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Post-operative Pancreatitis as a Predictor of Post-operative Pancreatic Fistula in Patients Following Pancreaticoduodenectomy

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ABSTRACT

Background: Postoperative pancreatic fistula remains the single most important determinant of morbidity and mortality following pancreaticoduodenectomy. A new entity was proposed by Saxon Connor "Post-Operative pancreatitis", which is defined by raised serum amylase more than the upper limit of institutional serum amylase value on Post-Operative day 0 or 1. There has been shown to be an association between postoperative pancreatitis and postoperative pancreatic fistula. We have conducted this study to see the incidence of postoperative pancreatitis and its association with postoperative pancreatic fistula.

Methods: This was a prospective observational study. All patients undergoing pancreaticoduodenectomy at a tertiary care center for one and a half years were included. A cut-off value of serum amylase 80U/L was used to make a diagnosis of postoperative pancreatitis. The patients were followed up for one month. Pancreas specific complications were defined according to the definition given by the International Study Group of Pancreatic Surgery.

Results: A total of 49 pancreaticoduodenectomies were done in the given period. The incidence of postoperative pancreatitis was 31(63.3%) and postoperative pancreatic fistula was 19(38.8%). Postoperative pancreatic fistula was seen in 19(61.2%) of patients having postoperative pancreatitis ($P<0.001$). Post-operative pancreatitis was also significantly associated with post pancreatectomy hemorrhage, increased hospital stay, and mortality. In multivariate analysis, preoperative endoscopic biliary drainage and increased serum amylase on the first postoperative day came out to be an independent predictor of postoperative pancreatic fistula.

Conclusions: Post-operative Pancreatitis was associated with an increased incidence of Post-operative pancreatic fistula and other postoperative complications like Post pancreatectomy hemorrhage and mortality.

Keywords: Pancreaticoduodenectomy; postoperative pancreatitis; postoperative pancreatic fistula; post pancreatectomy haemorrhage

INTRODUCTION

Pancreaticoduodenectomy(PD) is one of the complex surgery of the gastrointestinal tract with a high complication rate.[1] Pancreaticoduodenectomy is associated with high morbidity of around 40-60% even at high volume center.[2] Post-operative pancreatic fistula(POPF) is one of the most common complications following PD and attributes for most of the post-operative morbidities. Post-operative pancreatic fistula causes abdominal collection, abscess formation and hemorrhage.[3]

The novel concept post-operative pancreatitis has been proposed by Connors, according to this hypothesis- there are ischemic changes in pancreatic remnant that eventually lead to the pancreatitis of the pancreatic remnant, and the POPF is the sequelae of the POP.[4] For diagnosing POP a raised serum amylase level more than institutional normal serum amylase level on the day zero and the first post-operative day was proposed.[4]

Some retrospective studies have shown association between POP and POPF,[5,6] but another study did not show any association.[7] Hence In the light of conflicting evidences, lack of prospective studies and no study in this topic in our country this study was conducted.

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METHODS

A prospective observational study was done between June 2019 to February 2021 after ethical clearance from the Institutional review committee, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. The study was done at the Department of GI and general surgery, Tribhuvan university teaching hospital(TUTH), Kathmandu, Nepal. All the patients with age more than 18 years that had undergone PD in the study period were included, those patients who had mortality before the third postoperative day and who refused to participate in the study were excluded.

All preoperative assessments were done, preoperative biliary drainage was done in those patients who were in cholangitis or nutritionally unfit, by either percutaneous transhepatic biliary drainage(PTBD) or endoscopic retrograde cholangiopancreatography(ERCP) and stenting. Classical PD was done which included removal of the gall bladder with CBD, antrectomy, excision of head of the pancreas and duodenum and 10 cm of jejunum.[8] Pancreatojejunostomy(PJ) was done in all the patients and the anastomotic technique depended on the surgeon's preference, either a dunking PJ or duct to mucosa PJ was done. An end to side Hepaticojejunostomy(HJ), retro colic gastrojejunostomy, and a Braun's jejunojejunostomy was routinely performed.

All patients received prophylactic antibiotics and octreotide intraoperatively and for three days postoperatively, further continuation of octreotide dependent on surgeon discretion. Two drains were placed, one at the PJ site and another at the HJ site.

Serum amylase was checked four hours following surgery and on the morning of the first POD. Drain fluid amylase was checked on the third POD and subsequently as per treating physician discretion. Pancreas specific complications like POPF[9], postpancreatectomy haemorrhage(PPH)[10], Delayed gastric emptying(DGE)[11], Chyle leak[12] were defined according to that given by the international study group of pancreatic surgery(ISGPS). Bile leak was defined as that given by International study group of liver surgery.[13] Other complications were graded according to Clavien Dindo(CD).[14] Patients were followed up to 30 days following surgery.

The General objective of the study was to assess POP as a predictor of POPF and the secondary objectives were to look for the incidence of POP and the association of POP with other postoperative morbidities and mortality.

The quantitative continuous data (Age, Body mass index, Preoperative albumin, Intraoperative blood loss, Operative time, Serum amylase)were expressed as mean ± SD, The categorical data(Sex, Preoperative biliary drainage, pancreas texture, type of PJ and all the postoperative complications) were expressed in number (percentage) . Patients were divided into two groups on the basis of development of POP, development of POPF and Mortality. The difference between two quantitative continuous data were compared using the Student *t*-Test as a parametric test and Mann–Whitney U-Test as a nonparametric test, categorical date were compared using the x 2 test (parametric test) or Fisher's exact test (nonparametric test). The predictive value of the S. Amylase for predicting POPF was assessed using a receiver operating characteristic (ROC) curve analysis. Variables with a significant impact on POPF and mortality as determined by univariate analysis were analysed in multivariate logistic regression analysis to examine the relationship. The P-value < 0.05 was taken as statistically significant. All data were analysed using SPSS (version 23.0).

RESULTS

A total of 49 consecutive PDs were done in the study period. The mean age of the patients was 53.67 ± 11.2 years and the male: female ratio was almost similar(25:24). More than half(n=25, 51%) of the patients had preoperative biliary drainage, ERCP stenting in eight(16.3%) cases, and PTBD in 17 (34.6%) cases. The mean duration between drainage and surgery was 25± 20.54 days. The mean BMI of the patients was 19.96± 2.44 Kg/m^2 with mean albumin of 34.49± 6.6 g/L. The mean duration of surgery was 428.98±106.28 mins and mean blood loss was 545.92± 341.84ml. Most(n=42,85.7%) of the patients had a soft pancreas and only seven(14.3%) patients had firm pancreas, the mean diameter of the main pancreatic duct was 3.35±1.37mm. Ampullary carcinoma(n=31,63.3%) was the most common final histopathology, followed by distal cholangiocarcinoma in ten(20.4%) patients, carcinoma head of the pancreas was present in only three(6.1%) patients, chronic pancreatitis in two(4.1%) and other diagnosis in three(6.1%) patients.

The mean serum amylase on POD0 was 179.55 U/ml with a range of 10-1100 U/ml and the mean serum amylase on POD1 was 215.47 with a range of 10-1377 U/ml. Out of 49 patients, 31(63.2%) developed POP. Among all preoperative and intraoperative parameters, the mean MPD diameter was smaller(3.03± 1.01 vs 3.89± 1.74mm, p=0.034) in those patients who developed POP. Rest other parameters like age, sex, preoperative biliary drainage, type of biliary drainage, preoperative

albumin, BMI, operative duration, blood loss, pancreas texture were similar as shown in Table 1.

On comparing patient with POP and without POP; POPF rate was 19(61.2%) vs 0(p<0.001), PPH rate was 12(24.5%) vs 2(4.1%)(p=0.039), Mortality rate was 10(20.4%) vs 0(p=0.07), CD≥IIIA complications rate was 18(36.7%) vs 2(4.1%) (p=0.001) respectively . Rest other postoperative events like DGE, Chyle leak, bile leak and hospital stay were similar as shown in the table 1.

Out of 31 patients that developed POP, 19(61.2%, p<0.001) developed POPF. The Sensitivity of POP to diagnose POPF was 100%, Specificity of 60%. The positive predictive value of POP for diagnosing POPF was 61.3%, whereas the negative predictive value was 100%. As POP was determined by serum amylase on POD 0 and POD 1, we plotted the ROC curve of serum amylase levels and its association with POPF, the AUC for POD 0 and POD 1 was .785 and .881 respectively(Figure1).

As POP is functional on serum amylase on POD0/1, initially in multivariate analysis only POP and ERCP were included, but POP had a very high odds ratio, hence it was dropped. Due to the multicollinearity of POD 0, it was excluded from the model. Hence, serum amylase on POD 1 and ERCP were included in the multivariate analysis. High serum amylase on POD1 and preoperative ERCP were independent predictors of POPF(Table 2).

Table 1. Comparing preoperative and intraoperative parameters between the two groups who developed and did not develop Post Operative Pancreatitis. (α: Fisher exact test, β: Student's T-test, rest other parameters: Chi-square test.)

Parameters		POP(Present)N=31	POP(Absent)N=18	P-Value
Age[β]		52.52±10.80	55.67±11.89	0.866
Sex(M: F)		17:14	8:10	0.685
Preoperative Biliary drainage	Yes	18(58.1%)	7(38.9%)	0.196
	No	13(41.9%)	11(61.1%)	
ERCP[α]		7(22.6%)	1(5.6%)	0.229
PTBD		10(32.3%)	6(33.3%)	0.938
BMI(Kg/m^2)[β]		20±2.5	19.37±2.26	0.176
Pre-operative Albumin(g/l)[β]		35.19±6.64	33.38±6.64	0.335
Operative time(mins) [β]		434.52±109.14	419.44±103.55	0.637
Intra-operative blood loss[β]		569.35±397.21	505.56±220.88	0.534
Consistency of pancreas[α]	Soft	28(90.3%)	14(77.8%)	0.226
	Firm	3(9.7%)	4(22.2%)	
Main pancreatic duct diameter(mm)		3.03±1.01	3.89±1.74	0.034
PJ[α]	Dunking	28(66.7%)	14(33.3%)	0.398
	DTM	3(42.9%)	4(57.1%)	
POPF		19(61.2%)	0	<0.001
PPH		12(24.5%)	2(4.1%)	0.039
DGE[α]		0	1(2.0%)	0.185
Chyle leak[α]		1(2.0%)	18(36.7%)	0.441
Bile leak[α]		5(10.2%)	2(2.0%)	0.276
Hospital stay(In days) [β]		21±14.57	18±12.39	0.186
Mortality[α]		10(20.4%)	0	0.007
CD≥IIIA		18(36.7%)	2(4.1%)	0.001

Table 2. Univariate and multivariate analysis of different preoperative, intra-operative and post-operative predictors of POPF. (α: Fisher exact test, β: Student's T-test, rest other parameters: Chi-square test.)

	POPF univariate analysis			Multivariate analysis		
	Yes(n=19)	No(n=30)	P-value	O.R	C.I	P-value
Age(in years) [β]	54.42±10.80	53.20±11.59	0.714			
Sex	10:9	15:15	0.545			

Preoperative biliary drainage	Yes	12(63.2%)	13(43.3%)	0.145			
	No	7(36.8%)	17(56.7%)				
ERCP[α]		7(36.8%)	1(3.3%)	0.004	17.164	1.592-185.02	0.019
PTBD		5(26.3%)	11(36.7%)	0.541			
BMI(kg/m^2) [β]		20.8±2.43	19.46±2.32	0.053			
Pre-Operative Albumin(mmol/l) [β]		35.32±6.74	33.97±6.63	0.494			
Operative time(min) [β]		448.42±98.56	416.67±110.74	0.313			
Intraoperative blood loss(ml) [β]		610.53±473.92	505±222.58	0.297			
Pancreas consistency[α]	Soft	18(94.7%)	24(80%)	0.155			
	Firm	1(5.3%)	6(20%)				
PJ[α]	Dunking	17(89.5%)	25(83.3%)	0.691			
	DTM	2(10.5%)	5(16.7%)				
S.A POD0(U/ml) [β]		297.42±323.10	104.9±103.22	0.004			
S.A POD1(U/ml) [β]		387.63±366.67	106.43±117.697	<0.001	1.009	1.003-1.015	0.019
POP		19(100%)	12(40%)	<0.001			

Table 3. Univariate and multivariate analysis of different preoperative, intra-operative and post-operative predictors of mortality. (α: Fisher exact test, β: Student's T-test, rest other parameters: Chi-square test.)

		Mortality (Univariate analysis)			Multivariate analysis		
		Yes(n=10)	No(n=39)	P-value	O.R	C.I	P value
Age(yrs) [β]		57±11.36	52.82±11.14	0.297			
Sex(M: F) [α]		5:5	20:19	1.000			
Preoperative Biliary drainage[α]	Yes	6(60%)	19(48.7%)	0.725			
	No	4(40%)	20(51.3%)				
ERCP[α]		3(30%)	5(12.8%)	0.197			
PTBD[α]		3(30%)	14(33.3%)	1.00			
BMI[β]		20.20±3.36	19.9±2.19	0.766			
Preoperative Albumin(mmol/L) [β]		32.30±7.07	35.0519.9±	0.246			
Operative Time(min) [β]		478.00±105.28	416.41±104.16	0.103			
Blood loss(ml) [β]		800.00±545.18	480.77±236.63	0.007	1.005	1.00-1.01	0.041
Pancreas texture[α]	Soft	10(1005)	32(82.1%)	0.179			
	Firm	0	7(17.9%)				
Main Pancreatic duct diameter[β]		3.00±1.15	3.44±1.42	0.0378			
PJ[α]	Dunking	10(23.8%)	32(82.1%)	0.319			
	DTM	0	7(17.9%)				
S.A POD0[β]		294.30±323.77	150.13±119.36	0.082			
S.A POD1[β]		356.50±372.17	179.31±243.06	0.073			
POP[α]		10(100%)	21(53.8%)	0.008			
POPF[α]		8(80%)	11(28.2%)	0.008			
PPH[α]		9(90%)	5(12.8%)	<0.001	49.14	1.85-1299.90	0.02
Bile leak[α]		6(60%)	2(5.1%)	0.012			
DGE[α]		0	1(2.6%)	0.796			
Chyle leak[α]		0	1(2.6%)	0.796			
Rexploration[α]		6(60%)	0	<0.001			

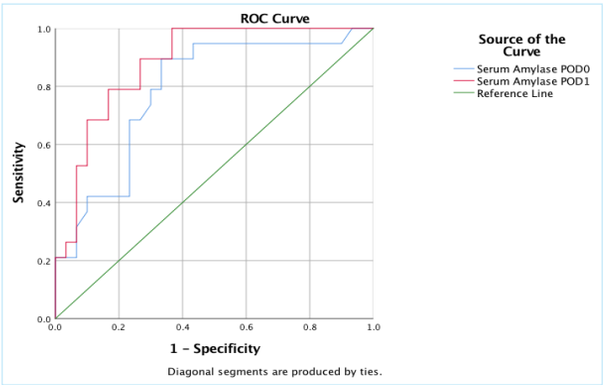

Figure 1. Showing ROC curves to assess the relationship between postoperative serum amylase values and POPF.

DISCUSSION

In our study post-operative pancreatitis was significantly associated with POPF and other postoperative complications . The incidence of POP in our study was 63.2% and is similar to other studies where the incidence ranges between41%-63.4%. Similar to other studies, we observed a statistically significant association between POP and POPF, PPH, CD>IIIA complications, and mortality.[5,6] The AUC of POD1 serum amylase was 88.1 for diagnosing POPF, which is a very good discrimination capacity and the negative predictive value for POP for POPF is very high, it was similar to a review of 292 patients who underwent PD in Verona, Italy in 2018.[5] Hence, by the morning of the first POD, we can identify those patients who are at high risk of developing POPF.

Out of the different parameters in our study, those patients developing POP had smaller main Pancreatic duct(MPD) than those who did not. Smaller MPD is a proven risk factor for POPF. It is seen that small MPD is seen in cases other than Carcinoma Head of Pancreas or chronic pancreatitis like ampullary carcinoma, distal cholangiocarcinoma, duodenal adenocarcinoma, in these pathologies the acinar cell density is high. In our cohort of patient the common pathology is ampullary carcinoma . Nahm et. al studied the acinar cell density of the pancreatic stump and found that the increase in acinar cell density in the pancreatic stump was significantly associated with POP.[15] In another retrospective study, it was shown that smaller MPD, normal bilirubin, high-risk pathology, female sex, and robotic surgery was associated with developing POP.[16]

The most common histopathology in our study was ampullary carcinoma which is different to the literature published from the West, where the most common diagnosis is pancreatic ductal adenocarcinoma, [5-7,17] therefore most of the pancreas we operate on have soft consistency(85.7%). The mean MPD diameter in our patients is 3.35±1.37mm. Small duct and soft pancreas are already proven risk factors for POPF.[18] This might be one explanation for the higher POPF rate(38.2%) in our study compared to other studies. One new thing found in our study was ERCP with stenting as a risk factor of POPF.

Higher intraoperative blood loss and PPH were independent predictors of mortality in this study. Similarly, in another study done in our center showed that PPH with higher intra-operative blood loss was significantly associated with mortality.[19] There was a high mortality rate in our study compared to the previous study done in our center.[20]

The DGE rate was very low in our study, seen in only one case(2.3%) compared to 13.01% and 30.5% in western literature. One of the reasons behind DGE is said to be intra-abdominal collection secondary to POPF.[18] In our study, despite the POPF rate being such high as ~ 32%, the DGE rate is very low. We perform a Braun's jejunojejunostomy regularly at our centre and our patients have a lower BMI which might be the reason for such low DGE.[21,22]

Various authors have used other additional parameters along with serum amylase for better characterization of POP. Measurement of CRP on POD 2[5,7], CECT abdomen[23] or trend of Serum amylase from POD0-3.[24] The addition of these parameters has increased the predictivity rate of POPF.

There are very few studies regarding the management of POP. In a study, it was shown that in patients at high risk for POP, near-zero fluid management was associated with a higher rate of POP (24.6 vs. 0%, P < 0.01) and POPF (27.6 vs. 11.4%, P 1/4 0.05) than liberal fluid management.[5] In an RCT where ulinastatin(a trypsin inhibitor) and placebo were compared, ulinastatin decreased the incidence of POP and decreased the drain amylase level on POD 2-3 significantly but the study was not powered enough to detect the change in the POPF rates.[25]

Recently, ISGPS has tried to define Post-pancreatectomy acute pancreatitis(PPAP) as an acute inflammatory condition of the pancreatic remnant beginning within the first three postoperative days following a partial pancreatic resection. The diagnosis requires (1) a sustained postoperative serum hyperamylasemia (POH) greater than the institutional upper limit of normal for

at least the first 48 hours postoperatively; (2) associated with clinically relevant features; and (3) radiologic alterations consistent with PPAP. Three different PPAP grades were defined based on the clinical impact: (1) grade POH, biochemical changes only; (2) grade B, mild or moderate complications; and (3) grade C, severe life-threatening complications.[26]

There are a few drawbacks of our study, first is the observational bias: in our study, the complications rates were higher than our previous studies,[21,27] which might have increased the predictability of POP. The second, is lacking of use of other additional parameters, as previously mentioned, we could have added CECT abdomen to look for features of acute pancreatitis in the patients who had postoperative CT for any complications. Third is that we could have taken a biopsy from the pancreas in the reexplored patients, which could have given a histopathological evidence of pancreatitis. Nevertheless, this study has increased our interest in this new entity. The Recent definition given by ISGPS will help in better characterization in future studies.[26]

CONCLUSIONS

Post-operative Pancreatitis was associated with an increased incidence of Post-operative pancreatic fistula and other postoperative complications like Post pancreatectomy hemorrhage and mortality.

CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg. 2015;220(4):530-536.[Article]
2. Bergquist JR, Shubert CR, Ubl DS, Thiels CA, Kendrick ML, Truty MJ et al. Risk by indication for pancreaticoduodenectomy in patients 80 years and older: a study from the American College of Surgeons National Surgical Quality Improvement Program. HPB (Oxford). 2016;18(11):900-907. [Article]
3. Nahm CB, Connor SJ, Samra JS, Mittal A. Postoperative pancreatic fistula: a review of traditional and emerging concepts. *Clin Exp Gastroenterol*. 2018;11:105-118.[Article]
4. Connor S. Defining post-operative pancreatitis as a new pancreatic specific complication following pancreatic resection. HPB (Oxford). 2016;18(8):642-651. [Article]
5. Bannone E, Andrianello S, Marchegiani G, Masini G, Malleo G, Bassi C et al. Postoperative Acute Pancreatitis Following Pancreaticoduodenectomy: A Determinant of Fistula Potentially Driven by the Intraoperative Fluid Management. Ann Surg. 2018;268(5):815-822.[Article]
6. Chen H, Wang W, Ying X, Deng X, Peng C, Cheng D et al. Predictive factors for postoperative pancreatitis after pancreaticoduodenectomy: A single-center retrospective analysis of 1465 patients. Pancreatology. 2020;20(2):211-216.[Article]
7. Birgin E, Reeg A, Téoule P, Rahbari NN, Post S, Reissfelder C et al. Early postoperative pancreatitis following pancreaticoduodenectomy: what is clinically relevant postoperative pancreatitis?. HPB (Oxford). 2019;21(8):972-980.[Article]
8. He J, Ahuja N, Makary MA, Cameron JL, Eckhauser FE, Choti MA et al. 2564 resected periampullary adenocarcinomas at a single institution: trends over three decades. HPB (Oxford). 2014;16(1):83-90.[Article]
9. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017;161(3):584-591.[Article]
10. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery. 2007;142(1):20-25.[Article]
11. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142(5):761-768.[Article]
12. Besselink MG, van Rijssen LB, Bassi C, Dervenis C, Montorsi M, Adham M, et al. Definition and classification of chyle leak after pancreatic operation: A consensus statement by the International Study Group on Pancreatic Surgery. Surgery. 2017;161(2):365-372.[Article]
13. Koch M, Garden OJ, Padbury R, Rahbari NN, Adam R, Capussotti L, et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. Surgery. 2011;149(5):680-688.[Article]
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-213.[Article]
15. Nahm CB, Brown KM, Townend PJ, Colvin E, Howell VM, Gill AJ, et al. Acinar cell density at the pancreatic resection

margin is associated with post-pancreatectomy pancreatitis and the development of postoperative pancreatic fistula. HPB (Oxford). 2018;20(5):432-440.[Article]

16. Ikenaga N, Ohtsuka T, Nakata K, Watanabe Y, Mori Y, Nakamura M. Clinical significance of postoperative acute pancreatitis after pancreatoduodenectomy and distal pancreatectomy. Surgery. 2021;169(4):732-737. [Article]
17. Partelli S, Tamburrino D, Andreasi V, Mazzocato S, Crippa S, Perretti E, et al. Implications of increased serum amylase after pancreaticoduodenectomy: toward a better definition of clinically relevant postoperative acute pancreatitis. HPB (Oxford). 2020;22(11):1645-1653. [Article]
18. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg. 2013;216(1):1-14.[Article]
19. Subedi, N., B. Kandel, B. Ghimire, P. B. Kansakar, R. S. Bhandari, and P. Joshi Lakhey. Management of Postpancreatectomy Hemorrhage Following Pancreaticoduodenectomy at a Tertiary Care Center in Nepal". Journal of Institute of Medicine Nepal, vol. 42, no. 3, Dec. 2020, pp. 26-31.[Article]
20. Shah S, Ghimire B, Paudel S, Singh YP. Pancreatic Configuration Index in Predicting Postoperative Pancreatic Fistula in a Tertiary Care Center in Nepal. J Nepal Health Res Counc. 2020;18(2):172-177. Published 2020 Sep 7. [Article]
21. Zhou Y, Hu B, Wei K, Si X. Braun anastomosis lowers the incidence of delayed gastric emptying following pancreaticoduodenectomy: a meta-analysis. BMC Gastroenterology. 2018 Nov 26;18(1):176.[Article]
22. Robinson JR, Marincola P, Shelton J, Merchant NB, Idrees K, Parikh AA. Peri-operative risk factors for delayed gastric emptying after a pancreaticoduodenectomy. HPB (Oxford). 2015 Jun;17(6):495–501.[Article]
23. Loos M, Strobel O, Dietrich M, Mehrabi A, Ramouz A, Al-Saeedi M, et al. Hyperamylasemia and acute pancreatitis after pancreatoduodenectomy: Two different entities. Surgery. 2021;169(2):369-376.[Article]
24. Bann Bannone E, Andrianello S, Marchegiani G, Malleo G, Paiella S, Salvia R, et al. Postoperative hyperamylasemia (POH) and acute pancreatitis after pancreatoduodenectomy (POAP): State of the art and systematic review. Surgery. 2021;169(2):377-387.[Article]
25. Uemura K, Murakami Y, Hayashidani Y, Sudo T, Hashimoto Y, Ohge H, et al. Randomized clinical trial to assess the efficacy of ulinastatin for postoperative pancreatitis following pancreaticoduodenectomy. J Surg Oncol. 2008;98(5):309-313.[Article]
26. Marchegiani G, Barreto SG, Bannone E, Sarr M, Vollmer CM, Connor S, et al. Postpancreatectomy Acute Pancreatitis (PPAP): Definition and Grading From the International Study Group for Pancreatic Surgery (ISGPS). Ann Surg. 2022;275(4):663-672.[Article]
27. Lakhey PJ, Bhandari RS, Ghimire B, Khakurel M. Perioperative outcomes of pancreaticoduodenectomy: Nepalese experience. World J Surg. 2010;34(8):1916-1921.[Article]