

PREMALIGNANT AND MALIGNANT EPITHELIAL LESIONS OF THE PANCREAS

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Some of the terminology used for epithelial lesions in the pancreas is confusing. Those lesions that should not be considered premalignant will be mentioned but the lecture will concentrate on precursors of pancreatic adenocarcinoma. Malignant epithelial lesions will only be discussed briefly, highlighting recently described entities.

The three main premalignant epithelial lesions of the pancreas are Pancreatic Intraepithelial Neoplasia (PanIN), Mucinous Cystic Neoplasms (MCNs) and Intraductal Papillary Mucinous Neoplasms (IPMNs). The PanIN nomenclature was developed in 1999 and defined as neoplastic epithelial proliferations in the smaller calibre ducts (ie. <5 mm diameter).^[1] However, it is now recognised that PanINs may arise in any part of the pancreatic duct system, including the large ducts.^[2] The PanINs are classified into three grades (PanIN-1A&1B, PanIN-2 and PanIN-3) based on the degree of architectural and cytological atypia and there is morphological progression through the PanINs to invasive ductal adenocarcinoma. The standardisation of this terminology has allowed clearer study of the molecular progression from normal to invasive pancreatic carcinoma, sometimes referred to as the 'PanINgram'.^[3,4]

MCNs and IPMNs are cystic lesions of the pancreas (reviewed in [5]) and precursors of invasive adenocarcinoma. MCNs are less common than IPMNs and, when invasive, usually give rise to ductal type adenocarcinoma. IPMNs can be classified in three ways: (i) by the site of origin, namely branch duct type, main duct type or combined/mixed type, (ii) by the epithelial phenotype, and (iii) by the degree of dysplasia and whether there is invasive carcinoma or not. The invasive carcinoma in IPMN may be colloid (mucinous non-cystic) carcinoma or ductal adenocarcinoma. The prognosis for MCNs or IPMNs with invasive carcinoma is much better than that for conventional (non-MCN and non-IPMN associated) pancreatic ductal adenocarcinoma and, therefore, it is important to recognise the precursor lesion.^[2,6-8]

REFERENCES

1. Hruban RH, Adsay NV, Albores-Saavedra J et al. Pancreatic intraepithelial neoplasia: a new nomenclature and classification system for pancreatic ductal lesions. *Am J Surg Pathol* 2001;25:579-86.
2. Hruban RH, Takaori K, Klimstra DS et al. An illustrated consensus on the classification of pancreatic intraepithelial neoplasia and Intraductal papillary mucinous neoplasms. *Am J Surg Pathol* 2004;28:977-87.
3. Wilentz RE, Iacobuzio-Donahue CA, Argani P et al. Loss of expression of DPC4 in pancreatic intraepithelial neoplasia: evidence that DPC4 inactivation occurs late in neoplastic progression. *Cancer Res* 2000;60:2002-6.
4. Feldmann G, Beaty R, Hruban RH, Maitra A. Molecular genetics of pancreatic intraepithelial neoplasia. *J Hepatobiliary Pancreat Surg* 2007;14:224-32.
5. Campbell F, Azadeh B. Cystic neoplasms of the exocrine pancreas. *Histopathology* 2008;52:539-51.
6. Crippa S, Salvia R, Warshaw AL et al. Mucinous cystic neoplasm of the pancreas is not an aggressive entity. *Ann Surg* 2008;247:571-9.
7. Nagata K, Horinouchi M, Saitou M et al. Mucin expression profile in pancreatic cancer and the precursor lesions. *J Hepatobiliary Pancreat Surg* 2007;14:243-54.
8. Maire F, Hammel P, Terris B et al. Prognosis of malignant intraductal papillary mucinous tumours of the pancreas after surgical resection. Comparison with pancreatic ductal adenocarcinoma. *Gut* 2002;51:717-22.

