PANCREAS NEWS

The Effect of Pathological Types of Intraductal Papillary Mucinous Neoplasms of the Pancreas on Survival

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Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas consist of papillary growths within the pancreatic ductal system and they are at risk of malignant transformation. They were first described by Ohhashi *et al*. in 1982 [1] and represent more than one third of all cystic neoplasms of the pancreas but less than 1% of all pancreatic tumors [2, 3].

The World Health Organization has classified IPMNs into four categories based upon the degree of epithelial dysplasia: adenoma, borderline carcinoma, carcinoma in situ or invasive carcinoma [4] From a morphologic point of view, IPMNs may involve the main pancreatic duct, a side branch or both. The latter is termed "mixed" type.

The consensus panel of the International Association of Pancreatology convened in Sendai and reviewed the collected series of patients with IPMNs involving the main pancreatic duct and found that the majority had carcinoma in situ or invasive cancer while the risk of malignancy was much lower in patients with side branch disease [5]. Thus, main duct IPMNs have a significant risk of malignancy, and surgery is recommended regardless of the presence of symptoms, whereas the surgery is warranted for side branch IPMNs in the presence of symptoms, mural nodules, positive cytology or a cyst size less than 3 cm.

From a pathological point of view we are able to recognize four morphological types of intraductal papillary mucinous neoplasms of the pancreas based on their microscopic morphology and immunohisto-chemical reactivity against anti-mucin 1, anti-mucin 2 and anti-mucin 5AC antibodies: gastric, intestinal, pancreatobiliary, and oncocytic [6]. From a practical point of view, we do not have enough information regarding the differences in the clinical manifestations and prognostic parameters among the morphological types of IPMNs. For this reason, the paper by Furukawa *et al*. is worthy of mention because, even if is a retrospective study, it is based on a consistent number of patients who had undergone surgery [7]. These authors found that gastric-type IPMNs were associated with a lower histological grade, involvement of the branch ducts, absence of invasion and a fair survival rate. Intestinal-type IPMNs were associated with non-invasive mucinous carcinoma, invasive colloid carcinomas in those cases with invasion, involvement of the main duct and a less favorable prognosis. Invasive mucinous carcinoma with colloid carcinomas was exclusively associated with intestinal-type IPMNs and had a better prognosis than invasive mucinous carcinoma with tubular adenocarcinoma. Pancreatobiliary-type IPMNs occur with a slight preference for older women and are associated with high histological grades, invasive phenotypes characterized by tubular adenocarcinoma and a poor prognosis. For the first time, the predominance of this type of IPMN was found in women and it is quite distinctive from the sex distribution of other IPMN types. Pancreatobiliary-type IPMNs had the highest prognostic risk of the four types; this was a distinctive feature in a cohort of patients with invasive disease and may be due to the high susceptibility of this IPMN type to develop invasive tubular adenocarcinoma. Onco-cytic-type IPMNs were more likely to develop in younger people than were the other IPMN types. These IPMNs were associated with a high histological grade, minimal invasion, invasive oncocytic carcinoma in the cases with invasion and a less favorable prognosis. In the study of Furukawa *et al*., patients with oncocytic-type IPMNs exhibited survival rates of 80% at 5 years and 70% at 10 years, similar to those of patients with intestinal-type IPMNs.

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The data of Mino-Kenudson *et al*. [8] complete and better define those of Furukawa *et al*. [7] in patients with invasive IMPNs. The data of Mino-Kenudson *et al*. are also retrospective; they are based on 271 patients with surgically resected, pathologically confirmed IPMNs identified from a prospectively collected database. Of these, 61 were found to have invasive carcinoma arising in the background of IPMNs, including 12 with minimally invasive carcinoma. The authors also used a control group involving 570 patients resected for pancreatic ductal adenocarcinoma. What conclusions can be reached? First: tubular, colloid and oncocytic invasive IPMNs arise from different epithelial subtypes. Second: patients with invasive IPMNs have a better outcome than those with pancreatic ductal adenocarcinoma. Third: the outcome remained favorable only for colloid and oncocytic carcinomas; on the contrary, tubular adenocarcinoma was associated with worse overall survival, not significantly different from that of pancreatic ductal adenocarcinoma.

In summary, the results of these two studies, when confirmed by prospective data, will help us to better define the prognosis of patients with IPMN who have undergone surgery. They also underscore the continuum existing from IPMNs to ductal adenocarcinoma, and are able to stimulate both the search for the molecular substances present in the various types of IPMNs for diagnostic and therapeutic use as well as the epidemiological, clinical and biological relationship between IPMNs and ductal pancreatic adenocarcinoma. Finally, these data are of paramount importance in clinical practice because patients having pancreatic ductal adenocarcinoma concomitant with IPMNs and those having pancreatic ductal adenocarcinoma deriving from IPMNs, have a more favorable outcome and can be diagnosed earlier than ordinary pancreatic adenocarcinoma [9].

Conflict of interest None

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