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THESE

Pour obtenir le titre de

DOCTEUR EN MEDECINE

Présentée et soutenue publiquement

Par

Nicolas ROLLIN

Le 30 mars 2021

EVALUATION RETROSPECTIVE DES FACTEURS DE RISQUE DE FISTULE
PANCREATIQUE APRES PANCREATECTOMIE DISTALE.
ETABLISSEMENT D'UN SCORE PREDICTIF.

Directeur de thèse : Dr Jean Christophe VALATS

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RESUME

La fistule pancréatique est une complication fréquente et grave après une pancréatectomie distale. Le nombre et le poids des différents facteurs de risque rapportés dans la littérature restent encore controversés et il n'existe pas de score pour prédire la survenue de fistule pancréatique de grade B et C (cliniquement pertinente).

Les données concernant 103 patients consécutifs subissant une pancréatectomie ont été collectées.

Trente-trois patients ont développé une fistule pancréatique : 24 fistules de grade B et 9 fistules de grade C. Le temps opératoire supérieur à 4 heures, le taux d'amylase sur le liquide de drainage abdominal supérieur à 500 UI/L à J3 post opératoire, l'épaisseur du pancréas supérieur à 10 mm et un IMC supérieur à 30 se sont avérés prédictifs fistule pancréatique cliniquement pertinente. Un score de 4 points a été créé à partir des variables sélectionnées dans le modèle multivarié. La capacité de discrimination a été testée sur la courbe ROC, montrant une aire sous la courbe de 0,83 (IC 95% [0,75 - 0,92]). Le seuil du score a été déterminé à 2 points / 4, ce qui a la valeur la plus élevée selon l'indice de Youden (0,53). La sensibilité est calculée à 82% (IC95% [69 - 95]) et la spécificité à 71 (IC95% [61 - 82]). Un seuil à 3 points / 4 permet d'atteindre une spécificité de 99% (IC95% [99-100]).

MOTS CLES : Fistule Pancréatique, Pancréatectomie distale, Score prédictif, Temps opératoire, Obésité, Amylase, Epaisseur pancréatique.

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1) ABBREVIATIONS

BL : Biochemichal leak

BMI : Body Mass Index

CR : Clinically Relevant

DFA : Drain Fluid Amylase

DP : Distal pancreatectomy

ERCP : Endoscopic Retrograde Cholangiopancreaticography

IQR : Interquartile Range

IPMN : Intraductal Papillary Mucinous Neoplasia

ISGPF : International Study Group Pancreatic Fistula

POD : Post-Operative Day

POPF Postoperative pancreatic fistula

ROC : Receiver Operating Characteristic

SD : Standard Deviation

2) INTRODUCTION

Distal pancreatectomy (DP) is a standardized and frequently performed surgical procedure for the resection of pancreatic diseases located in the body and/or tail of the pancreas^{1,2}. The occurrence of a postoperative pancreatic fistula (POPF) is a common and serious complication such as bleeding, hemorrhage, septic complications, prolonged ileus, which can lead to reoperation or death^{3,4}. The incidence of this complication ranges between 25-40%, despite surgical technical progress^{5,6} and the sharp increase in the pancreatic adenocarcinoma's incidence predicts a parallel increase in pancreatic fistulas⁷. Moreover, POPF cause a delay of adjuvant chemotherapy or radiotherapy treatment³, leading to a worse therapeutic management of the oncologic patient.

The treatment of POPF is multidisciplinary, involving anesthesiologists, radiologists, digestive surgeons and also gastroenterologists. Treatment of clinically relevant (CR) POPF complications may also involve radiologic and endoscopic procedures, such as gastrocystostomy, duodenocystostomy or ERCP^{8,9}. Indeed, a well codified therapy of the fistula itself still does not exist and the best management strategy is still debated. For these reasons, a major challenge for surgeons is to understand the risk factors of POPF in order to prevent its occurrence, and to come to an early diagnosis to avoid timely complications.

The ISGPF (International Study Group Pancreatic Fistula) redefined POPF in 2016, differentiating three situations¹⁰. The biochemical leak is defined by measurable drain output on after postoperative day 3 with drain fluid amylase (DFA) concentration equals or higher than 3 times the upper limit of normal

serum value (no longer defined as a fistula). The grade B POPF is defined with a pancreatic leak that requires a therapeutic intervention (radiological or endoscopic) or the presence of abdominal drains for more than 21 days. The grade C POPF occurs when the fistula is complicated by organ failure or further surgery is needed.

The risk factors for pancreatic fistula after distal pancreatectomy were the subject of many studies, with soft pancreas, significant intraoperative blood loss, and long operating time most commonly described^{11,12}. Biochemical leak itself, no longer corresponding to a pancreatic fistula since the new definitions, is considered a good predictor of the occurrence of a POPF¹³. However, the number and the weight of the different risk factors still remain controversial¹⁴.

The main objective of our study is to define a new score, easy to use, to identify patients at high risk of developing a pancreatic fistula grade B or C (clinically relevant; CR) after DP.

3) PATIENTS AND METHODS

A/ Study design and patient selection

The study had a single-center retrospective cohort design and was conducted at the Montpellier University Hospital. All patients who underwent a distal pancreatectomy between January 2015 and December 2019 were included, regardless of the indication, with or without splenectomy in addition. Exclusion criteria was age younger than 18.

B/ Data collection

From a prospectively collected database, preoperative demographic and medical data were collected (age, BMI, medical history). Pancreatic isthmus diameter was measured on a preoperative imaging test, where available. Amylase level on drain fluids was performed on post-operative day (POD) 1, 3, 5, and every two days if positive for a BL or a POPF. If several drainages were positioned, that one with the highest value was considered. Pancreatic fibrosis and tumor histology were recorded from pathological report. Data regarding both mini-invasive and laparotomic surgery were recorded. The technique used for pancreatic remnant closure was always a stapler closure, already known to be safe and effective^{15,16}. Drain were always positioned during surgery. On the first post-operative day patients were observed in a sub-intensive care unit. They were re-admitted in the surgical ward based on their clinical conditions. BL and POPF were defined according to POPF definition of ISGPF¹⁰.

C/ Statistical analysis

The categorical data were described by frequencies and percentages, whereas continuous data by mean \pm standard deviation (SD) or median \pm interquartile range (IQR) depending on whether or not they have a normal distribution.

Categorical variables were compared by using the χ^2 test or Fischer exact test, while the distribution of continuous variables were compared by applying

Student's t-test or Mann-Whitney test, when appropriated. An univariate analysis of variables predictive of POPF according to literature was performed via logistic regression with a p value set to 0,05. Then a multivariate analysis of variables potentially predictive of fistula risk via multivariate logistic regression with backward selection. The variables were checked for collinearity via tolerance.

The variables finally were selected to build a simplified score if the p value at multivariate analysis was $<0,10$. The predictive performance of this score was then tested on the population studied. The accuracy of a continuous variable in predicting a categorical outcome was evaluated using the Receiver Operating Characteristic (ROC) curves. The specificity and the sensitivity of the different thresholds are presented with their 95% confidence intervals. Youden's J test was performed to evaluate the performance of a positive score on the POPF occurrence.

The primary endpoint was the developing of a POPF grade B or C during the post-operative course.

The statistical analysis was conducted using the SPSS software (version 26.0).

4) RESULTS

A/ General results

103 patients who underwent a distal pancreatectomy (DP) were included, 45 males and 58 females. The medium age of the population was 62 years, without difference between patients with and without CR-POPF. Patients characteristics are shown in Table 1. Almost all surgeries were performed for oncological purpose, accounting for 69,5% of cases (Table 2), with 35 patients had a diagnosis of Adenocarcinoma (34%), 24 of Neuroendocrine Tumor (23.3%) and 12 (11.7%) of Intraductal Papillary Mucinous Neoplasia (IPMN).

Thirty-three patients developed a CR-POPF : 24 grade B fistulas and 9 grade C fistulas. In the group of grade B POPF, 27 patients had abdominal drains which were left more than 21 days, 6 patients were treated with a complementary interventional procedure, by radiology for 4 of them, and by endoscopy for the other two.

In the group of grade C PF, 4 patients underwent additional interventional endoscopy treatment but a surgical intervention was still necessary for 3 of these patients. In total, 8 patients underwent a reoperation and 4 of them underwent 2 interventions. Six surgeries consisted of collection drainage and 5 surgeries were for hemostatic purposes. One patient underwent a complementary gastrectomy for oncologic purpose. Only one patient died in the month following the DP, due to the progression of his neuroendocrine disease.

Data of univariate and multivariate analysis are shown in Table 2. The average BMI was 24,7 and obesity (defined as a BMI > 30) was associated with PF at univariate analysis, but was not statistically significative at multivariate analysis

(OR= 1,33; 95%CI 0.35 - 5.02; p value 0.067). The average operating time was 3 hours and twelve minutes. An operating time longer than 4 hours was associated with a higher risk of PF (OR=5,28 ; IC95%= [1,61 - 17,31]). Laparoscopy was performed slightly more than laparotomy (58% vs 42%), without correlation with POPF. The median level of amylase in abdominal drains at post-operative day (POD) 3 were higher for patients with POPF than those without POPF (656,0 vs 132,5; p=0,002). A preoperative imaging test was available in 64 patients. The median diameter of the pancreatic isthmus was 10,5 mm. Pancreas thickness superior to 10 mm was found to be a prognostic indicator for PF (OR=7,12; IC95%=[2,32 - 21,87], p<0,01).

		Clinically Relevant Post-Operative Pancreatic Fistula (CR-POPF)			
		Population	No	Yes	p
Pancreas thickness	<i>Mean (± SD)</i>	11.3 (± 3.5)	10.2 (± 3.0)	12.9 (± 3.5)	0.0003
	<i>Median (Q1;Q3)</i>	10.5 (9.0 ;13.0)	9.0 (8.0;11.0)	13.0 (11.0;15.0)	
Length of stay	<i>Mean (± SD)</i>	13.5 (± 8.3)	10.8 (± 4.8)	19.4 (± 10.9)	<0.0001
	<i>Median (Q1;Q3)</i>	11.0 (8.0 ;16.0)	10.0 (8.0;12.0)	18.0 (11.0;24.0)	
Age	<i>Mean (± SD)</i>	62.2 (± 13.6)	63.1 (±14.2)	60.2 (± 11.9)	0.1131
	<i>Median (Q1;Q3)</i>	64.0 (54.0 ;71.0)	67.5 (57.0;73.0)	62.0 (50.0;69.0)	
BMI	<i>Mean (± SD)</i>	24.7 (± 4.6)	24.4 (± 4.0)	25.5 (± 5.7)	0.2704
	<i>Median (Q1;Q3)</i>	24.0 (21.0 ;28.0)	24.0 (21.0;27.0)	25.0 (22.0;30.0)	
Drain Fluids Amylase POD 3	<i>Mean (± SD)</i>	2095.9 (±7806.7)	1089.8 (±3229.5)	4296.6 (±12963.8)	<0.0001
	<i>Median (Q1;Q3)</i>	196.0 (67.0 ;864.0)	132.5 (45.0;45.0)	656.0 (243.5;2076.0)	
	<i>Median (Q1;Q3)</i>	744.0 (156.0 ;3321.0)	292.0 (111.0;2619.0)	2176.5(521.0;6209.0)	

Operating Time	<i>Mean (± SD)</i>	3.5 (± 1.2)	3.2 (± 1.1)	4.0 (± 1.3)	0.0090
	<i>Median (Q1;Q3)</i>	3.3 (2.5 ; 4.3)	3.1 (2.4;3.7)	4.0 (2.9;5.0)	
Surgical technique	<i>Laparoscopy (%)</i>	60 (58.3)	45 (64.3)	15 (45.5)	0.0705
	<i>Laparotomy (%)</i>	43 (41.7)	25 (35.7)	18 (54.5)	
Gender	<i>Man (%)</i>	45 (43.7)	26 (37.1)	19 (57.6)	0.0511
	<i>Woman (%)</i>	58 (56.3)	44 (62.9)	14 (42.4)	
BMI	<i>Normal (%)</i>	86 (83.5)	63 (90.0)	23 (69.7)	0.0096
	<i>BMI > 30 (%)</i>	17 (16.5)	7 (10.0)	10 (30.3)	
Hypertension	<i>No (%)</i>	74 (71.8)	51 (72.9)	23 (69.7)	0.7393
	<i>Yes (%)</i>	29 (28.2)	19 (27.1)	10 (30.3)	
Tobacco	<i>No (%)</i>	72 (69.9)	49 (70.0)	23 (69.7)	0.9750
	<i>Yes (%)</i>	31 (30.1)	21 (30.0)	10 (30.3)	
Dyslipidemia	<i>No (%)</i>	93 (90.3)	64 (91.4)	29 (87.9)	0.7228
	<i>Yes (%)</i>	10 (9.7)	6 (8.6)	4 (12.1)	
Diabetes	<i>No (%)</i>	85 (82.5)	59 (84.3)	26 (78.8)	0.4930
	<i>Yes (%)</i>	18 (17.5)	11 (15.7)	7 (21.2)	
Alcohol	<i>No (%)</i>	97 (94.2)	65 (92.9)	32 (97.0)	0.6614
	<i>Yes (%)</i>	6 (5.8)	5 (7.1)	1 (3.0)	
Chronic pancreatitis	<i>No (%)</i>	97 (94.2)	68 (97.1)	29 (87.9)	0.0815
	<i>Yes (%)</i>	6 (5.8)	2 (2.9)	4 (12.1)	
OSAS	<i>No (%)</i>	97 (94.2)	66 (94.3)	31 (93.9)	1.0000
	<i>Yes (%)</i>	6 (5.8)	4 (5.7)	2 (6.1)	
Chronic liver disease	<i>No (%)</i>	96 (93.2)	66 (94.3)	30 (90.9)	0.6775
	<i>Yes (%)</i>	7 (6.8)	4 (5.7)	3 (9.1)	
Histologic fibrosis	<i>No (%)</i>	73 (70.9)	49 (70.0)	24 (72.7)	0.7762
	<i>Yes (%)</i>	30 (29.1)	21 (30.0)	9 (27.3)	

Table 1: Patients' characteristics according to CR-POPF presence. BMI: Body Mass Index; POD: Post-operative day; OSAS: Obstructive Sleep Apnea Syndrome

	Univariate		Multivariate	
	Odds ratio [CI95%]	p-value	Odds ratio [CI95%]	p-value
Obesity (BMI >30)	3,37 [1,09 - 10,43]	0,0347	1,33 [0,35 - ,02]	0.0672
Laparotomy vs Laparoscopy	1,89 [0,78 - 4,54]	0,1569		
Gender (Woman)	0,4 [0,17 - 0,97]	0,0535		
Amylase > 500 U/L	3,92 [1,64 - 9,4]	0,0022	4,62 [1,56 - 13,62]	0.0026
Pancreas thickness (>10 mm)	7,17 [2,85 - 18,02]	<.0001	7,70 [2,65 - 22,31]	0.0006
Operating time >4h	4.13 [1,66 - 10,26]	0,0023	5,66 [1,66 - 19,29]	0.0060

Table 2: Univariate and Multivariate analysis for Post-operative Pancreatic Fistula

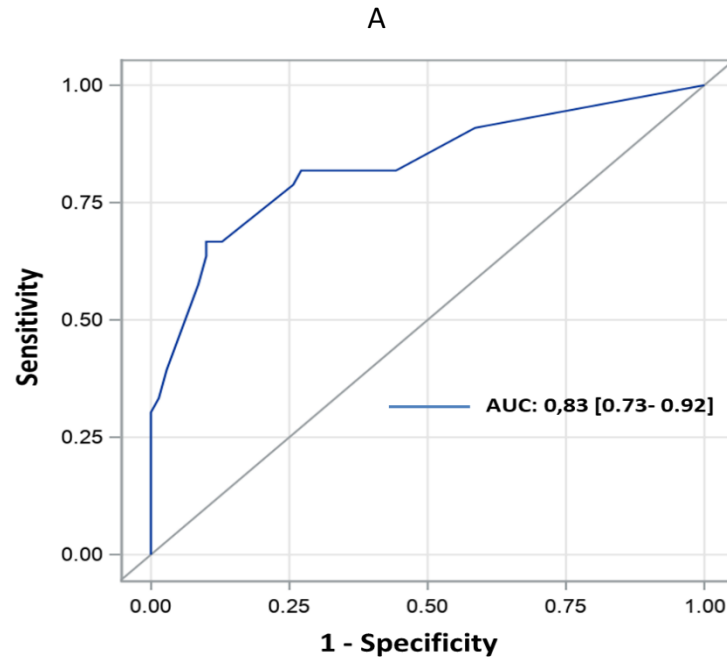
B/ Building a predictive score

A 4 points score was created from the variables selected in the multivariate model.

One point was assigned if the patient had a pancreas thickness greater than 10 mm, as well as if he has an operation lasting more than 4 hours, if the amylase level on drain on POD 3 was higher than 500/L and if the patient had BMI >30. Obesity was chosen for the score because of the results of univariate analysis and because it well fitted the model on the ROC curves. The discriminating ability was tested on the ROC curve, showing an AUC (area under the curve) of 0.83 (IC 95%= [0.75 - 0.92]). On the Hosmer-Lemeshow test, the difference between the prediction of the model and the observed value is not significant (p-value = 0.44), which validates a relatively good fit of the model.

The score threshold was determined at 2 points/4, which has the highest value according to the Youden index (0.53). The sensitivity is calculated at 82%

(CI95%69 - 95) and the specificity at 71 (CI95%= [61 - 82]). A threshold at 3 points/4 is also very interesting, allowing to reach a specificity of 99% (CI95%= [99 – 100]).



B

Cutoff	Sensitivity [CI95%]	Specificity [CI95%]	Youden Index
4	0.12 [0.01 - 0.23]	1 [1 - 1]	0.12
3	0.42 [0,26 - 0,59]	0.99 [0,96 - 1,00]	0.41
2	0.82 [0.69 - 0.95]	0.71 [0.61 - 0.82]	0.53
1	0.97 [0.91 - 1.03]	0.24 [0.14 - 0,34]	0,21

Figure 1: Receiving Operating Characteristic Curves (A) with their specificity and sensitivity (B) of the different thresholds.

5) DISCUSSION

A simple score using the pancreas thickness, obesity, amylase level in abdominal drain on POD 3 and operating time seems to be able to predict with sensitivity of 82% and specificity of 71% with a cutoff at 2 points/4. The specificity of this score can be increased at 99% by raising the threshold at 3 point/4.

The risk factors found in our study (amylase on drains' fluid on POD 3, pancreatic thickness > 10mm, operating time) are concordant with the literature. As the texture of the pancreas was not provided in all the operative reports, we used a new variable which consists of measuring the pancreas at the level of the isthmus. Previous studies have already reported pancreatic thickness to be related with POPF¹⁷. Indeed, preoperative CT or MRI imaging has been reported to be a useful modality for surgeons to stratify the risk of severe POPF after pancreatic surgery, helping to select specific and tailored perioperative strategies¹⁸. Pancreatic thickness seems to be objective and can be obtained preoperatively, has showed to be a risk factor for the occurrence of CR-POPF at multivariate analysis with an ODDS Ratio higher than seven. This result can have different reasons, like the technical difficulty of suturing or stapling a thicker tissue, as already investigated in literature¹⁹. We tested the amylase level in abdominal drains instead of lipase, because of its wider diffusion and usefulness for pancreatic fistula diagnosis and prognosis, as stated by many papers^{20,21}. The amylase cutoff at 500 U / L was associated with better statistical performance in constructing the score. Longer operative time have been known to correlate with increased morbidity²² and confirmed in our series to increase the risk for CR-

POPF. Cutoff of 4 hours had the best performance and was coherent with previous study²². Finally, obesity was chosen for our risk score, even if not significantly associated with POPF. After multivariate analysis its p value was not far from significance, and in literature there are a lot of previous papers reporting its role as a prognostic factor^{20,23}. For these reasons we tried to build a score by using this parameter, obtaining a discriminating ability on the ROC curves with an AUC of 0.83.

The main strength of this study lies in the creation of a score very easy to use, by using the risk factors identified in our study and already known in literature. If a patient has a score of 3, you can be almost sure that he will develop a grade B or C pancreatic fistula. Obviously, these are preliminary results, which need to be validated in an external cohort on a larger sample size. Nevertheless, they seem very promising and they could be very useful in everyday clinical practice, as well as in research.

Despite there are no sufficient evidences to suggest substantial changes in clinical practice, having a score suggestive for developing CR-POPF could help the surgeons to perform a more strict observation of the patient even in absence of specific suspicious symptoms or laboratory findings. It may be useful to plan postoperative radiological investigations to detect POPF before the occurrence of its fearsome complications, and to choose with a good likelihood rate which patient needs further investigations.

Strategies to reduce the occurrence of CR-POPF may include intraperitoneal drains, prophylactic somatostatin analogues, surgical tissue/fibrin sealants²⁴. The usefulness of the aforementioned strategies is still debated, but having the

possibility to choose a subpopulation in which to implement them may be very important. In particular, the decisions on drainage management could be influenced by a positive score, thanks to an additional parameter, strong but very simple to apply. The usefulness of the score on the conduct to be kept on the removal or not of the abdominal drains after DP is still to be studied, but we are convinced that it would be very useful and interesting, as evidenced by the numerous papers existing in the literature that highlight an enormous disparity and uncertainty in the daily practice of pancreatic surgeons^{25,26}.

Given the absence of a consolidated therapy, having a score to classify patients at high risk of developing a POPF could allow you to select a population on which to test a possible prophylactic therapy, also invasive, given the high risk and severity of the complication itself. For example, endoscopic drainage by sphincterotomy and placement of a pancreatic prosthesis has already shown curative efficacy, and it could be studied in patients with a score greater than 2 in prophylaxis²⁷.

The study had important limitations. First of all, the small sample size that gave less statistical power to our conclusions. The score has not yet been validated on an external cohort, for sure this will be the next step. Then, the lack of information on operative transfusions in our database didn't allow to consider this parameter in our analysis, even if some previous study described it as a predictive factor for POPF. Finally, the retrospective and single-center design of the study was certainly another important limitation. An evaluation of the score on larger and external cohorts, possibly within a prospective multicentric study, is needed.

A simple score based on operation time, BMI > 30, amylase level >500 UI on abdominal drains on POD 3 and pancreatic thickness > 10 mm, measured at the isthmus on preoperative CT, can predict the postoperative risk of developing CR-POPF with a sensitivity of 82% (CI95%= [69 - 95]) and a specificity of 71% (CI95%= [61 - 82]) using a cutoff of 2 point, and even higher by choosing a threshold at 3 points/4. It seems very interesting for future clinical and research applications, further studies might go in this direction in order to validate it and to be able to benefit from its use.

5) REFERENCES

1. Parikh PY, Lillemoe KD. Surgical management of pancreatic cancer - Distal pancreatectomy. *Semin Oncol.* 2015. doi:10.1053/j.seminoncol.2014.12.010
2. Lillemoe KD, Kaushal S, Cameron JL, Sohn TA, Pitt HA, Yeo CJ. Distal pancreatectomy: Indications and outcomes in 235 patients. In: *Annals of Surgery.* ; 1999. doi:10.1097/00000658-199905000-00012
3. Fuks D, Piessen G, Huet E, et al. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prognosis, and risk factors. *Am J Surg.* 2009. doi:10.1016/j.amjsurg.2008.03.004
4. Lermite E, Sommacale D, Piardi T, et al. Complications after pancreatic resection: Diagnosis, prevention and management. *Clin Res Hepatol Gastroenterol.* 2013. doi:10.1016/j.clinre.2013.01.003
5. Oneil MacHado N. Pancreatic fistula after pancreatectomy: Definitions, risk factors, preventive measures, and management - Review. *Int J Surg Oncol.* 2012. doi:10.1155/2012/602478
6. Miyasaka Y, Mori Y, Nakata K, Ohtsuka T, Nakamura M. Attempts to prevent postoperative pancreatic fistula after distal pancreatectomy. *Surg Today.* 2017. doi:10.1007/s00595-016-1367-8
7. Bouvier AM, Uhry Z, Jooste V, et al. Focus on an unusual rise in pancreatic cancer incidence in France. *Int J Epidemiol.* 2017. doi:10.1093/ije/dyx088
8. Fujino Y. Perioperative management of distal pancreatectomy. *World J Gastroenterol.* 2015. doi:10.3748/wjg.v21.i11.3166

9. Goasguen N, Bourrier A, Ponsot P, et al. Endoscopic management of pancreatic fistula after distal pancreatectomy and enucleation. *Am J Surg*. 2009. doi:10.1016/j.amjsurg.2008.03.005
10. 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. *Surg (United States)*. 2017. doi:10.1016/j.surg.2016.11.014
11. Kleeff J, Diener MK, Z'graggen K, et al. Distal pancreatectomy: Risk factors for surgical failure in 302 consecutive cases. *Ann Surg*. 2007. doi:10.1097/01.sla.0000251438.43135.fb
12. Hackert T, Werner J, Büchler MW. Postoperative pancreatic fistula. *Surgeon*. 2011. doi:10.1016/j.surge.2010.10.011
13. 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. doi:10.1016/j.ijssu.2015.07.007
14. Peng YP, Zhu X Le, Yin L Di, et al. Risk factors of Postoperative pancreatic fistula in patients after distal pancreatectomy: A systematic review and metaanalysis. *Sci Rep*. 2017. doi:10.1038/s41598-017-00311-8
15. Probst P, Hüttner FJ, Klaiber U, et al. Stapler versus scalpel resection followed by hand-sewn closure of the pancreatic remnant for distal pancreatectomy. *Cochrane Database Syst Rev*. 2015. doi:10.1002/14651858.CD008688.pub2

16. Zhang H, Zhu F, Shen M, et al. Systematic review and meta-analysis comparing three techniques for pancreatic remnant closure following distal pancreatectomy. *Br J Surg*. 2015. doi:10.1002/bjs.9653
17. Chang YR, Kang JS, Jang JY, et al. Prediction of Pancreatic Fistula After Distal Pancreatectomy Based on Cross-Sectional Images. *World J Surg*. 2017. doi:10.1007/s00268-017-3872-3
18. Sandini M, Bernasconi DP, Ippolito D, et al. Preoperative computed tomography to predict and stratify the risk of severe pancreatic fistula after pancreatoduodenectomy. *Med (United States)*. 2015. doi:10.1097/MD.0000000000001152
19. Kawai M, Tani M, Okada KI, et al. Stump closure of a thick pancreas using stapler closure increases pancreatic fistula after distal pancreatectomy. *Am J Surg*. 2013. doi:10.1016/j.amjsurg.2012.11.023
20. Lee CW, Pitt H, Riall TS, et al. 751 Does Drain Fluid Amylase Accurately Predict Pancreatic Fistula? *Gastroenterology*. 2014. doi:10.1016/s0016-5085(14)63747-1
21. Shinchu H, Wada K, Traverso LW. The Usefulness of Drain Data to Identify a Clinically Relevant Pancreatic Anastomotic Leak After Pancreaticoduodenectomy? *J Gastrointest Surg*. 2006. doi:10.1016/j.gassur.2005.08.029
22. Ball CG, Pitt HA, Kilbane ME, Dixon E, Sutherland FR, Lillemoe KD. Perioperative blood transfusion and operative time are quality indicators for pancreatoduodenectomy. *HPB*. 2010. doi:10.1111/j.1477-2574.2010.00209.x

23. Gaujoux S, Cortes A, Couvelard A, et al. Fatty pancreas and increased body mass index are risk factors of pancreatic fistula after pancreaticoduodenectomy. *Surgery*. 2010. doi:10.1016/j.surg.2009.12.005
24. Ecker BL, McMillan MT, Allegrini V, 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*. 2019. doi:10.1097/SLA.0000000000002491
25. Villafane-Ferriol N, Shah RM, Mohammed S, et al. Evidence-Based Management of Drains Following Pancreatic Resection: A Systematic Review. *Pancreas*. 2018. doi:10.1097/MPA.0000000000000961
26. Beane JD, House MG, Ceppa EP, Dolejs SC, Pitt HA. Variation in Drain Management After Pancreatoduodenectomy: Early Versus Delayed Removal. *Ann Surg*. 2019. doi:10.1097/SLA.0000000000002570
27. Dumonceau JM. Distal pancreatectomy: Another indication for prophylactic pancreatic stenting? *Gastrointest Endosc*. 2010. doi:10.1016/j.gie.2010.05.016

6) ANNEXES

Histological diagnosis	Clinically Relevant Post-Operative Pancreatic Fistula (CR-POPF)		
	No	Yes	p
<i>Adenocarcinoma (%)</i> 35 (34.0)	27 (38.6)	8 (24.2)	0.1862
<i>Neuroendocrine tumor (%)</i> 24 (23.3)	14 (20.0)	10 (30.3)	
<i>IPMN (%)</i> 12 (11.7)	9 (12.9)	3 (9.1)	
<i>Serous Cystadenocarcinoma (%)</i> 5 (4.9)	2 (2.9)	3 (9.1)	
<i>Mucinous cystadenocarcinoma (%)</i> 9 (8.7)	8 (11.4)	1 (3.0)	
<i>Other (%)</i> 18 (17.5)	10 (14.3)	8 (24.2)	

Table 3: Histological diagnosis on pathological examination. IPMN: Intraductal papillary mucinous neoplasm

7) SERMENT D'HIPPOCRATE

En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure, au nom de l'Être suprême, d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine.

Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail.

Admis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

8) ABSTRACT

INTRODUCTION

Postoperative Pancreatic Fistula (POPF) is a common and serious complication after Distal Pancreatectomy (DP). The number and the weight of the different risk factors reported in literature still remain controversial and an effective and accepted score to predict the occurrence of grade B and C (Clinically Relevant; CR) POPF does not exist.

METHODS

Data regarding 103 consecutive patients undergoing DP were collected. A multivariate analysis of variables potentially predictive of fistula risk via multivariate logistic regression with backward selection was performed, in order to build a simplified score. The predictive performance of the score was then tested on the population studied. The accuracy in predicting a categorical outcome was evaluated using the Receiver Operating Characteristic (ROC) curves. Youden's J test was performed to evaluate the performance of a positive score on the POPF occurrence.

RESULTS

Thirty-three patients developed a CR-POPF : 24 grade B fistulas and 9 grade C fistulas. Operation time >4 hours, amylase levels on drains' fluid >500 UI on POD 3 and pancreatic thickness >10mm were found to be predictive of CR-POPF on multivariate analysis. A 4 points score was created from the variables selected in the multivariate model, by assigning 1 point for each of the previous parameters and 1 if the patient had a BMI > 30. The discriminating ability was tested on the ROC curve, showing an area under the curve of 0.83 (CI 95%=

[0.75 - 0.92]). On the Hosmer-Lemeshow test, the difference between the prediction of the model and the observed value is not significant (p-value = 0.44). The score threshold was determined at 2 points/4, which has the highest value according to the Youden index (0.53). The sensitivity is calculated at 82% (CI95%= [69 - 95]) and the specificity at 71 (CI95%= [61 - 82]). A threshold at 3 points/4 allows to reach a specificity of 99% (CI95%= [99 - 100]).

CONCLUSION

A simple score based on operation time, obesity, amylase level on abdominal drains on POD3 and pancreatic thickness measured at the isthmus on preoperative CT can predict the postoperative risk of developing CR-POPF with good sensitivity using a cutoff of 2 or more point.

9) RESUME

La fistule pancréatique est une complication fréquente et grave après une pancréatectomie distale. Le nombre et le poids des différents facteurs de risque rapportés dans la littérature restent encore controversés et il n'existe pas de score pour prédire la survenue de fistule pancréatique de grade B et C (cliniquement pertinente).

Les données concernant 103 patients consécutifs subissant une pancréatectomie ont été collectées.

Trente-trois patients ont développé une fistule pancréatique : 24 fistules de grade B et 9 fistules de grade C. Le temps opératoire supérieur à 4 heures, le taux d'amylase sur le liquide de drainage abdominal supérieur à 500 UI/L à J3 post opératoire, l'épaisseur du pancréas supérieur à 10 mm et un IMC supérieur à 30 se sont avérés prédictifs fistule pancréatique cliniquement pertinente. Un score de 4 points a été créé à partir des variables sélectionnées dans le modèle multivarié. La capacité de discrimination a été testée sur la courbe ROC, montrant une aire sous la courbe de 0,83 (IC 95% [0,75 - 0,92]). Le seuil du score a été déterminé à 2 points / 4, ce qui a la valeur la plus élevée selon l'indice de Youden (0,53). La sensibilité est calculée à 82% (IC95% [69 - 95]) et la spécificité à 71 (IC95% [61 - 82]). Un seuil à 3 points / 4 permet d'atteindre une spécificité de 99% (IC95% [99-100]).

MOTS CLES : Fistule Pancréatique, Pancréatectomie distale, Score prédictif, Temps opératoire, Obésité, Amylase, Epaisseur pancréatique.