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ORIGINAL ARTICLE

Observational Study

# Comparing acid steatocrit and faecal elastase estimations for use in M-ANNHEIM staging for pancreatitis

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## Abstract

***AIM***

To compare two tests for exocrine pancreatic function (EPF) for use in M-ANNHEIM staging for pancreatitis.

***METHODS***

One hundred and ninety four consecutive patients with acute pancreatitis (AP; $n$ = 13), recurrent acute pancreatitis (RAP; $n$ = 65) and chronic pancreatitis (CP; $n$ = 116) were enrolled. EPF was assessed by faecal elastase-1 (FE-1) estimation and stool fat excretion by the acid steatocrit method. Patients were classified as per M-ANNHEIM stages separately based on the results of the two tests for comparison. Independent Student's $t$-test, $\chi^2$ test, Kruskal-Wallis test, Mann-Whitney $U$ test and McNemar's test were used as appropriate.

***RESULTS***

Sixty-one (52.5%) patients with CP had steatorrhoea when assessed by the acid steatocrit method; 79

(68.1%) with CP had exocrine insufficiency by the FE-1 test ($\chi^2$ test, $P < 0.001$). The results of acid steatocrit and FE-1 showed a significant negative correlation (Spearman's rho = -0.376, $P < 0.001$). A statistically significant difference was seen between the M-ANNHEIM stages as classified separately by acid steatocrit and the FE-1. Thirteen (6.7%), 87 (44.8%), 89 (45.8%) and 5 (2.5%) patients were placed in M-ANNHEIM stages 0, Ⅰ, Ⅱ, and Ⅲ respectively, with the use of acid steatocrit as against 13 (6.7%), 85 (43.8%), 75 (38.6%), and 21 (10.8%) respectively by FE-1 in stages 0, Ⅰ, Ⅱ, and Ⅲ thereby altering the stage in 28 (14.4%) patients ($P < 0.001$, McNemar's test).

***CONCLUSION***

FE-1 estimation performed better than the acid steatocrit test for use in the staging of pancreatitis by the M-ANNHEIM classification since it diagnosed a higher proportion of patients with exocrine insufficiency.

**Key words:** Chronic pancreatitis; Pancreatic function tests; Pancreatic elastase; Staging; Steatorrhoea



**Core tip:** Patients with acute, recurrent acute and chronic pancreatitis were classified as per M-ANNHEIM stages, separately based on the results of two exocrine function tests (acid steatocrit method and faecal elastase test) for comparison. A statistically significant difference was seen between the M-ANNHEIM stages as classified separately by the two tests. Faecal elastase-1 estimation performed better than the acid steatocrit test for use in the staging of pancreatitis by the M-ANNHEIM classification since it diagnosed a higher proportion of patients with exocrine dysfunction.

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## INTRODUCTION

Steatorrhoea from pancreatic insufficiency increases in frequency as chronic pancreatitis (CP) advances and forms an important parameter for staging the disease in various classification systems[1-3]. The M-ANNHEIM classification, a new system for staging and assessing the severity of pancreatitis, subdivides the disease into 5 stages based on pain and pancreatic functions[1]. Different pancreatic function tests (PFT) and tests for assessing steatorrhoea have been in use for assessing exocrine pancreatic function (EPF) in patients with CP[4]. PFT have also been used for diagnosing CP when imaging studies are inconclusive for the same as happens in early stages of the disease[4]. Direct PFT like the secretin test have a greater sensitivity and help in diagnosing CP in its moderate to late stages as compared to early stages of the disease[4]. However, the test is cumbersome, not easily available, poorly standardised across centres, poses difficulty in measuring the enzyme output and is poorly tolerated by some patients due to the need for oro-duodenal intubation[5]. The 72-h quantitative faecal fat estimation is considered the best method for assessing steatorrhoea. A major drawback of this method has been the need to collect stool specimen for 72 h and to store and process them[6].

The acid steatocrit method correlates well with the 72-h quantitative faecal fat estimation and has a sensitivity, specificity and positive predictive value of 100%, 95% and 90% respectively, and acts as an easier alternative[7,8]. The other advantages of this method are its simplicity, reliability and cost-effectiveness for evaluating steatorrhoea in CP[8-11].

Faecal elastase-1 (FE-1), is a useful indirect pancreatic function test in which a random spot stool sample can be used to identify exocrine pancreatic insufficiency (EPI) in well established CP, the situation in which steatorrhoea commonly occurs[12-14]. Studies indicate that FE-1 is useful in estimating fat malabsorption in CP and correlates well with the acid steatocrit method[15].

Not many studies have compared FE-1 and the acid steatocrit method for evaluating EPF in CP. The aim of our study was to determine the usefulness of stool fat analysis by the acid steatocrit method and FE-1 estimation in the staging of pancreatitis using the M-ANNHEIM classification system.

## MATERIALS AND METHODS

### *Patients*

Consecutive patients with pancreatitis presenting to the Department of Gastroenterology and Hepatology, Kasturba Hospital, Manipal between June 2009 and June 2013 were prospectively enrolled in this cross sectional study. Patients underwent detailed clinical evaluation and were classified to have AP, RAP and CP. AP was defined as a single episode of any two of typical upper abdominal pain, raised serum amylase and/or lipase three times above the upper limit of normal and evidence of pancreatitis on imaging[16]. Patients presenting with more than one episode of acute pancreatitis with complete resolution of symptoms in between the episodes and no evidence of CP on imaging were considered to have RAP[17,18]. CP was defined by the presence of pancreatic calcifications and/or ductal changes, visualized by ultrasonography, computed tomography (CT), endoscopic ultrasound (EUS) ("consistent with" and "suggestive of" CP by the Rosemont criteria), endoscopic retrograde cholangiopancreatography or magnetic resonance

**Table 1 Demographic and clinical features of patients identified with pancreatitis based on imaging criteria**

| | AP ($n$ = 13) | RAP ($n$ = 65) | CP ($n$ = 116) | $P$ value |
|---|---|---|---|---|
| Age (yr) (mean ± SD) | 29.8 ± 11.6 | 29.0 ± 11.5 | 33.3 ± 14.2 | 0.10 |
| Male: female | 12 : 1 | 57 : 8 | 96 : 20 | 0.53 |
| Alcoholic pancreatitis (≥ 50 g/d) | 2 (15.4) | 19 (29.2) | 28 (24.1) | 0.10 |
| Idiopathic pancreatitis | 11 (84.6) | 46 (70.8) | 88 (75.9) | 0.52 |
| Duration of symptoms (in months) [median (interquartile range)] | 0 (0-0.2) | 7.0 (3.5-24.0) | 24.0 (4.0-48.0) | < 0.001 |
| VAS (mean ± SD) | 5.4 ± 2.0 | 6.4 ± 2.31 | 5.4 ± 2.5 | 0.02 |

A $P$ value of < 0.05 was considered statistically significant.

cholangiopancreatography (MRCP)[19,20].

Stool samples were collected from all patients in two separate containers and one sample was stored at -80 ℃, for estimation of FE-1 by ELISA by using a monoclonal antibody based ELISA kit (ScheBo Biotech, Giessen, Germany) as per manufacturer's instructions. Values of ≥ 200 μg per gram of stool, 100 and 200 μg per gram and < 100 μg per gram were categorised as normal, mild to moderate EPI and severe insufficiency respectively[21].

### Stool fat estimation by the acid steatocrit method

Semiquantitative stool fat estimation by the acid steatocrit method was done on random spot stool samples as proposed by Tran *et al*[11]. 500 mg of stool was diluted with water and homogenized for 2 to 5 min. 500-μL aliquot of the homogenized stool were added with 100 mL of Perchloric acid and the pH was confirmed to be < 1. The mixture was aspirated into a capillary tube, sealed at one end and centrifuged at 13000 revolutions per minute for exactly 15 min[9,11]. The length of the fatty layer and the length of the solid layer were measured. Acid steatocrit (%) was obtained by the formula: fatty layer/(fatty layer + solid layer) × 100. The stool fat (in grams/day) was calculated by the equation: -0.43 + (0.45 × acid steatocrit %)[9]. Steatorrhoea was diagnosed when the stool fat excretion was 7 g/d or higher[4].

Patients were classified as per the M-ANNHEIM staging system first using the acid steatocrit method and then by using the FE-1 test also for comparison.

### Statistical analysis

Independent Student's $t$-test and the $\chi^2$ test were used as appropriate. Spearman's rho was used to analyse the correlation between the results of the two tests for exocrine function. The Kruskal-Wallis test was used to compare non normal continuous variables between the various M-ANNHEIM stages. A $P$ value of < 0.05 was considered as statistically significant. The Mann-Whitney $U$ test was used to compare continuous variables between any two M-ANNHEIM stages with Boneferonni adjustments for multiple pairwise comparisons considering a $P$ value of < 0.008 as statistically significant for 6-pairwise comparison. The McNemar's test was used to compare the nominal data. A $P$ value of < 0.05 was considered as statistically significant. The statistical review for this study was performed by a biomedical statistician.

The study protocol was approved by the Ethics Committee of Manipal University. All study participants or their legal guardians provided written informed consent prior to study enrolment.

## RESULTS

Of the 194 consecutive patients recruited, 13 (6.8%) had AP, 65 (33.5%) had RAP and 116 (59.7%) had CP. Their baseline characteristics are shown in Table 1.

### Correlation between exocrine insufficiency assessed by acid steatocrit and FE-1 estimation

EPI was tested by acid steatocrit and FE-1 by ELISA in all 194 patients. Stool fat analysis by acid steatocrit method showed a significant negative correlation (Spearman's rho = -0.376, $P$ < 0.001) with FE-1 indicating that both methods had a good agreement for assessing EPI. None of the patients with AP or RAP showed evidence of EPI by either test. Among a total of 116 patients with CP, 61 (52.5%) and 79 (68.1%) patients showed the presence of EPI by the acid steatocrit method and FE-1 respectively. This difference was statistically significant ($\chi^2$ test, $P$ < 0.001).

### M-ANNHEIM staging using the acid steatocrit test

Since all patients in the present study consulted for abdominal pain, there were no patients with stage Ⅳ disease as per the M-ANNHEIM classification. The median (IQR) stool fat excretion levels as assessed by the acid steatocrit method were significantly different between the M-ANNHEIM stages 0, Ⅰ, Ⅱ and Ⅲ in a 6-pairwise comparison ($P$ < 0.001, by Kruskal-Wallis test; Table 2). The stool fat excretion was also significantly different when compared between any two stages except between stages 0 and Ⅰ (Table 2).

### M-ANNHEIM staging using FE-1 estimation

The median (IQR) FE-1 values were significantly different between the different M-ANNHEIM stages in

**Table 2 Stool fat in grams/day by acid steatocrit in M-ANNHEIM stages of pancreatitis**

| M-ANNHEIM stage (*n* %) | Median (IQ range) of stool fat in g/d |
|---|---|
| 0, 13 (6.7) | 6.3 (6.0-6.6) |
| Ⅰ, 87 (44.8) | 6.3 (5.9-6.4) |
| Ⅱ, 89 (45.8) | 7.5 (6.4-10.8) |
| Ⅲ, 5 (2.5) | 15.3 (12.0-15.6) |

A statistically significant difference was present between the different M-ANNHEIM stages ($P < 0.001$, Kruskal-Wallis test). Comparison between any two stages showed a statistically significant difference between stages 0 and Ⅱ, and stages Ⅱ and Ⅲ ($P = 0.002$, Mann-Whitney *U* test) and also between stages 0 and Ⅲ, Ⅰ and Ⅱ, Ⅰ and Ⅲ ($P < 0.001$; Mann-Whitney *U* test). A *P* value of < 0.008 was considered statistically significant for such comparisons between any two groups after Alpha adjustment.

**Table 3 Faecal elastase-1 levels in M-ANNHEIM stages of pancreatitis**

| M-ANNHEIM stage (*n* %) | Median (IQ range) of stool fat in g/d |
|---|---|
| 0, 13 (6.7) | 289.0 (249.0-383.2) |
| Ⅰ, 85 (43.8) | 389.1 (263.2-436.1) |
| Ⅱ, 75 (38.6) | 144.3 (108.9-219.0) |
| Ⅲ, 21 (10.8) | 87.6 (41.1-119.1) |

A statistically significant difference was present between the different M-ANNHEIM stages ($P < 0.001$, Kruskal-Wallis test). Comparison between stages 0 and Ⅱ, 0 and Ⅲ, Ⅰ and Ⅱ, and Ⅱ and Ⅲ showed a statistically significant difference ($P < 0.001$ for all comparisons, Mann-Whitney *U* test). A *P* value of < 0.008 was considered statistically significant for such comparisons between any two groups after Alpha adjustment.

a 6-pairwise comparison ($P < 0.001$, by Kruskal-Wallis test, Table 3). These values were also significantly different when compared between any two stages except between stages 0 and Ⅰ (Table 3).

### *Tests for exocrine function - relevance to M-ANNHEIM staging*

To determine the usefulness of the two methods of assessing EPI for use in the M-ANNHEIM staging, we compared the number of patients in M-ANNHEIM stages obtained separately by using acid steatocrit and FE-1 estimations. As shown in Table 4, 28 (14.4%) patients had a change in stage by using FE-1 as against the use of acid steatocrit. 7 (3.6%), 5 (2.5%), 16 (8.2%) shifted from stage Ⅰ to Ⅱ, Ⅱ to Ⅰ and Ⅱ to Ⅲ respectively. This difference was statistically significant ($P < 0.001$, Mc Nemar's test; Table 4).

## DISCUSSION

By comparing M-ANNHEIM stages of pancreatitis as determined by using the acid steatocrit method and FE-1 levels we have shown that 14.4% of patients had a change in stage, most often a move to a higher stage, with the use of the latter. This is because FE-1 estimation confirmed EPI in a significantly higher

**Table 4 Comparing the number of patients based on M-ANNHEIM staging by acid steatocrit and faecal elastase-1 estimations *n* (%)**

| M-ANNHEIM stages | Acid steatocrit method | FE-1 test |
|---|---|---|
| 0 | 13 (06.7) | 13 (06.7) |
| Ⅰ | 87 (44.8) | 85 (43.8) |
| Ⅱ | 89 (45.8) | 75 (38.6) |
| Ⅲ | 05 (2.5) | 21 (10.8) |

A *P* value < 0.05 was considered statistically significant. A statistically significant difference was present between the number of those assessed by both methods in M-ANNHEIM stages ($P < 0.001$, Mc Nemar's test). FE-1: Faecal elastase-1.

number of patients compared to the acid steatocrit method. Though the tests used in our study measure different aspects of EPI *i.e.*, enzyme secretion and fat excretion respectively, the results of the two showed a high degree of correlation as expected. The lower rate of detection of EPI by the acid steatocrit test could possibly be attributed to the disadvantages this method. These include a lack of standardisation of the test and the effect of dietary fat intake at the time of sample collection on the test results[15,22]. The number of patients in M-ANNHEIM stages 0 and Ⅲ were smaller and a higher number would have enhanced the quality of this study.

Unlike with the acid steatocrit method FE-1 estimation offers many advantages. In addition to its high sensitivity for assessing moderate to severe EPI, it correlates well with the findings of imaging studies in patients with CP and unlike other pancreatic enzymes such as chymotrypsin, elastase is not degraded as it passes through the gut[6,15,23-26]. Bian *et al*[27] have shown that the secretin-enhanced MRCP (sMRCP) significantly correlates with the FE-1 test to quantify the pancreatic exocrine function in patients with CP based on the M-ANNHEIM staging. However, sMRCP has its own limitations in the detection of EPI in patients with CP, given its high cost, the semiquantitaive nature of its results and a modest sensitivity of 69%[28]. The limitations of FE-1 estimation such as its lower sensitivity for detecting mild EPI should however be kept in mind while using this test[4,6].

Estimation of 72-h stool fat excretion and the secretin test are considered the gold standard for assessing steatorrhoea and EPI respectively. It is likely that these tests would have provided different results if we had used them in the M-ANNHEIM staging of pancreatitis. A recent study showed that FE-1 is highly sensitive to diagnose EPI, but low on specificity as compared to the 72-h stool fat excretion test[29]. However, 72-h stool fat excretion and the secretin test are demanding on patients and laboratories alike and are hence uncommonly used at present[6]. It is unlikely that a simple test for steatorrhoea like the spot faecal fat test using Sudan staining would have performed

any better than FE-1 estimation but this needs to be evaluated in future studies.

Accurate staging of pancreatitis is important to study the natural history of the disease and the effect of interventions on the same. It will also help in comparing the results of different studies. It is possible that the additional use of biomarkers will improve the staging systems and this needs to be explored in future studies. An earlier report from our centre showed that serum MCP-1 levels were lower in patients with CP and EPI as compared to those diagnosed with CP but without EPI[30]. Future studies combining tests for pancreatic function and biomarkers may help in the early detection of CP.

While the assessment of EPF by acid steatocrit and FE-1 correlated well with each other the latter detected EPI in a significantly higher number, thereby placing a larger number of patients in higher stages of disease as per the M-ANNHEIM classification. We recommend that the FE-1 test should be used for staging pancreatitis by the M-ANNHEIM classification.

## COMMENTS

### Background

Exocrine pancreatic insufficiency (EPI) increases as chronic pancreatitis advances and this forms an important parameter for staging of chronic pancreatitis (CP) in various classification systems.

### Research frontiers

Various pancreatic function tests are available to assess the exocrine pancreatic function (EPF). This study focussed on comparing faecal elastase-1 (FE-1) estimation and the results of acid steatocrit test for evaluating EPF for use in the staging of pancreatitis by the M-ANNHEIM system.

### Innovations and breakthroughs

The results of this study show that stool fat analysis by acid steatocrit and FE-1 correlate well with each other. The estimation of FE-1 detected EPI, in a significantly higher number, thereby placing a larger number of patients in higher stages of disease as per the M-ANNHEIM classification.

### Applications

This study shows that FE-1 is a more appropriate pancreatic function test to determine EPI and to stage pancreatitis using the M-ANNHEIM classification.

### Terminology

FE-1 measures the amount of pancreatic elastase enzyme secreted into the gut by the pancreas and is estimated by the enzyme-linked immunosorbent assay technique. FE-1 is a tubeless indirect pancreatic function test which relies on the stability of pancreatic elastase as it transits through the intestine before excretion in stool. FE-1 is highly sensitive in estimating EPI during advanced stages of CP. Steatorrhoea by the acid steatocrit method is determined by diluting the stool with distilled water and homogenising it followed by mixing the stool with Perchloric acid to a pH of less than 1. The stool mixture is transferred to a capillary tube, and centrifuged to obtain a fat layer and a solid layer, which is measured by the appropriate formula to measure the stool fat content in the given stool sample.

### Peer-review

The authors have produced a well designed and constructed study with useful clinical results. The design is clear, the outcomes well presented and the conclusion is also clear.

## REFERENCES


1 **Schneider A**, Löhr JM, Singer MV. The M-ANNHEIM classification of chronic pancreatitis: introduction of a unifying classification system based on a review of previous classifications of the disease. *J Gastroenterol* 2007; **42**: 101-119 [PMID: 17351799]

2 **Ramesh H**. Proposal for a new grading system for chronic pancreatitis: the ABC system. *J Clin Gastroenterol* 2002; **35**: 67-70 [PMID: 12080229]

3 **Büchler MW**, Martignoni ME, Friess H, Malfertheiner P. A proposal for a new clinical classification of chronic pancreatitis. *BMC Gastroenterol* 2009; **9**: 93 [PMID: 20003450 DOI: 10.1186/1471-230X-9-93]

4 **Duggan SN**, Ní Chonchubhair HM, Lawal O, O'Connor DB, Conlon KC. Chronic pancreatitis: A diagnostic dilemma. *World J Gastroenterol* 2016; **22**: 2304-2313 [PMID: 26900292 DOI: 10.3748/wjg.v22.i7.2304]

5 **Chowdhury RS**, Forsmark CE. Review article: Pancreatic function testing. *Aliment Pharmacol Ther* 2003; **17**: 733-750 [PMID: 12641496]

6 **Lieb JG**, Draganov PV. Pancreatic function testing: here to stay for the 21st century. *World J Gastroenterol* 2008; **14**: 3149-3158 [PMID: 18506918 DOI: 10.3748/wjg.14.3149]

7 **Amann ST**, Josephson SA, Toskes PP. Acid steatocrit: a simple, rapid gravimetric method to determine steatorrhea. *Am J Gastroenterol* 1997; **92**: 2280-2284 [PMID: 9399770]

8 **Dumasy V**, Delhaye M, Cotton F, Deviere J. Fat malabsorption screening in chronic pancreatitis. *Am J Gastroenterol* 2004; **99**: 1350-1354 [PMID: 15233677 DOI: 10.1111/j.1572-0241.2004.30661.x]

9 **Bijoor AR**, Geetha S, Venkatesh T. Faecal fat content in healthy adults by the 'acid steatocrit method'. *Indian J Clin Biochem* 2004; **19**: 20-22 [PMID: 23105451 DOI: 10.1007/BF02894252]

10 **Guarino A**, Tarallo L, Greco L, Cesarano L, Guandalini S, Rubino A. Reference values of the steatocrit and its modifications in diarrheal diseases. *J Pediatr Gastroenterol Nutr* 1992; **14**: 268-274 [PMID: 1619531]

11 **Tran M**, Forget P, Van den Neucker A, Strik J, van Kreel B, Kuijten R. The acid steatocrit: a much improved method. *J Pediatr Gastroenterol Nutr* 1994; **19**: 299-303 [PMID: 7815261]

12 **Tod J**, Fine D. Fecal elastase: a useful test for pancreatic insufficiency? *Dig Dis Sci* 2010; **55**: 2709-2711 [PMID: 20838890 DOI: 10.1007/s10620-010-1409-9]

13 **Beharry S**, Ellis L, Corey M, Marcon M, Durie P. How useful is fecal pancreatic elastase 1 as a marker of exocrine pancreatic disease? *J Pediatr* 2002; **141**: 84-90 [PMID: 12091856 DOI: 10.1067/mpd.2002.124829]

14 **Carroccio A**, Verghi F, Santini B, Lucidi V, Iacono G, Cavataio F, Soresi M, Ansaldi N, Castro M, Montalto G. Diagnostic accuracy of fecal elastase 1 assay in patients with pancreatic maldigestion or intestinal malabsorption: a collaborative study of the Italian Society of Pediatric Gastroenterology and Hepatology. *Dig Dis Sci* 2001; **46**: 1335-1342 [PMID: 11414313]

15 **Girish BN**, Rajesh G, Vaidyanathan K, Balakrishnan V. Fecal elastase1 and acid steatocrit estimation in chronic pancreatitis. *Indian J Gastroenterol* 2009; **28**: 201-205 [PMID: 20177867 DOI: 10.1007/s12664-009-0079-z]

16 **Banks PA**, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013; **62**: 102-111 [PMID: 23100216 DOI: 10.1136/gutjnl-2012-302779]

17 **Guda NM**, Romagnuolo J, Freeman ML. Recurrent and relapsing pancreatitis. *Curr Gastroenterol Rep* 2011; **13**: 140-149 [PMID: 21286872 DOI: 10.1007/s11894-011-0176-x]

18 **Yadav D**, Hawes RH, Brand RE, Anderson MA, Money ME, Banks PA, Bishop MD, Baillie J, Sherman S, DiSario J, Burton FR, Gardner TB, Amann ST, Gelrud A, Lawrence C, Elinoff B, Greer JB, O'Connell M, Barmada MM, Slivka A, Whitcomb DC. Alcohol consumption, cigarette smoking, and the risk of recurrent acute

and chronic pancreatitis. *Arch Intern Med* 2009; **169**: 1035-1045 [PMID: 19506173 DOI: 10.1001/archinternmed.2009.125]

19 **Catalano MF**, Sahai A, Levy M, Romagnuolo J, Wiersema M, Brugge W, Freeman M, Yamao K, Canto M, Hernandez LV. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. *Gastrointest Endosc* 2009; **69**: 1251-1261 [PMID: 19243769 DOI: 10.1016/j.gie.2008.07.043]

20 **Conwell DL**, Lee LS, Yadav D, Longnecker DS, Miller FH, Mortele KJ, Levy MJ, Kwon R, Lieb JG, Stevens T, Toskes PP, Gardner TB, Gelrud A, Wu BU, Forsmark CE, Vege SS. American Pancreatic Association Practice Guidelines in Chronic Pancreatitis: evidence-based report on diagnostic guidelines. *Pancreas* 2014; **43**: 1143-1162 [PMID: 25333398 DOI: 10.1097/MPA.0000000000000237]

21 **Ewald N**, Raspe A, Kaufmann C, Bretzel RG, Kloer HU, Hardt PD. Determinants of Exocrine Pancreatic Function as Measured by Fecal Elastase-1 Concentrations (FEC) in Patients with Diabetes mellitus. *Eur J Med Res* 2009; **14**: 118-122 [PMID: 19380282]

22 **Ramakrishna BS**. The steatocrit as a measure of fecal fat excretion: uses and pitfalls. *Indian J Gastroenterol* 2009; **28**: 195-197 [PMID: 20177864 DOI: 10.1007/s12664-009-0076-2]

23 **Dominici R**, Franzini C. Fecal elastase-1 as a test for pancreatic function: a review. *Clin Chem Lab Med* 2002; **40**: 325-332 [PMID: 12059069 DOI: 10.1515/CCLM.2002.051]

24 **Lüth S**, Teyssen S, Forssmann K, Kölbel C, Krummenauer F, Singer MV. Fecal elastase-1 determination: 'gold standard' of indirect pancreatic function tests? *Scand J Gastroenterol* 2001; **36**: 1092-1099 [PMID: 11589385]

25 **Usküdar O**, Oğuz D, Akdoğan M, Altiparmak E, Sahin B. Comparison of endoscopic retrograde cholangiopancreatography, endoscopic ultrasonography, and fecal elastase 1 in chronic pancreatitis and clinical correlation. *Pancreas* 2009; **38**: 503-506 [PMID: 19287334 DOI: 10.1097/MPA.0b013e31819f639f]

26 **Walkowiak J**, Cichy WK, Herzig KH. Comparison of fecal elastase-1 determination with the secretin-cholecystokinin test in patients with cystic fibrosis. *Scand J Gastroenterol* 1999; **34**: 202-207 [PMID: 10192202]

27 **Bian Y**, Wang L, Chen C, Lu JP, Fan JB, Chen SY, Zhao BH. Quantification of pancreatic exocrine function of chronic pancreatitis with secretin-enhanced MRCP. *World J Gastroenterol* 2013; **19**: 7177-7182 [PMID: 24222963 DOI: 10.3748/wjg.v19.i41.7177]

28 **Schneider AR**, Hammerstingl R, Heller M, Povse N, Murzynski L, Vogl TJ, Caspary WF, Stein J. Does secretin-stimulated MRCP predict exocrine pancreatic insufficiency?: A comparison with noninvasive exocrine pancreatic function tests. *J Clin Gastroenterol* 2006; **40**: 851-855 [PMID: 17016144 DOI: 10.1097/01.mcg.0000225652.00308.a2]

29 **Chowdhury SD**, Kurien RT, Ramachandran A, Joseph AJ, Simon EG, Dutta AK, David D, Kumar C B, Samuel P, Balasubramaniam KA. Pancreatic exocrine insufficiency: Comparing fecal elastase 1 with 72-h stool for fecal fat estimation. *Indian J Gastroenterol* 2016; **35**: 441-444 [PMID: 27878466 DOI: 10.1007/s12664-016-0714-4]

30 **Kamath MG**, Pai CG, Kamath A, Kurien A. Monocyte chemoattractant protein-1, transforming growth factor-beta1, nerve growth factor, resistin and hyaluronic acid as serum markers: comparison between recurrent acute and chronic pancreatitis. *Hepatobiliary Pancreat Dis Int* 2016; **15**: 209-215 [PMID: 27020638]

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