CAPER Collaborative Alliance for Pancreatic Education and Research

JOHNS HOPKINS MEDICINE

Exocrine Pancreatic Insufficiency in Chronic Pancreatitis

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Chronic Pancreatitis (CP)

- Fibro-inflammatory disorder of the pancreas
- Features include:
  - pancreatic calcifications
  - ductal changes
  - **exocrine pancreatic insufficiency**
  - histological changes

Exocrine Pancreatic Insufficiency (EPI)

- Definition:
  - inability of the pancreas to secrete fluids for adequate digestion
  - usually manifests after 90% of acinar cell parenchyma is lost
- Symptoms: Steatorrhea, abdominal pain
- Diagnosis: made by direct or indirect testing
- Sequela: weight loss/malnutrition, fat soluble vitamin deficiency, bone demineralization
- Treatment: pancreatic enzyme replacement therapy (PERT)
  - Low-dosing < 60,000 USP/day
  - High-dosing ≥ 60,000 USP/day
  - Appropriate dosing: 40-50,000 USP/meal

Study Aims

Aims:

1. What percentage of patients with CP are on PERT?
2. What clinical factors influence PERT use?
3. What percentage of patients on PERT are dosed with high-dosing, or low-dosing or appropriate dosing?
4. What clinical factors affect the dosing of PERT?

Cohort of CP by M-ANNHEIM

Definite CP is established by one or more of the following additional criteria:

1. **Pancreatic calcifications**
2. **Moderate or marked ductal lesions**
3. Marked and persistent exocrine insufficiency defined as pancreatic steatorrhea markedly reduced by enzyme supplementation
4. Typical histology of an adequate histological specimen

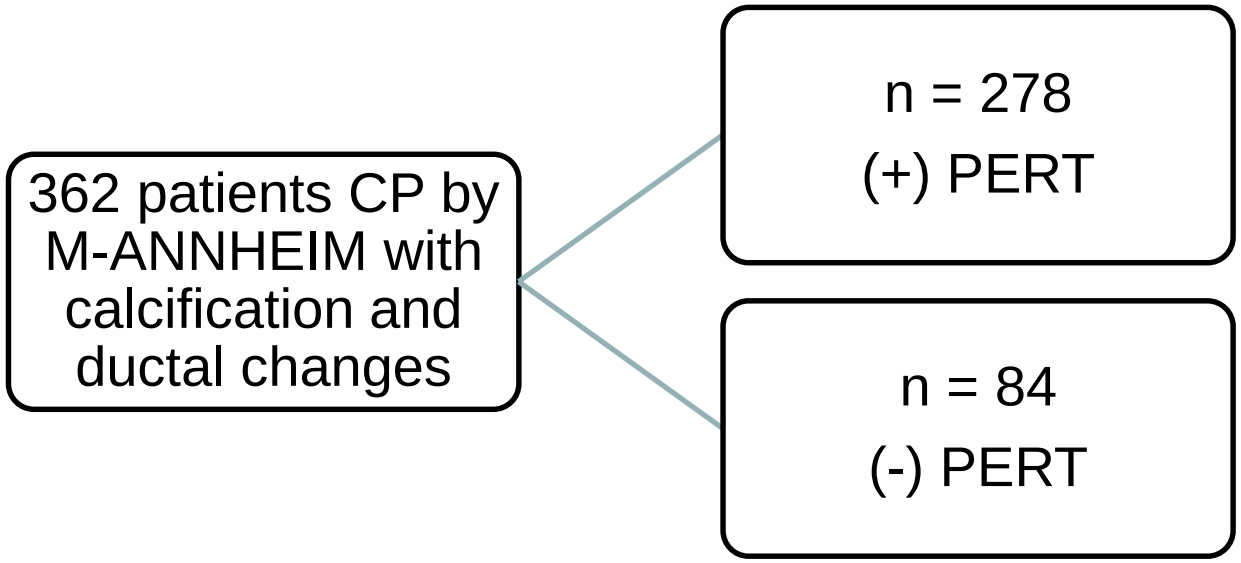
Seen in Pancreas Clinic at JHH from 2011-2019

Chronic Pancreatitis by M-ANNHEIM

	Total (n=362)
Age, (y)	49.27 ± 15.8
Gender, (Male)	198(54.7)
Race	
White	266(73.9)
Black	64(17.9)
Other	30(8.3)
Etiology	
Toxic	170(46.9)
Idiopathic	88(24.3)
Genetic	76(21.0)
Other	28(7.73)
BMI (kg/m^2)	24.76 ± 5.6

MANNHIEM	
Calcification only	139(38)
Moderate-Marked Ductal Changes only	111(31)
Calcification and ductal changes	112(31)
Endocrine Insufficiency	
Insulin-independent Diabetes	74(31)
Insulin-dependent Diabetes	15(6.2)
Exocrine Insufficiency	n = 208
Fecal Elastase (<100)	99(48)
Fecal Elastase (100-200)	29(13)
Fecal Elastase (>200)	80(38)

PERT



77% of patients with CP by M-ANNHEIM criteria were on PERT

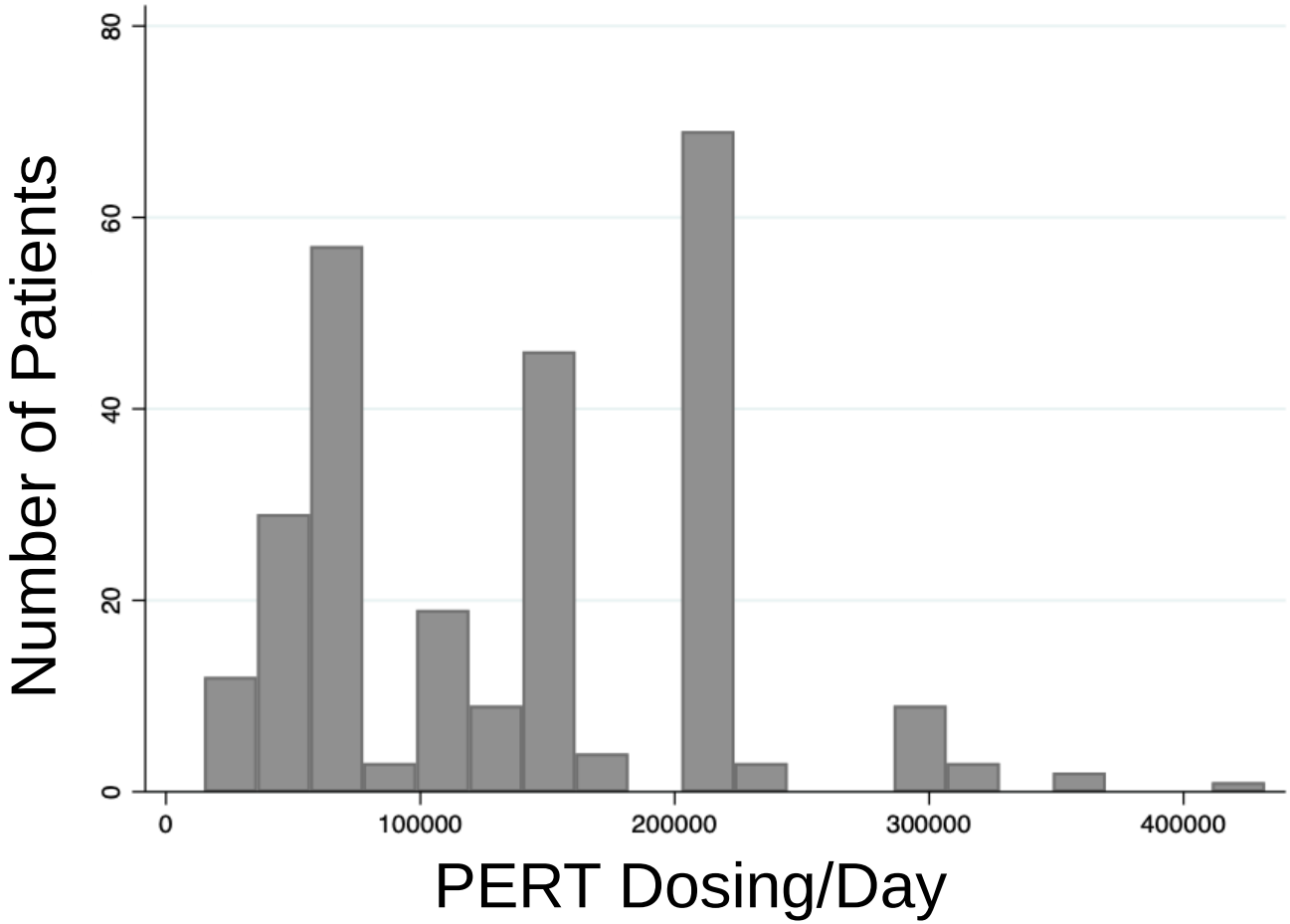
Differences in patients on PERT vs No PERT

	Total (n=362)	On PERT (n=278)	No PERT (n=84)	OR [95%CI]	P value
Age, y	49.27 ± 15.8	49.4 ± 15.8	50 ± 15.6	-	0.6
Gender, Male	198(54.7)	153(50)	45(53.5)	-	0.8
Race					
White	266(73.89)	207(74.7)	59(71)	-	
Black	64(17.88)	50(18)	14(16.7)	-	0.4
Other	30(8.3)	20(7)	10(12)	-	
Etiology					
Toxic	170(46.9)	139(50)	31(36.9)	1.7[1.03,2.8]	**0.03**
Genetic	76(20.99)	61(21.9)	15(17.8)	1.2[0.6,2.4]	0.4
Idiopathic	88(24.3)	58(20)	30(35.7)	0.4[0.2,0.8]	**0.006**
Other	28(7.73)	20(7.1)	8(9.5)		
BMI (kg/m^2)	24.76 ± 5.6	24.2 ± 5.1	26.8 ± 6.7	0.9[0.8,0.9]	**0.003**
MANNHIEM					
Calcification only	139(38.4)	105(37.7)	34(40.4)	0.8[0.5,1.4]	0.6
Moderate-Marked Ductal Changes only	111(30.66)	75(26.9)	36(42.8)	0.4[0.2,0.8]	**0.006**
Calcification and ductal changes	112(30.9)	98(35.2)	14(16.7)	2.7[1.4,5.2]	**0.002**

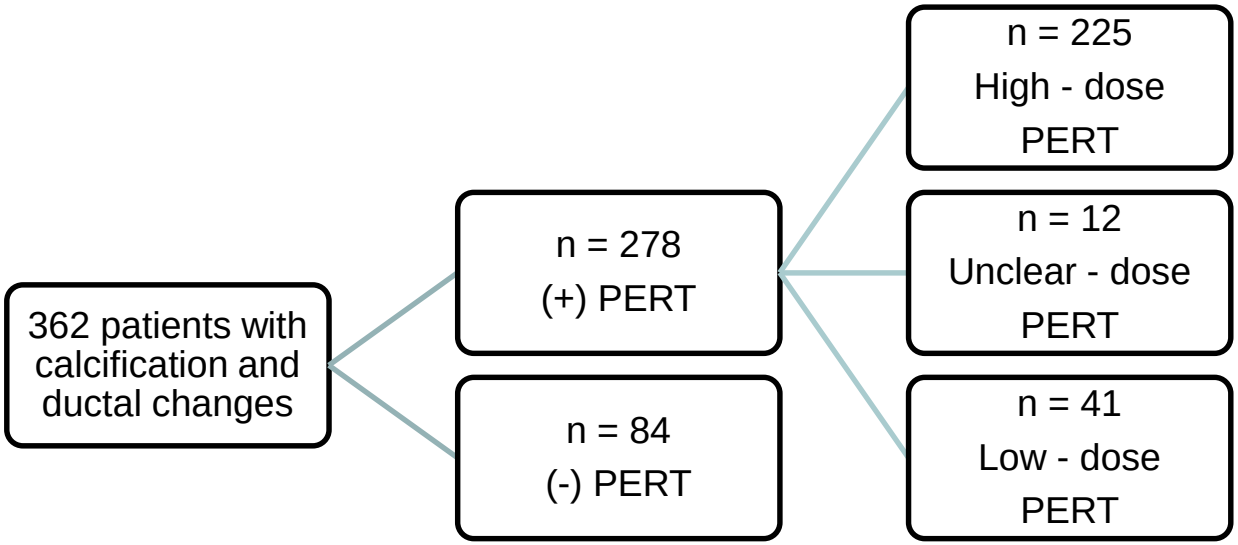
Patients with Steatorrhea and FE < 100 are on PERT

	Total (n=362)	On PERT (n=278)	No PERT (n=84)	OR [95%CI]	P value
Exocrine Insufficiency Clinical Symptoms					
Steatorrhea	160 (44)	148 (53)	12 (14)		
No Steatorrhea	136 (38)	80 (29)	56 (67)	8.6[4.3,17]	**<0.001**
Unclear	66(18)	50 (18)	16 (19)		
Fecal Elastase (FE) Tested (n)	208	182	26	-	-
FE-1 <100	99 (48)	94 (52)	5 (19)	4.5[1.6,12]	**0.003**
FE-1 100-200	29 (14)	26 (14)	3 (12)	1.2[0.3,4.5]	0.7
FE-1 >200	80 (38)	62 (34)	18 (69)	0.2[0.09,0.5]	**0.001**

Range of PERT dosing



Majority of patients are on high dose PERT



84% of patients with CP by M-ANNHEIM were on High-dose > 60,000

15% of patients with CP by M-ANNHEIM were on Low-dose < 60,000

50% of patients with CP by M-ANNHEIM were on > 120,000 USP/day

23% (52/225) on High-Dose PERT and 4.8% (2/41) on Low-Dose PERT had idiopathic etiology(p=0.017, OR =5.8[1.3,25])

Strengths

- Well defined cohort of definite CP
- EPI testing was conducted on a majority of these patients
- Higher prevalence of genetic CP

Limitations

- Referral center
- FE-1 test characteristics
- Unclear why patients were initiated on PERT
- Unclear of the duration of CP
- Histology not present for most patients

Future Directions

- Better diagnostics for EPI
- Nutrition assessment and longitudinal follow of these patients
- Assess for endocrine insufficiency
- Assess the prevalence of EPI in CP patients via subgroup analysis

Study Conclusions

In a well-defined cohort of CP at a referral center:

- 77% of patients were on PERT therapy
- 84% of patients with CP by M-ANNHEIM were on High-dose PERT
- 15% of patients with CP by M-ANNHEIM were on Low-dose PERT
- 50% of patients with CP by M-ANNHEIM were on > 120,000 USP/day

Study Conclusions

- Patients with 1) idiopathic CP and 2) only moderate to marked ductal changes were less likely to be on PERT
- Patients with 1) toxic CP and 2) BOTH moderate to marked ductal changes and pancreatic calcifications were more likely to be on PERT
- BMI was lower for patients on PERT
- Patients with FE< 100, more of these patients were on PERT
- Patients with FE > 200, less patients were on PERT.

Thank You

UPMC and Pancreas Fest

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CAPER Pancreas Scholars Program

JHH

- Vikesh Singh
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- Venkata Akshintala

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