Postoperative pancreatic fistula: Low preoperative ejection fraction may be another contributing factor

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Original Article

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ABSTRACT

Objective: We investigated if ejection fraction (EF) was a predisposing factor for postoperative pancreatic fistula (POPF) as a perfusion indicator, or not.

Design: This was a retrospective single center study.

Setting: Clinic of Gastroenterology Surgery, Türkiye Yüksek İhtisas Training and Research Hospital, Ankara, Turkey

Subjects: A total of 77 patients who underwent pancreaticoduodenectomy

Intervention: EF values were divided into 3 groups with demographic similarity as 40-49, 50-59, and 60 and above. Investigated relationship between EF and POPF.

Main outcome measures: Preoperative EF, albumin, bilirubin, hemoglobin, CRP, WBC, neutrophil, lymphocyte, AST, ALT, GGT, CEA, CA19-9 values; intraoperative data such as operation types, ductus diameter in pancreas after resection, the presence of porta resection; postoperative pathology results, fistula grades, 1st and 3rd days drain and blood amylases were retrospectively recorded.

Results: EF value was found to be between 40-49 in 10 (13%) patients, between 50-59 in 37 (48%) patients, and 60 or above in 30 (39%) patients. EF values of cases with leakage were found to be statistically significantly lower than the cases without leakage ($p<0.05$). In case of leakage, optimal cut-off value was calculated as ≤52.

Conclusion: EF values of cases with leakage in pancreas fistulas were found to be statistically significantly lower than the cases without leakage ($p<0.05$). Cut-off value was found as 52 (AUC, with 93% interval of confidence). EF value below 52 in patients underwent pancreaticoduodenectomy, statistically increases pancreatic fistulas.

KEY WORDS: ejection fraction, postoperative pancreatic fistula, pancreaticoduodenectomy

INTRODUCTION

Pancreaticoduodenectomy (PD) is a standard treatment method for many benign and malign diseases in pancreas head and in the periampullary region. PD associated mortality has decreased below 5% in recent years. Despite such a decrease in mortality, morbidity remains close to 50%[1-2].

Pancreaticojejunostomy is the Achilles heel of this procedure. Any problem at this point causes POPF, which increases hospital stay, cost, morbidity and mortality[3]. Many factors such as age, gender, pancreatic duct diameter, operation time, anastomosis techniques, structure of the remaining pancreas, presence of pancreatic stent, hepatitis, intraoperative blood loss and perfusion disorders were searched as predisposing factors in pancreatic fistula, developing by the deterioration of Achilles heel[4-6]. However, there is no particular test that can preoperatively measure the perfusion capacity of the tissue. In our study, we sought the answer to the question whether ejection fraction (EF), representing the ratio of the blood pumped from ventricle to the amount of blood remaining in the ventricle at the end of diastole, could be used as a preoperative indicator for anastomotic leakage or not.

SUBJECTS AND METHOD

Patients

A total of 390 PD cases operated between 2014-2018 in Türkiye Yüksek Ihtisas Training and Research Hospital Gastroenterology Surgery Clinic were analysed in electronic environment. Seventy-seven patients on whom preoperative echocardiography (ECO) was performed and who had their EF values recorded were included in the study.

Data collection

Preoperative EF, albumin, bilirubin, hemoglobin, CRP, WBC, neutrophil, lymphocyte, AST, ALT, GGT, CEA, CA19-9 values; intraoperative operation types, ductus diameter in the remaining pancreas, presence of major vein resection; postoperative pathology results, fistula grades, 1st and 3rd days drain and blood amylases were retrospectively recorded. EF values were divided into 3 groups with demographic similarity as 40-49, 50-59, and 60 and above.

Peroperative management

Decision of operation for preoperative patients were made by a council of physicians composed of gastroenterologists, gastroenterology surgeons, medical oncologists, radiation oncologists, radiologists and pathologists. The patients with distant metastases were directed to medical oncology. Prophylactic antibiotherapy was administered to all intraoperative patients (1gr, cefazolin sodium, generic drug, Turkey). All patients underwent PD were implanted internal stents, and generally duct-to-mucosa technique was performed in pancreaticojejunostomy anastomosis (PJ), with 12 mm synthetic monofilament absorbable 5-0 (maxon, covidien, USA). If end-to-end anastomis is not suitable after port resection in patients with portal invasion, either iliac arter Y-graft or falciform patch from cadaver was used in our clinic where liver transplantation is also accomplished. Falciform patch was preferably used in lateral port resection operations, while in resections greater than 4 cm, first choice was artery graft from cadaver. Vein graft was preferred when there was no artery graft available. Ductal diameter and pancreatic consistency were noted. Routine drainage was placed in all patients. Drain amylase content was checked in postoperative 1st and 3rd days, and in case it was 3 fold higher than blood amylase, then it was evaluated as significant for fistula. In patients who had fistula, Sandostatin was used, but it was not used routinely. Drains were removed when drainage decreased below <50 ml in 24 hours. In cases where percutaneous drain was required, it was placed by interventional radiology. Discharged patients were called to control at 1st week, 1st month, 3rd month, 6th month and 12th month, and every 6 months at the 2nd and the following years.

Statistical analysis

Statistical analysis of the data was performed by IBM SPSS Statics Version 24 package software. Pearson Chi-Square, Fisher's Exact test and Chi-square trend analysis were used for comparing categorical variables between groups, while Mann Whitney U statistical analyses were used for comparing continuous variables between groups. Cut-off value of EF results was calculated by ROC analysis, in case of leakage. $P<0.05$ was considered as statistically significant.

This research did not receive any specific grant from funding agencies in the public, commercial. The study was performed in compliance with the Declaration of Helsinki. We confirm that all patient identifiers have been removed or disguised so that the patients described are not identifiable and cannot be identified through the details of the script.

RESULTS

As for gender, 45 of the patients were male and 32 were female. Median age was 77 years. Leakage was observed in 36 (46%) patients, out of which, 23% were found as grade A, 18% as grade B and 5% as grade C. Major vascular revision was performed in six (7.8%) patients, porta repair in three patients, superior mezenteric ven (SMV) resection in two patients, and graft repair between hepatic artery and aorta by arter graft in one patient. We preferred Wirsung jejunostomy in 63 patients (81.8%), pancreaticojejunostomy (PJ) in 11 patients (14.3%) and dunkıng in 3 (3.9%) patients.

The most preferred choice was Wirsung jejunostomy (WJ) anastomosis, and most frequently observed case was adenocarcinoma in pathology results. EF value was between 40-49 in 10 (13%) patients, between 50-59 in 37 (48%) patients and 60 and above in 30 (39%) patients. EF values of the cases with leakage were found to be statistically significantly lower than that of the cases without leakage ($p<0.05$). Also 1st and 3rd days drain and serum amylases values of the cases with leakage were statistically significantly higher than those of the cases without leakage ($p<0.05$). Ductal diameters of the cases with leakage were significantly smaller than those of the cases without leakage ($p<0.05$). ASA scores of the cases with leakage were found to be significantly higher than those of the cases without leakage ($p<0.05$). Pancreatic consistency of the cases with leakage were significantly softer than the cases without leakage (Table 1). In the subgroup analysis, and when the distribution of pathology results and EF were analysed with respect to leakage types, statistically significant difference was not found between groups ($p>0.05$) (Table 2).

Statistically significant difference was not determined between groups in grade B and grade C cases with regard to EF groups ($p>0.05$)(Table 3).

Optimal cut off value in the presence of leakage was found as ≤52. Accordingly, area under curve (AUC) value was calculated as 93.3% and this value was found to be statistically significant ($p<0.001$). (Table 4).

DISCUSSION

Disruption of pancreaticojejunostomy anastomosis, known as the Achilles heel of whipple operation, causes post operative pancreatic fistula (POPF). The factors leading to POPF were found in our study as ASA score, pancreatic consistency, ductal diameter, as well as ejection fraction (EF) which is particular to our study.

Pancreaticoduodenectomy is the primary treatment method for the tumors at the head of pancreas, at distal of biliary tract and at duodenal ampulla[7,8]. As indicated in the studies in the literature, the rate of pancreatic fistula that develops after PD varies between 11.4% and 64.3%[9]. POPF is a risk factor for delayed gastric emptying, sepsis and post operative bleeding[10-12].

International Study Group for Postoperative Pancreatic Fistula (ISGPF) was established in 2005 under the leadership of Claudio Bassi[13] from Verona University Surgical Gastroenterology Department. ISGPF defined POPF biochemically as amylase value in drains determined as 3 times higher than blood amylase in any measurement from postoperative 3rd day on. Also, they indicated that abdominal pain, distension, delay in gastric emptying, fever (>38 ºC), CRP increase, and leucocyte increase (>10.000 cells/mm^3) can be observed clinically.

Pancreatic fistula is divided into 3 groups as grade A, grade B and grade C. Grade A fistula: It represents the most frequently observed fistula group, also known as “transient fistula’’, which doesn’t reveal any finding clinically. It is only defined biochemically as a fistula. It doesn’t increase hospital stay and therapy costs. Grade B fistula: Pancreatic fluid is observed in abdominal tomography and this particularly requires drainage. Abdominal pain and fever may accompany. Antibiotic and sandostatin may be needed. It increases hospital stay and the cost. Grade C Fistula: Sepsis and organ dysfunction may accompany. Re-operation may be needed. The risk of mortality is high.

After 11 years, again Bassi *et al* updated the grading in 2016. The term biochemical leak (BL) was used instead of Grade A, and the gray area between grade B and Grade C was clarified[14].

Van Berge Henegouwen *et al*[5] related the small size of pancreatic duct and ampullary carcinoma with POPF. In our study, ampullary carcinoma was not found as a risk factor (p=0.96), while the ductal diameter of small size was found to be a significant risk factor (p<0.01).

It was highlighted in many studies that the hardness of the remaining pancreatic tissue was advantageous for the fistula. Because it was thought that, the more hard the tissue was, the easier it was to suture without laser[3]. In our study too, the hardness of the pancreatic tissue was found to be a significant risk factor in the development of pancreatic fistula (p<0.01).

Velu *et al* found that postoperative 0th day serum amylase value >130 IU/L was a risk factor for POPF[15]. In our study, 1st and 3rd day drain amylase and serum amylase values were found to be significant for POPF. As regards the ratio of drain amylase over serum amylase, however, only 3rd day was found to be significant (p<0.01)(Table 1).

Dengl *et al* however, showed that fibrosis below <%25, pancreatic channel <3mm, and BMI >25 were prognostic factors[16]. Kawai *et al* found male gender as a risk factor in a retrospective study investigating 1239 patients[17]. The other risk factors such as Carkopenia and visceral obesity and post operative 1st day drain amylase were found to be independent risk factors for POPF[18,19].

No effect of octreotide use could be shown to decrease POPF, in the randomized controlled studies[20]. We also used octreotide in POPF patients, however we didn’t observe any statistically significant remission.

Cohort studies showed that excessively delivered intravenous fluids increased POPF risk[21]. In patients with fluid limitation by means of hypertonic saline, hospital stay and mortality decreased too, along with POPF[22]. We used saline in our cases and did not perform any fluid limitation.

Anastomosis techniques: Pancreatogastrostomy (PG) was thought to decrease POPF, since there was no enterokinase to activate trypsin at gastric epithelium and pancreas enzymes could not be activated in stomach acid. A multicenter prospective randomized study comparing PG and PJ was conducted with

440 patients and no statistically significant difference was observed (20%-22%, p:0.617)[23]. PJ techniques were compared within themselves as duct-to-mucosa versus invagination. No significant difference regarding POPF was determined between these two techniques, in two randomized controlled studies (RCT)[24,25]. Only, it was shown in the subgroup analysis in one of the studies that invagination was more advantageous in soft pancreas (10%-42%, p=0.010)[24]. We also used invagination technique of PG in our study with smaller size ductal diameter, but used WJ in cases with ductal diameter greater than 5mm. However, we couldn't find any signficant difference regarding POPF.

In their study with 522 high risk patients, Ecker *et al* observed that POPF risk decreased with external stent and increased with internal stent (external 15.2%, internal 43.8%, no stent 33.8%, p<001)[26]. We routinely used internal stent in our patients.

In 2016 PANDRA study, 395 patients were included and they were divided into two groups as the ones who were inserted intraoperative drain and those not. In the group without drain, POPF speed (5.9% vs 11.9%, p=0.030) and fistula related complications (13.0% vs 26.4%, p=0.0008) were found to be less[27]. However in multivariable analyses, it was noticed that the majority of the patients without drain had neoadjuvant therapy, and used somatostatin analogs. Hence, drain was not assessed as an independent risk factor in POPF development. We used drains routinely in all our patients.

Another important factor providing integrity of anastomosis is the perfusion of the tissues. Tissues with poor perfusion develop ischemia by time thus disrupt anastomosis. In our study we hypothesized that EF, which represents the ratio of the blood pumped out from the left ventricle to the amount of blood remaining in the ventricle at the end of diastole, could be used as an indicator for preoperative perfusion. In this sense, our study is a first in the literature. (Any similar publication was not seen in PUBMED search).

Ejection fraction is the rate of pumping of the left ventricle wall. As of today, reliable measurements can be accomplished by three-dimensional echocardiography (3DE)[28]. It is the numerical value of the pumping power of the heart. Therefore, it can be an indicator for blood perfusion of pancreas and jejunum.

We determined that EF is an effective risk factor in determining the risk of leakage, like the other factors such as ductal diameter, pancreatic consistency and ASA score (Table 1, p<0.001). We found optimal cut-off value as ≤52 in case of leakage. Accordingly we calculated AUC value as 93.3% and this AUC value was assessed statistically significant (p<0.001) (Table-4). When EF was divided into 3 groups as 40-49, 50-59 and 60 and above then compared with grade A, B and C fistulas, we couldn't find any significant relationship (Table 2, p=0.152).

CONCLUSION

In conclusion, EF is a predisposing factor in POPF (p<0.05). Cut-off value was found as 52 (AUC, with interval of confidence of 93%). EF value below 52 statistically increases pancreatic fistula, in patients underwent pancreaticoduodenectomy. In such an operation having so high mortality and morbidity, preoperative EF measurement should be taken into acccount.

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Author Contribution:

Concept - M.A.Ü., E.B.B.; Design - M.A.Ü, Y.M.Ö.; Supervision – E.A., E.P.; Resources - EEŞ., O.A.; Materials – E.E.Ş., M.A.Ü; Data Collection and/or Processing – M.A.Ü., E.P.; Analysis and/or Interpretation – M.A.Ü., E.B.B.; Literature Search – E.A., Y.M.Ö.; Writing Manuscript – M.A.Ü., E.B.B.; Critical Review - M.A.Ü., E.B.B.

REFERENCES

1. Bassi C, Massimo F, Salvia R, *et al.* Management of complications after pancreticoduodenectomy in a high volume center: results on 150 consecutive patients. Dig Surg 2001; 18:453-458.

2. Gouma DJ, van Geenen RC, van Gulik TM, *et al*. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. Ann Surg 2000; 232:786-795.

3. Liang TB, Bai XL, Zheng SS. Pancreatic Fistula after Pancreaticoduodenectomy: Diagnosed according to International Study Group Pancreatic Fistula (ISGPF) Definition. Pancreatology 2007; 7:325-331.

4. Hosotani R, Doi R, Imamura M. Duct-tomucosa pancreaticojejunostomy reduces the risk of pancreatic leakage after pancreatoduodenectomy. World J Surg 2002; 26:99-104.

5. Van Berge Henegouwen MI, De Wit LT, Van Gulik TM, Obertop H, Gouma DJ Incidence, risk factors, and treatment of pancreatic leakage after pancreaticoduodenectomy: drainage versus resection of the pancreatic remnant. J Am Coll Surg 1997; 185:18-25.

6. Yang YM, Tian XD, Zhuang Y, *et al*. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 2005; 11:2456-2461.

7. Brown EG, Yang A, Canter RJ, Bold RJ. Outcomes of pancreaticoduodenectomy: where should we focus our efforts on improving outcomes? JAMA Surg 2014; 149:694-699 .

8. Yamashita Y, Shirabe K, Tsujita E, *et al*. Surgical outcomes of pancreaticoduodenectomy for periampullary tumors in elderly patients. Langenbecks Arch Surg 2013; 398:539-545.

9. Hu BY, Wan T, Zhang WZ, Dong JH. Risk factors for postoperative pancreatic fistula: Analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 2016; 22(34):7797-7805.

10. Reid-Lombardo KM, Farnell MB, Crippa S, *et al*. Pancreatic anastomotic leakage after pancreaticoduodenectomy in 1,507 patients: a report from the Pancreatic Anastomotic Leak Study Group. J Gastrointest Surg 2007; 11:1451-1458.

11. Lermite E, Pessaux P, Brehant O, *et al*. Risk factors of pancreatic fistula and delayed gastric emptying after pancreaticoduodenectomy with pancreaticogastrostomy. J Am Coll Surg 2007; 204:588-596.

12. Schmidt CM, Choi J, Powell ES, *et al*. Pancreatic fistula following pancreaticoduodenectomy: clinical predictors and patient outcomes. HPB Surgery, Volume 2009, Article ID 404520, 8 pages http://dx.doi.org/10.1155/2009/404520.

13. Bassi C, Dervenis C, Butturini G, *et al*. For the International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: An international study group (ISGPF) definition. Surgery 2005;138:8-13.

14. Bassi C, Marchegiani G, Dervenis C, *et al*. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 2017; 161:584-59.

15. Velu LKP, Chandrabalan VV, Jabbar S, *et al*. Serum amylase on the night of surgery predicts clinically significant pancreatic fistula after pancreaticoduodenectomy. HPB 2014; 16:610-619.

16. Deng Y, Zhao B, Yang M , Li , Zhang L. association between the ıncidence of pancreatic fistula after pancreaticoduodenectomy and the degree of pancreatic fibrosis. Journal of Gastrointestinal Surgery 2018; 22:438-443.

17. Kawai M, Kondo S, Yamaue H, *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 HepatoBiliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2011; 18:601-608 .

18. Pecorelli N, Carrara G, De Cobelli F, *et al*. Effect of sarcopenia and visceral obesity on mortality and pancreatic fistula following pancreatic cancer surgery. BJS 2016; 103:434-442.

19. Liu Y ,Li Y,Wang L, MMb, Peng CJ. Predictive value of drain pancreatic amylase concentration for postoperative pancreatic fistula on postoperative day 1 after pancreatic resection. An updated meta-analysis. Medicine 2018; 97:38.

20. Yeo CJ, Cameron JL, Lillemoe KD, *et al*. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. Ann Surg 2000; 232(3):419-429.

21. Han IW, Kim H, Heo J, *et al*. Excess intraoperative fluid volume administration is associated with pancreatic fistula after pancreaticoduodenectomy: a retrospective multicenter study. Medicine Baltimore 2017; 96(22):6893.

22. Lavu H, Sell NM, Carter TI, *et al*. The HYSLAR trial: a prospective randomized controlled trial of the use of a restrictive fluid regimen with 3% hypertonic saline versus lactated Ringers in patients undergoing pancreaticoduodenectomy. Ann Surg 2014; 260(3):445-453.

23. Keck T, Wellner UF, Bahra M, *et al*. Pancreatogastrostomy versus pancreatojejunostomy for RECOnstruction after PANCreatoduodenectomy (RECOPANC, DRKS 00000767): perioperative and longterm results of a multicenter randomized controlled trial. Ann Surg 2016;263(3):440-449.

24. Senda Y, Shimizu Y, Natsume S, *et al*. Randomized clinical trial of duct-to-mucosa versus invagination pancreaticojejunostomy after pancreatoduodenectomy. Br J Surg 2018; 105(1):48-57.

25. Singh AN, Pal S, Mangla V, *et al*. Pancreaticojejunostomy: does the technique matter? A randomized trial. J Surg Oncol 2018; 117(3):389-396.

26. Ecker BL, McMillan MT, Asbun HJ, *et al*. Characterization and optimal management of high-risk pancreatic anastomoses during pancreatoduodenectomy. Ann Surg 2018; 267(4):608-616.

27. Witzigmann H, Diener MK, Kienkotter S, *et al*. No need for routine drainage after pancreatic head resection: the dual-center, randomized, controlled PANDRA trial (ISRCTN04937707). Ann Surg 2016; 264(3):528-537.

28. Wu VCC, Kitano T, Nabeshimal Y, *et al*. Optimal threshold of three-dimensional echocardiographic fully automated software for quantification of left ventricular volumes and ejection fraction: Comparison with cardiac magnetic resonance disk-area summation method and feature tracking method. PLOS ONE 2019.(January 28, 2019, at https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0211154).

Table 1: General features of fistula/non fistula cases

General Features	Non fistula cases	Fistula cases	Z	p
	Median (Min.-Max.)	Median (Min.-Max.)		
EF	65 (40-70)	50 (40-62)	-6.716	***<0.001***
Drain amylase 1 (U/L)	151 (13-54000)	1521.5 (13-63000)	-3.696	***<0.001***
Blood amylase 1(U/L)	62 (13-933)	291.5 (12-3246)	-3.870	***<0.001***
Drain amylase1 / blood amylase rate	1.88 (0.18-819.49)	5.5 (0.17-238.64)	-1.634	0.102
Drain amylase 3(U/L)	34.5 (1.77-20000)	486 (4-6729)	-4.832	***<0.001***
Blood amylase 3(U/L)	22 (6-300)	49 (6-227)	-3.326	***0.001***
Drain amylase 3 /blood amylase 3 rate	1.33 (0.15-194.17)	5.95 (0.35-129.4)	-3.993	***<0.001***
Ductal diameter (mm)	6 (1-12)	2.5 (2-4)	-5.979	***<0.001***
Bilirubin levels(mg/Dl)	2.26 (0.25-33.53)	1.49 (0.3-19)	-0.664	0.507
Albumin (g/L)	3.7 (2.69-4.74)	3.55 (2.2-5)	-0.391	0.696
CRP(mg/L)	9 (0.4-130)	7.08 (0.6-258)	-0.153	0.878
Wbc(x10^3/uL)	7 (4-17.2)	7.8 (4.32-13.3)	-1.205	0.228
Neutrofıl (%)(x10^3/uL)	65 (31.8-90)	63.55 (20.4-79)	-0.730	0.465
Lenfosit(x10^3/uL)	25 (13-50.1)	25.7 (11-73)	-0.944	0.345
Hgb(g/Dl)	12.6 (8.4-16)	12.55 (7.8-15.5)	-1.047	0.295
ASA 1-2	30	10	16.948	***<0.001***
ASA 3-4	10	26		
Pancreatic consistency Hard Middle Soft	 30 8 10	 8 7 21	44.811	***<0.001***
CEA(ng/Ml)	2 (0-16.69)	2.13 (0-104)	-0.155	0.877
Ca-19-9(ng/Ml)	64.35 (0-2016)	33.3 (0-2044)	-0.436	0.663

Mann Whitney U analysis; EF:ejection fraction

Table 2: Distribution of pathology results, EF, presence of comorbid diseases and major vein resection rates with respect to leakage types

General Features		Fistula grade (ABC)						X^2	p
		Grade A		Grade B		Grade C			
		n	%	n	%	n	%		
Pathology	Adenoca	12	66.7	9	64.3	4	100	10.891	0.966
	Pancreatitis	1	5.6	-	-	-	-		
	IPMN	1	5.6	2	14.3	-	-		
	Tubulovillous Adenoma	1	5.6	-	-	-	-		
	NET	-	-	1	7.1	-	-		
	Serous cyst adenoma	2	11.1	1	7.1	-	-		
	GİST	-	-	1	7.1	-	-		
	Groove pancreatitis	1	5.6	-	-	-	-		
Adeno Ca	Others	6	33.3	5	35.7	-	-	1.658	0.531
	Adeno Ca	12	66.7	9	64.3	4	100		
Serous cyst adenoma	Others	16	88.9	13	92.9	4	100	0.544	1.000
	serous cyst adenoma	2	11.1	1	7.1	-	-		
IPMN	Others	17	94.4	12	85.7	4	100	1.080	0.696
	IPMN	1	5.6	2	14.3	-	-		
NET	Others	18	100	13	92.9	4	100	2.104	0.500
	NET	-	-	1	7.1	-	-		
EF	40-49	2	11.1	4	28.6	2	50	2.051	**0.152**
	50-59	16	88.9	9	64.3	2	50		
	60 and over	-	-	1	7.1	-	-		

Fisher's Exact test, Qui-square test for trend analysis.

IPMN: ıntraductal papillary mucinous neoplasia; NET: neuroendocrine tumor; EF: ejection fraction

Table 3: The relationship beween EF Groups and Grade B and Grade C fistulas

EF	Grade B		Grade C		X^2	p
	n	%	n	%		
40-49	4	28.6	2	50.0	1.157	0.681
50-59	9	64.3	2	50.0		
60-70	1	7.1	-	-		

Fisher's Exact test; EF: ejection fraction

Table 4: Results of ROC analysis, executed to determine the cut-off value of EF values in the presence of leakage/ graph