41

Pancreatic Incidentaloma

Miguel F. Herrera Juan Pablo Pantoja Mauricio Sierra Salazar, and David Velázquez-Fernández

Introduction

The widespread use of highly sensitive imaging techniques has led to the serendipitous identifi- cation of subclinical tumors in some organs [1]. Pancreatic incidentaloma (PI) has been defined as a mass that is incidentally discovered during an image study for symptoms other than the ones of the mass itself or the organ affected. The term 'pancreatic incidentaloma' was first described by Ho and Kostiuk [2, 3]. The incidence of PI varies among different studies. In a series of 333 asymptomatic potential kidney donors, two cases of PI (0.6%) were found [4]. In a recent report analyzing the Japanese experience of PET for cancer screening in 39,785 asymptomatic subjects, six cases of unsuspected pancreatic can- cer (0.01%) were discovered [5]. Some studies have suggested that the incidence is rising [6].

When encountering a PI, the aim is to deter- mine the benign or malignant nature of the lesion. There is a general idea that early treat- ment of incidental malignant lesions may ren- der a higher cure rate and prolonged survival. However, series studying subclinical tumors in different organs have shown that the rate of malignancy and the impact of early treatment vary. The outcome is thus related not only to the stage of the disease at the time of diagnosis but also to the biologic aggressiveness of the tumor. Some authors have suggested that the identi- fication and early treatment of an incidental

lesion in certain organs, such as the kidney, reduces morbidity and mortality. In a study of 633 patients with renal carcinoma, earlier stages were significantly more frequent, and the 5-year cancer-specific survival rate was higher in the 15% of tumors discovered incidentally, when compared with patients with overt disease [7].

Studies analyzing the benefit of identifying hepatic incidentalomas have reported contra- dicting results. Little and colleagues in a series of 64 hepatic incidentalomas found that only 11 (17%) of patients were benefited from the early identification of a tumor. In contrast, 83% of the patients did not experience any benefit in terms of quality of life or prolonged survival [8]. Lui et al., in a study where 58% of hepatic inciden- talomas were malignant, found that patients with hepatocellular carcinoma had a signifi- cantly better survival than those patients with clinically suspected malignancy who underwent treatment during the same period of time [9].

Obsessive search for small incidental tumors has, on the other hand, the risk that a significant number of patients may undergo extensive diag- nostic evaluation and treatment without any posi- tive impact on their health status, with the added risk of well-known surgical complications [10].

Etiology of PI involves a variety of benign and malignant diseases, which are depicted in Table 41.1. Demographic characteristics of PI located in the pancreatic head (age, gender, and comorbidities) have been shown to be simi- lar to those of patients with symptomatic

J.G.H. Hubbard et al. (eds.), *Endocrine Surgery*, Springer Specialist Surgery Series, DOI 10.1007/978-1-84628-881-4_41, © Springer-Verlag London Limited 2009

Table 41.1. Etiology of pancreatic incidentaloma

Exocrine

Benign
- Serous cystadenoma
- Mucinous cystadenoma
- Intraductal papillary mucinous adenoma
- Mature cystic teratoma

Borderline
- Mucinous cystic tumor with moderate dysplasia
- Intraductal papillary mucinous tumor with moderate dysplasia
- Solid pseudopapillary tumor

Malignant
- Ductal adenocarcinoma
- Osteoclast-like Giant Cell tumor
- Serous cystadenocarcinoma
- Mucinous cystadenocarcinoma
- Intraductal papillary mucinous carcinoma
- Acinar cell carcinoma
- Pancreatoblastoma
- Solid-pseudopapillary carcinoma
- Ampullary adenocarcinoma

Endocrine
- ACTH secreting tumor
- Carcinoid tumor
- Gastrinoma
- Glucagonoma
- GRF-secreting tumor
- Insulinoma
- PP secreting tumor
- Somatostatinoma
- VIPoma

Cystic lesions
- Benign pancreatic cysts
- Dysontogenic cysts
- Hydatid cyst
- Lymphoepithelial cysts (LECs)
- Pancreatic dermoid cysts
- Parasitic cysts (echinococcus granulosis and multilocularis cysts)
- Retention pancreatic cysts

Congenital
- Choledochocele cyst
- Congenital cyst
- Intrapancreatic accessory spleen

Infectious masses
- Ascaris lumbricoides
- Candida albicans
- CMV
- Coxsackievirus
- Cryptosporidiosis
- Mumps
- Mycobacterium avium complex
- Mycobacterium tuberculosis

Mesenchymal tumors
- Kaposi's Sarcoma
- Lipoma
- Lymphangioma
- Pancreatic Castleman's disease
- Pancreatic hamartoma
- Pancreatic sarcoma
- Plexiform neurofibroma
- Schwannoma
- Teratoma

Metastatic lesions
- Breast
- Colon
- Lung
- Lymphoma
- Melanoma
- Renal cell carcinoma

Nonislet cell tumors
- Adenosquamous carcinoma
- Anaplastic tumors
- Clear cell "sugar" tumor
- Colloid carcinoma
- Granulocytic sarcoma
- Leukemia
- Lymphoma
- Primitive neuroectodermal tumor

Pancreatic inflammatory mass
- Eosinophilic pancreatitis
- Focal pancreatitis
- Inflammatory myofibroblastic tumor
- Lymphoid hyperplasia
- Phlegmon
- Pseudocyst
- Traumatic pancreatitis
- Wagener's disease
- Xanthogranulomatous pancreatitis

pancreatic tumors [6]. The rate of malignancy in PI has been reported to be as high as 32%, which is higher than the percentage of malig- nancy reported in other organs such as the liver, the kidney, and the adrenal glands [6–11]. The malignancy rate of PI (32%) is lower than the percentage found in patients with clinical suspi- cion of a PC (75.9%) [6]. When TNM staging was compared, the PI group also had a signifi- cantly higher proportion of patients in lower stages (stage I, 34.4 vs 10.4%) and significantly fewer positive lymph nodes. Adjusted survival rate after resection in this study was also sig- nificantly higher in patients with PI than in symptomatic patients [6]. These findings favor a more aggressive approach toward PI.

The term 'imaging incidentalomas' has been proposed for the tumors identified by conventional imaging techniques. Asympto- matic pancreatic masses can also be identified by endoscopy or endoscopic ultrasound (US), giving them the name 'endoscopic incidenta- lomas' [6]. Series where PI have been detected by endoscopy show a higher percentage of ampullary and neuroendocrine tumors.

PI can be grossly divided into solid or cystic.

We discuss both groups separately.

Solid Tumors

The incidence of benign disease in solid pancrea- tic tumors suspicious of cancer ranges from 6 to 21%. Chronic pancreatitis accounts for almost 70% of the benign lesions [12], alcoholic pan- creatitis being the most common cause (60%). In the past, the diagnosis of 'idiopathic pancreati- tis' was established in one third of the cases. It is now known that up to 11% of those patients have autoimmune pancreatitis [13–15]. Specific char- acteristics on image studies can help to differ- entiate malignant from benign lesions.

The likelihood of identifying a PI on an image study depends basically on three factors. One is tumor features such as size, density, echogenicity, calcifications, and duct dilatation. The second is the quality of the study, and the last one is the experience of the person inter- preting the study [16]. All three factors are of atmost importance, since it has been described that changes compatible with malignancy occur as early as 18 months before diagnosis [17].

In the following sections we describe relevant image features of pancreatic tumors that may be of help to the differential diagnosis.

Pancreatic Cancer

The most frequent solid lesion in the pancreas is pancreatic carcinoma (PC). At the time of diag- nosis in symptomatic patients, advanced dis- ease is the most frequent scenario (extensive local disease in about 40% and metastases in 40–55%), leaving less than 20% of patients as candidates for potentially curative resection [18, 19]. The earliest imaging finding of a PC before a mass becomes apparent is pancreatic duct dilatation or pancreatic duct cutoff [17].

On the arterial phase of a dynamic helical CT scan, PC presents as a hypovascular, hypoen- hanced lesion when compared with the sur- rounding pancreatic parenchyma [20, 21]. Necrosis may be present in larger tumors, and it is represented by nonstaining areas in the center of the mass. When these findings are present, the hypodense mass is highly likely to be ductal carcinoma [20]. When the disease is more advanced it can show local invasion or vascular encasement [21]. Multidetector row spiral CT allows for a better and faster image acquisition, leading to more refined images.

The sensitivity and specificity of FDG PET for the diagnosis of PC in patients with normal blood glucose levels range from 85 to 100% and from 67 to 99%, respectively. False-positive studies are associated with the presence of inflammation or history of radiation, and false-negative studies can occur in patients with hyperglycemia and in some small tumors. In contrast with CT alone where size is an important factor, FDG PET sensitivity is independent of tumor size. Recent reports have shown that the amount of FDG uptake may be of prognostic value. Combination of PET and CT may offer a better accuracy [22–23].

Most PC on MRI are hypointense on unen- hanced T1-weighted sequences when compared with the surrounding pancreas, and they are hypointense or isointense on T2-weighted images. Unfortunately, up to 44% of PC can be mildly hyperintense on T2-weighted images, which causes some confusion [24].

Sensitivity and specificity of simple MRI and CT scan in the evaluation of solid pancreatic masses are similar [19, 22]. Magnetic resonance

cholangiopancreatography can be added to bet- ter define pancreatic duct characteristics, and angiography to assess vascular involvement. Time–signal intensity curve on MRI may help to distinguish PC from chronic pancreatitis when there is a focal mass in the pancreas and to identify a PC in patients with long-standing chronic pancreatitis [25].

On endoscopic US, PC is often observed as a hypoechoic, nonhomogeneous irregularly shaped mass when compared with the surround- ing parenchyma. Tumors less than 2 cm may have a more homogeneous echogenicity and smooth borders [26]. Factors associated with failure to detect PC on endoscopic US include the presence of chronic pancreatitis, diffuse infil- tration of the tumor, and recent history of acute pancreatitis [27]. In a recent study, the sensitivity of endoscopic US and multidetector row spiral CT for detecting a pancreatic tumor was 98 and 86%, respectively. Tumors smaller than 25 mm were detected more frequently by endoscopic US [28]. In a different study where endoscopic US was compared with MRI and PET, sensitivity was 98, 87.5, and 87.5%, respectively [29].

Endoscopic US has the possibility of perform- ing US-guided fine-needle aspiration with a sensi- tivity from 64 to 98% and a specificity from 71 to 100% for the cytological diagnosis of PC [12, 19]. The overall rate of complications of the procedure ranges from 2 to 5% [30, 31]. Chronic pancreatitis can be a confounding factor. In a recent study, sensitivity of fine-needle aspiration for detecting PC in patients with and without chronic pancrea- titis is 73.9 and 91.3%, respectively [32].

Serum tumor markers can be helpful in differ- entiating benign from malignant pancreatic masses. The addition of other tumor markers such as Ca-125 does not increase the diagnostic accuracy of Ca 19-9 is the gold standard marker for PC with a sensitivity and specificity as high as 87 and 98%. False-positive diagnosis can occur in the presence of hyperbilirubinemia, and false-negative diagnosis can be established in patients with rare blood groups (Le(a b) blood group) and fucosyltransferase deficiency. The combination of Ca 19-9 with other tumor markers such as Ca 125 does not increase the diagnostic accuracy [33]. Promising studies of plasma proteomic profile, DNA array, and micro RNA expression may be used for the early detec- tion of PC and for the differential diagnosis between PC and chronic pancreatitis [34–37].

Islet Cell Tumors

In general, ICT are rare. They account for 2–4% of all pancreatic neoplasms with an incidence of 1.5 in 100,000 inhabitants. Nearly 60% secrete one or more biologically active peptides, result- ing in clinical syndromes. The most frequent functioning tumors are insulinoma, gastri- noma, glucagonoma, VIPoma, and somatostati- noma. Because each has a different clinical pre- sentation and some specific image characteristics, it is not frequent that diagnosis of an unsuspected functioning ICT by imaging studies only is made.

Between 30 and 40% of ICT are nonfunction- ing, and this is more likely to be discovered incidentally when symptoms due to the pre- sence of the mass are not yet obvious [38]. Multiple ICT are generally associated with other endocrinopathies as part of the multiple endocrine neoplasia or the Von Hippel-Lindau syndromes.

On CT scan, most ICT present as isodense or moderately hypodense masses with important IV enhancement. Calcification, necrosis, and cystic degeneration seem to be more common in large nonfunctioning tumors. It is important to acquire images in arterial, venous, and portal phases. The portal phase has proven to be the phase in which most small tumors can be iden- tified [39].

MRI has a diagnostic sensitivity of 78–91% [16, 40], which is equivalent to dynamic CT [40]. MRI, on the other hand, is more sensitive than CT for liver and bone metastases [41]. ICT show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images [24, 42, 43].

Endoscopic US can identify lesions as small as 5 mm in size. Tumors located in the tail of the pancreas are less likely to be identified by endoscopic US [40, 44, 45]. In a recent prospective study, sensitivity and spe- cificity of endoscopic US was 93 and 95%, respectively [45].

Scintigraphy using ^{111}In-octreotide has shown to have a sensitivity of 67–91% for the detection of ICT, and it is used for diagnosis, staging, and follow-up [40, 46, 47]. ^{11}C-5-hydro- xytryptophan PET has recently shown good results in detecting small gastrinomas and non-functioning ICT [48].

Pancreatic Metastases

Metastases to the pancreatic parenchyma are uncommon. The incidence of patients with advanced malignant tumors in autopsy studies varies from 3 to 12%. The more frequent tumors metastasizing to the pancreas are renal cell, bronchogenic, and breast carcinomas as well as melanoma; they can be found as part of the initial work-up for their primary tumor or during follow-up. Time interval between the primary lesion and the pancreatic metastatic disease can be up to 20 years, particularly in patients with renal cell carcinoma [49, 50].

On CT scan, pancreatic metastases can have three different patterns. The most common pre- sentation is as a single mass (50–73%). Lesions have well-defined margins and tend to be ovoid. They are isodense or hypodense on the noncon- trasted phase. Vascular invasion is rare. However, splenic vein obstruction and portal hypertension have been reported. Irregularities in the main pancreatic duct can also occur, making it difficult to differentiate metastases from chronic pancrea- titis. Another form of presentation is as a diffuse enlargement of the pancreatic gland (15–44%). The presence of multiple pancreatic masses is the least common presentation (5-10%) [50]. IV enhancement of the metastases seems to correlate with the enhancement characteristics of the pri-mary tumor [50]. On MRI, metastases are fre- quently hypointense on T1 and hyperintense on T2. On endoscopic US metastatic lesions are hypoechoic or isoechoic, round, and well-defined [51]. In a series of 23 patients with pancreatic metastases from renal cell carcinomas, 52% were diagnosed in asymptomatic patients at fol- low-up of, and 44% in patients with suspicion of recurrence [52]. Metastases to other organs can be as frequent as 95%. This finding supports the metastatic nature of the disease [50].

Chronic Pancreatitis

Morphologic changes due to chronic inflamma- tion of the pancreas are atrophy of the parench- yma and calcifications. Focal enlargement and the development of a pancreatic mass may also occur. Chronic pancreatitis often represents a real dilemma since it may resemble a pancreatic tumor.

When fibrosis is present, it is uniformly dis- tributed throughout the entire gland. If fibrosis is nonuniform, it may resemble a pancreatic mass on image studies. Although there has been intensive research in this field, it is still very difficult to differentiate PC from chronic pancreatitis [53].

Endoscopic US criteria for chronic pancreati- tis include at least three of the following findings: heterogeneous echogenicity, lobularity, lobular gland margins, hyperechoic stranding, hypere- choic foci, duct irregularity, atrophy, the pre- sence of a cyst, stone, calcifications, ductal dila- tion, or side branch dilation [54]. In a recent study FDG PET had a sensitivity and specificity of 100 and 97%, respectively, for the diagnosis of chronic pancreatitis and 96 and 100% for PC [55].

Autoimmune pancreatitis occurs in 4–11% of patients with chronic pancreatitis [14]. Up to 33% of patients with autoimmune pancreati- tis may present a discrete mass mimicking a pancreatic tumor. High serum level of g-globulin, IgG, IgG4, or the presence of positive autoanti- bodies including antinuclear, antilactoferrin, and anticarbonic anhydrase antibodies, and rheumatoid factor can help for the diagnosis. When a biopsy is performed, marked interlob- ular fibrosis and prominent infiltration of lymphocytes and plasma cells in the periductal area are present [56]. A summary of image characteristics is shown in Table 41.2.

Cystic Tumors

Most cystic lesions of the pancreas are benign [57–59]. It is important, however, to characterize such lesions and to distinguish true cystic lesions from pancreatic pseudocysts. The different his- tologic types of pancreatic cystic neoplasms are shown in Table 41.3. Serous cystadenomas, mucinous cystic lesions, and intraductal papil- lary mucinous neoplasms account for more than 90% of primary cystic pancreatic tumors [58]. Whilst pure cystic asymptomatic lesions are benign and can be safely followed, mucin-producing lesions are potentially malignant and warrant surgical resection [57-59].

Most cystic pancreatic lesions are inciden- tally found on imaging studies performed for other pathologies, and as many as 35% of patients are totally asymptomatic at the time of discovery [57–59].

Table 41.2. Differential diagnosis of solid tumors

	CT	FDG-PET	MRI	Endoscopic US	Confounding factors
Pancreatic carcinoma	• Hypovascular • Hypoenhanced in arterial phase	• Focal FDG uptake	• T1 hypointense, T2 hypo- or isointense	• Hypoechoic, non homogeneous, irregular shape	• T2 Mild hyperintensity in 44% of Mets and ICT
Islet cell tumors	• Iso- or hypodense w/o contrast • Important contrast enhancement • In MEN multiple lesions	• Variable uptake depending on the tumor • Limited accuracy (better accuracy with 5-hydroxitryptophan)	• T1 hypointensity T2 hyperintensity	• Homogeneous, regular shape hypoechoic	• Multiple can also be Mets
Metastases	• Well defined margins • Ovoid, iso- or hypodense w/o contrast • Diffuse enlargement • Multiple lesions	• Focal uptake depending on the primary tumor	• T1 hypointense • T2 hyperintense	• Hypo- or isoechoic well-defined round lesions	• Multiple can be ICT associated with MEN
Chronic pancreatitis	• Atrophy, calcifications	• Diffusely increased uptake	• Atrophy, calcifications	• Heterogeneous echogenicity, hyperechoic stranding	• Focal pancreatitis can be mistaken with PC

Table 41.3. Image patterns for cystic pancreatic tumors with clinical association

Lesion	Morphology	Associated lesion	Management
Unilocular cysts	• No septa • Solid component • Central-cyst wall calcification	• Pseudocyst • IPMNs • Unilocular serous cystadenomas • Lymphoepithelial cysts	• Observation if <3 cm • EUS cyst content analysis of suspicious lesions
Microcystic	• Polycystic or microcystic pattern (>6 compartments) • Stellate pattern calcification	• Serous cystadenoma	• Observation
Macrocystic	• Multilocular (<6 compartments) • Larger compartments	• Mucinous cystadenomas • IPMNs	• Surgery
Solid component	• Uni or multilocular with solid component	• Mucinous cystadenomas • IPMNs	• Surgery

Symptomatic patients may refer abdominal pain as the chief complaint. Jaundice is infre- quent and is usually associated with large lesions obstructing the common bile duct. Recurrent episodes of pancreatitis can be related to the abdominal pain episodes [57–60].

Following Bosniaḱs classification for renal cysts, a radiographic classification of pancreatic cysts based on imaging features was proposed [61]. Accordingly, the four different types of cystic lesions recognized today are (1) unilocu- lar cysts, (2) microcystic lesions, (3) macrocys- tic lesions, and (4) mixed lesions or cysts with a solid component. This classification has both diagnostic and therapeutic implications, asso- ciating the radiographic features with the spe- cific clinical entities, and eventually defining the therapeutic approach.

Unilocular Cysts

Pancreatic pseudocysts are the most commonly found unilocular cysts. Others include intraduc- tal papillary mucinous neoplasms, serous cystadenomas, and lymphoepithelial cysts [62, 63]. The absence of clinical symptoms or laboratory or imaging signs related to pancrea- titis may help to differentiate true cystic lesions from pseudocysts. A unilocular lesion in a patient with a clinical history of pancreatitis is almost always a pseudocyst. A thin-walled pan- creatic duct is consistent with the diagnosis. MRI cholangiopancreatography or fine cut CT may find communication between the pseudo- cyst and the pancreatic duct. A lobulated uni- locular cyst located in the head of the pancreas should raise the suspicion of a serous cystadenoma [63].

Microcystic Lesions

Serous cystadenoma usually demonstrate a polycystic or microcystic pattern consisting of a cyst collection that ranges from few milli- meters to 2 cm in size [64]. They are usually lobulated. The septa and wall are enhanced on imaging studies. A stellate pattern of calcification is visible in 30% of the patients and is considered characteristic of a serous

cystadenoma [64–69]. Pancreatic duct dilation is rare. In 20% of the cases, a honeycomb or sponge pattern is found on CT scan as a result of the microcystic nature of the tumor [64, 65]. In patients with indeterminate findings, MRI or endoscopic US can help to characterize the lesions. A similar honeycomb pattern can also be found on T2-weighted MRI images. Endo- scopic US usually shows discrete small anechoic areas [65, 67, 68]. The benign nature of these lesions allows follow-up in asymptomatic patients [59, 69].

Macrocystic Lesions

Mucinous cystic neoplasms (cystadenomas) and intraductal papillary mucinous neoplasms usually present as macrocystic lesions. Mucinous cystadenomas mainly involve the body and tail of the pancreas. They do not communicate with the main pancreatic duct, but they can cause partial ductal obstruction [69]. MRI and/or endoscopic US are helpful in defining the architecture of the cyst, which helps to differentiate them from ser- ous cystadenomas [64, 70, 71]. A peripheral egg- shell calcification is highly suggestive of a poten- tially malignant mucinous cystic neoplasm [71]. Only 25% of patients are symptomatic at the time of diagnosis. Surgical treatment is advocated for all mucinous lesions [57, 59, 69. 72]. Patients with totally resected malignant tumors have a 50–75% long-term survival [57, 59, 69. 72].

Cysts with a Solid Component

Intraductal papillary mucinous neoplasms can be classified as main duct, branch duct, or mixed lesions. Side branch or mixed tumors are lesions that extend outside the main pan- creatic duct. It may be difficult to differentiate them from a mucinous cystic neoplasm because they both share similar morphological features. MRI is considered the best modality to charac- terize these tumors. Endoscopic retrograde colangiopancreatography (ERCP) is seldom needed today for diagnosis. Computed tomogra- phy, with high-resolution multidetector row technology, can help to define the morphologic features of the cyst [61, 73]. These lesions are

Table 41.4. Cystic fluid aspirate analysis, biologic markers with malignant potential and probable clinical diagnosis

Marker	Cutoff levels	Probable diagnosis	Malignant potential	Experimental markers
Amylase	>5,000 U/l	Pseudocyst	Low	–
Ca 19-9	>50,000 U/ml	Mucinous cystadenoma	High	kRAS LOH analysis
CEA	>400 ng/ml	Mucinous cystadenoma	High	kRAS LOH analysis
CEA	<5 ng/ml	Serous cystadenoma	Low	VHL testing
Ca 72.4	>40 U/ml	Mucinous cystadenoma	High	kRAS LOH analysis
Mucin	>1,200/ml	Mucinous Cystadenoma	High	kRAS LOH analysis

VHL: Von Hippel-Lindau gene mutation, LOH: Loss of heterozygosity at chromosome 3p25; kRas: kRAS mutation.

considered premalignant and surgical treatment is thus advocated [58, 59, 74]. The incidence of malignancy is higher in main duct and mixed tumors than in side-branch neoplasms [75].

Cysts with a solid component can be uni- locular or multilocular. Included in this cate- gory are true cystic tumors as well as solid pancreatic neoplasms with a cystic compo- nent or cystic degeneration. The latter include islet cell tumors (ICT), solid pseudo-papillary, adenocarcinoma, and metastasis. Most tumors in this category are malignant and should be surgically treated [59, 76]. MR cholangiopancreatography is superior to sin- gle-section helical CT to characterize these tumors [75]. For small mural nodules, typi- cally undetected by MR or CT scanning, high-resolution US is extremely sensitive.

Endoscopic US

When the image techniques cannot establish a definitive diagnosis, endoscopic US may add more detailed information about the lesion [77–79]. It is important to realize that endo- scopic US can only differentiate solid from cys- tic lesions but cannot make the differential diag- nosis between benign and malignant tumors. Cytological examination and fluid content analy- sis for biochemical and tumor markers can help to differentiate mucinous from nonmucinous tumors, preventing unnecessary pancreatic resec- tion of benign lesions [78, 80]. The biochemical

and tumor markers that can help in the diagnos- tic process are shown in Table 41.4.

Surgical Treatment

Most authors agree that the presence of a potentially resectable solid pancreatic mass in a CT scan or endoscopic US in an other- wise healthy patient, with no clinical or bio- chemical characteristics suggesting a benign condition such as autoimmune pancreatitis, should prompt us to offer surgical treatment. A proposed algorithm for the management of PI is shown in Fig. 41.1 [12]. Indications for biopsy are (a) a neoadjuvant chemotherapy protocol, (b) irresectability, (c) significant comorbidities that contraindicate a major surgical procedure, (d) undetermined diagno- sis (inflammatory vs neoplastic), and (e) an apparently resectable lesion with suspicious lymph node enlargement.

The extent of surgery in patients with solid PI should be dictated by tumor location, number of lesions, and feasibility of establishing the diagnosis. If malignancy is confirmed or cannot be ruled out, a standard resection depending on the location of the PC should be performed (pancreatoduodenectomy or distal pancreatect- omy). Enucleation or resection of ICT is per- formed depending on the location of the tumor and its relationship to the pancreatic duct; cen- tral pancreatectomy may also be considered in selected patients.

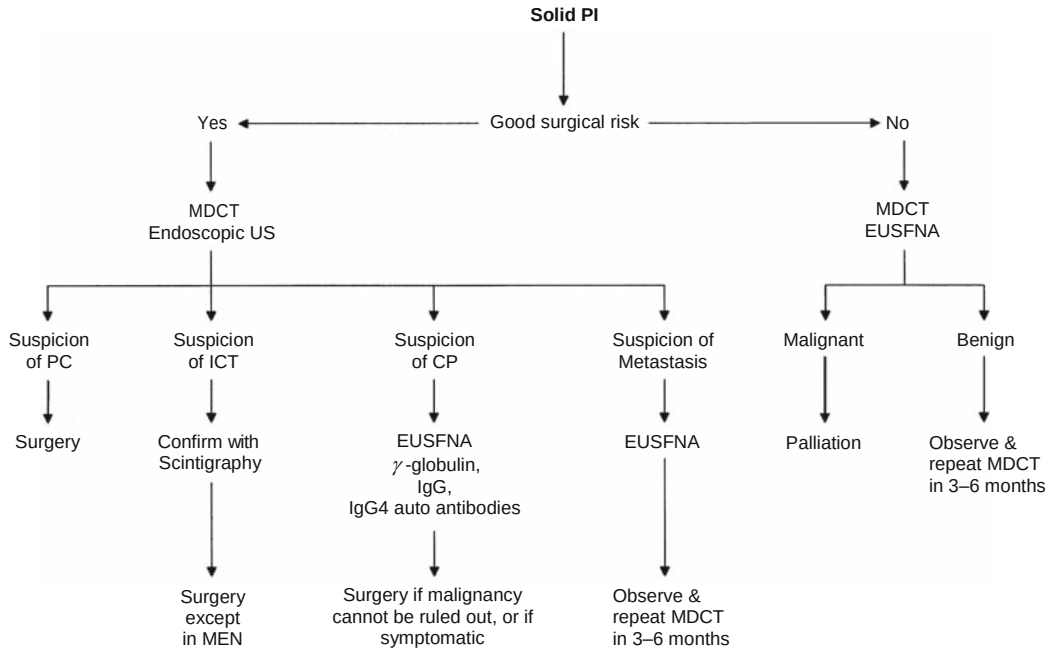

Fig. 41.1. Management algorithm for solid PI. CP: chronic pancreatitis; EUSFNA: endoscopic ultrasound-guided fine-needle aspiration; ICT: islet cell tumor; MDCT: multidetector row spiral CT scan; PC: pancreatic cancer; PI: pancreatic incidentaloma.

Some authors have advocated aggressive surgical treatment for pancreatic metastases, based on the fact that a reasonably good long-term survival can be achieved in some patients [52].

General rules for the management of cystic lesions are to resect potentially malignant tumors such as mucinous cystadenomas and intraductal papillary mucinous neoplasms and to observe benign lesions such as serous cystadenoma [80, 81]. Data from recent stu- dies have confirmed the benign course of cystadenomas. Surgical treatment is then reserved for symptomatic lesions or for tumors with significant growth during fol- low-up. Allen and colleagues [59] reported symptoms in 35% of lesions with a mean diameter of 4.9 cm; whereas Tseng and col- leagues described symptoms in 72% of patients with lesions >4 cm [82]. Resection has generally been recommended for tumors equal to or larger than 3 cm (Fig. 41.2).

In a series of 221 patients with cystic neo- plasms [83], nonoperative treatment was

offered to patients who were asymptomatic, older than 62 years of age, or had small cysts (median 2.4 cm). The majority of patients were followed by image studies (67%). After a mean follow-up of 24 months, 19% of the tumors demonstrated an increase in size. All resected lesions were benign.

Similarly, two studies from the Massachu- setts General Hospital have recommended nonoperative management for patients with asymptomatic incidentally discovered cystic lesions <2 cm in size and in elderly patients with nonmucinous lesions with normal CEA levels on fluid analysis [57, 82]. The inci- dence of malignancy in patients with small lesions (<2 cm) who underwent resection was only 3% [57].

A study from the Memorial Sloan Kettering Cancer Center analyzed predictive factors for malignancy in PI [59]. The presence of a solid component in a mucinous cyst lesion was the most important predictive factor (61%); growth of a cystic lesion was also associated with malignancy.

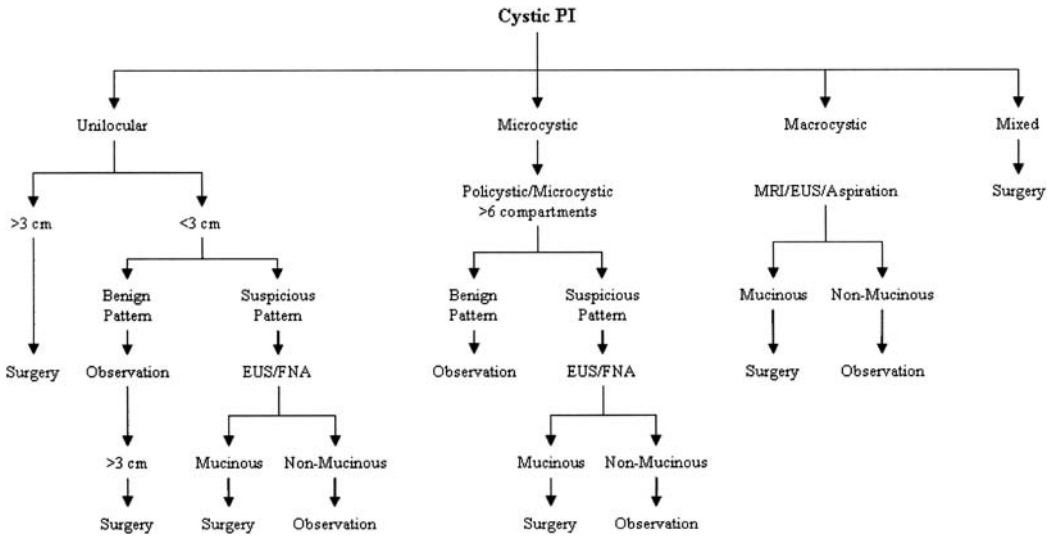

Fig. 41.2. Management algorithm for cystic PI. EUSFNA: endoscopic ultrasound-guided fine-needle aspiration; MRI: magnetic resonance imaging; EUS: endoscopic ultrasound.

References

1. Prinz RA, Brooks MH, Churchill R, et al. Incidental asymptomatic adrenal masses detected by computed tomographic scanning. Is operation required? JAMA. 1982;248:701–4.
2. Kostiuk TS. Observation of pancreatic incidentaloma. Klin Khir. 2001;9:62–3.
3. Ho CL, Dehdashti F, Griffeth LK, et al. FDG-PET evalua- tion of indeterminate pancreatic masses. J Comput Assist Tomogr. 1996;20:363–9.
4. Strang AM, Lockhart ME, Kenney PJ, et al. Computer- ized tomographic angiography for renal donor evalua- tion leads to a higher exclusion rate. J Urol. 2007;177:1826–9.
5. Ide M, Suzuki Y. Is whole-body FDG-PET valuable for health screening? Eur J Nucl Med Mol Imaging. 2005;32:339–41.
6. Winter JM, Cameron JL, Lillemoe KD, et al. Periampul- lary and pancreatic incidentaloma: a single institution's experience with an increasingly common diagnosis. Ann Surg. 2006;243:673–80.
7. Tsui KH, Shvarts O, Smith RB, et al. Renal cell carci- noma: prognostic significance of incidentally detected tumors. J Urol. 2000;163:426–30.
8. Little JM, Richardson A, Tait N. Hepatic dystychoma: a five year experience. HPB Surg. 1991;4:291–7.
9. Liu CL, Fan ST, Lo CM, et al. Hepatic resection for incidentaloma. J Gastrointest Surg 2004;8:785–93.
10. Westbrook JI, Braithwaite J, McIntosh JH. The out- comes for patients with incidental lesions: serendipitous or iatrogenic? Am J Roetnol. 1998;171:1193–6.
11. Herrera MF, Grant CS, van Heerden JA, et al. Inciden- tally discovered adrenal tumors: an institutional per- spective. Surgery. 1991;110:1014–21.

12. Wolfson D, Barkin JS, Chari ST, et al. Management of pancreatic masses. Pancreas. 2005;31:203–17.
13. Steer ML, Waxman I, Freedman S. Chronic pancreatitis. N Engl J Med. 1995;332:1482–90.
14. Finkelberg DL, Sahani D, Deshpande V, Brugge WR. Autoimmune pancreatitis. N Engl J Med. 2006;355:2670–6.
15. Yadav D, Notahara K, Smyrk TC, et al. Idiopathic tume- factive chronic pancreatitis: clinical profile, histology, and natural history after resection. Clin Gastroenterol Hepatol. 2003;1:129–35.
16. Hammel P. Tumeurs pancréatiques de découverte for- tuite: diagnostic et prise en charge. Gastroenterol Clin Biol. 2002;26:700–8.
17. Gangi S, Fletcher JG, Nathan MA, et al. Time interval between abnormalities seen on CT and the clinical diag- nosis of pancreatic cancer: retrospective review of CT scans obtained before diagnosis. AJR Am J Roentgenol. 2004;182:897–903.
18. McMahon PM, Halpern EF, Fernandez-del Castillo C, et al. Pancreatic cancer: cost-effectiveness of imaging technologies for assessing resectability. Radiology. 2001;221:93–106.
19. Nichols MT, Russ PD, Chen YK. Pancreatic imaging: current and emerging technologies. Pancreas. 2006;33:211–20.
20. Saisho H, Yamaguchi T. Diagnostic imaging for pan- creatic cancer: computed tomography, magnetic reso- nance imaging, and positron emission tomography. Pancreas. 2004;28:273–8.
21. Choi EK, Park SH, Kim DY, et al. Unusual manifestations of primary pancreatic neoplasia: radiologic-pathologic correlation. J Comput Assist Tomogr. 2006;30:610–7.
22. Delbeke D, Pinson CW. Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. J Hepatobiliary Pancreat Surg. 2004;11:4–10.

23. Kalra MK, Maher MM, Boland GW, et al. Correlation of positron emission tomography and CT in evaluating pancreatic tumors: technical and clinical implications. AJR Am J Roentgenol. 2003;181:387–93.
24. Lopez Hänninen E, Amthauer H, Hosten N, et al. Pro- spective evaluation of pancreatic tumors: accuracy of MR Imaging with MR cholangiopancreatography and MR Angiography. Radiology. 2002;224:34–41.
25. Tajima Y, Kuroki T, Tsutsumi R, et al. Pancreatic carci- noma coexisting with chronic pancreatitis versus tumor-forming pancreatitis: diagnostic utility of the time-signal intensity curve from dynamic contrast- enhanced MR imaging. World J Gastroenterol. 2007;13:858–65.
26. Horwhat JD, Gress FG. Defining the diagnostic algo- rithm in pancreatic cancer. JOP. 2004;5:289–303.
27. Bhutani MS, Gress FG, Giovannini M, et al. The no endosonographic detection of tumor (NEST) study: a case series of pancreatic cancers missed on endoscopic ultrasonography. Endoscopy. 2004;36:385–9.
28. DeWitt J, Devereaux B, Chriswell M, et al. Comparison of endoscopic ultrasonography and multidetector com- puted tomography for detecting and staging pancreatic cancer. Ann Intern Med. 2004;141:753–63.
29. Borbath I, Van Beers BE, Lonneux M, et al. Preoperative assessment of pancreatic tumors using magnetic reso- nance imaging, endoscopic ultrasonography, positron emission tomography and laparoscopy. Pancreatology. 2005;5:553–61.
30. Horwhat JD, Paulson EK, McGrath K, et al. A rando- mized comparison of EUS-guided FNA versus CT or US- guided FNA for the evaluation of pancreatic mass lesions. Gastrointest Endosc. 2006;63:966–75.
31. Voss M, Hammel P, Molas G, et al. Value of endoscopic ultrasound guided fine needle aspiration biopsy in the diagnosis of solid pancreatic masses. Gut. 2000;46:244–9.
32. Varadarajulu S, Tamhane A, Eloubeidi MA. Yield of EUS-guided FNA of pancreatic masses in the presence or the absence of chronic pancreatitis. Gastrointest Endosc. 2005;62:728–36.
33. Cwik G, Wallner G, Skoczylas T, et al. Cancer antigens 19-9 and 125 in the differential diagnosis of pancreatic mass lesions. Arch Surg. 2006;141:968–74.
34. Bloomston M, Frankel WL, Petrocca F, et al. MicroRNA expression patterns to differentiate pancreatic adeno- carcinoma from normal pancreas and chronic pancrea- titis. JAMA. 2007;297:1901–8.
35. Koopmann J, Zhang Z, White N, et al. Serum diagnosis of pancreatic adenocarcinoma using surface-enhanced laser desorption and ionization mass spectrometry. Clin Cancer Res. 2004;10:860–8.
36. Buchholz M, Kestler HA, Bauer A, et al. Specialized DNA arrays for the differentiation of pancreatic tumors. Clin Cancer Res. 2005;11:8048–54.
37. Honda K, Hayashida Y, Umaki T, et al. Possible detec- tion of pancreatic cancer by plasma protein profiling. Cancer Res. 2005;65:10613–22.
38. Brentjens R, Saltz L. Islet cell tumor of the pancreas: the medical oncologist's perspective. Surg Clin North Am. 2001;3,527–42.
39. Horton KM, Hruban RH, Yeo C, Fishman EK. Multi- detector row CT of pancreatic islet cell tumors. Radio- graphics. 2006;26:453–64.

40. Kaltsas GA, Besser GM, Grossman AB. The diagnosis and medical management of advanced neuroendocrine tumors. Endocr Rev. 2004;25:458–511.
41. Debray MP, Geoffroy O, Laissy JP, et al. Imaging appear- ances of metastases from neuroendocrine tumours of the pancreas. Br J Radiol. 2001;74:1065–70.
42. Thoeni RF, Mueller-Lisse UG, Chan R, et al. Detection of small, functional islet cell tumors in the pancreas: selec- tion of MR imaging sequences for optimal sensitivity. Radiology. 2000;214:483–90.
43. Semelka RC, Custodio CM, Cem-Balci N, Woosley JT. Neuroendocrine tumors of the pancreas: spectrum of appearances on MRI. J Magn Reson Imaging. 2000;11:141–8.
44. Rösch T, Lightdale CJ, Botet JF, et al. Localization of pancreatic endocrine tumors by endoscopic ultrasono- graphy. N Engl J Med. 1992;326:1721–6.
45. Anderson MA, Carpenter S, Thompson NW, et al. Endo- scopic ultrasound is highly accurate and directs man- agement in patients with neuroendocrine tumors of the pancreas. Am J Gastroenterol. 2000:95:2271–7.
46. Kaltsas GA, Mukherjee JJ, Grossman AB. The value of radiolabelled MIBG and octreotide in the diagnosis and management of neuroendocrine tumours. Ann Oncol. 2001;12(Suppl 2):S47–50.
47. Wiedenmann B, Jensen RT, Mignon M, et al. Preoperative diagnosis and surgical management of neuroendocrine gastroenteropancreatic tumors: generalrecommendations by a consensus workshop. World J Surg. 1998;22:309–18.
48. Orlefors H, Sundin A, Garske U, et al. Whole-body (11)C-5-hydroxytryptophan positron emission tomo- graphy as a universal imaging technique for neuroendo- crine tumors: comparison with somatostatin receptor scintigraphy and computed tomography. J Clin Endo- crinol Metab. 2005;90:3392–400.
49. Merkle EM, Boaz T, Kolokythas O, et al. Metastases to the pancreas. Br J Radiol. 1998;71:1208–14.
50. Scatarige JC, Horton KM, Sheth S, Fishman EK. Pan- creatic parenchymal metastases: observations on helical CT. AJR Am J Roentgenol. 2001;176:695–9.
51. Palazzo L, Borotto E, Cellier C, et al. Endosonographic features of pancreatic metastases. Gastrointest Endosc. 1996;44:433–6.
52. Ghavamian R, Klein KA, Stephens DH, et al. Renal cell carcinoma metastatic to the pancreas: clinical and radi- ological features. Mayo Clin Proced. 2000;75:581–5.
53. Kim T, Murakami T, Takamura M, et al. Pancreatic mass due to chronic pancreatitis: correlation of CT and MR imaging features with pathologic findings. AJR Am J Roentgenol. 2001;177:367–71.
54. Kwon RS, Brugge WR. New advances in pancreatic ima- ging. Curr Opin Gastroenterol. 2005;21:561–7.
55. Imdahl A. Nitzsche E, Krautmann F, et al. Evaluation of positron emission tomography with 2-[(18) F] fluoro- 2-deoxy-D-glucose for the differentiation of chronic pancreatitis and pancreatic cancer. Br J Surg. 1999;86:194–9.
56. Okazaki K, Kawa S, Kamisawa T, et al. Clinical diagnos- tic criteria of autoimmune pancreatitis: revised propo- sal. J Gastroenterol. 2006;41:626–31.
57. Fernández-del Castillo C, Targarona J, Thayer SP, et al.
Incidental pancreatic cysts: clinicopathologic character- istics and comparison with symptomatic patients. Arch Surg. 2003;138:427–34.

58. Allen PJ, Jaques DP, D'Angelica M, et al. Cystic lesions of the pancreas: selection criteria for operative and non- operative management in 209 patients. J Gastrointest Surg. 2003;7:970–7.
59. Allen PJ, D'Angelica M, Gonen M, et al. A selective approach to the resection of cystic lesions of the pan- creas: results from 539 consecutive patients. Ann Surg. 2006;244:572–82.
60. Sheehan MK, Beck K, Pickleman J, Aranha GV. Spec- trum of cystic neoplasms of the pancreas and their surgical management. Arch Surg. 2003;138:657–62.
61. Sahani DV, Kadavigere R, Saokar A, et al. Cystic pan- creatic lesions: a simple imaging-based classification system for guiding management. Radiographics. 2005;25:1471–84.
62. Holzheimer RG, Mannick JA (eds). Surgical treatment: evidence-based and problem-oriented. Munich, Ger- many: Zuckschwerdt, 2001.
63. Cohen-Scali F, Vilgrain V, Brancatelli G, et al. Discrimi- nation of unilocular macrocystic serous cystadenoma from pancreatic pseudocyst and mucinous cystadenoma with CT: initial observations. Radiology. 2003;228:727–33.
64. Sarr MG, Murr M, Smyrk TC, et al. Primary cystic neoplasms of the pancreas. Neoplastic disorders of emerging importance-current state-of-the-art and unanswered questions. J Gastrointest Surg. 2003;7:417–28.
65. Curry CA, Eng J, Horton KM, et al. CT of primary cystic pancreatic neoplasms: can CT be used for patient triage and treatment? AJR Am J Roentgenol. 2000;175:99–103.
66. Fernandez-del Castillo C, Warshaw AL. Current man- agement of cystic neoplasms of the pancreas. Adv Surg. 2000;34:237–48.
67. Procacci C, Biasiutti C, Carbognin G, et al. Characteriza- tion of cystic tumors of the pancreas: CT accuracy. J Comput Assist Tomogr. 1999;23:906–12.
68. Procacci C, Graziani R, Bicego E, et al. Serous cystade- noma of the pancreas: report of 30 cases with emphasis on imaging findings. J Comput Assist Tomogr. 1997;21:373–82.
69. Warshaw AL, Compton CC, Lewandrowski K, et al. Cys- tic tumors of the pancreas. New clinical, radiologic, and pathologic observations in 67 patients. Ann Surg. 1990;212:432–43.
70. Sahani D, Prasad S, Saini S, Mueller P. Cystic pancreatic neoplasms evaluation by CT and magnetic resonance cholangiopancreatography. Gastrointest Endosc Clin N Am. 2002;12:657–72.
71. Mathieu D, Guigui B, Valette PJ, et al. Pancreatic cystic neoplasms. Radiol Clin North Am. 1989;27:163–76.
72. Horvath KD, Chabot JA. An aggressive resectional approach to cystic neoplasms of the pancreas. Am J Surg. 1999;178:269–74.
73. McNulty NJ, Francis IR, Platt JF, et al. Multi–detector row helical CT of the pancreas: effect of contrast- enhanced multiphasic imaging on enhancement of the pancreas, peripancreatic vasculature, and pancreatic adenocarcinoma. Radiology. 2001;220:97–102.
74. Siech M, Tripp K, Schmidt-Rohlfing B, et al. Intraductal papillary mucinous tumor of the pancreas. Am J Surg. 1999;177:117–20.
75. Taouli B, Vilgrain V, Vullierme MP, et al. Intraductal papillary mucinous tumors of the pancreas: helical CT with histopathologic correlation. Radiology. 2000;217:757–64.
76. Kloppel G, Kosmahl M. Cystic lesions and neoplasms of the pancreas: the features are becoming clearer. Pan- creatology. 2001;1:648–55.
77. Mallery S, Quirk D, Lewandrowski K, et al. EUS-guided FNA with cyst fluid analysis in pancreatic cystic lesions (abstr). Gastrointest Endosc. 1998;47:AB149.
78. Brugge WR. Evaluation of pancreatic cystic lesions with EUS. Gastrointest Endosc. 2004;59:698–707.
79. Sedlack R, Affi A, Vazquez-Sequeiros E, et al. Utility of EUS in the evaluation of cystic pancreatic lesions. Gas- trointest Endosc. 2002;56:543–7.
80. Brugge WR, Lauwers GY, Sahani D, et al. Cystic neo- plasms of the pancreas. N Engl J Med. 2004;351(12):1218–26.
81. Sakorafas GH, Sarr MG. Cystic neoplasms of the pan- creas: what a clinician should know. Cancer Treat Rev. 2005;31:507–35.
82. Tseng JF, Warshaw AL, Sahani DV, et al. Serous cysta- denoma of the pancreas: tumor growth rates and recommendations for treatment. Ann Surg. 2005;242:413–19.
83. Walsh RM, Vogt DP, Henderson JM, et al. Natural his- tory of indeterminate pancreatic cysts. Surgery. 2005;138:665–71.