Management of Postpancreatectomy Hemorrhage Following Pancreaticoduodenectomy at a Tertiary Care Center in Nepal

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ABSTRACT

Introduction

Postpancreatectomy hemorrhage (PPH) is an important complication which significantly increases morbidity and mortality following pancreaticoduodenectomy (PD). This study aims to find the incidence, classification, management, and mortality associated with PPH following PD. This study also describes the changes in management and outcomes between the period of 2004-2014 and 2015-2019 in our institute as in the later time period there was use of CT angiography and interventional radiology (IR) to identify and control the bleeding site.

Methods

This is a retrospective study in which medical records of patients having PPH following PD between 2004-2019 were analyzed. The grading and classification were done according to the International Study Group of Pancreatic Surgery (ISGPS). Management and outcomes were analyzed using standard descriptive statistics.

Results

A total of 43 patients developed PPH out of 336 PDs. Out of 43 patients, 4 (9.3%) had Grade A, 16 (37.2%) had Grade B and 23 (53.5%) had Grade C PPH. Fifteen (35%) patients were managed conservatively, seven (16.2%) with IR procedure and 21 (48.8%) were reexplored. There were 16 (37.2%) mortalities, out of different factors- intraoperative blood loss >500 ml showed the predictability for mortality (p= 0.01). On comparing two time periods it was seen that the PPH rate was almost similar but the mortality decreased from 58.8% to 23.07%.

Conclusion

PPH following PD is associated with high mortality. Increased use of IR procedure and CT angiography can decrease the relaparotomy rates and eventually decrease mortality.

Keywords

Interventional radiology, pancreaticoduodenectomy, postpancreatectomy hemorrhage

INTRODUCTION

Pancreaticoduodenectomy (PD) is a major and morbid procedure and it has been increasing in number every year with advances in imaging and increase in several centers performing it. Though the mortality has now decreased up to 5%, morbidity remains up to 40%.[1] Postoperative pancreatic fistula (POPF)[2] remains the most common complication and also an important determinant for other complications[3] like post pancreatectomy hemorrhage (PPH)[4], delayed gastric emptying (DGE)[5] and chyle leak[6]. These complications have been defined and revised by the International Study Group of Pancreatic Surgery (ISGPS). PPH though not frequently seen as POPF but significantly increases morbidity and mortality of the patient.[7] Early PPH (<24hr) is considered to be technical failure whereas delayed (>24hr) is usually related to vessel erosion or pseudoaneurysm. The mortality/morbidity related to PPH has decreased due to the availability of CT angiography, advances in Intervention Radiology(IR) procedure like stenting and angioembolization. These procedure have led to decreased relaparotomy and mortality as well.[8]

In this study, we report our experience in the management of PPH at our institution. This study aimed to investigate the incidence, classification, management, and mortality associated with PPH after PD at a tertiary care center in Nepal. There has been change in the management and outcome of PPH between 2004 to 2014 and 2015 till 2019 in our institute and we have tried to show in our study as in the later time period there was easy availability and liberal use of CT angiography and interventional radiology (IR) to find and control the bleeding site.

METHODS

The study was approved by the Institutional Review Committee, Institute of Medicine (IOM), Kathmandu, Nepal. This is a retrospective study of all the patients who developed PPH following PD between 2004 to 2019 at Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal. All the procedures were carried out at the Department of GI and General surgery TUTH, Kathmandu. Details of patients were extracted from the hospital clinical records. All the patients with benign or malignant periampullary disease who underwent PD were included.

Any episode of bleeding, like blood in nasogastric (NG) tube, blood in the drain or passage of melenic stool was considered as PPH. Severity, timing and grade all were defined according to ISGPS.[4] The classification is shown in Table 1.

All the cases of mild PPH were managed conservatively. The management of severe PPH is depicted in Figure 1. Due to the availability of the CT angiography and angioembolization techniques, there was difference in management of severe PPH between 2004-2014 and 2015-2019. As shown in Figure 1, before easy availability of CT angiography and IR, laparotomy was only method to identify the bleeding spot and control it. In later period any severe PPH cases were stabilized and urgent CT angiography was done, if the bleeder was identified then angioembolization was done. If no active bleed was seen in CT angiography but patient had features of ongoing bleed then a conventional angiography was done. On conventional angiography if bleeding was not seen then patient was taken for laparotomy. Hence the difference in the management of PPH and outcome between these two different time period has been shown here.

Statistical analysis was performed with SPSS software (SPSS Inc., version 16 for Macintosh, IBM, Chicago, IL, USA). Continuous variables were expressed as the mean and SD or as the median with a range when appropriate. Student's t-test was used to compare the means between groups. Nonparametric tests were used when appropriate. A Chi-squared test was used for nominal data. Univariate logistic regression analysis was done for different factors like age, sex, pre-operative biliary drainage, Pancreatic consistency, diameter of main pancreatic duct, presence of POPF, time and severity of PPH, blood loss, duration of surgery and final histopathology to predict mortality in PPH

Table 1. Classification of PPH according to ISGPS[4]

Class	Description
Time of onset	
Early	<24 hr from surgery
Late	>24 hr from Surgery
Location	
Extraluminal	Bleeding inside abdominal cavity
Intraluminal	Intra enteric
Severity	
Mild	• Hb drop <3 g/dL
	• Mild clinical impairment
	• No therapeutic consequence -
	• 2–3 PRBC if <24 hr from surgery
	• 1–3 PRBC if >24 hr from surgery
Severe	• Large blood loss
	• Hb drop >3 g/dL
	• Significant clinical impairment >3 PRBC
	• invasive treatment
Grade	
Grade A	Early mild
Grade B	Early severe
	Late mild
Grade C	Late severe

Severe PPH

Before 2014

- Blood transfusion
- Correction of coagulopathy

Failure to improve

After 2014

CT Angiography

No active contrast extravasation

Active contrast extravasation

Clinical suspicion of active bleed

Clinical improvement

Conventional angiography

Observation

No active contrast extravasation

Active contrast extravasation

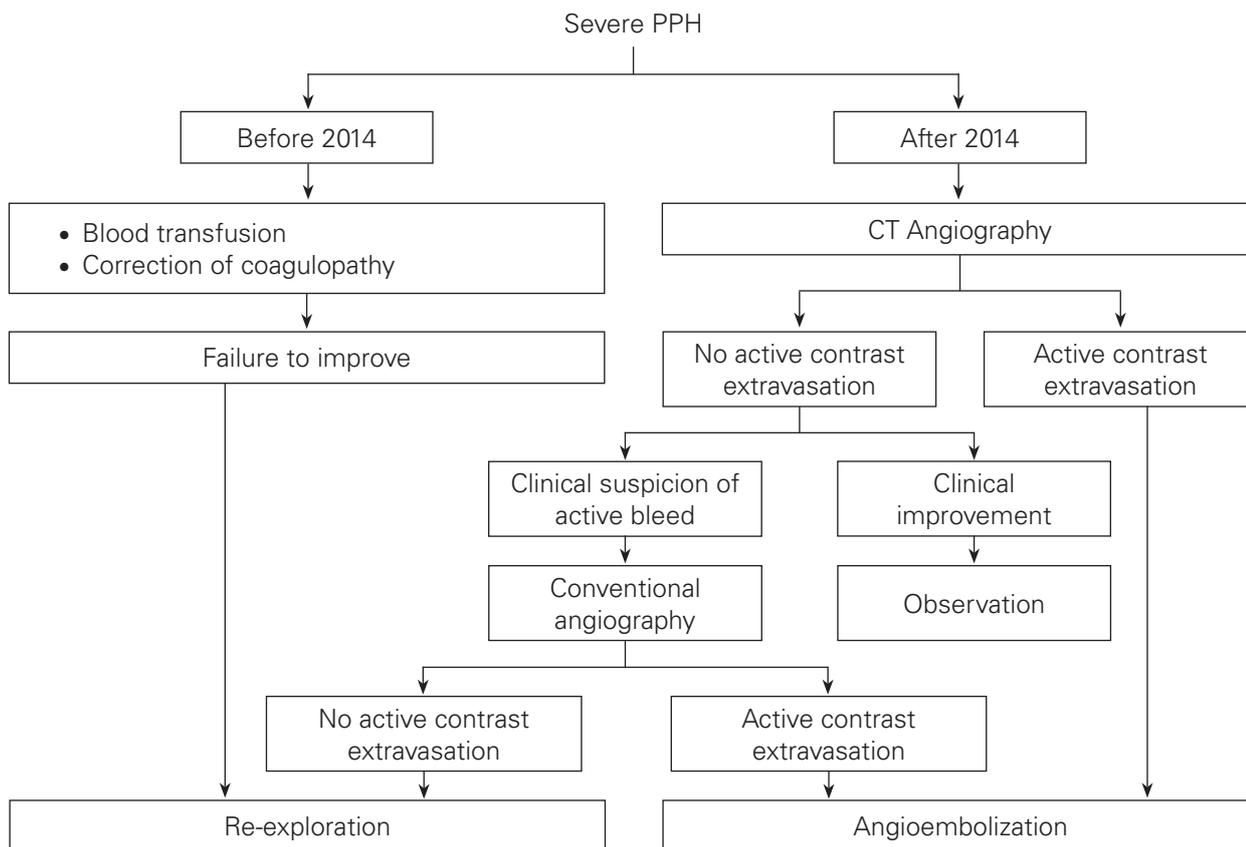Re-exploration

Angioembolization

Fig 1. Management algorithm of severe PPH

patients. All tests were 2- tailed. P values < 0.05 were considered statistically significant.

RESULTS

The clinical characteristics of the patients that developed PPH are summarized in Table 2. A total of 43 patients developed PPH out of 336 PDs. The mean age of those developing PPH was 51 years. Percutaneous transhepatic biliary drainage (PTBD) was preferred method of biliary drainage, done in10(23.3%) patients whereas Endoscopic retrograde cholangiopancreatography (ERCP) and stenting was done in two (4.7%) cases only. No biliary drainage was done in 31 (72%) patients. Mean operative duration was 412.79 ±294.51 mins and mean estimated blood loss was 553.95 ± 295.48 ml. The indication for PD was ampullary carcinoma in 34(79.1%) patients, distal cholangiocarcinoma in four(11.6%) patients, carcinoma head of the pancreas (Ca HOP) in one (2.3%) patient and other pathology were seen in four (7%)patients.

Out of 43 patients, four patients developed Grade A PPH (9.3%). Sixteen patients developed Grade B PPH (37.2%) and 23 patients (53.5%) developed Grade C PPH. POPF was associated in 35 (83.1%) patients that had PPH. The grade and timing of PPH are shown in Table 3. Location wise 19 (44.2%) patients had intraluminal bleed, 22 (51%) had

extraluminal bleed and two (4.7%) patients had both intra and extra luminal bleed.

There were total four Grade A PPH and all of them were managed conservatively. There were

Table 2. Characteristics of patients with PPH (n=43)

Characteristics	Number
Age (years)	51.65±13.07
Sex (F/M)	24/19
BMI (kg/m^2)	21.79±3.3
Pre-operative biliary drainage	
No	31 (72.0%)
PTBD	10(23.3%)
ERCP+ Stenting	2(4.7%)
Pancreatic consistency	
Soft	37(86)%
Firm	6 (14%)
Main pancreatic duct diameter(mm)	3.42±0.85
Duration of Surgery (mins)	412.79±294.51
Blood loss (ml)	553.95±295.48
Final diagnosis	
Ampullary carcinoma	34 (79.1%)
Distal cholangiocarcinoma	4 (11.6%)
Ca HOP	1 (2.3%)
Others	4 (7%)

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Table 3. Characteristics of patients with PPH according to ISGPS (n=43)

Chracteristics	Frequency
PPH Time	
Early	12 (27.9%)
Late	31 (72.1%)
PPH Severity	
Mild	13 (30.2%)
Severe	30 (69.8%)
Location	
Intraluminal	19 (44.2%)
Extraluminal	22 (51.1%)
Both	2 (4.7%)
PPH Grade	
Grade A	4 (9.3%)
Grade B	16 (37.2%)
Grade C	23 (53.5%)
Associated with POPF	
Yes	35 (83.1%)
No	8 (16.9%)

a total of 16 Grade B PPH Patients. Out of those 16 Patients, seven patients had early severe PPH and nine patients had late mild PPH. Six (85.7%) out of seven early severe PPH patients were reexplored, one (14.3%) patient was managed with glue embolization. There were two (28.5%) mortalities among six reexplored patients. All of the late mild PPH cases were managed conservatively. There were three (33.3%) mortalities in the late mild group. There were a total of 23 Grade C PPH patients. Two (8.6%) were managed conservatively, six (26.0%) patients were managed with IR procedures and 15 (65.4%) were reexplored. There were a total of 11 (47.8%) mortalities in Grade C PPH group, nine (81.3%) of the 15 reexplored patient had mortality. One (16.67%) of the six patients that was managed with an IR procedure had mortality. One (50%) of the two patients that was managed conservatively had mortality.

There were total 16 (37.2%) mortalities of the patients having PPH. Amongst various factors as shown in Table 4 that were considered for predicting mortality in PPH patients, blood loss more than 500 ml showed the predictability of mortality after undergoing surgery. (p= 0.01 OR=5.8 (CI- 1.5-22.7) This signifies that the chances of mortality were 5.8 times higher in patients having intraoperative blood loss more than 500 ml in comparison to surgeries with blood loss less than 500ml. However, other risk factors did not show any significant association.

We have compared our data between 2004-2014 and 2015-2019 (Table 5). The number of PDs has almost doubled in the last five years, though the PPH rate is almost similar 13.2% and 12.5% respectively. In the last five years, use of IR

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Table 4. Predictive risk factors of mortality in patients with PPH (n=16)

Risk factors	No.	p-value/OR
Age (years)		
<50	8	p= 0.28
≥50	8	OR= 0.5(0.14-1.7)
Sex		
Female	7	p= 0.22
Male	9	OR= 2.18 (0.62-7.7)
Ampullary Malignancy		
No	4	p= 0.61
Yes	12	OR= 0.68(0.15-3.02)
Pancreatic Consistency		
Soft	13	p= 0.48
Firm	3	OR= 1.84(0.32-10.4)
MPD>3 mm		
No	11	p= 0.28
Yes	5	OR= 0.49(0.13-1.8)
POPF		
No	3	p= 0.78
Yes	13	OR= 1.23 (0.26-5.8)
PPH Time		
Early	2	p= 0.9
Late	14	OR= 4.1(0.77-21.9.6)
PPH severity		
Mild	3	p= 0.21
Severe	13	OR= 2.5(0.58-11.1)
Blood loss>500ml		
No	6	p= 0.01
Yes	10	OR= 5.8 (1.5-22.7)
Preop Drainage		
No	12	p= 0.74
Yes	4	OR= 0.79(0.19-3.2)
Surgery time> 300mins		
No	5	p= 0.88
Yes	11	OR= 1.1(0.29-4.1)

Table 5. Incidence, grade and management of PPH between 2004-2014 and 2015-2019

Details	2004-2014	2015-2019
Total PD	128	208
PPH	17 (13.2%)	26 (12.5%)
Grade of PPH		
Grade A	-	4
Grade B	7	9
Grade C	10	13
Management		
Conservative	7 (41.2%)	8 (30.7%)
Angioembolisation	-	7 (26.9%)
Reexploration	10 (58.8%)	11 (42.3%)
Mortality	10 (58.8%)	6 (23.07%)

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procedures have decreased the relaparotomy rate of 58.8% vs 42.3%. Out of seven patients that had IR intervention, five(71.4%) had coil embolization done, glue embolization and gel foam embolization was done in one(14.3%) patient each. Though PPH rates are similar, mortality rate has decreased from 58.8% to 23.07%.

DISCUSSION

Pancreaticoduodenectomy is one of the major surgeries done in surgical gastroenterology units. TUTH is one of the high volumes centers in Nepal and on average more than 50 PDs are performed every year. One of the unique features is that we have more ampullary cases than carcinoma head of the pancreas, so the pancreas we operate are soft and have non dilated pancreatic duct and also dunking method of pancreaticojejunostomy (PJ) is done in most of the cases.

PPH rate in our center is 12.7% which is higher than that shown by Alvaro et al[7], Gallego et .al[8] and Feng[9] et al which is 3%, 6.8% and 8.7% respectively. There can be multiple explanations for high PPH, first the pancreas we operate have soft consistency leading to higher chances of POPF and eventually PPH. Second is the dunking method of PJ, as shown in RECOPANC trial where pancreatogastrostomy (PG) was compared with PJ and PG in this study was done by dunking method, the PG group had higher incidence of intraluminal PPH.[10]

In our series, we had Grade C PPH as the most frequent type. Incidence of Grade B/C PPH was 90.7% of all the PPH patients. Okoda et.al[11] had B and C PPH rate of 38% whereas in series by Ansari et al[12] it was 6.8% of overall patients. Most of the studies consider Grade B/C as clinically relevant PPH and consider Grade A PPH just as part of a normal postoperative course. Hence there is a suggestion to reconsider the grading of PPH like that of POPF.[8]

The mortality rate in our series was 37.2% of those who had PPH. The mortality rate is higher than Asari et al[13], Izumo et al[14] with 20% and 11% respectively but the mortality rate was almost similar to Wolk et.al[15] of 32%. Amongst the factors that predicts mortality in patients that had PPH, we found intra operative blood loss >500 ml to be an independent predictor. Wellener et al[16] in his series showed that Age>79, BMI > 26, Bilirubin >1.25 and presence of POPF to be an independent predictor of mortality.

In our cohort of patients, ampullary carcinoma was the most common final diagnosis which was in 79.7% patients and carcinoma head of the pancreas was only in 2.3% patients. In a study by Ansari et.al[12] the most common histopathology was PDAC 33.8% and ampullary carcinoma was in 9% patients. Similarly, Wellner et.al[16] also showed that pancreatic ductal adenocarcinoma (PDAC) was the most common type in 33.8% cases and periampullary was in 14.6% cases but in the study by Wolk et.al[15], ampullary carcinoma was seen as the most common type, seen in 74.8% cases and PDAC was seen only in 18.3% as final diagnosis. Most of the data from the west shows PDAC as the most common type of histopathology whereas we have ampullary carcinoma as the most common pathology. Hence our pancreas are softer so, have higher chances of POPF and its sequalae like PPH.

In our series 81.3% cases that had PPH had POPF and 80.6% of the late PPH patients had POPF. Also in the study by Ansari et al and Wellner et al POPF was significantly associated with PPH. POPF has been closely related to PPH, the amylase rich fluid erodes the branch of blood vessels, causes pseudoaneurysm or intra-abdominal collection which can cause pressure effect eventually leading to haemorrhage.[4]

In a study the authors argued that Grade B PPH is a heterogeneous group. In Grade B both early severe and delayed Mild PPH are included. They argued that management and the clinical course of two groups is entirely different hence advocating for a reappraisal of classification.[8] In our Study also, out of 16 patients that had Grade B PPH, seven out of eight patients in the early severe group were reexplored whereas rest nine that had late mild were managed conservatively.

In our center, there has been a shift in paradigm in the management of PPH. The factors may be more experienced, more vigilant working staff and good support of IR. The mortality due to PPH has decreased from 58.8% to 23%. In a study done by Wolk,[15] the use of angiography has been significantly increased between period 1994 to 2009 and 2010 to 2014 but the relaparotomy and mortality rate were similar 45.6% vs 42.1% and 26.2% and 28.2%.

Being a retrospective study our study carries all the inherent problems like loss of data, selection bias and loss to follow up, still it gives some insight about a lethal complication of a complex surgery in a developing country. We are still in the stage of evolution, our preferred method for biliary drainage is PTBD rather than ERCP. Five years back reexploration was the only method of addressing severe PPH. We are still far away from minimally invasive pancreatic surgery. With an increased number of cases, knowledge and good support from Department of Critical Care and Department of Intervention Radiology, we have decreased the mortality rates but morbidity remains high.

CONCLUSION

Postpancreatectomy hemorrhage following pancreaticoduodenectomy is associated with high

mortality. Increased use of IR procedure and CT angiography can decrease the relaparotomy rates and eventually decrease mortality.

CONFLICT OF INTEREST

None declared.

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