Pancreatic cyst dilemma: Between physical and biochemical markers

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Author contributions: Khamaysi I designed and wrote the letter; and Eyal Zussman revised the letter; the manuscript has been read and approved by all the authors.

Conflict-of-interest statement: The authors declare no conflicts of interest.

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Specialty type: Gastroenterology and Hepatology

Country/Territory of origin: Israel

Peer-review report’s scientific quality classification
Grade A (Excellent): 0

Abstract

Physical analysis of the pancreatic cystic lesions (PCLs) fluid as expressed by the rheological behavior (“string sign”) can improve the diagnostic yield and should be integrated in every multimodal PCLs workup.

Key Words: Pancreatic cyst; Fluid analysis; String sign; Rheology

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Core Tip: No single optimal test reliably determines the pancreatic cyst subtype including all imaging modalities and biochemical fluid analysis. Physical analysis of the fluid as expressed by the string sign can improve the diagnostic yield and should be integrated in every multimodal pancreatic cystic lesions workup. The string sign as it is currently performed, suffers from significant shortcoming due to its subjective nature. Rheological (physical) properties, instead, can overcome the disadvantages of the standard string sign and replace it in clinical practice.

Citation: Khamaysi I, Zussman E. Pancreatic cyst dilemma: Between physical and biochemical markers. World J Gastroenterol 2021; 27(41): 7207-7209

URL: https://www.wjgnet.com/1007-9327/full/v27/i41/7207.htm
DOI: https://dx.doi.org/10.3748/wjg.v27.i41.7207
Grade B (Very good): 0  
Grade C (Good): C, C  
Grade D (Fair): 0  
Grade E (Poor): 0  

Received: June 6, 2021  
Peer-review started: June 6, 2021  
First decision: June 30, 2021  
Revised: July 1, 2021  
Accepted: September 30, 2021  
Article in press: September 30, 2021  
Published online: November 7, 2021  
P-Reviewer: Kikuyama M, Masuda A  
S-Editor: Wang JL  
L-Editor: A  
P-Editor: Wang JL

Figure 1 Representative types I, II and III flow curves. The graph inset shows the values of infinite viscosity, ηc, depicting the difference between the minimal value of type III and the maximum value of types I and II.

TO THE EDITOR

We read with great interest the frontier by Okasha et al[1] regarding the diagnosis of pancreatic cystic lesions (PCLs) and the benefits of various diagnostic models. The authors described a vast array of available diagnostic test and concluded that the combination of both endoscopic ultrasound-fine needle aspiration (EUS-FNA) findings with cystic fluid tumor markers analysis, along with clinical, radiologic, histologic, genetic, and molecular characteristics, enhances the diagnostic accuracy and helps to construct a novel model in the era of PCLs[1].

Unfortunately, the authors did not mention the viscosity of the cystic fluid as an important marker for differentiation between PCLs subtypes (mucinous and non-mucinous cysts).

The string sign, as a surrogate marker of fluid viscosity, is a useful and reliable test that can be used to improve the diagnostic accuracy of other pancreatic cyst fluid studies when used in combination[2], however, the string sign suffers from, relatively, high interobserver variability regarding its positivity and should be interpreted with caution and not used as a single test but in combination with other tests to differentiate mucinous from non-mucinous cysts[3].

String sign is inherently a subjective test and lacks a theoretical framework for predicting the viscoelastic nature of the fluid, which can be objectively characterized by the viscous and elastic response of a fluid under deformation (rheological behavior).

In order to overcome the subjective nature of the string sign, we developed a new rheological assay in which (using a rheometer) a wide array of viscoelastic properties (rheological curves) can be generated and recorded.

Use of a rotational viscometer supports simulation of true rheological conditions (the stepping change of either the shear stress or the shear rate is programmed but the parameter remains constant during each step). The viscosity of the samples was measured with a DHR-2 Rheometer (TA Instruments, USA) at 25 °C. The preferred geometry was cone-and-plate, with a cone diameter of 40 mm and a surface-plate angle of 1°. The rheometer was operated in shear rate control mode. Several time sweep tests at different constant shear rates (5-2000 1/s) were performed. The measured steady-state shear viscosity values (when the viscosity was constant in time) were used to construct flow curves of the fluids.

In our study[4], we found that the cutoff value of pancreatic cyst fluid viscosity, ηc, can serve as an independent marker to distinguish between mucinous and non-mucinous cysts. It was found that ηc > 1.3 cP characterizes mucinous cysts, whereas ηc > 1.3 cP is typical for non-mucinous cysts. Moreover, we could differentiate between three distinct flow curves of the rheological behavior of pancreatic cyst fluids according to dynamic viscoelastic properties. Types I and II hypothesized to correlate with non-mucinous cysts, and type III with mucinous cysts (Figure 1). This simple and rapid diagnostic tool can be immediately implemented after EUS-FNA sampling, and provides for a low variability rate compared to the commonly used, subjective string sign technique. Although the findings are promising, they must be further confirmed in a large-scale study.
In conclusion, no single optimal test reliably determines the pancreatic cyst subtype including all imaging modalities and biochemical fluid analysis. Physical analysis of the fluid as expressed by the string sign can improve the diagnostic yield and should be integrated in every multimodal PCLs workup.

The string sign as it is currently performed, suffers from significant shortcoming due to its subjective nature. Rheological (physical) properties, instead, can overcome the disadvantages of the standard string sign and replace it in clinical practice.

REFERENCES

1 Okasha HH, Awad A, El-Meligui A, Ezzat R, Aboubakr A, AbouElenin S, El-Husseiny R, Alzamzamy A. Cystic pancreatic lesions, the endless dilemma. *World J Gastroenterol* 2021; 27: 2664-2680 [PMID: 34135548 DOI: 10.3748/wjg.v27.i21.2664]

2 European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut* 2018; 67: 789-804 [PMID: 29574408 DOI: 10.1136/gutjnl-2018-316027]

3 Hakim S, Coronel E, González GMN, Ge PS, Chari ST, Thosani N, Ramireddy S, Badillo R, DaVee T, Catalano MF, Sealock RJ, Parupudi S, Hernandez LV, Joshi V, Irisawa A, Rana S, Lakhtakia S, Viölmann P, Safford A, Sun S, Giovannini M, Katz MH, Kim MP, Bhutani MS. An international study of interobserver variability of "string sign" of pancreatic cysts among experienced endosonographers. *Endosc Ultrasound* 2021; 10: 39-50 [PMID: 33473044 DOI: 10.4103/eus.eus_73_20]

4 Khamaysi I, Abu Ammar A, Vasilyev G, Arinstein A, Chowers Y, Zussman E. Differentiation of Pancreatic Cyst Types by Analysis of Rheological Behavior of Pancreatic Cyst Fluid. *Sci Rep* 2017; 7: 45589 [PMID: 28358122 DOI: 10.1038/srep45589]
