

RE: Proteomic Mucin Profiling for the Identification of Cystic Precursors of Pancreatic Cancer

Pancreatic cystic lesions pose a clinical relevant problem, because they are discovered frequently on modern imaging (up to 20%) (1) and because they might be precursors of pancreatic ductal adenocarcinoma.

Jabbar et al. have shown in a cohort of 78 patients with various cystic lesions of the pancreas that proteomic mucin profiling identified with 97.5% accuracy those lesions that had a malignant potential (2). These data are impressive and relevant on first sight, but fail to have a clinically significant impact on closer look.

First, pseudocysts (37 of 78 patients) can in most cases be diagnosed by a combination of patient history, imaging, and cyst fluid analysis, and rarely pose a diagnostic challenge (3). Similarly, pancreatic ductal adenocarcinoma, main-duct, or combined-type intraductal papillary mucinous neoplasm (IPMN) (19 of 78 patients) are readily diagnosed by modern imaging, endoscopic ultrasound (EUS), and cyst fluid analysis, represent a clear indication for surgery, and do not pose a diagnostic challenge in most cases as well (4).

Second, to include symptomatic patients is equally questionable, since incidental, nonsymptomatic cysts represent the diagnostic challenge (only 17 of 78 patients) (5).

Thirdly, histology is the gold standard for diagnosis (only 29 of 78 patients), and any study relying on cytology and “multi-disciplinary boards” has to be interpreted cautiously, especially if claiming high diagnostic accuracy.

The problem of differentiating cystic lesions with or without malignant potential is currently not the clinically relevant one; it is rather to define those lesions that are likely to progress to overt malignancy. A large number of incidental cystic lesions in the pancreas are side-branch IPMNs (6) that are known to have a malignant potential; what is not known, however, is which lesions are going to progress and should be resected.

A number of features and risk factors have been identified that better stratify side branch IPMNs (4). Nonetheless, even when applying these factors, the controversy remains, because some centers advocate surgery for most of these lesions (7), while others favor a more conservative approach (4).

The present paper does not help in better stratification of these lesions. MUC1 expression was present in seven of 14 side-branch IPMNs, but no information is presented with regards to whether those lesions had higher grades of dysplasia or were in situ cancers. Main-duct IPMNs, on the other hand, were MUC1-negative in two of three cases, which is in line with what is known about the MUC1 profile of these lesions; ie, 50% of main-duct IPMNs show intestinal differentiation and do not express MUC1. Main-duct IPMNs have a higher risk to progress to invasive cancers and are generally an indication for surgery (4).

In conclusion, the study of Jabbar et al. shows that proteomic mucin profiling can identify cystic lesions with malignant potential. This is where we have been for several years; ie, with modern imaging, EUS/cyst fluid analysis, and cytology, we can fairly well identify those lesions. What we cannot reliably answer at the moment is a different, yet highly important clinical question,

namely: What is the risk of malignant transformation? And, thus, what is the best therapy for patients harboring these cysts?

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