Review

Pancreatic tumors imaging: An update

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Abstract

Currently, ultrasound (US), computed tomography (CT) and Magnetic Resonance Imaging (MRI) represent the mainstay in the evaluation of pancreatic solid and cystic tumors affecting pancreas in 80–85% and 10–15% of the cases respectively. Integration of US, CT or MR imaging is essential for an accurate assessment of pancreatic parenchyma, ducts and adjacent soft tissues in order to detect and to stage the tumor, to differentiate solid from cystic lesions and to establish an appropriate treatment. The purpose of this review is to provide an overview of pancreatic tumors and the role of imaging in their diagnosis and management.

In order to a prompt and accurate diagnosis and appropriate management of pancreatic lesions, it is crucial for radiologists to know the key findings of the most frequent tumors of the pancreas and the current role of imaging modalities.

A multimodality approach is often helpful. If multidetector-row CT (MDCT) is the preferred initial imaging modality in patients with clinical suspicion for pancreatic cancer, multiparametric MRI provides essential information for the detection and characterization of a wide variety of pancreatic lesions and can be used as a problem-solving tool at diagnosis and during follow-up.

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1. Introduction

Currently, ultrasound (US), computed tomography (CT) and Magnetic Resonance Imaging (MRI) represent the mainstay in the evaluation of pancreatic solid and cystic tumors affecting pancreas in 80–85% and 10–15% of the cases respectively [1,2]. Integration of US, CT or MR imaging is essential for an accurate assessment of pancreatic parenchyma, ducts and adjacent soft tissues in order to detect and to stage the tumor, to differentiate solid from cystic lesions and to establish an appropriate treatment. The purpose of this review is to provide an overview of pancreatic tumors and the role of imaging in their diagnosis and management.

2. Classification

Pancreatic tumors including a heterogeneous group of primary lesions: adenocarcinoma, neuroendocrine tumor (NET), pancreatic cystic neoplasms, solid pseudopapillary tumor, pancreatoblastoma, pancreatic lymphoma and rare miscellaneous neoplasms [1] (Table 1).

Pancreatic ductal adenocarcinoma (PDA) represents 85–95% of all pancreatic solid pancreatic malignant neoplasms while neuroendocrine tumors are frequently benign and include insulinoma, gastrinoma, glucagonoma, somatostatinoma, vasoactive intestinal polypeptide tumor (VIPoma), Pancreatic polypeptide secreting tumors (PPomas) and non-functioning tumors, amounting to 3–4% of the cases [1].

3. Clinical presentation

Early pancreatic cancer is often asymptomatic. Tumors in the
pancreatic head (75% of the cases), often present early with biliary obstruction. However, tumors in the body and tail can remain asymptomatic till late in disease stage [3].

Weight loss, poor appetite, abdominal discomfort, abdominal or midback pain and obstructive jaundice and related symptoms are relatively common and generally occur late in the clinical development; pancreatitis is less common as presenting symptoms [1,4,5]. Digestive problems, nausea and vomiting occur more frequently when the cancer presses on the stomach. Rarely, pancreatic cancers cause diabetes due to the destruction of insulin-making cells. Encasement of vascular structures, infiltration of adjacent bowel and superior mesenteric vein thrombosis may all occur later.

PDA is associated with several rare paraneoplastic syndromes: Trousseau syndrome is traditionally defined as migratory thrombophlebitis [6,7]. Panniculitis is associated with acinar cell carcinoma in 8% of cases; eczematous dermatitis, fibrous cutaneous hand changes, plantar keratoderma, polyomysitis, neurological and hematologic manifestation represent other paraneoplastic syndromes [1,8–10].

Signs and symptoms of pancreatic functioning NET are different and dependent on an excessive secretion of hormones. Insulinoma (50%) reveals itself with hypoglycemic attacks featuring neuroglycopenia and sympathetic over-stimulation, including weakness, confusion, sweating, and rapid heartbeat, and/or atypical seizures [11–13]. Gastrinomas (20%) produce too much gastrin, causing a condition known as Zollinger-Ellison syndrome, resulting in peptic ulcers which can cause pain, nausea, loss of appetite and anemia [1,11,14–17]. VIPomas (3%) make vasoactive intestinal peptide (VIP) and result in watery diarrhea and hypokalemia [1,11,12,18], Glucagonomas (1%) produce glucagon that increases glucose levels in the blood; most of the symptoms are often nonspecific, as diarrhea, weight loss, malnutrition and rarely hyperglycemia. The most distinctive feature of a glucagonoma is necrotic migratory erythema, a red rash with swelling and blisters that often travels place to place on the skin [1,11,12,19]. Somatostatinomas (≤1%) produce somatostatin; symptoms can include diarrhea, steatorrhea, nausea, poor appetite and weight loss, gallstones, and symptoms of diabetes [1,11,20]. Pompas cause an increase in the production of pancreatic polypeptide (PP), but they are rare and have not been associated with any clinical syndrome [21]; some patients also get watery diarrhea.

Signs and symptoms of non-functioning neuroendocrine tumors are caused by mass effect (mainly jaundice, belly pain and weight loss) [11].

Moreover, asymptomatic cancer can be incidentally detected on abdominal scans obtained for other reasons.

4. Imaging

4.1. Plain radiograph

Plain abdominal radiograph has a very limited role in imaging of the pancreas; sometimes it can show coarse parenchymal calcification of the pancreas in 25–59% of patients with chronic pancreatitis; however, calcifications near the pancreas can be confused with splenic artery calcifications.

4.2. Ultrasound

Ultrasound (US) is usually limited in the evaluation of pancreas due to body habitus (adipose tissue) and the interposed intestinal and gastric bloating [22–24]. However, US is the first non-invasive imaging test for the evaluation of pancreas. Abdominal conventional US allows to assess size, site and echogenicity of pancreatic lesions and to evaluate the Wirsung duct caliber; with a sensitivity and specificity respectively of 75% [24] and an accuracy of 50–70% [25]. Most focal pancreatic lesions are hypoechoic compared to normal parenchyma. Typically dilatation of the common bile duct and pancreatic duct (double duct sign), which is very suggestive for a mass in the pancreatic head, even in the absence of a visible mass, is seen in patients with a pancreatic head tumor.

Endoscopic US (EUS) provides ultra-high resolution images and is commonly accepted as the most sensitive technique for detection of small pancreatic head tumors (<2 cm) [26,27].

4.3. Contrast-enhanced US

The introduction of microbubble contrast agents has improved the diagnostic accuracy of US in the study of pancreatic pathologies [28,29]. Contrast-enhanced US (CEUS) is a cost-effective real-time method that allows the evaluation of the enhancement of pancreatic lesions during the dynamic phases [29] and provides useful findings for differentiating pancreatic carcinoma from chronic focal pancreatitis [30]; moreover CEUS is very accurate in demonstrating NET vascularisation [31].

Even if the Authors themselves suggest that CEUS is an accurate method for the characterization of pancreatic masses [32], CEUS is not sufficient to characterize the tumor, but rather it can improve the accuracy of US of pancreatic lesions incidentally detected as
complementary dynamic imaging [31]; contrast-enhanced CT and/or MRI allow a more accurate evaluation of the local extension and metastatic spread [33,34]. Nevertheless, CEUS can be used during follow-up in patients with severe acute pancreatitis, after an initial CT evaluation, because it may help in identifying and in delineating necrotic areas, which do not enhance [28,35].

Technique — After contrast agent injection, enhancement of the pancreas begins immediately after aortic enhancement during an early arterial phase (10–30 s); subsequently there is a transient venous phase (30 to approximately 120 s) [28]. The main limitation is represented by the different pharmacokinetics of microbubble contrast agents in comparison to the contrast medium of CT or MRI, due to their confine in vessel lumen without extravascular phase; consequently the late phase of CEUS does not correspond to the interstitial or parenchymal equilibrium phase described in CT and/or MRI [23].

4.4. Multidetector-row CT

Multidetector-row Computed Tomography (MDCT) is the most widely used imaging modality for pancreatic tumors evaluation with a sensitivity between 76% and 92% for diagnosing pancreatic cancer [3,36,37]. Brennan et al. assert that CT has an accuracy of 85–95% for tumor detection, a positive predictive value of 89–100% for resectability and a negative predictive value of 45–79% for resectability [38].

MDCT allows to accurately assess tumor morphology, ductal anatomy, and its relationship to surrounding organs and vascular structures, permitting a surgical planning. High-resolution MDCT and image-processing techniques (multiplanar reconstructions and curved reformations) can provide additional details and can define the pancreatic ductal course and anatomy. CT is also easily able to detect the “double duct sign”, whereas tumors in the pancreatic body may cause upstream MPD dilatation.

Since the tumor may be isodennuating, no pancreatic mass is visualized in 10% of cases [38].

Indirect signs, such as abrupt cut-off of the pancreatic duct PDA dilatation (interrupted duct sign), mass effect on the pancreatic parenchyma and atrophic distal parenchyma, should be considered as indicators of tumors when mass cannot be clearly identified on CT [39]; the knowledge of pancreatic cancer and surrounding parenchyma at CT is essential to improve research on methods to detect isoattenuated tumor [40]. The quantitative analysis at triphasic MDCT increases tumor detection with respect to visual analysis, showing a higher sensitivity in all phases, even for small PDAs isodense to the pancreatic parenchyma upstream to the tumor [40].

Technique — Many CT protocols for pancreatic enhancement and pancreatic tumor staging are described in the literature. In patients with suspected pancreatic tumor, the majority of standard CT protocols [41–44] involves non-contrast study followed by pancreatic parenchymal phase (PPP) and portal venous phase (PVP) and delayed phase (DP), after the administration of intravenous contrast material.

An arterial phase (AP) may be performed if a hypervascular pancreatic lesion such as a neuroendocrine tumor is suspected, while PPP (typically 40–45 s after start of contrast injection at flow rate of 4 ml/s) allows maximal differentiation between the normal parenchyma and the hypodense pancreatic lesions, becoming the most sensitive phase for the evaluation of pancreatic parenchyma (e.g. adenocarcinoma) [37,41]. PVP (70 s after start of contrast injection) is optimal for detecting liver metastases.

Nevertheless, multiphase CT exposes patient to a high radiation dose. Recently, the split-bolus CT protocol has been proposed for the detection and staging of pancreatic cancer [45].

Split-bolus MDCT technique, combining arterial phase (AP) and PVP, allows an optimal pancreatic enhancement to detect normal pancreatic parenchyma and to maximize the difference in attenuation between the tumor and the background pancreatic parenchyma with a better tumor conspicuity, provides optimal synchronous arterial and mesenteric venous opacification evaluating potential tumor resectability, and reduces radiation dose [45–47]. In addition, split-bolus allows lymph nodes assessment, detection and characterization of the focal liver lesions [46].

In Fig. 1 is reported a schematic view of split-bolus MDCT protocol in a patient weighting 75 Kg.

4.5. MRI

MRI, including morphologic and functional sequences, has become widely used in the diagnosis of pancreatic pathologies because of its very high soft-tissue contrast resolution, with an accuracy in the detection and staging of adenocarcinoma of 90–100% [48]; MR cholangiopancreatography (MRCP) permits the evaluation of pancreatic ductal system anatomy and abnormalities and can be used to depict relationship between cystic lesions and pancreatic duct [49,50]. MRI is used as a problem-solving tool for diagnosis and during follow-up in patients with cystic pancreatic tumors [51].

Furthermore, diffusion-weighted imaging (DWI), almost becomes part of the MRI protocol, may provide additional information about a wide variety of solid and cystic lesions of the pancreas and can help radiologists, especially to detect solid pancreatic tumors with a high cellularity or fibrosis, which show a low ADC (apparent diffusion coefficient) values [49], and potentially to distinguish focal pancreatitis from adenocarcinoma, as reported in literature [52].

MRI can be performed with scanning at 1.5T or 3T: studies comparing 1.5T and 3T abdominal MRI suggest that 3T does not offer substantial improvement in image quality for unenhanced images; however, the signal–noise ratio (SNR) of contrast-enhanced images is thought to be superior at 3T [52–60].

Technique — A complete evaluation of the pancreas and the pancreaticobiliary ductal system includes a multiparametric MRI (mpMRI) T2-weighted (T2W) and diffusion-weighted imaging (DWI), as well as contrast-enhanced MRI and cholangiopancreatography (MRCP) pulse sequences (HASTE) using the following sequences: axial T1W gradient-echo, with and without fat saturation, using breath-hold or gated respirations, axial and coronal T2W images with and without fat saturation, either fast spin echo (FSE) or turbo spin echo (TSE), T1W breath-hold fat-suppressed 3D gradient-echo images before and after gadolinium (Gd-DTPA) administration and spin echo EPI single shot (DWI) with b value 0, 800, 1000 and ADC maps reconstruction. Contrast-enhanced MRI includes multiphase (PPP, PVP and DP) study after intravenous administration of Gd-DTPA.

The MRCP sequences can be obtained by 3-dimensional (3D) acquisition that produces high resolution images of the pancreaticobiliary ductal system. Pineapple and blueberry juice have been used as oral contrast agents to reduce the signal from the overlying stomach and duodenum.

Secretin MR cholangiopancreatography (S-MRCP) sequence, which entails administration of secretin to stimulate the exocrine function of the pancreas, have been developed for a more complete assessment of pancreatic ducts and glandular function, useful in assessment of complex ductal anomalies and to quantitatively assess the exocrine function of the pancreas [50].

4.6. PET/CT

Nuclear medicine is able to provide a functional imaging of
pancreatic tumours of different histology and its contribution is of pivotal importance to better diagnose and follow up pancreatic lesions.

Many papers investigated the diagnostic ability of pancreatic cancer of Positron Emission Tomography (PET) with 2-deoxy-[18F] fluoro-d-glucose ([18F]FDG), a radiocompound labelled with [18F]Fluorine ([18F]) that uses glycolytic pathways and has an uptake mechanism in tumour cells depending on the increased number of functional glucose transporters and glycolytic enzymes [61–62]. The wide diffusion of hybrid systems, combining nuclear medicine (SPECT and PET) and radiology devices (CT, MRI) mounted on the same gantry to obtain co-registered and fused functional and anatomical images, improves diagnostic results in clinical practice [61,62]. In a recent meta-analysis the sensitivity and specificity of 18FDG-PET to confirm suspected pancreatic cancer resulted up to 95% and 100%, respectively [62].

A further promising radiopharmaceutical has been proposed to image pancreatic cancer, the thymidine analogue 3-deoxy-3'-[18F] fluorothymidine ([18F]FLT) [63]. This radiocompound allows to visualize proliferating lesions and it has been shown that it selectively accumulates in malignant tumours of the pancreas [64], but its use is still limited.

Furthermore pancreas is a site of neuroendocrine tumours (NETs). Pancreatic NETs are less frequent than endocrine gastrointestinal tumours and, although generally asymptomatic, they may cause hypersecrection of several hormones (gastrin, insulin, glucagon, vasoactive intestinal peptide) and usually over-express somatostatin receptors (SSR) 1–5 [65–68].

Among positron emitting radiopharmaceuticals, [18F]FDG does not represent the option of choice because it better detects highly metabolic undifferentiated tumours, while other radiotracers such as [18F]-DOPA (3,4-dihydroxy-L-phenylalanine labelled with [18F]) and peptides labelled with [68Ga]Ga provide better results [69]. NETs are avid of [18F]-DOPA because they derive from cells belonging to the amine precursor uptake and decarboxylation (APUD) cell system and therefore show a high [18F]-DOPA decarboxylase activity [70] while [68Ga]-DOTA peptides are radiolabelled somatostatin analogues binding to somatostatin receptors (SR) that are over-expressed on NET tumour cell surface [71].

The most known PET tracer for SR imaging are [68Ga]-DOTAO-Tyr3/octreotate ([68Ga]-DOTATATE), [68Ga]-DOTAO-Tyr3/octreotide ([68Ga]-DOTATOC) and 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid)-1-Nal3-octreotide ([68Ga]-DOTANOC) and they are useful to evaluate SR expression in order to treat the patients with β-emitting labelled somatostatin analogues [61,71], such as radiocompounds labelled by 90Yttrium (90Y) and 177Lutetium (177Lu).

Despite the clinical relevance of [68Ga]-labelled radiocompounds also due to the high spatial resolution of PET scan comparing with SPECT, the γ-emitting somatostatin analogues maintain a certain role. 111In-DTPA-octreotide is commercially available and is the most commonly used agent for SR imaging [71,72]. It shares with positron-emitting radiopharmaceuticals the clinical indications including the diagnosis of primary and metastatic NETs, the staging and the follow-up of patients and the selection of subjects with inoperable and/or metastatic tumours candidates to peptide receptor radionuclide therapy.

5. Solid lesions

5.1. Pancreatic ductal adenocarcinoma

Pancreatic ductal adenocarcinoma (PDA), 85–95% of all pancreatic solid pancreatic malignant neoplasms, represents the fourth leading cause to cancer-related deaths and affects men more frequently between 60 and 80 years of age [1–4]. PDA is located in the pancreatic head 60–70%, less commonly in the body (10–20%) and 5–10% in the tail [1–3]. Postoperative survival rate at 5-year is of 20% [1,3], furthermore the cancer is resectable at diagnosis in only about 20–15% of cases [50]. CA 19.9 can be elevated, but it is useful during follow-up because its rise up precedes imaging manifestation of relapse [50].

On PPP of the conventional bi- or triphasic CT and on mixed (PPP/PVP) phase of split-bolus MDCT protocol, most tumors are hypovascular. On intravenous contrast medium injection (Fig. 2); the 10% of cases may be isodensities [1,38,40]: mass effect, abnormal contour of the pancreas, ductal obstruction with “double duct sign,” and vascular invasion (vessel deformity, thrombosis, and development of collateral vessels) are indirect signs of pancreatic cancer [1,2]. Rarely (8% of cases) can be see cystic-necrotic degeneration [73].

At MRI PDA shows low signal intensity on T1W images and appears hypovascular than the normal pancreas after paramagnetic contrast medium administration; sometimes exhibit delayed enhancement [49]. On dynamic images the PPI allows the greatest attenuation difference between cancer and normal pancreatic parenchyma; T2W images shows less tumor conspicuity, furthermore is useful to emphasize secondary signs as upstream pancreatic ductal dilatation.

In addition to morphological and multiphasic contrast-
enhanced imaging, functional informations on cellularity provided by DWI further improve MRI diagnostic accuracy [74,75]. Since malignant tumors are characterized by limited diffusion due to fibrosis and hypercellularity, DWI and apparent diffusion coefficient (ADC) values provide a high degree of contrast between PDA and normal pancreatic parenchyma: pancreatic tumours have increased signal intensity on diffusion weighted images with high b values (b > 500 s/mm²) and relatively low ADC values [49]. In addition, DWI may be helpful in the earlier detection of cancer and lymph nodes and/or liver metastases [49,76–78]. Instead, it is difficult to differentiate between mass-forming focal pancreatitis and poorly differentiated PDA [49].

Representative case of PDA evaluated by mpMRI is reported in Fig. 3.

Endoscopic US, specially used to perform biopsies, plays a key role in the detection and staging of small tumors (up to 0.2 cm) and clarify equivocal cases at CT or MRI showing an ill-defined, heterogeneous hypoechoic mass [1].

On 18FDG PET evaluation PDA generally shows intense focal FDG uptake due to enhanced glucose metabolism. 18FDG PET is potentially useful to detection small metastases that can be underestimate at MDCT and MRI.

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**Fig. 2.** 60-years-old male patient with unresectable pancreatic ductal adenocarcinoma with liver metastasis at initial 64-slice split-bolus CT protocol. Mixed phase (a) and delayed phase (b) show inhomogeneous lesion in the body of the pancreas. Note dilatation of the Wirsung in the pancreas up-stream to the tumor.

**Fig. 3.** 28-years-old male patient with pancreatic ductal adenocarcinoma with multiple liver metastasis at 3T mpMRI evaluation. Fat-suppressed T2-weighted images (a) shows a slightly inhomogeneous hyperintense lesion (arrow in a) in the body of the pancreas determining dilatation of the Wirsung in the pancreas up-stream to the tumor. MRCP (b) shows the interrupted duct sign (head arrow in b). At multiphase TIW breath-hold fat-suppressed 3D gradient-echo images after intravenous administration of gadolinium (Gd-DTPA) (c–f) the lesion appears inhomogeneous with maximum enhancement on delayed phase (f). On DWI with b = 1000 values (g) and ADC map (h) the tumor (arrow in g and h) show restriction of the diffusion of the water molecules.
5.2. Pancreatic neuroendocrine tumor

Pancreatic neuroendocrine tumors (NET) represent about 1%–5% of all pancreatic tumors and occur sporadically in patients in their third to sixth decades [79]. In some cases, association with multiple endocrine neoplasia type 1 (MEN1), neurofibromatosis type 1, von Hippel-Lindau syndrome and tuberous sclerosis can been observed.

The NET often shows a homogeneous or heterogeneous hyper-enhancing pattern at the early stage in CEUS, depending on the amount of the stroma within the lesion [80–82].

On AP or PPP of the conventional bi- or triphasic MDCT and in mixed (PPP/PVP) phase of split-bolus MDCT protocol, the NET appears hyperattenueted in comparison to adjacent pancreatic parenchyma. Small NET (<2 cm) shows typical homogeneous intense enhancement during the arterial phase whereas greatest lesions show heterogeneous enhancement, a finding due to areas of cystic degeneration, necrosis, fibrosis and calcification [1,83,84].

NET are usually more conspicuous on T1-weighted images; the presence of cystic component (necrosis or cystic degeneration) are typically hyperintense on T2 MRI. Malignant NET may show high signal intensity on DWI with high b values and low ADC values due to restriction by dense tumor cellularity; benign small NET can have a relatively high ADC values [49].

As previously reported pancreatic NET can be successfully evaluated by imaging with somatostatin analogues labeled by γ and β-emitting radiopharmaceuticals, while 18FDG can be used to evaluate more aggressive and less differentiated tumors.

Representative cases of functional and non-functional NET (US, split-bolus MDTC, mp-MRI) are reported in Figs. 4–6.

5.3. Solid pseudopapillary tumor

Solid pseudopapillary tumor (SPT), most commonly localized in the pancreatic tail and in young females, constitute approximately 1%–2% of all pancreatic neoplasms [85,86], with an excellent prognosis following complete resection. Rarely malignant degeneration can occur, just as in liver and peritoneum metastases [1,87].

On CT, SPT usually can be seen as a large well-encapsulated mass with cystic, solid or hemorrhagic components [1,82,88].
that displace surrounding structures without obstruction of the bile duct or pancreatic duct; peripheral calcification can be seen in 30% of cases [86]. The pseudocapsule (compressed pancreatic tissue and fibrosis) is an important feature to distinguish these neoplasms.

After contrast medium injection, the SPT shows peripheral slow early heterogeneous enhancement during arterial phase of solid component with central cystic spaces [85].

MRI demonstrates the small tumors, most frequently functioning tumors, as solid and homogeneous and larger tumors, most frequently nonfunctioning tumors, as heterogeneous mass with an heterogeneous signal intensity on T1- and T2W images. The degree of diffusion and ADC values are dependent to cystic or hemorrhagic fluid; solid component usually can show relatively low ADC values [49].

Most of the papers on 18FDC PET in pancreatic tumours concern PDA, but a recent interesting paper [89] retrospectively reviewed the records of 11 subjects with SPT and 46 patients with pancreatic ductal adenocarcinoma, showing high 18FDC uptake also in SPT and concluding that this rare tumour should be considered when a solid pancreatic mass with increased 18FDC uptake is revealed at PET/CT scan.

Fig. 6. 34-years-old male patient with incidental finding of non-functioning pancreatic neuroendocrine tumor (arrow). Mixed phase at 64-slice split-bolus CT protocol (a) shows a well defined lesion that exhibits intense enhancement which persists into the delayed phase (b) in the tail of the pancreas. US (c) shows a hypoechoic lesion and CEUS (d) demonstrates hyperenhancing pattern at the early phase. At 3T MRI evaluation on T2W images the NET appears as slightly inhomogeneous hyperintense lesion (e) that exhibits intense enhancement at arterial phase T1W breath-hold fat-suppressed 3D gradient-echo images after intravenous administration of gadolinium (Gd-DTPA) (f). On DWI with b = 1000 values (g) and ADC map (h) the tumor (arrow in g and h) shows restriction to water diffusion due to increased cellular density.
5.4. Pancreatoblastoma

Pancreatoblastoma, the most common pancreatic tumor in young children (mean 5 years), is rare in adults (<1% of all pancreatic tumors) [49,90]. Pancreatoblastoma is typically an asymptomatic, well-encapsulated and heterogeneous large mass; it coexists with an increase of serum alpha-fetoprotein level in 25-33% of cases [1]. Metastases are rare.

This tumor is heterogeneous with hypoechoic cystic spaces and hyperechoic internal septa at US evaluation [91].

On MRI pancreatoblastoma shows intermediate signal intensity at T1-and T2-weighted with small hyperintense areas in T2. The solid component exhibits rapid enhancement during arterial phase and wash-out in delayed phase after contrast medium administration and restricted diffusion due to dense cellularity on DWI [85].

5.5. Pancreatic lymphoma

Primary pancreatic lymphoma, most frequent in immunocompromised patients, constitutes 0.5% of pancreatic tumors and is most commonly a B-cell subtype of non-Hodgkin lymphoma [1,92]. More common is a secondary lymphoma as result of direct extension from peripancreatic lymphadenopathy. Clinical presentation
of primary pancreatic lymphoma is nonspecific; the most common findings were abdominal pain and weight loss.

Pancreatic lymphoma occurs in a focal well-circumscribed form (uniform low attenuation and minimal enhancement at CT; hypointensity on T1W images and intermediate signal intensity on T2W images and slight contrast enhancement at MRI) and a diffuse pattern (diffuse enlargement and hypointensity on T1-and T2 w images and moderate homogeneous enhancement at MRI) that can simulate the appearance of acute pancreatitis [1,93]. Imaging findings can show encasement of peripancreatic vessels [94].

Imaging findings are not specific in the differentiation of pancreatic lymphoma and pancreatic cancer, but a bulky homogeneous tumoral mass without alteration of Wirsung’s duct should suggest the diagnosis [95].

6. Cystic lesions

Cystic lesions represents 10–15% of all pancreatic tumors. An important distinction among neoplastic cysts is the categorization into four subtypes unilocular, macrocystic: multilocular, microcystic and cystic with a solid component and in mucinous versus nonmucinous. The first aim of imaging is to characterize cystic neoplasms, to confirm or to exclude a communication between the cystic lesion and the pancreatic duct and to distinguish these from pseudocysts (encapsulated fluid collections without necrosis after 4 week from onset of acute pancreatitis) [96].

When small (<3 cm) cysts are represented by unilocular lesions, well defined and without internal septa, calcification or internal soft-tissues nodules, it is suggested a close surveillance with serial
imaging at 6-months intervals for the first year and annual follow-up for next three years.

Usually imaging shows a cystic mass with a thick wall that exhibits mild enhancement after intravenous contrast injection.

6.1. Serous cystadenoma

Serous cystadenomas are benign cystic tumors (20% of all pancreatic cystic neoplasms), typically diagnosed incidentally in asymptomatic patients, most frequently in older women, which do not require surgical excision. The lesion appears as a cystic mass with a thick wall that exhibits mild enhancement after intravenous contrast injection.

Fig. 10. 36-years-old female patient with main-duct intraductal papillary mucinous neoplasm. Axial (a) and coronal multiplanar reconstruction (b) mixed phase at 64-slice split-bolus CT protocol shows a significant cystic dilatation of the main pancreatic duct with linear parietal calcifications without mural nodules and/or areas of pathological enhancement. On 1.5T MRI the lesion appears homogeneously hyperintense on the axial (c) and coronal (d) T2W images, and site of communication with the Wirsung is recognizable on the MRCP sequences (arrow in e). At multiphase TIW breath-hold fat-suppressed 3D gradient-echo images after intravenous administration of gadolinium (Gd-DTPA) (f–h) the lesion doesn't exhibit enhancement neither restriction of diffusion on DWI with high b values (i) and ADC sequences (l).

Serous cystadenomas are benign cystic tumors (20% of all pancreatic cystic neoplasms), typically diagnosed incidentally in asymptomatic patients, most frequently in older women, which do not require surgical excision. The lesion appears as a cluster of cysts well-defined (without visible communication with pancreatic duct) with a high signal intensity on MRI T2W images (Figs. 7–8), with a thin fibrous septa that can show delayed enhancement after contrast medium administration. Two subtypes of lesions are known: microcystic serous cystadenomas, composed of multiple

Fig. 11. 75-years-old female patient with metastatic small cell lung cancer at 64-slice Split-bolus CT protocol during follow-up. Mixed phase shows the primitive inhomogeneous mass at the right upper lobe of the lung (a) and a heterogeneous metastasis in the liver and in the tail of the pancreas (b).
cysts (each < 2 cm), separated by fibrous septa originated from a central calcified scar, and macrocystic serous cystadenomas, uncommon, composed of large cysts (1–8 cm). A central calcified scar is highly specific and best demonstrated at CT [49]. When associated with von Hippel–Lindau (VHL) disease, multifocal cystic lesions can involve the pancreatic gland diffusely [96]. The features in DWI and ADC are depending on the amount of fibrous septa or fluid in the lesion; occasionally serous cystadenomas with fibrous septa can show relatively higher signal intensity on DWI and lower ADC values compared with non-neoplastic cysts. On the bases of DWI the differential diagnosis between these lesions and non-neoplastic cysts is difficult [49].

6.2. Mucinous cystic neoplasm (mucinous cystadenoma/cystadenocarcinoma)

Mucinous cystic neoplasm (10% of all pancreatic cystic neoplasms), are most frequently diagnosed in women (80%) in their sixth decade of life [89,97] and are preferentially localized in body and pancreatic tail without communication with pancreatic duct [unlike intraductal papillary mucinous neoplasms (IPMNs)].

The lesion appears as a multicocular or unicocular or mildly septated cysts well-defined, usually >2 cm (Fig. 9). In relation to the degree of hemorrhage or the amount of protein in the mucoid cysts, CT shows different levels of attenuation [96] and the lesion may be hyperintense on T1W images.

Imaging is unable to distinguish cystadenoma from cystadenocarcinoma, furthermore intracystic enhancing soft tissues, invasion of adjacent organs and vascular invasion are suspicious for malignancy, as metastatic disease too. The rare (16%) presence of peripheral eggshell calcifications has a highly predictive value for malignancy. DWI will not distinguish between mucinous cystic neoplasm and non-neoplastic mucinous cystic neoplasm due to the relatively high ADC values [49].

6.3. Intraductal papillary mucinous tumor of the pancreas

IPMNs of the pancreas represent 20% of cystic pancreatic lesions and occur more frequently in elderly men [86,94]. The histopathologic characteristics of IPMNs are papillary growth and hyperproduction of mucina which causes dilatation of the main pancreatic duct, its branches or both [49,50,97,98]. The characteristic imaging feature of IPMNs is the communication of lesion with pancreatic ducts, demonstrate on MRI [49], useful to differentiate them from mucinous cystadenoma (Fig. 10).

IPMNs may frequently be multifocal and may have benign or
malignant behavior on the basis of the degree of dysplasia; when it affects the main duct, the lesion is more likely to be malignant. The features suggestive of invasive carcinoma are the large size of the mass (>3 cm), presence of mural nodules, dilatation of the main pancreatic duct > 1 cm and multifocal involvement [50].

DWI does not allow a differential diagnosis because IPMNs usually show an high ADC value even in cases of carcinomas in situ [49].

7. Metastases

Pancreatic metastases occur in 2–5% of all malignant neoplasms and originate most frequently from renal cell carcinoma, lung carcinoma, breast carcinoma, colorectal carcinoma, ovarian carcinoma and melanoma [99]. Imaging features are non-specific: metastases can be solid or cystic, hypo- or hypervascular depending on primary tumor and can be solitary (50–70%), multifocal or diffuse [1,99–102] (Figs. 11–12).

8. Imaging after surgery

The knowledge of the type of surgical procedures (Whipple procedure, distal pancreatectomy, central pancreatectomy or total pancreatectomy) and the normal post-operative appearances are essential for an accurate evaluation of the complications and recurrent disease.

Several imaging techniques can be used after pancreatic surgery. US plays a limited role in the early post-operative period useful only for the peritoneal fluid detection.

In the immediate post-operative period the most common findings are fluid peritoneal or peri-pancreatic collections, increased density of the mesenteric fat tissue, reactive adenopathy and pneumobilia; early and late surgical complications as anastomosis leakage, pancreatico-jejunal fistula, peritonitis, abscess, aneurysms, anastomoticstenosis, perianastomotic ulcers, biloma and intra-abdominal bleeding, are better detected on CT imaging.

CT represents the first choice for the evaluation of tumor recurrence and for the assessment of lymph nodes and liver metastasis [102].

MRI may be used as alternative imaging modality to CT or in cases of inconclusive CT findings; furthermore, MRI combined with functional DWI potentially provides helpful information about locally recurrent disease.

Also 18FDG PET is useful to detect recurrent disease after surgery, but PET scan has to be performed for some months after surgical treatment to avoid unspecific uptake of the radio-compound due to inflammatory reaction after therapy (Fig. 13).

9. Conclusion

Imaging play an essential role in the assessment of neoplastic and non-neoplastic diseases [103–106]. In order to a prompt and accurate diagnosis and appropriate management of pancreatic lesions, it is crucial for radiologists to know the key findings of the most frequent tumors of the pancreas and the current role of imaging modalities.

A multimodality approach is often helpful. If MDCT is the preferred initial imaging modality in patients with clinical suspicion for pancreatic cancer, mpMRI provides essential information for the detection and characterization of a wide variety of pancreatic lesions and can be used as a problem-solving tool for diagnosis and during follow-up.

Ethical approval

Ethical approval was requested and obtained from the “Second University of Naples ethical committee”.

Conflicts of interest

All Authors have no conflict of interests.

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Author contribution

Michele Scialpi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

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Alfredo D’Andrea: Participated substantially in execution of the study and in the analysis and interpretation of data.

Sabrina Gravante: Participated substantially in the drafting and editing of the manuscript.

Giuseppe Falcone: Participated substantially in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

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Lucia Manganaro: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

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