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Predictive value of drain fluid amylase level on postoperative day one after pancreatic resection for predicting postoperative pancreatic fistula

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ABSTRACT

Objective: The aim of this study was to evaluate the predictive value of the first postoperative day (POD1) drain fluid amylase in predicting pancreatic fistula formation following pancreaticoduodenectomy (PD).

Material and Methods: One-hundred and eighty-five prospective patients undergoing PD between April 2014 and April 2018 were studied retrospectively. Cut-off point to predict the development of POPF was determined by median values for drain fluid amylase of 1883 U/L. Patients were classified into two groups according to POD1 drain fluid amylase values: <1883 U/L (Group 1) and ≥1883 U/L (Group 2). Differences between the groups with clinically relevant POPF and without POPF were evaluated.

Results: The incidence of POPF was 17.2%. POD1 amylase level was the strongest predictor of POPF, with levels of higher than 1883 U/L demonstrating the best accuracy (87.5%), sensitivity (78.1%), specificity (89.5%), positive predictive value (60.9%), and negative predictive value (95.1%). One-hundred and forty-four patients (77.8%) had a POD1 drain amylase level of less than 1883 U/L, and POPF developed in only seven (3.7%) cases, whereas in patients with POD1 drain amylase level of 1883 U/L or higher (n= 41), the POPF rate was 31.4% [OR: 22.24, 95% CI (7.930–62.396), p< 0.001].

Conclusion: The cut-off point of POD1 drain fluid amylase level (1883 U/L) might predict the clinically relevant POPF with adequate sensitivity and specificity rates in patients undergoing pancreatic resection.

Keywords: Pancreaticoduodenectomy, amylases, postoperative complications, pancreatic fistula

INTRODUCTION

Despite the implementation of advancing techniques into postoperative management of the patients, complication rates after pancreatic resection remain high. Postoperative pancreatic fistula (POPF) is a common complication that threatens the patient's life after pancreaticoduodenectomy (PD). POPF can cause adverse consequences, including the development of intra-abdominal abscesses and intra-abdominal or intramucosal hemorrhage (1,2). For that reason, identifying high-risk patients for POPF in the perioperative period is critical for appropriate patient management planning.

The cut-off values were different among studies. Differences in the definition of POPF, differences in the surgical procedure, and retrospective studies prevent the establishment of the optimal cut-off value. From the viewpoint of the mechanism of POPF, the differences in surgical procedures do not affect fistula formation. A large-scale prospective trial is warranted to establish an optimal cut-off value that applies to any surgical procedure (3). However, there is not any consensus on POD1 drain fluid amylase cut-off value. Several studies have suggested that drainage fluid analyses contribute to predicting POPF, although there has long been a debate on the preventive and therapeutic implementation of abdominal drains after performing a pancreatic resection (4-10). The controversial results may be explained by the fact that any cohort of patients undergoing PD may not be homogeneous to determine the diagnostic and therapeutic implications of prophylactic abdominal drainage, in the absence of objective criteria to be used to determine the individual risks for developing POPF. Recently, the levels of amylase in the drainage fluid have received considerable attention, with researchers asking whether they can serve to predict PF or to decide the optimum time for drain removal.

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In several studies, predictive values (sensitivity, specificity, and positive and negative predictive values) were investigated and reported as strongly favorable for POPF (11,12). For this reason, we aimed to determine the optimal predictive value of POD1 drain fluid amylase level in estimating POPF after PD.

MATERIAL and METHODS

This study was performed after obtaining the permission of Gazi University Faculty of Medicine Clinical Research Ethics Committee (Decision Number: 425). Patients who had elective pancreaticoduodenectomy in the General Surgery Clinic of Gazi University Medical Faculty during the period from April 2014 to April 2018 participated in the study. All patients included in the study were operated by two experienced surgeons, performing more than 50 operations per year. Demographic data of the study patients and their intraoperative, pathological, and postoperative data were logged by the surgeons.

The standard PD as described in the literature was performed on all patients (13). In addition, the lymph nodes between the coeliac trunk and the superior mesenteric artery (triangular area) were retrieved, and the proximal jejunum was pulled up for P-J through the Treitz hole that occurred after duodenectomy. Pyloric preservation was not performed on any patients. An internal stent at the appropriate size was placed between the pancreatic duct and the jejunal opening in all patients, and external drainage was not performed. Two abdominal drains were placed around the P-J and hepaticojejunostomy. Blumgart anastomosis was performed on all patients as described; three or four transpancreatic U-sutures were placed approximately 1 cm distal to the transected edge of the pancreas going from front to back with suture. The seromuscular back wall of the jejunum was utilized, nearer the mesenteric edge, and 10 to 15 mm longitudinal seromuscular stitches were placed. The suturing then reverted to back to front through the pancreas completing the U. A duct-to-mucosa anastomosis was constructed with four to six stitches of polydioxanone 5-6/0 after creating a small opening (about 2-3 mm) in the jejunal loop. The transpancreatic U-sutures were then passed through the seromuscular layer of the anterior wall of the jejunal loop in the direction of the short axis. Each of the U method sutures was placed at a distance of 5 to 10 mm from the last. This procedure completely covered the pancreatic stump with jejunal serosa and protected the knots from cutting through the pancreatic tissue.

Resection and reconstruction of the superior mesenteric vein and portal vein were accepted as vessel resection. To prevent the development of stress ulcerations, proton pump inhibitors were administered to all patients. The parenchymal texture of the pancreas was determined as soft or hard by the surgeon by manually palpating the pancreatic remnant. After the operation, one drain was placed adjacent to the pancreaticojejunostomy and hepaticojejunostomy. The drain fluid amylase (DFA) levels on POD 1-, 3-, and -5 were recorded daily after the operation.

Postoperative pancreatic fistula was defined and classified according to the International Study Group for Pancreatic Surgery-2016 (14). The diagnosis of POPF was made if the amylase level of the drain fluid was three times higher than the serum amylase level on the 3rd postoperative day. This was regarded as biochemical leakage (BL). Grade B fistula was defined as fistula requiring any changes in the treatment (need for antibiotics, enteral or parenteral nutrition, percutaneous, endoscopic, or angiographic interventions) or fistula with abdominal drainage lasting longer than 21 days. Fistula-related organ failure, reoperation, or death was accepted as Grade C fistula. Grade B and C fistulas were defined as clinically relevant POPF (CR-POPF).

First, univariate and multivariate analyses were used to retrospectively investigate the relationship between patient and tumor characteristics, intraoperative, and postoperative features. Cut-off points to predict the development of POPF were determined by median values. Patients were classified into two groups according to POD1 drain fluid amylase level; those with a value <1883 U/L were named the low amylase group, and those with ≥1883 U/L were named the high amylase group. Patient and tumor characteristics were recorded, including age, sex, body mass index (BMI), pathological diagnosis (malignant or benign), operation time (min), estimated blood loss (mL), vascular resection performed/none, soft or hard pancreas parenchyma, main pancreatic duct size (mm), postoperative day one, two, and three drain fluid amylase levels, the median value of POD1 drain amylase value level (≥1883 U/L vs. <1883 U/L), Clavien-Dindo complication classification, and the re-operation rate.

The main pancreatic duct diameter was measured perioperatively by the surgeon who performed the operation. The morbidity rate in the postoperative period was determined by including all complications developing just after the surgery and throughout the postoperative period until the patient was discharged from the hospital. The Clavien-Dindo classification was used for complications (15). Delayed gastric emptying in the postoperative period was diagnosed by the International Study Group on Pancreatic Surgery.

Statistical Analysis

All data were summarized as mean ± standard deviation (SD). For univariate analysis, non-paired t-test and χ^2 test were used, and for multivariate analyses, logistic regression analysis was used. P-values <0.05 were considered statistically significant. Cut-off points to predict the development of POPF were determined by median values. Analysis of data and the

assessment of sensitivity, specificity, predictive values, and accuracy were performed with diagnostic formulas. SPSS program was used for statistical analysis.

RESULTS

Patient Characteristics

One-hundred and eighty-five patients undergoing PD were included in the study. Median age was 62 years (range= 24-85 years), and there were 104 male (56.2%) patients. Mean BMI of the patients was 26.3 ± 17.8 m^2/kg. Among the patients, 86 (46.5%) had comorbid factors; and 70 (37.8%) patients had ASA III/IV scores. Histopathological diagnosis was benign in 34 (18.4%) patients, and it was reported to be malignant in 81.6% of the patients. Ninety-nine (53.5%) patients were identified as having hard pancreatic parenchyma, and 86 (46.5%) patients had soft parenchyma. The main pancreatic duct diameter was <4 mm in 62 patients (33.5%), and 41 patients (22.2%) needed a blood transfusion during the operation. The postoperative pancreatic fistula rate was 17.3% (32). While the rate of POPF development was 25% (8) in patients with hard pancreatic parenchyma, it was 75% (24) in patients with soft pancreatic parenchyma. The postoperative pancreatic fistula was identified in 24 patients with soft and eight patients with hard pancreatic parenchyma. The main pancreatic duct diameter was less than 4 mm in 68% of patients with POPF (Table 1).

Using the median drain fluid amylase level (<1883 U/L vs. ≥1883 U/L) as a cut-off value.

Clinicopathological characteristics of the patients, intraoperative and postoperative features are presented in Tables 2, 3, and 4. Patients were divided into two groups: Patients with POD1 drain fluid amylase level lower than 1883 U/L (Group 1) and patients with POD1 drain fluid amylase ≥1883 U/L (Group 2). In 21.9% (n= 7) of the patients with POPF, POD1 drain fluid amylase levels were lower than 1883 U/L. Postoperative day one drain fluid amylase levels were higher than 1883 U/L in 78.1% (n= 25) of the patients who developed fistulas on POD1 (Table 2). There were more patients with hard pancreatic parenchyma (59.7% vs. 31.7%, p= 0.002) and ≥4 mm duct diameter (73% vs. 41%, p< 0.001) in Group 1 than Group 2. Patients with soft parenchyma were 46.5% (OR= 3.689, CI= 1.048-12.987) and more likely to form POPF compared to those patients with hard pancreatic parenchyma (p= 0.045). Patients with a small duct diameter (<4 mm) were 33.5% (OR= 3.732, CI= 1.333-10.447) and more likely to form POPF compared to those patients with a larger duct diameter (p= 0.012). It was determined that the need for blood transfusion was higher in Group 2 (36.6% vs. 18.1%, p= 0.012), and the results are shown in Table 3. Postoperative day one in Group 2 was related to a higher rate of overall morbidity that was significantly different (Table 4). There were no statistically significant differences between the groups in terms of demographic patients characteristics, ASA score, comorbidity, histopathological diagnosis, tumor location, vascular resection, estimated blood loss, internal stent replacement, operation time, or length of hospital stay (Tables 2, 3, and 4).

Predictors of PF

The multivariate analysis revealed that a POD1 drain fluid amylase level higher than 1883 U/L (OR= 22.24, 95% CI= 7.93-62.39), p= 0.0001), soft parenchyma (OR= 3.689, 95% CI= 1.04-12.98, p= 0.045), and <4 mm main pancreatic duct size (OR= 3.732, 95% CI= 1.33-10.44, p= 0.012) were the independent factors for POPF development, which is shown in Table 5.

Postoperative day one drain fluid amylase level was found to be the powerful predictor of POPF. The best accuracy (87.5%), sensitivity (78.1%), specificity (89.5%), positive predictive value (PPV) (60.9%), and negative predictive value (NPV) (95.1%) were found for POD1 drain fluid amylase level with 1883 U/L or higher (Table 6). The postoperative day one drain fluid amylase level was <1883 U/L in 144 patients (77.8%), and POPF was seen in seven patients (3.7%). The POPF incidence rate was 31.4% among 41 patients with ≥1883 U/L POD1 drain amylase level [OR= 22.24, 95% CI (7.930-62.396), p< 0.001].

DISCUSSION

Postoperative pancreatic fistula (POPF) formation following pancreatic surgery remains a challenge even in pancreatic centers with a high volume of patients. The reported incidence of POPF after PD ranges between 2% and 46% (16). Therefore, predicting the patients who will develop POPF might facilitate the management of this challenging complication and improve surgical outcomes. There are no clearly established tools to identify high-risk patients for developing POPF. The potential risk factors, such as soft parenchymal texture, narrow duct, intraoperative blood loss, and high BMI, have been suggested to be associated with POPF. But their predictive values are not adequate.

However, the early prediction of POPF remains controversial despite the availability of several various methods, proposed to estimate the development of POPF along with the associated risk factors. The precision of fistula according to the ISGPF in 2005 suggested that the drain fluid amylase level measured on postoperative day three or later and postoperative day one drain fluid amylase levels for diagnosis of POPF were not discussed in the ISGPF consensus meeting. This topic is controversial because there are conflicting results on using postoperative day one drain fluid amylase levels to predict the pancreatic fistula (10,17-22).

Table 1. Demographic, clinic, and operative characteristics of patients

	Total (n= 185)	POPF (n= 32)	No-POPF (n= 153)
Age, year			
<65	69 (37.3)	21 (65.6)	95 (62.1)
>65	116 (62.7)	11 (34.4)	58 (37.9)
Sex			
Male	104 (56.2)	19 (59.4)	85 (55.6)
Female	81 (43.8)	13 (40.6)	68 (44.4)
ASA Score			
I/II	115 (62.2)	21 (65.6)	94 (61.4)
III/IV	70 (37.8)	11 (34.4)	59 (38.6)
Comorbidity			
Yes	86 (46.5)	17 (53.1)	89 (45.1)
No	99 (53.5)	15 (46.9)	84 (54.9)
Pathologic Diagnosis			
Benign	34 (18.4)	3 (9.4)	31 (20.3)
Malign	151 (81.6)	29 (90.6)	122 (79.7)
Tumor Location			
Pancreas head	121 (65.4)	16 (50)	105 (68.6)
Distal choledoch	20 (10.8)	8 (25)	27 (17.6)
Ampulla tm	35 (18.9)	7 (21.9)	13 (8.5)
Duodenal tm	9 (4.9)	1 (3.2)	8 (5.2)
PJ Anastomosis Type			
Blumgart	144 (77.8)	23 (71.9)	135 (88.2)
Dunking	41 (22.2)	9 (28.1)	18 (11.8)
Pancreas Texture			
Soft	86 (46.5)	24 (75)	62 (40.5)
Hard	99 (53.5)	8 (25)	91 (59.5)
PD Diameter, mm			
≥4	123 (66.5)	10 (31.3)	113 (73.9)
<4	62 (33.5)	22 (68.7)	40 (26.1)
Blood Loss, mL			
≥400	46 (24.9)	10 (31.3)	36 (23.5)
<400	139 (25.1)	22 (68.7)	117 (76.5)
Blood Transfusion			
Yes	41 (22.2)	13 (40.6)	28 (18.3)
No	144 (77.8)	19 (59.4)	125 (81.7)
Operation Time, min			
≥240	137 (74.1)	27 (84.4)	110 (71.9)
<240	48 (25.9)	5 (15.6)	43 (28.1)
POD 1 Cut-off, U/L			
<1883	144 (77.8)	7 (21.9)	137 (89.5)
≥1883	41 (22.2)	25 (78.1)	16 (10.5)
POD 3 Cut-off, U/L			
<504	139 (75.1)	5 (15.6)	134 (87.6)
≥504	46 (24.9)	27 (84.4)	19 (12.4)
POD 5 Cut-off, U/L			
<98	142 (76.7)	4 (12.5)	138 (90.2)
≥98	43 (23.3)	28 (87.5)	15 (9.8)

Table 2. Comparison of the preoperative and demographic characteristics of the patients grouped according to the cut-off value of POD 1 drain amylase

		POD 1 Drain Amylase Cut-Off Value		
	All Patients (n= 185), %	**<1883 U/mL (n= 144)**	**≥1883 U/mL (n= 41)**	**p**
Age, year ≥65 <65	 69 (37.3) 116 (62.7)	 56 (38.9) 88 (61.1)	 13 (31.7) 28 (68.3)	0.402
Age, year, mean ± SD	60.0 ± 11.3	60.7 ± 11.3	57.5 ± 11.0	0.082
Sex Male Female	 104 (56.2) 81 (43.8)	 84 (58.3) 60 (41.7)	 20 (48.8) 21 (51.2)	0.359
BMI, m^2/kg	26.3 ± 17.8	27.8 ± 11.3	27.4 ± 3.4	**0.050**
ASA score I/II III/IV	 115 (62.2) 70 (37.8)	 87 (60.4) 57 (39.6)	 28 (68.3) 13 (31.7)	0.359
Comorbidity Yes No	 86 (46.5) 99 (53.5)	 76 (52.8) 68 (47.2)	 23 (56.1) 18 (43.9)	0.707
Pathologic Diagnosis Benign Malign	 34 (18.4) 151 (81.6)	 117 (81.3) 27 (18.8)	 34 (82.9) 7 (17.1)	0.807
Tumor Location Pancreas head Distal choledoch Ampulla tm Duodenal tm	 121 (65.4) 20 (10.8) 35 (18.9) 9 (4.9)	 99 (68.8) 25 (17.4) 14 (9.7) 6 (4.2)	 22 (53.7) 10 (24.4) 6 (14.6) 3 (7.3)	0.277

Table 3. Comparison of the intraoperative characteristics of the patients grouped according to the cut-off value of POD 1 drain amylase

		POD 1 Drain Amylase Cut-Off Value		
	All Patients (n= 185), %	**<1883 U/mL (n= 144), %**	**≥1883 U/mL (n= 41), %**	**p**
Pancreas Texture Soft Hard	 86 (46.5) 99 (53.5)	 58 (40.3) 86 (59.7)	 28 (68.3) 13 (31.7)	**0.002**
PJ Anastomosis Type Blumgart Dunking	 144 (77.8) 41 (22.2)	 127 (88.2) 17 (11.8)	 31 (75.6) 8 (24.4)	**0.017**
Vascular Resection Yes No	 16 (8.6) 169 (91.4)	 14 (9.7) 130 (90.3)	 2 (4.9) 39 (95.1)	0.330
Internal Stent No Yes	 156 (84.3) 29 (15.7)	 123 (85.4) 21 (14.6)	 33 (80.5) 8 (19.5)	0.444
PD Diameter, mm ≥4 <4	 123 (66.5) 62 (33.5)	 106 (73.6) 38 (26.4)	 17 (41.5) 24 (58.5)	**<0.001**
Operation Time, min ≥240 <240	 137 (74.1) 48 (25.9)	 106 (73.6) 38 (26.4)	 31 (75.6) 10 (24.4)	0.797
Blood Loss, mL ≥400 <400	 46 (24.9) 139 (25.1)	 33 (22.9) 111 (77.1)	 13 (31.7) 28 (68.3)	0.251
ES Transfusion Yes No	 41 (22.2) 144 (77.8)	 26 (18.1) 118 (81.9)	 15 (36.6) 26 (63.4)	**0.012**

Table 4. Comparison of the postoperative results of the patients grouped according to the cut-off value of POD 1 drain amylase

		POD 1 Drain Amylase Cut-Off Value		
	All Patients (n= 185), %	**<1883 U/mL (n= 144)**	**≥1883 U/mL (n= 41)**	**p**
POPF Yes No	 32 (17.3) 153 (82.7)	 7 (4.9) 137 (95.1)	 25 (61) 16 (39)	**<0.001**
POPF Grade Grade A Grade B Grade C	 19 (10.3) 10 (5.4) 3 (1.6)	 4 (2.8) 2 (1.4) 1 (0.6)	 15 (36.6) 8 (19.5) 2 (4.8)	0.216
DGE Yes No	 53 (28.6) 132 (71.4)	 37 (25.7) 107 (74.3)	 16 (39) 25 (61)	0.096
Bile Leakage Yes No	 6 (3.2) 179 (96.8)	 5 (3.5) 139 (96.5)	 1 (2.4) 40 (97.6)	0.742
Intraabd. Abses/Collection Yes No	 16 (8.6) 169 (91.4)	 12 (8.3) 132 (91.7)	 4 (9.8) 37 (90.2)	0.775
Intraabd. Haemoragia Yes No	 13 (7) 172 (93)	 9 (6.3) 135 (93.8)	 4 (9.8) 37 (90.2)	0.438
Other Complications Yes No	 11 (5.9) 174 (94.1)	 8 (5.6) 136 (94.4)	 3 (7.3) 38 (92.7)	0.674
LOH, day, median (range)	10 (5-96)	9.5 (5-96)	11 (5-55)	0.141
Morbidity Yes No	 81 (44.3) 104 (55.7)	 50 (34.7) 94 (65.3)	 32 (78) 9 (22)	**<0.001**

POD: Postoperative day, PD: Pancreaticoduodenectomy, POPF: Postoperative pancreatic fistula, DGE: Delayed gastric emptying, LOH: Length of hospital stay.

Table 5. Multivariate analysis of the predictors of POPF after PD

Variables	**n, %**	**OR (95% CI)**	**p**
Pancreatic Texture, Soft	86 (46.5)	3.689 (1.048-12.987)	**0.045**
Duct Diameter, <4 mm	62 (33.5)	3.732 (1.333-10.447)	**0.012**
Blood Transfusion, yes	41 (22.2)	0.488 (0.161-1.480)	0.205
POD 1 Amylase, ≥1883 U/mL	41 (22.2)	22.244 (7.930-62.396)	**<0.001**
POD 3 Amylase, ≥504 U/mL	46 (24.9)	4.802 (1.155-19.962)	**0.031**
POD 5 Amylase, ≥98 U/mL	43 (23.2)	22.468 (5.246-96.226)	**<0.001**

OR: Odds ratio, POD: Postoperative day, PD: Pancreaticoduodenectomy.

In our study, the cut-off value of postoperative day one drain fluid amylase level (1883 U/L) had 78.6% sensitivity, 89.5% specificity, and 87.5% accuracy rates for predicting POPF. A common point of the studies investigating this issue is that drain fluid amylase is very valuable in predicting the clinically relevant POPF on the POD1. However, in almost all studies, there is no consensus on what the cut-off value should be. When the cut-off value is 2365 U/L, 78% sensitivity, 80% specificity, 66% PPV, and 88% NPV have been reported (23). In another study, when the cut-off value was accepted as 350 U/L, the authors reported 79% specificity, 100% sensitivity, 41% PPV, and 100% NPV. Similarly, studies have reported that the cut-off values 4000 U/L and 5000 U/L are optimal for predicting the POPF (24,25). Our results are consistent with these trials, and we recommend that POD1 drain fluid amylase levels can be used in identifying high-risk patients to predict pancreatic fistula after PD.

Table 6. Predicted versus actual fistula formulation

		Actual		
		Fistula	**No-Fistula**	**Total**
Predicted	Fistula	25	16	41
	No-Fistula	7	137	144
	Total	32	153	185

Cut-off value 1883 U/L to maximize sensitivity (78.1%) and specificity (89.5%). Positive predictive value (PPV) 60.9%. Negative predictive value (NPV) 95.1%. False positive (FP) 21.9%. False negative (FN) 10.5%. accuracy 87.5%.

Yang Ji et al. reported that eight studies included in their meta-analysis provided published evidence indicating the predictive value of POD1 drain fluid amylase for developing POPF. Ansorge et al. investigated several clinical parameters for their predictive values for estimating the development of POPF and concluded that a POD1 drain fluid amylase level of 1322 U/L was the most clinically relevant parameter for predicting POPF (20).

Similarly, several studies have researched the significance of drain amylase levels for predicting POPF (8,11,26). El Nakeeb et al. investigated risk factors for POPF and recommended that a 1000 U/L cut-off value is best for predicting a clinically relevant pancreatic fistula (11). Facy et al. evaluated the levels of both lipase and amylase in the drain fluid in predicting POPF and found that the 500 U/L cut-off value of drain fluid amylase level was a good indicator for clinically relevant POPF (8). Kawai et al. retrospectively analyzed 1239 patients undergoing PD and demonstrated that a POD1 drain fluid amylase >4000 IU/L could predict POPF, based on a ROC curve analysis (18). The authors reported that this cut-off point was associated with a sensitivity of 62.2%, specificity of 89%, and accuracy of 84.8%. Another study reported that higher than 5000 U/L POD1 drain fluid amylase level is a significant predictive factor for POPF following distal pancreatectomy and PD (18). Similarly, another study reported that POD1 drain fluid amylase level higher than 5000 U/L is the best predictive marker for POPF, and they reported a sensitivity of 93% for PD and 100% for distal pancreatectomy (27). In another study that investigated whether POD1 drain fluid amylase could be used to estimate POPF following pancreatectomy, the authors reported that a low cut-off level of 100 U/L was associated with high sensitivity and NPV. Therefore, they recommended that early drain removal would be safe when drain amylase is lower than 100 U/L on the first postoperative day (19).

In our opinion, the wide range of proposed cut-off values depends on whether the drain amylase value is used to determine pancreatic fistula or patients who will not have a fistula. High cut-off values accurately predict those patients that will have a fistula, and low cut-off values predict those patients who will not have a fistula. Small differences in NPV for each cut-off value indicate that clinically relevant consequences of early drain removal should be reviewed from various aspects for the purposes of guiding management, rather than defining one POD1 drain amylase value as a cut-off. Therefore, the cut-off value may be different for each clinic.

In our opinion, it is important to determine the fistula or the patients who do not have a fistula. We believe that the cut-off value should then be determined according to the patient's fistula status. The comfort level of the surgeon should also be determined in selecting the cut-off point based on the small differences in NPV.

CONCLUSION

The cut-off point of POD1 drain fluid amylase level (1883 U/L) can help predict the clinically relevant POPF with adequate sensitivity and specificity rates in patients undergoing pancreatic resection. Multi-center, high-volume trials are now required to further investigate these findings.

Ethics Committee Approval: This study was approved by Gazi University Clinical Research Ethics Committee (Decision no: 425 Date: 06.07.2020).

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REFERENCES

1. *Poon RT, Fan ST, Lo CM, Ng KK, Yuen WK, Yeung C, et al. External drainage of pancreatic duct with a stent to reduce leakage rate of pancreaticojejunostomy after pancreaticoduodenectomy: A prospective randomized trial. Ann Surg 2007; 246: 425-33. https://doi.org/10.1097/SLA.0b013e3181492c28*
2. *de Castro SM, Busch OR, van Gulik TM, Obertop H, Gouma DJ. Incidence and management of pancreatic leakage after pancreatoduodenectomy. Br J Surg 2005; 92(9): 1117-23. https://doi.org/10.1002/bjs.5047*

3. *Nakanishi K, Kanda M, Sakamoto J, Kodera Y. Is the measurement of drain amylase content useful for predicting pancreas-related complications after gastrectomy with systematic lymphadenectomy? World J Gastroenterol 2020; 26(14): 1594-600. https://doi.org/10.3748/wjg.v26.i14.1594*
4. *Diener MK, Tadjalli-Mehr K, Wente MN, Kieser M, Büchler MW, Seiler CM. Risk-benefit assessment of closed intra-abdominal drains after pancreatic surgery: A systematic review and meta-analysis assessing the current state of evidence. Langenbecks Arch Surg 2011; 396: 41-52. https://doi.org/10.1007/s00423-010-0716-0*
5. *Bassi C, Molinari E, Malleo G, Crippa S, Butturini G, Salvia R, et al. Early versus late drain removal after standard pancreatic resections: Results of a prospective randomized trial. Ann Surg 2010; 252: 207-14. https://doi.org/10.1097/SLA.0b013e3181e61e88*
6. *Fisher WE, Hodges SE, Silberfein EJ, Artinyan A, Ahern CH, Jo E, et al. Pancreatic resection without routine intraperitoneal drainage. HPB (Oxford) 2011; 13: 503-10. https://doi.org/10.1111/j.1477-2574.2011.00331.x*
7. *Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R, et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: Prospective study for 104 consecutive patients. Ann Surg 2006; 244: 1-7. https://doi.org/10.1097/01.sla.0000218077.14035.a6*
8. *Facy O, Chalumeau C, Poussier M, Binquet C, Rat P, Ortega-Deballon P. Diagnosis of postoperative pancreatic fistula. Br J Surg 2012; 99: 1072-5. https://doi.org/10.1002/bjs.8774*
9. *Nissen NN, Menon VG, Puri V, Annamalai A, Boland B. A simple algorithm for drain management after pancreaticoduodenectomy. Am Surg 2012; 78: 1143-6. https://doi.org/10.1177/000313481207801029*
10. *Sutcliffe RP, Battula N, Haque A, Ali A, Srinivasan P, Atkinson SW, et al. Utility of drain fluid amylase measurement on the first postoperative day after pancreaticoduodenectomy. World J Surg 2012; 36: 879-83. https://doi.org/10.1007/s00268-012-1460-0*
11. *El Nakeeb A, Salah T, Sultan A, El Hemaly M, Askr W, Ezzat H, et al. Pancreatic anastomotic leakage after pancreaticoduodenectomy. Risk factors, clinical predictors, and management (single center experience). World J Surg 2013; 37: 1405-18. https://doi.org/10.1007/s00268-013-1998-5*
12. *Tsujie M, Nakamori S, Miyamoto A, Yasui M, Ikenaga M, Hirao M, et al. Risk factors of pancreatic fistula after pancreaticoduodenectomy: patients with low drain amylase level on postoperative day 1 are safe from developing pancreatic fistula. Hepatogastroenterology 2012; 59: 2657-60. https://doi.org/10.5754/hge12098*
13. *Warshaw AL, Thayer SP. Pancreaticoduodenectomy. J Gastrointest Surg 2004; 8: 733-41. https://doi.org/10.1016/j.gassur.2004.03.005*
14. *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: 584-91. https://doi.org/10.1016/j.surg.2016.11.014*
15. *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: 205-13. https://doi.org/10.1097/01.sla.0000133083.54934.ae*
16. *Yang J, Huang Q, Wang C. Postoperative drain amylase predicts pancreatic fistula in pancreatic surgery: A systematic review and meta-analysis. Int J Surg 2015; 22: 38-45. https://doi.org/10.1016/j.ijsu.2015.07.007*
17. *Molinari E, Bassi C, Salvia R, Butturini G, Crippa S, Talamini G, et al. Amylase value in drains after pancreatic resection as predictive factor of postoperative pancreatic fistula: Results of a prospective study in 137 patients. Ann Surg 2007; 246(2): 281-7. https://doi.org/10.1097/SLA.0b013e3180caa42f*
18. *Kawai M, Kondo S, Yamaue H, Wada K, Sano K, Motoi F, et al. Predictive risk factors for clinically relevant pancreatic fistula analyzed in 1,239 patients with pancreaticoduodenectomy: Multicenter data collection as a project study of pancreatic surgery by the Japanese Society of Hepato-Biliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2011; 18: 601-8. https://doi.org/10.1007/s00534-011-0373-x*
19. *Israel JS, Rettammel RJ, Leverson GE, Hanks LR, Cho CS, Winslow ER, et al. Does postoperative drain amylase predict pancreatic fistula after pancreatectomy? J Am Coll Surg 2014; 18: 978-87. https://doi.org/10.1016/j.jamcollsurg.2014.01.048*
20. *Ansorge C, Nordin JZ, Lundell L, Strömmer L, Rangelova E, Blomberg J, et al. Diagnostic value of abdominal drainage in individual risk assessment of pancreatic fistula following pancreaticoduodenectomy. Br J Surg 2014: 10(2): 100-8. https://doi.org/10.1002/bjs.9362*
21. *Hiyoshi M, Chijiiwa K, Fujii Y, Imamura N, Nagano M, Ohuchida J. Usefulness of drain amylase, serum C-reactive protein levels and body temperature to predict postoperative pancreatic fistula after pancreaticoduodenectomy. World J Surg 2013; 37: 2436-42. https://doi.org/10.1007/s00268-013-2149-8*
22. *Noji T, Nakamura T, Ambo Y, Suzuki O, Nakamura F, Kishida A, et al. Clinically relevant pancreas-related infectious complication after pancreaticoenteral anastomosis could be predicted by the parameters obtained on postoperative day 3. Pancreas 2012; 41: 916-21. https://doi.org/10.1097/MPA.0b013e31823e7705*
23. *Jin S, Shi XJ, Wang SY, Zhang P, Lv GY, Du XH, et al. Drainage fluid and serum amylase levels accurately predict development of postoperative pancreatic fistula. World J Gastroenterol 2017; 23(34): 6357-64. https://doi.org/10.3748/wjg.v23.i34.6357*
24. *Popiela T, Kedra B, Sierzega M, Gurda A. Risk factors of pancreatic fistula following pancreaticoduodenectomy for periampullary cancer. Hepatogastroenterology 2004; 51: 1484-8.*
25. *Kawai M, Tani M, Hirono S, Ina S, Miyazawa M, Yamaue H. How do we predict the clinically relevant pancreatic fistula after pancreaticoduodenectomy?--an analysis in 244 consecutive patients. World J Surg 2009; 33: 2670-8. https://doi.org/10.1007/s00268-009-0220-2*
26. *Conlon KC, Labow D, Leung D, Smith A, Jarnagin W, Coit DG, et al. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. Ann Surg 2001; 234: 487-93. https://doi.org/10.1097/00000658-200110000-00008*
27. *Partelli S, Tamburrino D, Crippa S, Facci E, Zardini C, Falconi M. Evaluation of a predictive model for pancreatic fistula based on amylase value in drains after pancreatic resection, Am J Surg 2014; 208: 634-9. https://doi.org/10.1016/j.amjsurg.2014.03.011*

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Pankreas rezeksiyonu sonrası postoperatif birinci günde dren sıvısı amilaz düzeyinin postoperatif pankreatik fistülü öngörmedeki değeri

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, pankreatikoduodenektomi (PD) sonrası pankreatik fistül oluşumunu öngörmede ameliyat sonrası ilk gün (POD1) drenaj sıvısı amilazının öngörücü değerini değerlendirmektir.

Gereç ve Yöntem: Nisan 2014 ile Nisan 2018 tarihleri arasında PD geçiren 185 hasta retrospektif olarak incelendi. Hastalar POD1 drenaj sıvısı amilaz değerlerine göre iki gruba ayrıldı: <1883 U/L (Grup 1) ve ≥1883 U/L (Grup 2). Klinik olarak anlamlı POPF'lu ve POPF'suz gruplar arasındaki farklar değerlendirildi. 1883 U/L drenaj sıvısı amilazı için Pearson korelasyon katsayıları ve alıcı işlem karakteristikleri (ROC) eğrileri hesaplandı.

Bulgular: POPF insidansı %17,2 idi. POD1 amilaz düzeyi postoperatif pankreatik fistülünün (POPF) en güçlü öngörücüsü olmuş, 1883 U/L'den yüksek düzeyler en iyi doğruluğu (%87,5), duyarlılığı (%78,1), özgüllüğü (%89,5), pozitif öngörü değerini (%60,9) ve negatif öngörü değerini (%95,1) göstermiştir. Yüz kırk dört hastanın (%77,8) POD1 drenaj amilaz düzeyi 1883 U/L'den düşüktü ve sadece yedi (%3,7) vakada POPF gelişirken, POD1 drenaj amilaz düzeyi 1883 U/L veya daha yüksek olan hastalarda (n= 41) POPF oranı %31,4'tü [OR: 22,24, %95 CI (7,930-62,396), p< 0,001].

Sonuç: POD1 drenaj sıvısı amilaz düzeyinin (1883 U/L) kesme noktası, pankreas rezeksiyonu yapılan hastalarda klinik olarak ilgili POPF'yi yeterli duyarlılık ve özgüllük oranlarıyla öngörebilir.

Anahtar Kelimeler: Pankreatikoduodenektomi, amilaz, postoperatif komplikasyonlar, pankreas fistülü

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