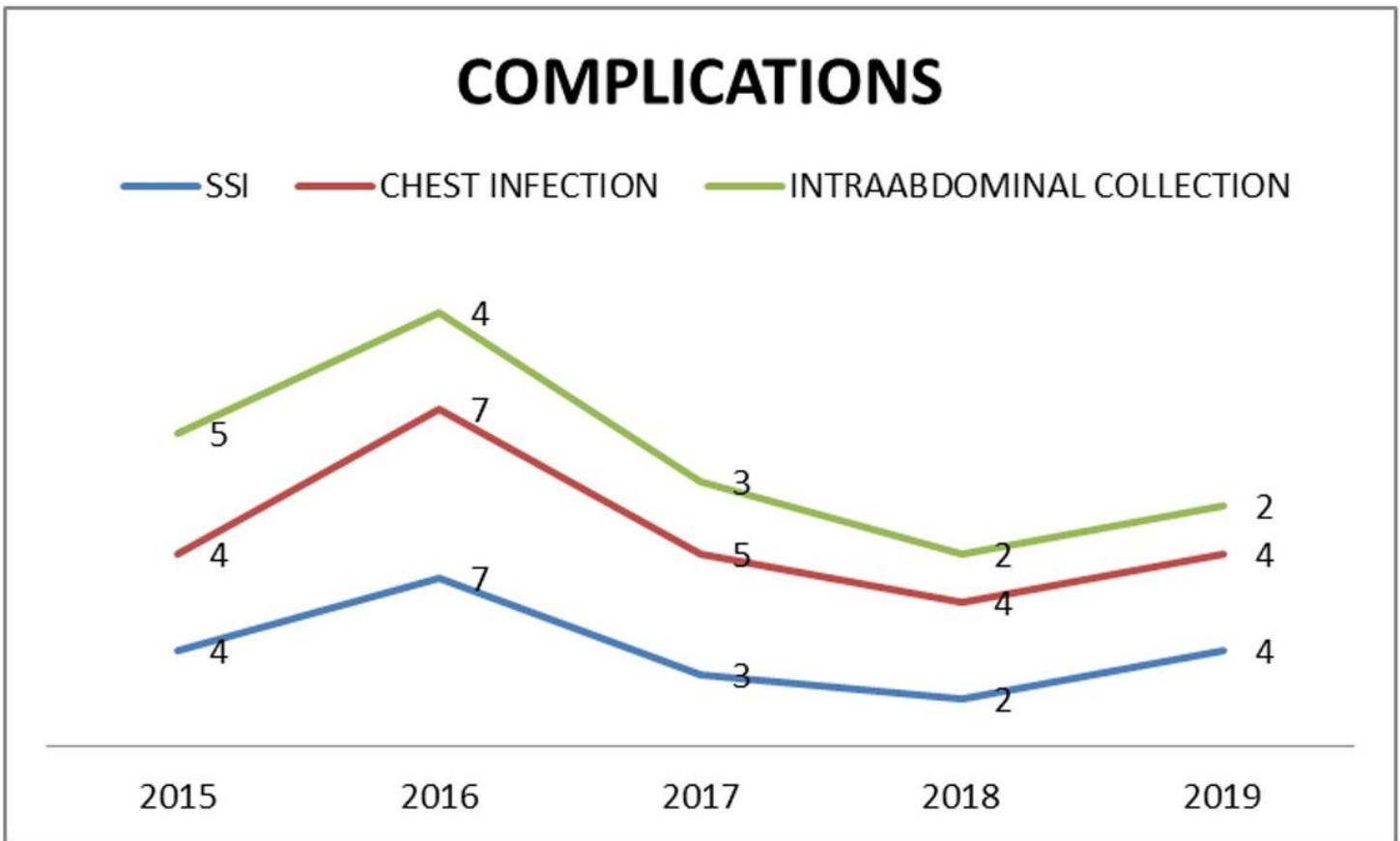


Figure 3

Year-wise trend of infective complication

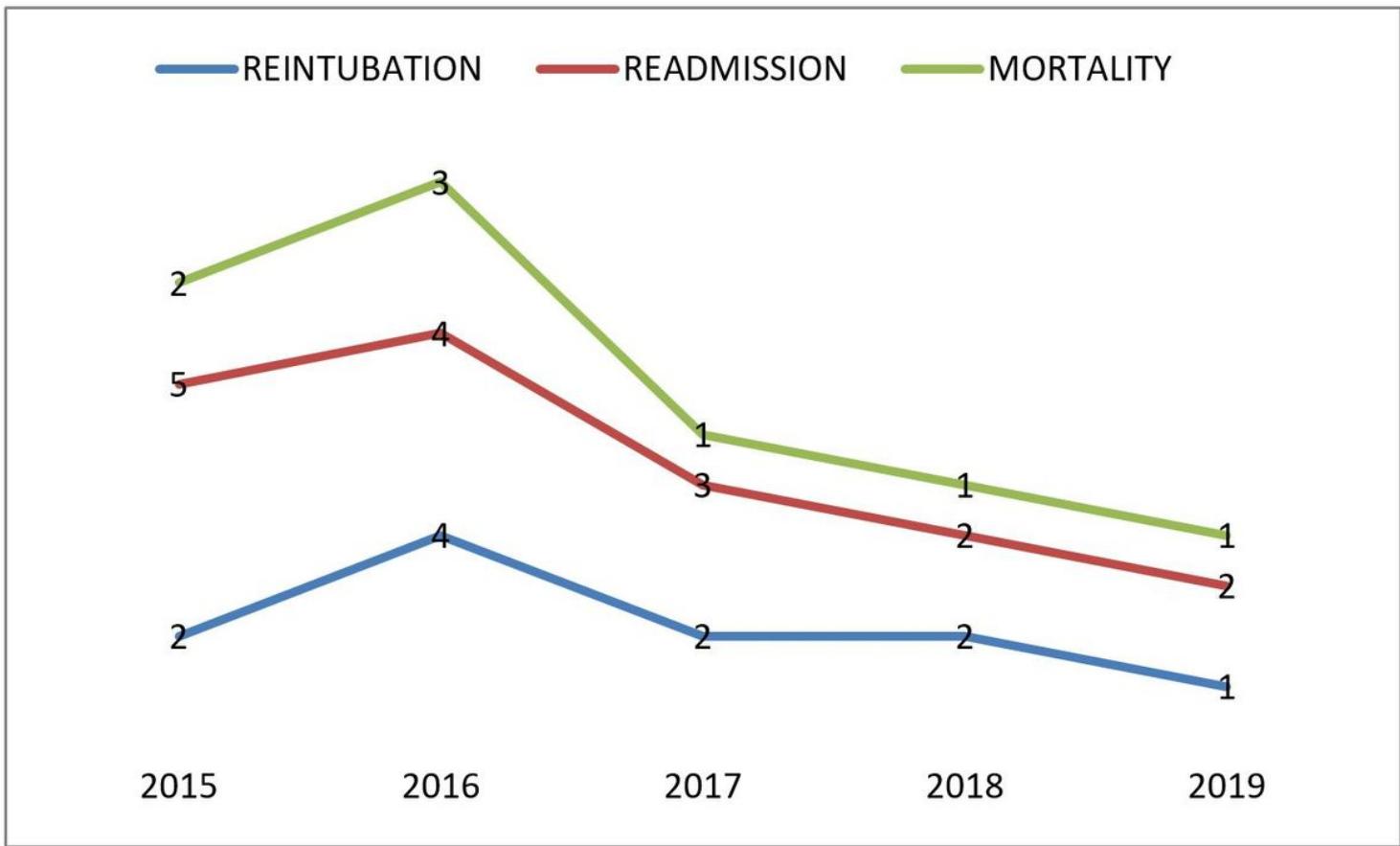


Figure 4

Trend of postoperative mortality and readmission