Low Drain Amylase Predicts the Absence of Pancreatic Fistula Following Pancreatectomy

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Study Aim: To determine the utility of DFA1 in predicting the absence of PF development following pancreatectomy and to identify a reliable DFA1 cutoff under which PF can be ruled out

Background

- Pancreatic fistula is a well known complication following pancreatectomy, carrying significant morbidity.
- Many studies have assessed the perioperative risk factors for development of PF, allowing the allocation of patients into high and low risk groups. These findings may improve patient outcomes by enhancing preoperative patient discussions and by improving patient understanding of postoperative outcomes.
- Recent studies have identified drain fluid amylase on post operative day 1 (DFA1) as a reliable predictor of PF. However, the DFA1 thresholds in these studies are highly variable, ranging from 100 to 5000 U/L.
- **As a result, little is offered for surgeons to determine at which DFA1 level it becomes possible to reliably rule out pancreatic fistula, so as to allow early drain removal.**

Methods

- The ACS-NSQIP Pancreatectomy Demonstration Project (ACS NSQIP PDP) was used to enroll patients who underwent partial pancreatectomy between November 2011 to December 2012.
- The definition of PF as described by the PDP intends to include patients with persistent drainage of amylase rich fluid, >3x normal serum amylase and one of the following 3 criteria: drain continuation beyond 7 post-operative days, percutaneous drainage of a pancreatic fluid collection or re-operation.
- Additionally, the patient is coded as having a PF if the surgeon states it in the health record.
- Drain volume was not a consideration in this definition.

Inclusion Criteria

- Patients who underwent pancreaticoduodenectomy, distal pancreatectomy or enucleation were included.
- Only patients with recorded fields for both DFA1 and PF.
- Statistical analyses were carried forth with univariate and multivariable regression models. An ROC curve was performed to elucidate the strength of association between DFA1 and PF.

Results

Patient Selection

- A total of 2805 patients were included from 43 institutions. Of these, 81 patients were excluded due to having undergone total pancreatectomy or unspecified procedures.
- Of the remaining 2724 patients, 110 patients were excluded because there was no PF data recorded and 2078 patients were excluded due to a lack of DFA1 data.
- The remaining 536 patients were eligible for analysis and included the final study group (Figure 1).

Predictor of Pancreatic Fistula

- On univariate analysis, high BMI, small pancreatic duct size and soft gland texture were significant factors associated with PF. 25% of obese patients experienced a PF. In patients with duct size <3 mm, PF occurred in 29%, and 28% in patients with soft pancreatic texture.
- In addition, DFA1 was analyzed as a continuous variable, and was strongly associated with PF formation (Table1).

Independent Predictors of Pancreatic Fistula

- Logistic regression analysis revealed significant associations of PF with BMI, duct size, texture and DFA1 with odds ratios noted here. DFA1 was similarly associated with PF formation (Table 2).
- Only factors with p<0.10 on univariate analysis were included in log regression analysis, which controlled for the above 4 factors.
- ROC curve confirmed the strength of association of DFA1 and PF development (Figure 2).

DFA1 as a Predictor of the Absence of Pancreatic Fistula

- The sensitivity, specificity, positive and negative predictive values of DFA1 at multiple DFA1 cutoffs was evaluated.
- as the DFA1 level decreases, the sensitivity and NPV increase. However, the PPV was relatively poor for all values.
- <90 U/L demonstrated the highest Se (97%) and NPV (98%) (Table 3).
- As DFA1 increases, PF rates increase accordingly by DFA1 intervals as shown below (Figure 3).

Results

FIGURE 1. PATIENT SELECTION

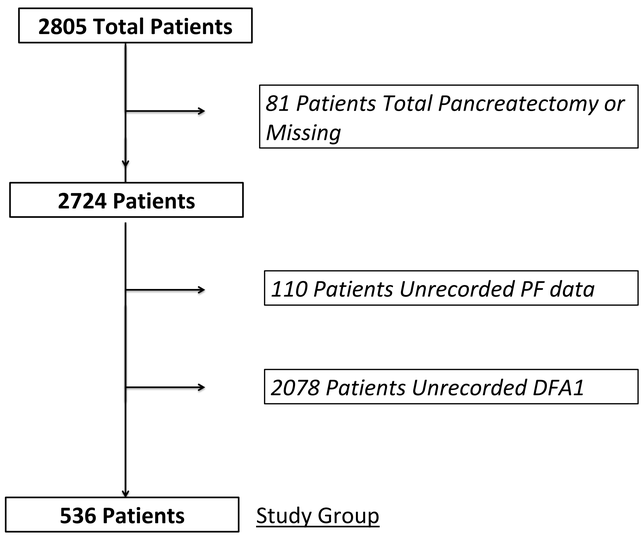


TABLE 1. PREDICTORS OF PANCREATIC FISTULA

Variable	Multivariable p-value	OR (95% CI)
BMI		
Normal	0.016	Referent
Overweight		1.084 (0.603 – 1.950)
Obese		2.197 (1.221 – 3.954)
Pancreatic Duct Size		
<3 mm	0.037	3.247 (1.062 – 9.933)
3-6 mm		1.482 (0.480 – 4.579)
>6 mm		Referent
Pancreatic Gland Texture		
Soft	0.033	2.521 (1.319 – 4.820)
Intermediate		1.644 (0.616 – 4.390)
Hard		Referent
DFA1 (continuous)	0.012	1.278 (1.056 – 1.546)

TABLE 2. INDEPENDENT PREDICTORS OF PANCREATIC FISTULA

Variable	PF rate (%)	Univariate p-value
BMI		
Normal	13	0.012
Overweight	17	
Obese	25	
Pancreatic Duct Size		
<3 mm	29	<0.001
3-6 mm	11	
>6 mm	7	
Pancreatic Gland Texture		
Soft	28	<0.001
Intermediate	16	
Hard	9	
DFA1 (continuous)		<0.001

FIGURE 2. STRENGTH OF RELATIONSHIP BETWEEN DFA1 AND PF

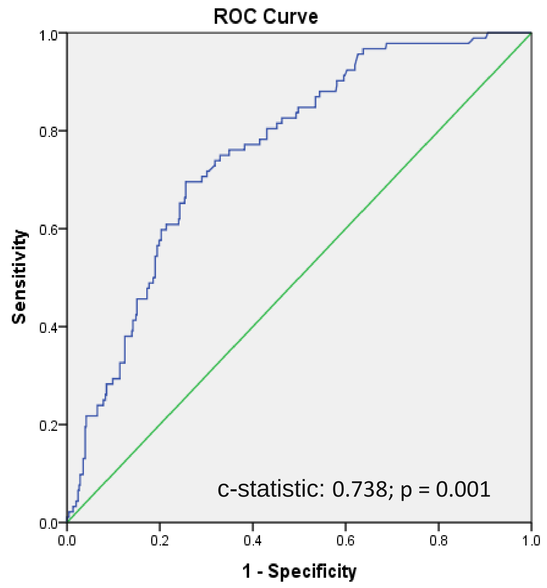
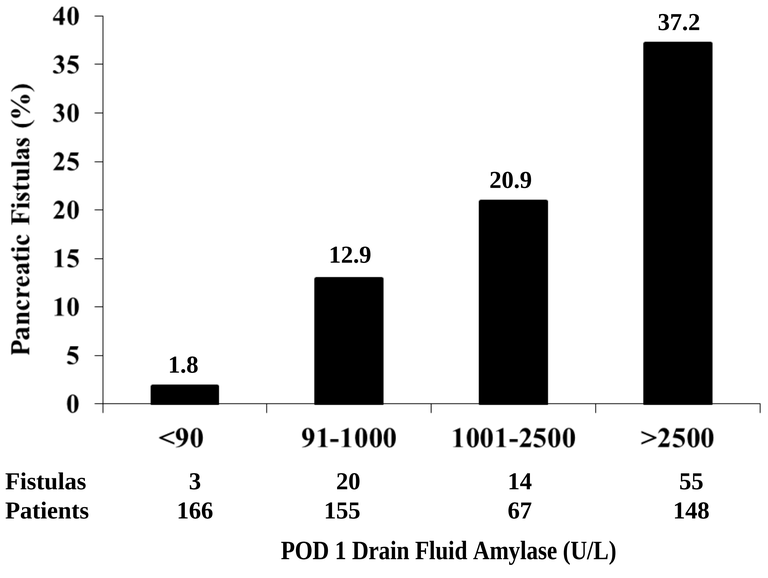


TABLE 3. ACCURACY OF DFA1 THRESHOLDS IN PREDICTING ABSENT PF

<DFA1 (U/L)	Se (%)	Sp (%)	NPV (%)	PPV (%)
5000	39	86	87	37
2500	60	79	91	37
1000	75	67	93	32
350	82	55	93	27
90	97	37	98	24

FIGURE 3. PANCREATIC FISTULA RATES ACCORDING TO DFA1 CUTOFF LEVEL



Conclusions

- Patients with very low DFA1, <90 U/L may be considered “very low risk” for pancreatic fistula development, with an associated sensitivity of 97% and NPV of 98%.
- This allows 31% patients in this study to have undergone early drain removal with a 3.3% false negative rate.
- Thus, early drain removal may be considered in patients with low DFA1.