Comparing American Gastroenterological Association Pancreatic Cyst Management Guidelines with Fukuoka Consensus Guidelines as Predictors of Advanced Neoplasia in Patients with Suspected Pancreatic Cystic Neoplasms

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BACKGROUND: In 2015, the American Gastroenterological Association (AGA) published guidelines to provide recommendations for management of suspected pancreatic cystic neoplasms (PCNs). The aim of this study was to compare efficacy of these with the Fukuoka consensus guidelines in predicting advanced neoplasia (AN) in patients with suspected PCNs.

STUDY DESIGN: We performed a retrospective study of 239 patients who underwent surgical resection for suspected mucinous PCN at a tertiary care center from 2000 to 2014. Surgical pathology was the gold standard. The AGA and Fukuoka criteria were applied, and their performance in predicting AN, defined as invasive cancer or high-grade dysplasia (HGD), was assessed.

RESULTS: Advanced neoplasia was found in 71 of 239 (29.7%) patients (28 invasive cancer, 43 HGD). The Fukuoka "high-risk" (FG-HR) and AGA "high-risk" (AGA-HR) criteria identified patients with AN with sensitivities of 28.2% and 35.2%, specificities of 95.8% and 94.0%, positive predictive values of 74.1% and 71.4%, and negative predictive values of 75.9% and 77.5%, respectively. Overall, there was no significant difference between the guidelines for prediction of AN. There were 7 and 6 cases with invasive cancer, and 23 and 24 cases with HGD missed by the FG-HR and AGA-HR guidelines, respectively.

CONCLUSIONS: In a retrospective analysis, the AGA guidelines are not superior to the Fukuoka guidelines in identifying AN in suspected PCNs. Both sets of guidelines have fair PPV for detection of AN, which would lead to avoidable resections in patients without AN. Additionally, the high-risk features of both guidelines do not accurately identify all patients with AN. (J Am Coll Surg 2016;223:729−737. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

The incidence of pancreatic cysts has been estimated to be as high as 41.6%, and their detection has increased as the use of cross-sectional imaging has become more common.[1] Clinical management of cysts revolves around accurate diagnosis and risk stratification for prediction of advanced neoplasia (AN).

To guide management of mucinous cystic neoplasms, the Sendai guidelines were developed in 2006. These were highly sensitive for correctly identifying malignant mucinous lesions, but had low specificity for AN, resulting in many avoidable resections. A subsequent revision, the Fukuoka Guidelines, was published in 2012 with the goal of improving specificity for predicting AN.[2,3] In 2015, the American Gastroenterological Association (AGA) published guidelines for the management of pancreatic cysts.[4] These were developed to raise the

Abbreviations and Acronyms

AGA   = American Gastroenterological Association
AN   = advanced neoplasia
EUS   = endoscopic ultrasound
FG   = Fukuoka guidelines
HGD   = high-grade dysplasia
HR   = high risk
IPMN = intraductal papillary mucinous neoplasm
PCN   = pancreatic cystic neoplasm
PDD   = pancreatic ductal dilation
W   = worrisome

threshold for surgery, therefore decreasing avoidable resections, and shift the paradigm to a more conservative approach for surveillance.

The aim of this study was to compare the performance of the Fukuoka consensus guidelines (FG) and the 2015 AGA pancreatic cyst management guidelines in predicting AN in patients with suspected mucinous pancreatic cystic neoplasms (PCNs).

METHODS

Chart review was conducted of 356 patients who underwent surgical resection for suspected mucinous PCN at the Hospital of the University of Pennsylvania, from 2000 to 2014. Inclusion criteria included cystic lesions of the pancreas in patients who underwent resection and had radiographic imaging of the pancreas (CT or MRI) performed at or reviewed formally at the Hospital of the University of Pennsylvania. The FG and the AGA guidelines were retrospectively applied to each case in the study cohort. Patients with known pancreatic pseudocysts, predominantly solid masses with a cystic component, or in whom imaging records were unavailable for review were excluded. Patient demographics and clinical, radiographic, and pathologic data were extracted. Cystic lesions of the pancreas were defined as incidental or symptomatic. Symptomatic cysts were defined as lesions identified on cross-sectional imaging in the presence of abdominal pain, jaundice, or pancreatitis. Endoscopic ultrasound (EUS) characteristics of the pancreatic lesions, including cytology when available, were recorded. When multiple cysts were present, the largest cyst or the cyst with the most significant features was evaluated.

Pathology from the surgical resection was used as the gold standard for the final diagnosis. The pathologic diagnosis was classified on the basis of the World Health Organization criteria.[5] Advanced neoplasia was defined as presence of invasive carcinoma or high-grade dysplasia (HGD). In the absence of AN, the following cysts were

characterized as cysts with malignant potential: intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms, neuroendocrine tumors, and pseudopapillary tumors. Pseudocysts, serous cystadenomas, nonneoplastic lymphoepithelial cysts, and hamartomatous malformations were classified as benign lesions. Pathology of the resected pancreatic cysts was correlated with the patient's clinical presentation and preoperative imaging.

Criteria that would result in a recommendation for surgical resection were considered high-risk (HR) features. The AGA high-risk criteria are solid component with pancreatic duct dilation (PDD) and concerning features on EUS-FNA (ie solid component with PDD or concerning cytology). Concerning cytology was defined as evidence of high-grade dysplasia (HGD), high-grade atypia, or adenocarcinoma. The FG high-risk features are jaundice, enhancing solid component, and PDD $\geq$ 10 mm. Criteria that would result in further diagnostic work-up or surveillance were considered "worrisome" features. The AGA worrisome features are solid component without PDD, PDD without solid component, increasing size of the pancreatic duct (PD), and cyst size $\geq$ 3cm; these were features that should prompt further work-up with EUS and fine needle aspiration (EUS-FNA). Worrisome criteria from FG are cyst size $\geq$ 3 cm, pancreatitis, thickened or enhancing cyst wall, PDD from 5 to 9 mm, nonenhancing solid component, and change in PD caliber with distal parenchymal atrophy. AGA and FG criteria are detailed in eTable 1.

The Institutional Review Board at the University of Pennsylvania approved the study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Statistical analysis

Descriptive statistics were used to summarize the demographic and clinical features of the cohort. Continuous variables were summarized and reported as means with standard deviations or medians and interquartile range. Categorical variables were summarized and reported as frequencies and percentages. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each criterion and its performance in detecting AN. McNemar's test was used to compare sensitivity and specificity. A p value of 0.05 was accepted as statistically significant. We calculated the area under the receiver operating characteristic curve for each set of criteria. Statistical analysis was performed with STATA V.14 (StataCorp).