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Editorial

Should We Be Concerned About Intraductal Papillary Mucinous Neoplasm's Unsettling Features?

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ABSTRACT

Although worrisome features represent an indication to perform endoscopic ultrasound study, recent studies have showed that these conditions are not strictly related to high risk of malignancy. Pancreatic resection for worrisome imaging features often demonstrates pathology consistent with low-grade dysplasia. Worrisome features should be considered as indicators of mostly low-grade dysplasia. High-risk stigmata are more consistent for diagnosis of malignant lesions.

Keywords
Worrisome features; High-risk stigmata; Intraductal papillary mucinous neoplasm (IPMN); Pancreatic neoplasm; Pancreatic high-grade dysplasia; Pancreatic low-grade dysplasia.

Pancreatic cystic neoplasms include different types of cysts with various biological behavior. The most prevalent are intraductal papillary mucinous neoplasm (IPMN). The majority of IPMN is located in the head of the pancreas. A single cystic mass as well as segmental involvement or involvement of the entire pancreatic duct can be present.

Management of IPMN should focus on the prevention of malignant progression, while avoiding unnecessary morbidity of surgery. This requires specialized centers with dedicated multidisciplinary teams.

Worrisome features are indicated and described during imaging study of IPMN.

These features, according to 2017 Fukuoka Consensus Guidelines are cyst size ≥3 cm, thickened or enhancing cyst walls, main duct size 5-9 mm, non-enhancing mural nodules, an abrupt change in pancreatic duct caliber with distal pancreatic atrophy, pancreatitis, and lymphadenopathy.[1]

Although these data represent an indication to perform endoscopic ultrasound study, recent studies have showed that these conditions are not strictly related to high-risk of malignancy.

Izumo et al[2] showed that an enhancing mural nodule ≥5 mm, pancreatitis, and thickened/enhancing cyst walls were independent predictive factors for high-grade dysplasia. However, none of worrisome features were pointed out.

Li et al[3] described a good correlation for prediction of high-grade dysplasia in presence of high-risk stigmata.

Furthermore, pancreatic resection for worrisome imaging features often demonstrates pathology consistent with low-grade dysplasia.

A recently published multi-institutional study on 324 patients by Wilson et al[4] found that 44% of specimens resected according to current guidelines had only low-grade dysplasia.

Sugimoto et al[5] confirmed in a single-center, retrospective analysis, that main pancreatic duct diameter of 7.2 mm (one of the high-risk stigmata) was identified as an optimal cutoff for a prognostic factor for malignant disease in IPMN (Table 1).

Shimizu et al[6] developed a nomogram to attempt to predict the probability of the presence of carcinoma in patients with IPMNs. Gender, type of lesion (MD-IPMN *vs.* BD-IPMN), size of mural nodules and pancreatic fluid cytology were all assigned

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Table 1. *Results of International Studies on Malignant Predictors for IPMN*

Paper	Number of patients	Results
Izumo et al[2]	295	Enhancing mural nodule ≥5 mm, pancreatitis and enhancing cyst walls were independent predictive factors for high-grade dysplasia.
Li et al[3]	363	48.3% of patients who met high-risk stigmata were respectively confirmed as high-grade dysplasia.
Wilson et al[4]	324	In the absence of high-risk features, high-grade dysplasia was present in 57.4% of patients with 2 or more worrisome features.
Sugimoto et al[5]	103	A main pancreatic duct diameter of 7.2 mm or greater was an independent prognostic factor for malignant neoplasms.
Shimizu et al[6]	81	On multivariate analysis, existing carcinoma was associated with female gender, main pancreatic duct IPMN, nodule size, and pancreatic juice cytology grade.

points: none of them is classified as worrisome feature.

On the base of the recent literature, we can start to consider "worrisome features" as indicators of mostly low-grade dysplasia and we should not based strict follow-up and/or indications to surgery on them.

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