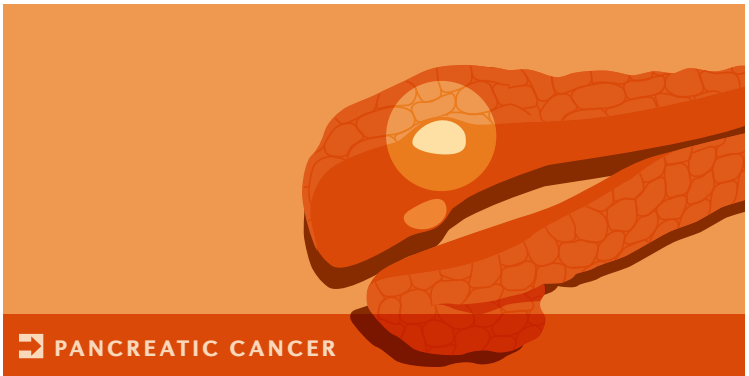
Nature Reviews Clinical Oncology | Published online 12 Dec 2017; doi:10.1038/nrclinonc.2017.199



PANCREATIC CANCER

Mass spectrometry indicates malignant potential

Pancreatic cyst lesions (PCLs) can be incidentally observed in up to 20% of patients undergoing abdominal MRI; although the majority of these lesions are entirely asymptomatic, current measures are often unable to discriminate between benign lesions and their malignant counterparts, which necessitate therapeutic intervention. Now, the findings of a phase II trial reveal the superiority of proteomic quantifications of three biomarkers in cyst-fluid samples over standard analyses (quantification of carcinoembryonic antigen (CEA) levels and cytology) in detecting malignant PCLs.

"This is a continuation of a previous study that was not quantitative and thus less accurate," lead author Gunnar Hansson explains, adding that "pancreatic cysts are closed cavities where secreted proteins typically accumulate in mucus over time, and thus provide an excellent source material for biomarker detection." In this study, the authors identified potential biomarkers in an exploratory cohort of 24 patients with established PCLs with or without pancreatic ductal adenocarcinoma (PDAC). Associations were then examined further in a test cohort of 80 patients with PCLs, followed by prospective validation in an independent cohort of 68 patients.

Researchers initially identified candidate biomarkers using cyst-fluid samples from patients in the exploratory cohort. Candidate biomarkers were limited to secreted and plasma membrane proteins only, and labelled peptides were then developed for the eight most promising candidates. In the training cohort, mucin 5AC proved to be the best marker for the presence of cystic cancer. When incorporated into a biomarker panel with mucin 2, this combination had a diagnostic accuracy for malignant potential of 97% versus 61% for CEA and 84% for cytology in the validation cohort, although many samples could not be analysed using either CEA or cytology owing to the need for higher volumes of cyst fluid. In combination with prostate stem cell antigen (PSCA), mucin 5AC enabled similarly high levels of detection of high-grade dysplasia and/or cancer in 95% of lesions compared with 35% for CEA and 50% for cytology.

"We have developed and validated a proteomic method that identified cystic pancreatic cancers and precursor lesions with very high accuracy, significantly exceeding that of current diagnostic tools," first author Karolina Jabbar summarizes. Jabbar also highlights the improved practicality provided by this approach: "similar to traditional assays, the method uses cyst fluid obtained using a routine outpatient procedure. Moreover, the low amount of cyst fluid required renders smaller lesions accessible for analysis." When asked about future directions, the authors state "the present method should be possible to directly apply in clinical chemistry laboratories of major hospitals."

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ORIGINAL ARTICLE Jabbar, K. S. *et al.* Highly accurate identification of cystic precursor lesions of pancreatic cancer through targeted mass spectrometry: a phase IIc diagnostic study. *J. Clin. Oncol.* http://dx.doi.org/10.1200/JCO.2017.73.7288 (2017)