Serum pancreatic enzymes as measurement for pancreatic exocrine insufficiency

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Introduction

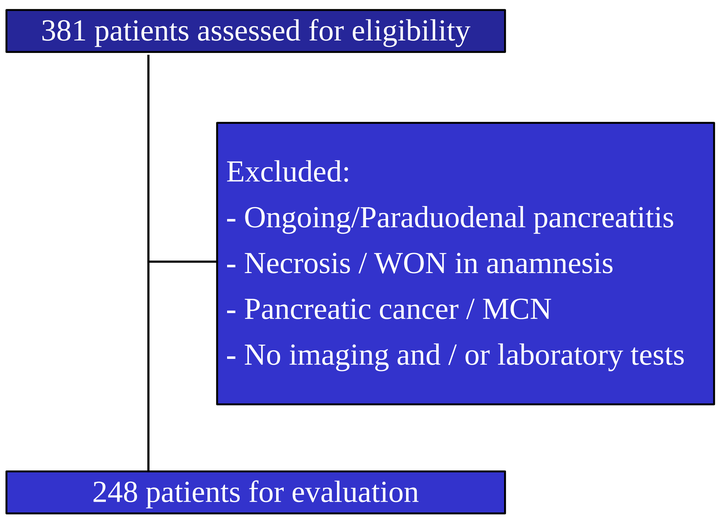
The pancreas as mixocrine gland is a crucial organ for the metabolic, endocrine system as well as for the exocrine, digestive system. Loss of the endocrine function results in diabetes mellitus, whereas the loss of the exocrine function results in pancreatic exocrine insufficiency (PEI) with insufficient secretion of the pancreatic enzymes and/or sodium bicarbonate. This may lead to a state of maldigestion and malabsorption with deficiencies especially in the fat-soluble vitamins A, D, E and K as well as a general state of malnutrition.

Over the last few decades, multiple tests - both direct and indirect - have been developed to measure the pancreatic function and to hence detect PEI. So far, fecal elastase 1 (FE-1) is most favored, but several studies have shown that the test only has a low sensitivity when it comes to detecting mild and moderate forms of PEI.

Aim of this retrospective study was to evaluate whether the serum pancreatic enzymes – so far only of diagnostic value for acute pancreatitis – are also suitable as marker for a pancreatic exocrine insufficiency.

Materials and Methods

For this study the data of 381 patients who had attended the Gastrocentrum of the Karolinska University Hospital for diagnosis/treatment of autoimunne pancreatitis (AIP), chronic pancreatitis (CP) and PEI as well as the data of control groups was collected. After excluding the data of 133 patients, 248 patients could be evaluated.



Up to two MRI/CT images were evaluated regarding the pancreatic function based on Matos and the size of the pancreas (atrophy vs- non-atrophy). These were compared with the lowest levels of pancreas amylase, lipase, vitamin D and CA 19-9 within 6 months as well as the lowest level of FE-1 within 1 year prior/after the imaging.
Furthermore we looked at diabetes mellitus as parameter for the endocrine function and risk factors such as smoking, alcohol and snus.

	CP	AIP	PEI	IBS / cystic lesions	IAR	IAR with cystic lesions	total	p
n	72	50	6	46	43	31	248	
Age (years)	53,4 ± 18,2	57,7 ± 19,7	43,2 ± 22,1	52,6 ± 14,8	53,3 ± 10,7	62,2 ± 12,1	54,9 ± 16,5	0,029
Gender								0,006
Females (%)	38 (53%)	21 (42%)	0	32 (70%)	27 (63%)	19 (61%)	137 (55%)	
Males (%)	34 (47%)	29 (58%)	6 (100%)	14 (30%)	16 (37%)	12 (39%)	111 (45%)	

Demographic data of the 248 patients included

Results

Imaging showed significant differences between the groups regarding pancreatic atrophy and the pancreatic duct breadth

	CP	AIP	PEI	IBS / cystic les.	IAR	IAR with cystic les.	total	p
Atrophy (set A / set B)								0,000 / 0,000
No	24 (34%) / 5 (19%)	15 (30%) / 2 (8%)	1 (20%) / 0	41 (89%) / 6 (67%)	43 (100%) / 13 (100%)	26 (84%) / 4 (50%)	150 (61%) / 20 (37%)	
Yes	47 (66%) / 21 (81%)	35 (70%) / 23 (92%)	4 (80%) / 1 (100%)	5 (11%) / 3 (33%)	0 / 0	5 (16%) / 4 (50%)	96 (39%) / 52 (63%)	
Ductus Pancreaticus (set A / set B)								0,000 / 0,000
Normal	18 (29%) / 5 (24%)	32 (89%) / 15 (83%)	4 (67%) / 1 (100%)	41 (98%) / 7 (100%)	42 (98%) / 13 (100%)	27 (100%) / 6 (100%)	164 (76%) / 47 (71%)	
Dilated	45 (71%) / 16 (76%)	4 (11%) / 3 (17%)	2 (33%) / 0	1 (2%) / 0	1 (2%) / 0	0 / 0	53 (24%) / 19 (29%)	

Whereas the majority of patients with AIP, CP and PEI showed pancreatic atrophy, there was no atrophy to be seen in the majority of the patients in the control groups.

A dilatation of the ductus pancreaticus could be seen in the majority of patients with CP, whereas the breadth of the ductus was normal in the majority of the patients from all other groups. Patients with CP, AIP and PEI seemed more likely to show a dilated ductus pancreaticus than patients from the control groups.

There was a significantly unequal distribution regarding the prevalence of Diabetes Mellitus

	CP	AIP	PEI	IBS / cystic les.	IAR	IAR with cystic les.	total	p
Diabetes Mellitus								0,000
No	54 (75%)	31 (62%)	5 (83%)	43 (94%)	41(95%)	30 (97%)	204 (82%)	
Type 1	2 (3%)	1 (2%)	1 (17%)	0	1 (2%)	0	5 (2%)	
Type 2	16 (22%)	18 (36%)	0	3 (7%)	1 (2%)	1 (3%)	39 (16%)	
Insulin treatment								0,611
No	6 (33%)	5 (26%)	0	2 (67%)	1 (50%)		14 (33%)	
Yes	12 (67%)	14 (74%)	1 (100%)	1 (33%)	1 (50%)		29 (67%)	

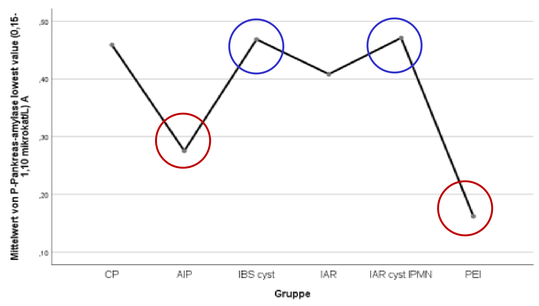
DM type I was most often seen in the patients with PEI (17%). The highest rate of DM type II could be seen in the patients with CP and AIP. The control groups had the lowest percentage of patients with DM, with over 90% of the patients in each control group not suffering from DM. Although only a minority of the patients with DM suffered from type I (5 out of 39 patients), the majority of patients with DM received treatment with insulin, indicating a significant loss of the endocrine function. However, there was no significant difference in the distribution of insulin treatment across all groups.

The levels of pancreas amylase and fecal elastasis measured differed significantly between the groups

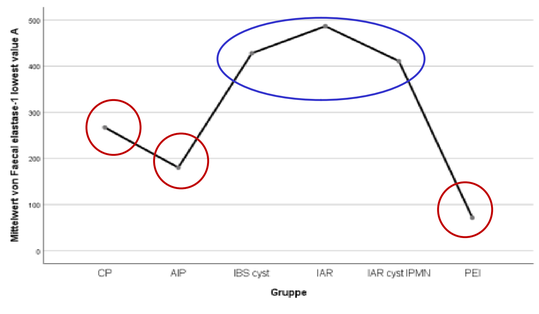
	CP	AIP	PEI	IBS / cystic lesions	IAR	IAR with cystic lesions	total	p
Mean value of pancreas amylase (0,15-1,10 mikrokat/L)								0,043 / 0,014
set A (n)	0,459 (58)	0,275 (39)	0,162 (5)	0,469 (41)	0,408 (30)	0,471 (18)	0,409 (191)	
set B (n)	0,326 (24)	0,204 (20)	0,100 (1)	0,479 (8)	0,467 (6)	0,413 (6)	0,325 (65)	
Fecal elastase (>200 µg/g faeces)								0,000 / 0,009
set A (n)	267 (53)	180 (37)	71 (6)	428 (36)	486 (7)	411 (7)	294 (146)	
set B (n)	225 (14)	130 (19)	14 (1)	379 (5)	501 (2)	387 (2)	216 (43)	

Patients with PEI and AIP had the lowest mean values of pancreatic amylase and FE-1.

For pancreatic amylase, a comparison of the groups with each other in set A showed a significant difference between
- Patients with PEI and patients with CP, IBS/cystic lesions as well as IAR with cystic lesions
- Patients with AIP and IAR with cystic lesions



For FE-1, a comparison in set A showed a significant difference between
- Patients with PEI and the control groups
- Patients with AIP and the control groups
- Patients with CP and patients with IBS/cystic lesions and IAR
- Patients with PEI and CP



Pancreatic amylase and lipase show high specifity but low sensitivity in detecting PEI

	FE-1 > 200 µg/g faeces	FE-1 < 200 µg/g faeces
P-lipase >0,22 / 0,36 mikrokat/L	45	16
P-lipase <0,22 / 0,36 mikrokat/L	6	18
	Specifity 0.8824	Sensitivity 0.5294
P-amylase >0,15 mikrokat/L	61	18
P-amlyase <0,15 mikrokat/L	7	25
	Specifity 0.8971	Sensitivity 0.5814

To determine the specifity and sensitivity of pancreatic enzymes in assessing PEI, patients were sorted into two groups according to their FE-1 value; a) patients with FE-1 <200 were defined as having pancreatic exocrine insufficiency, b) patients with FE-1 >200 were defined as healthy.
The corresponding pancreas amylase and/or lipase values were divided into a) under the lower level of normal (LLN) or b) above the LLN to see how well these values correlate with FE-1.
Pancreasamylase showed a sensitivity of 58% in assessing PEI and a specifity of 88%.
Pancreaslipase showed a sensitivity of 53% in assessing PEI and a specifity of 88%.

Summary and Conclusions

First results of ths project show that significant differences can be seen between patients with chronic pancreatitis, autoimmune pancreatitis or pancreatic exocrine insufficiency as opposed to control groups regarding
- Imaging
- Levels of pancreatic enzymes and FE-1
- Prevlence of Diabetes Mellitus

In detecting pancreatic exocrine insufficiency, pancreatic amylase and lipase show a high specifity, but low sensitivity, when comapred to FE-1.

Further evaluation is ongoing.

Abbreviations
CP: chronic pancreatitis
AIP: autoimmune pancreatitis
PEI: pancreatic exocrine insuficiency
IAR: Individuals at risk for pancreatic cancer
IBS: irritable bowel syndrome
IPMN: intraductal papillary mucinous neoplasm