Pancreatic Intraductal Papillary Mucinous Neoplasms.... Still Unanswered Questions!

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INTRODUCTION

Pancreatic intraductal papillary mucinous neoplasms (IPMN) are one of the precursors lesions of pancreatic adenocarcinoma. They have only been individualized as a specific disease in the mid 80’s and were first recognized by the World Health Organization in 1996. Since then, significant progress has been made in the diagnosis, understanding of the natural history and management of this frequent pancreatic neoplasm. Nevertheless, there are still numerous unanswered questions that make difficult patients management.

Pancreatic cyst “epidemic”

With the widespread use of high-quality cross-sectional imaging, an increased number of asymptomatic cystic pancreatic lesions are being identified. The prevalence of these so called “incidentalomas”, i.e. asymptomatic lesion fortuitously detected by imaging, is approximately 10% (1) in the population and may reach as high as 30% in older patients (2). Pancreatic cystic incidentaloma encompasses a wide spectrum of neoplasms, including serous cystadenomas (SCA), mucinous cystic neoplasms (MCN), mucinous cystadenocarcinomas, non-functional neuroendocrine tumors (PNET), solid and pseudopapillary neoplasm (SPPN) and intraductal papillary mucinous neoplasms (IPMN) (3).

The main issue in cystic pancreatic lesions management is that beyond their comforting presentation, this heterogeneous group of lesions can be premalignant or even malignant (Fig. 1). This concern has led to an increasing number of resections for pancreatic incidentaloma in order to eradicate potentially threatening pancreatic lesions in their earliest stages.

The diagnostic issue…

A “pancreatic cyst” is NOT a diagnosis. Knowing that there is various kind of pancreatic cystic lesions carrying different risk of cancer, having an accurate diagnosis is mandatory before any medical decision. You should always know what you are watching... you should always know what you are resecting. Nevertheless, even in high volume centers, there is in all surgical series, i.e.
already highly selected patients, a discrepancy between
the supposed preoperative diagnosis and the final
pathological diagnosis, in about 20% (2). This should
always be kept in mind when we select patients for
surgery, and make the assessment of the benefit risk
balance, especially for small asymptomatic pancreatic
cyst.

The benefit risk balance of surgery…
what you need to know!

Pancreatic surgery can be seen as one of the
most challenging surgery, because it is technically
challenging, but more importantly because of the
need of multiple skills in the management of these
patients, including surgeons, gastroenterologist,
diabetologist, oncologist, pancreateologist, radio-
logists, interventional radiologist, pathologist, psy-
chologist and nutritionist. The mortality of pancreatic
surgery ranges from 1% to 3% in high-volume centers
(4,5), but increases up to 6 to 10% when nationwide
centers are considered (6-8). Considering these
hetero-geneous results, there is a benefit to be
managed in high volume centers (3,4,5).

What are IPMN?

Intraductal papillary mucinous neoplasms (IPMN)
are cystic pancreatic mucin-producing neoplasms.
Histologically, they are categorized according to their
localization (main duct, branch duct involvement or
both), their grade of dysplasia (low or high) and their
phenotype (gastric, intestinal, pancreatobiliary or
oncocytic) (7, 8). Their clinical management remains
challenging, only based on imaging features and clinical
symptoms that are clearly imperfect and likely
overestimate the risk of cancer occurrence (19). It is actually demonstrated that only a minority
of IMPN are progressing to invasive lesions. If they
try to be «evidence-based medicine», the quality of
available study is poor for most of them, with no
randomized controlled trial, very few prospective
studies, and for most of them very few patients
followed more than 10 years. Guidelines (Fig. 3)
are quite consensual to select patient for surgery, i.e.
patient with pancreatic adenocarcinoma or at very
high risk to develop it. Patients with presence of
jaundice, cytology positive for high-grade dysplasia
or invasive cancer, with the presence of a contrast-
enhancing mural nodule (≥5 mm), with MPD diame-
ter >10 mm or solid mass should be considered as absolute indications for surgery as stated in international consensus. Recommendations are less consensual to select low-risk patients, i.e. patients with relative indications or “worrisome features”. for whom the benefit risk balance between surgery and surveillance is clearly more delicate to appreciate, and it remains possible that too many prophylactic surgery is performed for lesions that would never progress to invasive lesions.

Nevertheless, several questions remain unaddressed, including the following ones:

- what is the risk of cancer progression - within the cyst but also in the whole pancreas - in followed patients (22, 23).
- How to best select patient for surgery?
- what is the risk of relapse after surgery?
- What should be the surveillance modality for non-operated patients and operated ones.
- Can follow-up be discontinued for selected cyst and patients?
- What will be, in a near future, the input of molecular or genomic analysis, in the diagnosis and selection for surgery of patients with IPMN.
The new fear… the distant cancer

It has been proposed that IPMN represents a field defect, characterized by whole gland ductal instability (24). As such, the theoretical risk of developing carcinoma may not be limited the radiographically-identifiable target cyst, but rather applicable to the entire gland including regions separate from the initially identified target cyst. This “whole gland” risk, though, remains poorly defined as most studies have been limited to surgical series of patients who have undergone resection of the most radiographically concerning regions of the gland.

CONCLUSION

The best cancer is the one that never appears... and this justify pancreatic prophylactic surgery for IPMN, but of course not for all IPMN. Clear progresses have been made over the last decades, especially with recommendations and frequent actualization. Nevertheless, several questions remain unanswered, and only large long-term international medico-surgical collaboration will allow to answer them.

Conflict of interest

The author has any financial or other kinds of personal conflicts of interest.

REFERENCES