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Pancreatic cyst dilemma: Between physical and biochemical markers

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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.

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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 sting sign suffers from, relatively, high interobserver variability regarding its positivity and should be interpreted with caution and not 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.

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