Review

INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS – RISK OF MALIGNANCY

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Abstract

Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) are precancerous lesions. Anatomically, IPMNs are classified as main duct-type and branch duct-type. Histologically, these neoplasms are grouped into 4 categories: intestinal, pancreatobiliary, oncocytic, and gastric. Patients diagnosed with IPMN have been shown to have an increased risk of malignancy of the pancreatic tumor, but also an increased risk of associating cancers with extrapancreatic localization. Among the factors associated with the risk of malignancy of IPMNs are the involvement of the main pancreatic duct or branch duct, tumor size, diameter of the main pancreatic duct, and histological type. Regarding IPMN-associated extrapancreatic cancers, gastric adenocarcinoma and colorectal adenocarcinoma were the most reported.

Keywords: IPMN, main pancreatic duct, branch pancreatic duct, extrapancreatic cancers.

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1. Introduction

A series of cystic neoplasms can develop in the pancreas. These can be classified into several categories:

- mucinous cystic tumors;
- serous cystic tumors;
- cystic islet cell tumors;
- solid pseudopapillary neoplasms;
- intraductal papillary mucinous neoplasms of the pancreas (IPMNs) [1,2].

IPMNs are potentially malignant tumors that are also known as mucinous duct ectasias. These lesions can affect the main pancreatic duct, the branch ducts, or both [3]. Ohashi et al first described IPMN in 1982 in four patients diagnosed with pancreatic carcinoma but with a favorable outcome [4]. The particularities described in these patients were: dilated main pancreatic ducts, mucus secretion from the pancreatic duct, and patulous ampullary orifices [4]. Due to the small tumor size and absence of symptoms, the real incidence of IPMNs is not known. It is currently estimated that IPMNs account for approximately 1-3% of exocrine pancreatic neoplasms and 20-50% of cystic pancreatic neoplasms [5,6]. A study of 2832 computed tomography scans performed in patients without risk factors for pancreatic disease or a history of pancreatic lesions identified the presence of pancreatic cysts in 73 cases. The reported prevalence was 2.6 per 100 patients, and the size of the cysts ranged from 2 to 38 mm, with an average diameter of 8.9 mm [7]. The reported prevalence was 2.6 per 100 patients, and the size of these cysts ranged from 2 to 38 mm, with an average diameter of 8.9 mm [7]. Another study that looked at the

results of abdominal magnetic resonance imaging of 616 patients without a history of pancreatic lesions, identified the presence of incidental pancreatic cysts in 83 patients. In this case, the reported prevalence was higher, respectively 13.5% and the median diameter was 7.4 mm [8]. This study also reported an increase in the prevalence of pancreatic cysts, but also in their size, with age [8].

Among the risk factors associated with the development of IPMNs are:

- cigarette smoking;
- previous history of diabetes mellitus, chronic pancreatitis, or peptic ulcer;
- family history of pancreatic ductal adenocarcinoma;
- familial pancreatic carcinoma;
- familial adenomatous polyposis syndrome;
- Peutz-Jeghers syndrome [9-11].

IPMNs can be classified anatomically or histologically (Figures 1 and 2).

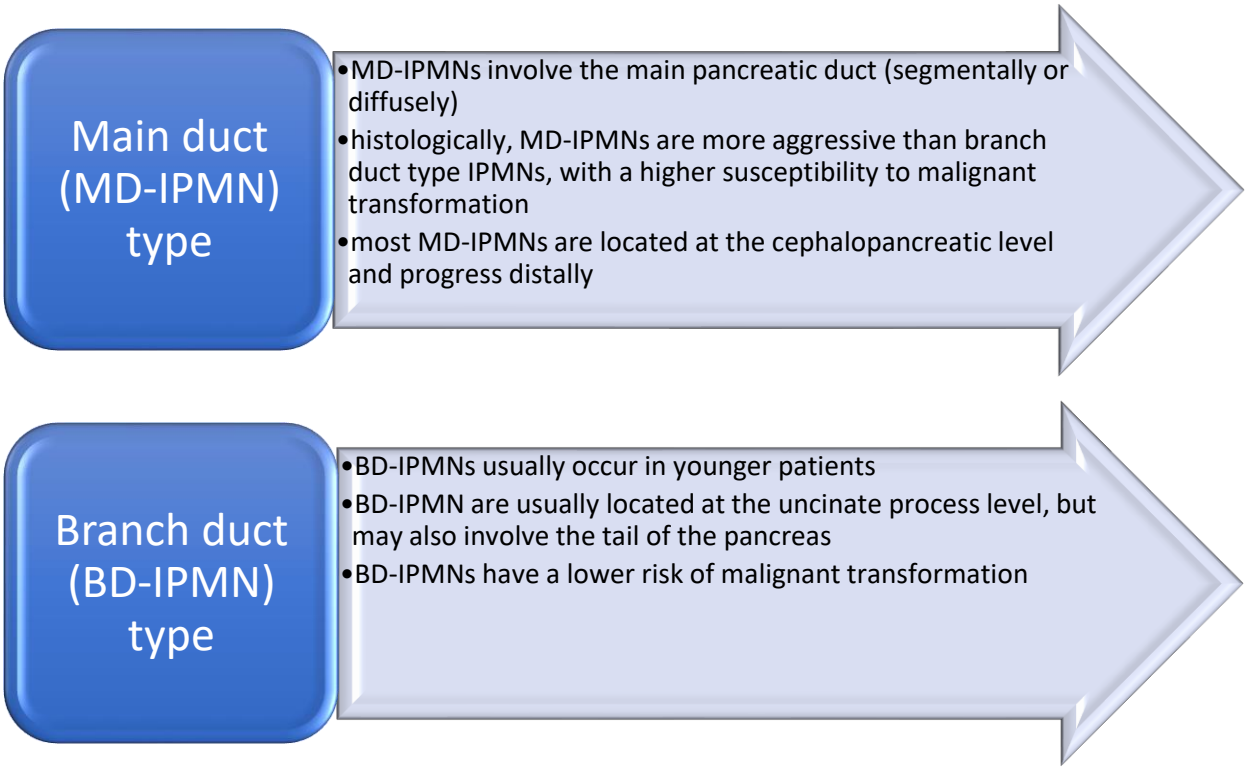

Figure 1. Anatomical classification of IPMNs [12,13].

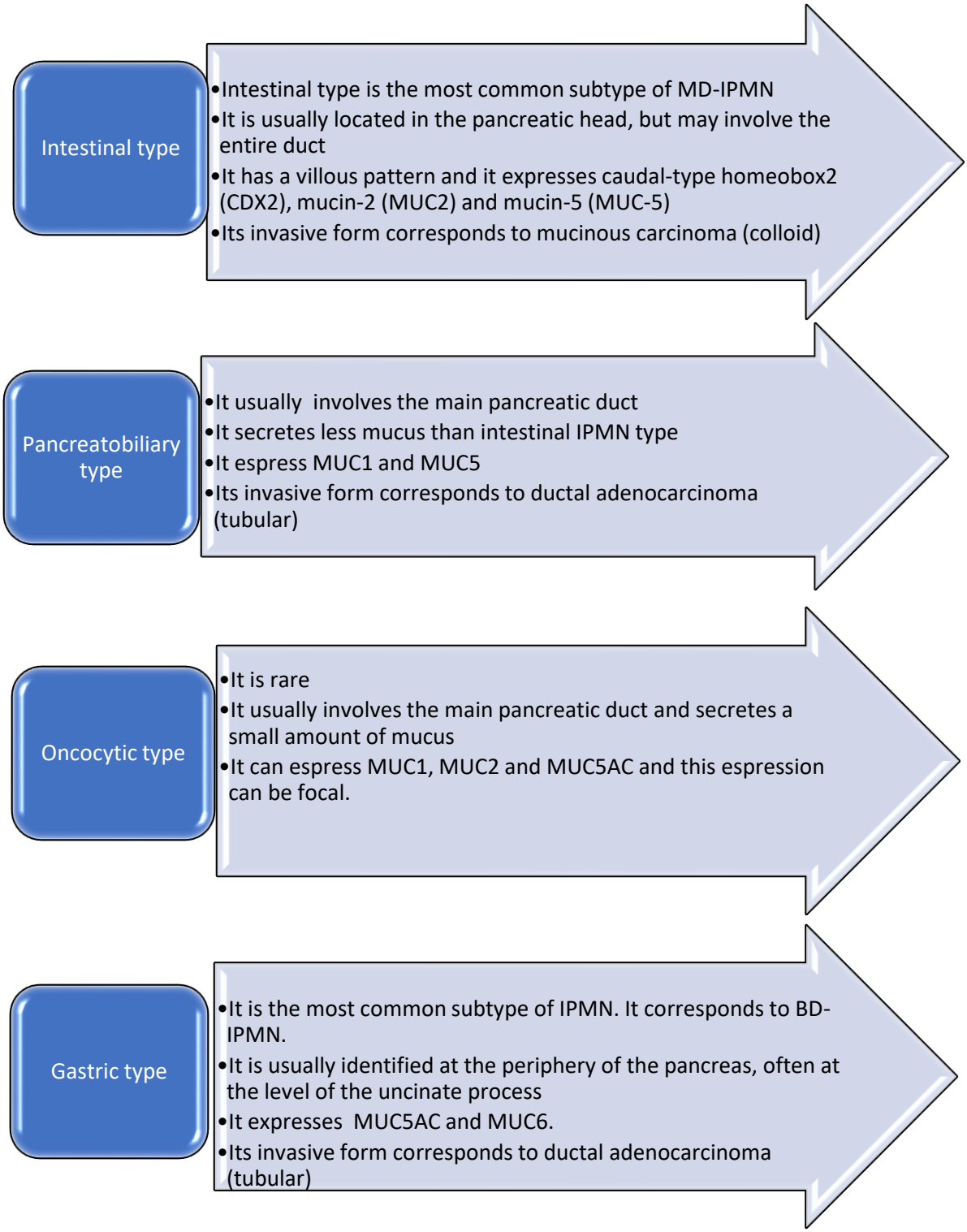

Figure 2. The histologic classification of IPMNs [14,15].

2. Risk of malignancy

Patients with IPMN have an increased risk of developing both pancreatic cancer and other extrapancreatic neoplasms. Depending on the degree of dysplasia, IPMNs are classified into 4 subtypes:

- Low-grade dysplasia – adenoma.
- Moderate dysplasia – borderline.
- High-grade dysplasia – carcinoma in situ.
- Invasive carcinoma [16].

In the case of MD-IPMN, the risk of progression to carcinoma in situ or invasive carcinoma is approximately 70%. Unfortunately, there are currently no symptoms or imaging features predictable for malignancy [17]. In the case of BD-IPMN, the risk of malignancy is lower [18]. Oyama et al studied the incidence of IPMN-derived carcinoma and concomitant ductal carcinoma among 1404 patients diagnosed with MD-IPMN over 20 years [19]. They reported a 5-year incidence rate of pancreatic malignancy of 3.3%, a 10-year incidence rate of 6.6%, and a 15-year incidence rate of 15% [19]. These authors also found a direct relationship between the size of MD-IPMN, the diameter of the main pancreatic duct, and the risk of developing IPMN-derived carcinoma, but not the risk of developing concomitant pancreatic duct adenocarcinoma [19]. Another study which included 62 patients with intraductal papillary-mucinous tumors identified the following as predictive factors for malignancy: tumor diameter >3 cm, the presence of mural nodules, and the diameter of the main pancreatic duct ≥ 7 mm [20]. For tumors with a diameter <3 cm, the risk of malignancy was lower, and among the risk factors associated with the progression to malignancy were:

- Older age.
- Male sex.
- Presence of symptoms.
- Some radiographic features such as solid components, the diameter of the main pancreatic duct ≥ 10 mm, or lymphadenopathy [20,21].

Another risk factor for malignancy in patients with IPMN is the histological subtype of the tumor. Thus, according to the literature, oncocytic-subtype IPMNs and pancreatobiliary-subtype IPMNs have a higher risk of malignancy than gastric-subtype IPMNs [22,23]. Distler et al analyzed histological subtypes of IPMNs and their prognostic value in 103 patients [23]. The intestinal type was identified in 45% of cases, pancreatobiliary type in 40% of cases, gastric type in 12% of cases, and oncocytic type in 4% of cases [24]. In terms of prognosis, the 5-year survival rate was significantly better among patients with intestinal IPMNs compared with patients with pancreatobiliary IPMNs (86.6% vs. 35.6%) [24]. The pancreatobiliary subtype was also associated with a significant risk of malignancy and recurrence, and the survival rate of these patients was comparable to that of pancreatic duct adenocarcinoma patients [24]. Another study that evaluated 213 patients with surgically resected IPMN identified 38 patients with low-grade dysplasia, 97 patients with intermediate-grade dysplasia, 18 patients with high-grade dysplasia, and 59 patients with associated invasive carcinoma [25]. From the group of patients with associated invasive carcinoma, the highest proportion corresponded to the oncocytic subtype (100%), followed by the pancreatobiliary subtype (57.9%), intestinal subtype (42.1%), and the lowest proportion to the gastric subtype (14.1%) [25].

Other neoplasms that can associate with IPMN are colorectal cancer, gastric cancer, bile duct cancer, thyroid carcinoma, and renal cancer [26-31]. The explanation for the relationship between IPMN and extrapancreatic cancers is currently unclear. Some data suggest that patients diagnosed with IPMNs are carefully evaluated, which leads to an increase in the detection rate of neoplasms with another location. Another explanation could be carcinogenic exposure or hereditary abnormalities, with a secondary increase in the risk of developing cancer. Choi MG et al. studied the incidence rate of extrapancreatic neoplasms among 61 patients

diagnosed with IPMNs [26]. Of these, 39% were associated with extrapancreatic neoplasms and 30% with extrapancreatic malignancies [26]. The most common were gastric adenocarcinoma (33%) and colorectal adenocarcinoma (17%). The authors also noted that the incidence rate of extrapancreatic neoplasms among patients with IPMN was significantly higher compared to other pancreatic neoplasms, such as mucinous cystic neoplasms (8%) or pancreatic ductal adenocarcinoma (10%) [26]. However, another study conducted in 2015, which followed 1340 patients over 3 years, concluded that patients with IPMNs do not have a higher rate of extrapancreatic cancers [31].

Conclusions

In conclusion, patients with IPMN have an increased risk of both malignancy of the pancreatic tumor and the association of neoplasms with extrapancreatic localization. If patients with MD-IPMNs have a 70% risk of malignancy, those with BD-IPMN have a risk of malignancy ranging from 3.3% to 15%. According to the literature, oncocytic-subtype IPMNs and pancreatobiliary- subtype IPMNs have a higher risk of malignancy than gastric-subtype IPMNs [22,23]. Of the extrapancreatic cancers, the most commonly associated with IPMNs were gastric adenocarcinoma and colorectal adenocarcinoma [26].

Author Contributions:

G.G. conceived the original draft preparation. G.C., G.G., and V-A.I. were responsible for conception and design of the review. VA.I., and G.C. were responsible for the data acquisition. G.C., and G.G. were responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. G.C., G.G., and VA.I. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article".

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