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C-reactive protein postoperative values to predict clinically relevant postoperative pancreatic fistula after distal pancreatectomy

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ABSTRACT

Introduction

Despite significant medical and technological advances, the incidence of Postoperative pancreatic fistula (POPF) after distal pancreatectomy (DP) is reported to be between 3-45%. The main objective of our study was to analyse the early post-surgical risk factors for developing POPF after DP.

Material and methods

A retrospective observational study was conducted on a prospective basis of patients undergoing PD in a tertiary hospital from January 2011 to December 2021. Sociodemographic, preoperative analytical, tumour-related and postoperative complications variables were analysed.

Results

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Of the 52 patients analysed, 71.8% of the sample had postoperative drains amylase elevation; however, 25.7% of the total had Grade-B and/or Grade-C POPF. Univariate logistic regression with the variables studied showed the following as risk factors for B-C o clinically relevant POPF: amylase values in drainage at 5th POD [p=0.097; 1.01 (1-1.01)] preoperative BMI [p=0.015; 1.27 (1.04-1.55)] and CRP value at 3rd POD [p=0.034; 1.01 (1.01-1.02)]. The ROC curve of CRP value at 3rd POD showed an area under the curve 0,764 (CI 95% 0,6-0,93) and the best cut-off point was 190 mg/L (Sensitivity 89% and Specificity 67%).

Conclusions

CRP value at 3rd POD is a predictive factor for POPF after DP. Early detection of patients at risk for POPF based on these characteristics could have an impact on their postoperative management.

Keywords: Pancreatectomy. Distal. CPR. Amylase. Fistula.

INTRODUCTION

Postoperative pancreatic fistula (POPF) is the most frequent and morbid complication following distal pancreatectomy (DP)(1). In fact, despite significant medical and technological advances, most series report an incidence between 3-45%, even in high volume centres(1,2). According to the latest ISGPF classification, POPF grade B or C is defined as an amylase elevation greater than three times the normal draining serum amylase value and which also has a clinical impact on the patient(3).

POPF is known to be a cause of significant postoperative morbidity such as intra-abdominal abscesses, post-surgical sepsis and haemorrhagic events, and it has also been negatively associated with short and long-term survival (3).

Therefore, it is not surprising that many studies have focused on identifying risk factors for developing POPF (4,5). However, most studies are either not specific to DP (small cohorts or large heterogeneity in POPF definitions) (6,7).

Moreover, many of the risk factors described are not modifiable or they are currently under study(8,9). In addition to trying to improve surgical outcomes, another good strategy would be to identify patients at risk of developing POPF early.

Many surgeons frequently leave surgical drains in place after distal pancreatectomy for early identification or even to mitigate the consequences of a POPF. Postoperative amylase values in surgical drains have been attempted to correlate with POPF(10). However, there are no internationally defined values that early predict the development of a clinically relevant POPF(3). In relation to the above, the predictive effect of postoperative C-reactive protein (CRP) on the evolution of POPF has recently been studied. However, virtually all studies are on cephalic duodenopancreatectomy (CDP)(11–13).

The main objective of our study was to analyse the association of CRP and postoperative amylase drainage values as risk factors for developing a clinically relevant POPF after a DP.

METHODS

Study design and participants

A retrospective observational study was conducted on a prospective basis of patients undergoing DP in the biliopancreatic surgery unit at tertiary hospital from January 2011 to December 2021. Central pancreatectomies, total pancreatectomies and patients under 18 years of age were excluded.

Variables

Sociodemographic variables were analysed: sex, age, body mass index in kg/m^2 (BMI), preoperative diabetes diagnosis and ASA classification; preoperative analytical variables: preoperative haemoglobin (mg/dL) and total protein (mg/dL); tumour-related variables: tumour location, preoperative anatomopathological diagnosis; surgical treatment variables: splenectomy, treatment of the pancreatic stump and

postoperative variables: amylase drainage at 3rd postoperative day (POD) in U/L, amylase in drainage at 5th POD (U/L), CRP at 3rd POD (mg/L), blood amylase at 3rd POD (U/L), postoperative complications according to Clavien-Dindo classification(14), as well as 30-day mortality rates.

Definition of postoperative pancreatic fistula

The diagnosis of POPF has been defined according to the modified 2016 International Postoperative Fistula Group classification. POPF was divided into biochemical fistula, Grade-B POPF and Grade-C POPF (3). The treatments for POPF have also been collected. Patients were divided into two groups: clinically relevant POPF (Grade-B and Grade-C) and no POPF.

Postoperative management

A prophylactic single dose of preoperative antibiotic therapy (cefazolin or amoxicillin-clavulanic acid) was administered to all patients 30 minutes before surgery.

No prophylactic antibiotic therapy or drain culture was routinely administered postoperatively. In case of suspected infectious complications, a drain culture as well as an urgent CT scan was requested. Furthermore, empirical broad-spectrum antibiotic therapy was started.

Drain removal was decided on the basis of appearance, outputs (ml) and amylase values in the drain. In case of POPF, the surgical drain was maintained until the POPF was resolved.

Statistical analysis

Categorical parameters were described as frequencies, and continuous variables were expressed as means or medians (depending on the normal distribution of the variables). Continuous variables were tested for normality using the non-parametric

Kolmogorov-Smirnov test. Quantitative variables were described with mean and standard deviation values if the distribution was normal and with median and interquartile range (IQR) in the opposite case. Categorical variables were expressed in absolute numbers and percentages.

For the statistical analysis of quantitative variables, Student's t-test was used. In case of non-normal variables, non-parametric tests were used. For categorical variables, Pearson's chi-square test was applied.

Bivariate analysis was calculated using Spearman ρ correlations. Multivariate logistic regression analysis was performed to identify independent risk factors based on statistically significant variables in bivariate analysis.

A p-value < 0.05 was considered statistically significant and odds ratio (OR) and 95% confidence intervals (95% CI) were calculated for each of the variables included.

To establish cut-off points for postoperative continuous variables as predictors of POPF, they were calculated by ROC curve analysis; in addition, the area under the curve (AUC) and its standard error were calculated. For the selected cut-off points, diagnostic reliability indices were calculated: sensitivity, specificity, positive predictive value and negative predictive value.

Data were analysed using Statistical Package for Social Sciences 23.0 (SPSSTM; SPSS Inc., Chicago, IL, USA).

Ethics committee

All procedures performed with human participants were in accordance with the ethical standards of the research committee and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards and the study was approved by our Drug Research Ethics Committee.

RESULTS

During the study period, 74 partial pancreatectomies were performed in our unit. Of the 74 patients, 22 patients were excluded (3 patients for a partial central pancreatectomy, 2 with a previous history of CPD and 17 patients due to missing data).

The mean age was 62.9±15 years with a predominance of females (64.1%). Most of patients were ASA II (55.8% - 29 patients) followed by ASA III (33.6% - 19 patients). Mean BMI was 26.06±5.7 Kg/m2. The most frequent pre-surgical diagnosis was adenocarcinoma in 32.7% of the sample (17 patients), followed by neuroendocrine tumours (23.1%- 12 patients). The next most frequent diagnostic group was pancreatic cystic neoplasms (intraductal papillary mucinous neoplasms, mucinous cystic neoplasm, pancreatic serous cystadenoma and solid pseudopapillary tumor- 13,6,5 and 1 patients respectively).

Regarding postoperative analytical values, the median amylase level at 3rd POD in surgical drain was 466,5 (230-2121) U/L; at 5th POD it decreased to 92 (57-886) U/L. Blood amylase had a median of 71,5 (36-125) U/L; in fact, only 2 patients had postoperative hyperamylasemia in the range of postoperative acute pancreatitis. The median CRP value at 3rd POD was 189 (97-247) U/L. These results are summarised in table 1.

POPF

Overall postoperative morbidity was described in 67.3% of patients. Of these, the 65.7% were Clavien-Dindo ≥III with 3.8% postoperative mortality (2 patients).

Specifically, in relation to POPF, 71.1% of the sample had postoperative amylase elevation in surgical drain. However, according to IGPS criteria (13), 17 patients or 32.7% of the total had clinically relevant POPF (Grade-B and/or Grade-C POPF) (Table 1).

Regarding the treatment of clinically relevant grade B POPF, 13 patients required percutaneous drainage. However, treatment with broad-spectrum antibiotic therapy and surgical drainage was sufficient in 2 patients. In patients with grade C post-operative fistula, urgent surgical drainage was necessary.

Bivariate analysis between patients who did and did not develop POPF in the study group detected statistically significant differences in preoperative haemoglobin values (p=0.021), preoperative BMI (p=0.055), surgical splenectomy (p=0.029), amylase in drainage 3rd POD (p=0.011), amylase in drainage 5th POD (p=0.034) and CRP values on postoperative day 3 (p=0.002) (Table 2).

To try to establish the risk factors associated with clinically relevant POPF, a logistic regression was performed with the variables studied (sex, Hb preoperative, splenectomy, BMI, Amylase drainage 5th POD and Serum CRP 3rd POD) and amylase in drainage at 5th POD POD [p=0.035; 7,1 (1,15-43,79)] and blood CRP value at 3rd POD [p=0.002; 18,41 (2,98-11,87)] were identified as a possible risk factors for POPF (Table 3).

Predictive accuracy of CRP values for POPF

In an attempt to establish cut-off points for both as predictors of POPF, ROC curve analysis were performed. A ROC curve analysis was performed comparing the values of amylase in drainage at 5th POD and serum CRP at 3rd POD. For postoperative CRP values at 3rd POD, ROC curve analysis demonstrated an AUC of 0.814 (95% CI 0.68-0.95; p=0.001). The 195 mg/L point was selected and it showed a Sensitivity (S) of 80% and a Specificity (S) of 80%. The positive predictive value was 81.25%. When the CRP at 3rd POD was ≥195 mg/L, the probability of correctly predicting the occurrence of a POPF would 81.25%. These results are shown graphically in Figure 1.

DISCUSSION

Our results suggest that CRP value at 3rd POD could be good predictor of POPF in PD. POPF after pancreatic surgery and specifically after PD is a source of postoperative morbidity (abscesses, sepsis, haemorrhagic events...) (3). In fact, POPF has sometimes been associated with poorer oncological outcomes or at least delaying adjuvant treatment if it would be necessary(15). Despite continuing medical advances, the results, including in high-volume centres, describe a fistula rate of around 3-45% (1,2). Therefore, although methods to fully prevent POPF continue to be studied(5,16), there

is a need to find a variable or measure to help us accurately and early predict patients at risk of developing POPF.

Blood CRP has been shown to be an early marker of postoperative abdominal infectious complications(11,12). In our sample, CRP at 3rd POD appears to be a good marker for POPF. Furthermore, when compared to the other analytical and/or drainage markers (amylase in drainage at 3rd POD and amylase in drainage at 5th POD), its AUC is lower (Figure 2).

The most important clinical value of this analytical parameter is that CRP blood values are elevated before the appearance of physical signs (fever, tachycardia, abdominal pain...). This could anticipate the management of infectious complications(17).

The relationship between postoperative complications and elevated CRP has been widely confirmed in colorectal cancer (18). In the meta-analysis by Warschkow et al, after an analysis of 1832 patients, CRP at 4th POD was a good marker of infectious postoperative complications. However, although the AUC curve was adequate, the sensitivity of CRP, as well as the PPV, was low, so that, in general, the usefulness of this parameter only allows for early and safe discharge (18).

In pancreatic surgery, this trend has recently been studied in CPD (13). In CPD, CRP values at 3rd POD was associated with POPF when the values ranged around 110-200 mg/L (19,20). However, in DP there is only one study that specifically refers to this relationship. In this retrospective study, Sakamoto et al, in a retrospective cohort of 97 PD patients, attempted to investigate predictors of POPF. With a 23.7% incidence of POPF, their results found that a CRP value >140 mg/L was an independent predictor of POPF (AUC 0.723). Therefore, they conclude that postoperative CRP could be a useful tool in the postoperative management of DP (21).

Our findings follow the trend reported by Sakamoto et al, with a very similar incidence of POPF and CRP values around those previously published (140 mg/L vs 195 mg/L). Furthermore, the PPV of CRP at 3rd POD was 90%. This could be translated as patients with CRP values >195mg/L at 3rd POD had a probability of 90% to being adequately classified as POPF patients.

Another topic of current debate is the need for postoperative prophylactic drains. The latest Cochrane review, with low certainty evidence, suggests that routine use of drains may reduce 90-day mortality(22). In our series, a closed postoperative aspiration drain was left in all patients and in 2 patients it was curative of the clinically relevant fistula.

In summary, according to our results, CRP values at 3rd POD could be adequate marker for predicting clinically relevant POPF; furthermore, this could have repercussions on postoperative management, such as: initiation of prophylactic antibiotic therapy, maintenance of drains regardless of amylase levels, early request for imaging tests, etc.

This study has two important limitations: sample size and retrospective nature (loss of cases as well as certain surgical characteristics). Nevertheless, we believe that these findings could be of great relevance given that CRP is a rapid and accessible marker, low-priced, and easily applicable in daily clinical practice. However, larger and prospective studies would be needed to contrast these findings.

CONCLUSION

CRP value at 3rd POD is a good marker for predicting clinically relevant POPF after distal pancreatectomy. Early detection of patients at risk for POPF based on these characteristics could have an impact on their postoperative management.

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Conflict of interest

The authors declare that there are no conflicts of interest in the reported results.

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REFERENCES

1. Ecker BL, McMillan MT, Allegrini V, Bassi C, Beane JD, Beckman RM, et al. Risk Factors and Mitigation Strategies for Pancreatic Fistula After Distal Pancreatectomy: Analysis of 2026 Resections From the International, Multi-institutional Distal Pancreatectomy Study Group. Ann Surg [Internet]. 2019;269(1). Available from: https://journals.lww.com/annalsofsurgery/Fulltext/2019/01000/Risk_Factors_and_Mitigation_Strategies_for.28.aspx

2. Beane JD, Pitt HA, Dolejs SC, Hogg ME, Zeh HJ, Zureikat AH. Assessing the impact of conversion on outcomes of minimally invasive distal pancreatectomy and pancreatoduodenectomy. HPB [Internet]. 2018;20(4):356–63. Available from: https://www.sciencedirect.com/science/article/pii/S1365182X17311061

3. Bassi C, Marchegiani G, Dervenis C, Sarr M. Pancreas The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula : 11 Years After. Surgery [Internet]. 2016;161(3):584–91. Available from: http://dx.doi.org/10.1016/j.surg.2016.11.014

4. Allen PJ, Gönen M, Brennan MF, Bucknor AA, Robinson LM, Pappas MM, et al. Pasireotide for Postoperative Pancreatic Fistula. N Engl J Med [Internet]. 2014 May 21;370(21):2014–22. Available from: https://doi.org/10.1056/NEJMoa1313688

5. Diener MK, Knaebel HP, Witte ST, Rossion I, Kieser M, Buchler MW, et al. DISPACT trial: a randomized controlled trial to compare two different surgical techniques of DIStal PAnCreaTectomy - study rationale and design. Clin Trials. 2008;5(5):534–45.

6. Chong E, Ratnayake B, Lee S, French JJ, Wilson C, Roberts KJ, et al. Systematic review and meta-analysis of risk factors of postoperative pancreatic fi stula after distal pancreatectomy in the era of 2016 International Study Group pancreatic fi stula de fi nition. Int Hepato-Pancreato-Biliary Assoc [Internet].

2021;23(8):1139–51. Available from: https://doi.org/10.1016/j.hpb.2021.02.015

7. Kawaida H, Kono H, Hosomura N, Amemiya H, Itakura J, Fujii H, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. 2019;25(28):3722–37.

8. Probst P, Schuh F, Dörr-Harim C, Sander A, Bruckner T, Klose C, et al. Protocol for a randomised controlled trial to compare postoperative complications between minimally invasive and open DIStal PAnCreaTectomy (DISPACT-2 trial). BMJ Open. 2021 Feb;11(2):e047867.

9. Yang F, Jin C, Hao S, Fu D. Drain Contamination after Distal Pancreatectomy: Incidence, Risk Factors, and Association with Postoperative Pancreatic Fistula. J Gastrointest Surg. 2019;23(12):2449–58.

10. Villafane-Ferriol N, Van Buren G, Mendez-Reyes JE, McElhany AL, Massarweh NN, Silberfein EJ, et al. Sequential drain amylase to guide drain removal following pancreatectomy. Hpb. 2018;20(6):514–20.

11. Uchida Y, Masui T, Nakano K, Yogo A, Yoh T, Nagai K, et al. Combination of postoperative C-reactive protein value and computed tomography imaging can predict severe pancreatic fistula after pancreatoduodenectomy. Hpb [Internet]. 2020;22(2):282–8. Available from: https://doi.org/10.1016/j.hpb.2019.06.020

12. Malya FU, Hasbahceci M, Tasci Y, Kadioglu H, Guzel M, Karatepe O, et al. The Role of C-Reactive Protein in the Early Prediction of Serious Pancreatic Fistula Development after Pancreaticoduodenectomy. Gastroenterol Res Pract [Internet]. 2018 Jan 28;2018:9157806. Available from: https://pubmed.ncbi.nlm.nih.gov/29619047

13. SAKAMOTO T, YAGYU Y, UCHINAKA EI, MORIMOTO M, HANAKI T, TOKUYASU N, et al. Predictive Significance of C-reactive Protein-to-albumin Ratio for Postoperative Pancreatic Fistula After Pancreaticoduodenectomy. Anticancer Res [Internet]. 2019 Nov 1;39(11):6283 LP – 6290. Available from: http://ar.iiarjournals.org/content/39/11/6283.abstract

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):205–13.

15. Bonaroti JW, Zenati MS, Al-abbas AI, Rieser CJ, Zureikat AH, Hogg ME, et al. Impact of postoperative pancreatic fistula on long-term oncologic outcomes after pancreatic resection. Hpb [Internet]. 2021;23(8):1269–76. Available from: https://doi.org/10.1016/j.hpb.2020.12.010

16. Watanabe N, Yamamoto Y, Sugiura T, Okamura Y, Ito T, Ashida R, et al. The Impact of Stump Closure Techniques on Pancreatic Fistula Stratified by the Thickness of the Pancreas in Distal Pancreatectomy. Dig Surg. 2020;37(4):340–7.

17. Singh PP, Zeng ISL, Srinivasa S, Lemanu DP, Connolly AB, Hill AG. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg. 2014;101(4):339–46.

18. Warschkow R, Beutner U, Steffen T, Müller SA, Schmied BM, Güller U, et al. Safe and early discharge after colorectal surgery due to C-reactive protein: A diagnostic meta-analysis of 1832 patients. Ann Surg. 2012;256(2):245–50.

19. Partelli S, Pecorelli N, Muffatti F, Belfiori G, Crippa S, Piazzai F, et al. Early Postoperative Prediction of Clinically Relevant Pancreatic Fistula after Pancreaticoduodenectomy: usefulness of C-reactive Protein. Hpb. 2017;19(7):580–6.

20. van Dongen JC, Smits FJ, van Santvoort HC, Molenaar IQ, Busch OR, Besselink MG, et al. C-reactive protein is superior to white blood cell count for early detection of complications after pancreatoduodenectomy: a retrospective multicenter cohort study. Hpb [Internet]. 2020;22(10):1504–12. Available from: https://doi.org/10.1016/j.hpb.2020.02.005

21. Sakamoto K, Ogawa K, Tamura K, Iwata M, Matsui T, Nishi Y, et al. Postoperative elevation of C-reactive protein levels and high drain fluid amylase output are strong predictors of pancreatic fistulas after distal pancreatectomy. J Hepatobiliary Pancreat Sci. 2021;28(10):874–82.

22. He S, Xia J, Zhang W, Lai M, Cheng N, Liu Z, et al. Prophylactic abdominal drainage for pancreatic surgery. Cochrane database Syst Rev. 2021 Dec;12(12):CD010583.

Table 1. Summary of sample characteristics

	Overall (n=52) n (%)
Age (years)	62.9±15
Sex	
• **Female**	29 (55.8)
Diabetes mellitus preoperative	20 (38.5)
Preoperative haemoglobin (g/dL)	14.02±1.4
Total proteins (g/dL)	6.65±0.6
ASA	
• **I**	3 (5.8)
• **II**	29 (55.8)
• **III**	19 (36.5)
• **IV**	1 (1.9)
BMI (Kg/m^2)	26.06 ±5.7
Tumour location	
• **Body**	34 (65.4)
• **Tail**	15 (28.8)
• **Body-tail**	3 (5.8)
Preoperative diagnosis	
• **Adenocarcinoma**	17 (32.7)
• **Neuroendocrine**	12 (23.1)
• **Intraductal papillary mucinous neoplasms**	13 (25)
• **Mucinous cystic neoplasm**	6 (11.5)
• **Pancreatic serous cystadenoma**	5 (9.69)
• **Solid pseudopapillary tumor**	1 (2.1)
Treatment of pancreatic stump	
• **Single suture**	30 (76.9)
• **Independent Wirsung closure**	4 (10.3)
• **Intraoperative transpapillary drainage**	5 (12.8)
Splenectomy	46 (90.2)
Laparoscopic approach	6 (11.5)
Teres ligament patch	18 (34.6)
Amylase in drainage 3rd POD (U/L)	466.5 (230-2121)

Serum amylase 3rd POD (U/L)	71.5 (36-125)
Amylase in drainage 5th POD (U/L)	92 (57-886)
Serum CRP 3r POD (mg/L)	189 (97-247)
Overall morbidity	67.3 (35)
Clavien-dindo classification • **I** • **II** • **IIIA** • **III B** • **IV** • **V**	 9 (25.7) 3 (8.6) 13 (37.1) 5 (14.3) 3 (8.6) 2 (5.7)
30-day postoperative mortality	2 (3.8)
POPF • **Biochemical leak** • **Grade B** • **Grade C**	 20 (54.1) 15 (40.5) 2 (5.4)
ASA: The American Society of Anesthesiologists classification; BMI: Body mass index; POD: postoperative day; CRP: C-reactive protein. POPF: Postoperative pancreatic fistula	

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Table 2. Univariate analysis of factor associated of PPF

	No PPF (n=35) n (%)	PPF (n=17) n (%)	p
Age (years)	63.93 ±15.2	60.97 ±15.6	0.516
Sex • **Female** • **Male**	 23 (65.7) 12 (31)	 6 (35.3) 11 (64.7)	0.073
Preoperative haemoglobin (g/dL)	13.73 ±1.47	14.68±1.1	0.021
Total proteins (g/dL)	6.62±0.6	6.71 ±0.7	0.701
ASA • **I** • **II** • **III** • **IV**	 3 (8.6) 19 (54.3) 13 (37.1) -	 - 10 (58.8) 6 (53.3) 1 (5.9)	0.312
Overweight (BMI >25 Kg/m^2)	10 (37)	7 (77.8)	0.055
Tumour location • **Body** • **Tail** • **Body-tail**	 24 (68.6) 8 (22.9) 3 (8.6)	 10 (58.8) 7 (41.2) -	0.228
Preoperative diagnosis • **Adenocarcinoma** • **Neuroendocrine** • **Other**	 15 (42.9) 6 (17.1) 14 (40)	 2 (11.8) 6 (35.3) 9 (52.9)	0.066
Treatment of pancreatic stump • **Single suture** • **Independent Wirsung closure** • **Intraoperative transpapillary drainage**	 20 (80) 2 (8) 3 (12)	 10 (71.4) 2 (14.3) 2 (14.3)	0.252
Splenectomy	34 (97.1)	12 (75)	0.029
Laparoscopic approach	4 (11.4)	2 (11.7)	0.081
Teres ligament patch	13 (37.1)	5 (29.4)	0.758
Amylase in drainage 3rd POD (U/L)	360 (209-1193)	1900 (551-7993)	0.011
Serum amylase 3rd POD (U/L)	61 (25-116)	90 (41-204)	0.130
Amylase in drainage 5th POD (U/L)	81 (51-209)	767 (66-6098)	0.034
Serum CRP 3r POD (mg/L)	114 (69-214)	215 (198-275)	0.002

ASA: The American Society of Anesthesiologists classification; BMI: Body mass index; POD: postoperative day; CRP: C-reactive protein. POPF: Postoperative pancreatic fistula

Table 3. Logistic regression of independent factor of clinically relevant POPF after distal pancreatectomy

	Inclusion model			**Optimized model (backward conditional)**		
Values	**Wald**	**OR CI 95%**	**P value**	**Wald**	**OR CI 95%**	**P value**
Sex (male)	4.11	3.51 (1.04-11.85)	0.015			
Hb preoperative	4.75	1.77 (1.06-2.96)	0.029			
Spenectomy	4.32	0.088 (0.01-0.87)	0.038			
BMI >25 (Kg/m^2)	5.79	1.23 (1.04-1.46)	0.016			
Amylase drainage 5th POD >150 **(U/L)**	5.30	4.58 (1.25-16.75)	0.021	4.45	7.1 (1.15-43.79)	0.035
Serum CRP 3rd POD >195**(mg/L)**	6.63	5.75 (1.52-21.93)	0.010	9.82	18.41 (2.98-11.87)	0.002

Hb: haemoglobin; BMI: Body mass index; POD: postoperative day; CRP: C-reactive protein. POPF: Postoperative pancreatic fistula; OR: odds ratio; CI confidence interval

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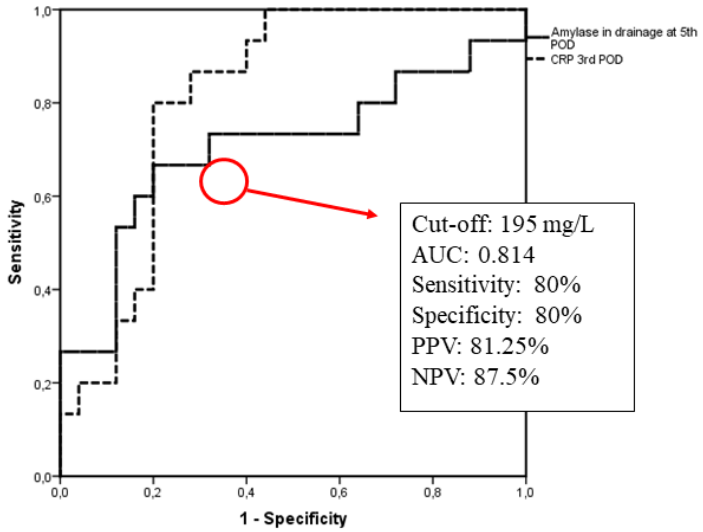
Figure 2. ROC curves for the prediction of clinically relevant postoperative pancreatic fistula (POPF).



Receiver Operating Characteristic (ROC) curve relating POPF to serum CRP (C-reactive protein) values at 3rd POD (postoperative day), amylase in drainage at 3rd POD and amylase in drainage at 5th POD. Area under the curve (AUC) of CRP 3rd DPO 0.814 [(95% CI 0.68-0.95); p=0.001] and amylase in drainage at 5th POD presented an AUC 0.707 [(95% CI 0.52-0.89); p=0.030].
PPV = positive predictive value; NPV = negative predictive value

Figure 1. ROC curves for the prediction of clinically relevant postoperative pancreatic fistula (POPF).

Receiver Operating Characteristic (ROC) curve relating POPF to serum CRP (C-reactive protein) values at 3rd POD (postoperative day), amylase in drainage at 3rd POD and

amylase in drainage at 5th POD. Area under the curve (AUC) of CRP 3rd DPO 0.814 [(95% CI 0.68-0.95); p=0.001] and amylase in drainage at 5th POD presented an AUC 0.707 [(95% CI 0.52-0.89); p=0.030].

PPV = positive predictive value; NPV = negative predictive value