Pancreatic Adenocarcinoma

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6.1 Overview

6.1.1 Epidemiology

The American Cancer Society estimates that about 48,960 new cases of pancreatic cancer (24,840 in men and 24,120 in women) will be diagnosed in the USA in 2015 [1]. The overall incidence of pancreatic cancer has been relatively stable for decades.

Although pancreatic cancer constitutes only about 3% of all cancers in the USA, it accounts for about 7% of all cancer-related deaths, being the fourth leading cause of cancer deaths in both men and women [2].

6.1.2 Risk Factors

Estimates indicate that 40% of pancreatic cancer cases are sporadic in nature, up to 30% are related to smoking, and 20% may be associated with dietary factors. Only 5–10% are hereditary in nature [3].

Diabetes mellitus increases the risk for pancreatic adenocarcinoma. The National Comprehensive Cancer Network (NCCN) guideline for pancreatic adenocarcinoma (2.2011 version) acknowledges long-standing diabetes mellitus as a risk factor for pancreatic cancer.

Another important risk factor is chronic pancreatitis: the risk increases linearly with time, with 4% of patients who had chronic pancreatitis for 20 years duration developing pancreatic cancer.

The risk is even higher in patients with hereditary pancreatitis (increased more than 50-fold).

6.1.3 Pathology

Ductal adenocarcinoma arises from, and is phenotypically similar to, pancreatic duct epithelium, with mucin production and expression of a characteristic cytokeratin pattern.

Most ductal adenocarcinomas are well to moderately differentiated. They usually consist of well-developed glandular structures, which more or less imitate normal pancreatic ducts, embedded in a fibrous desmoplastic stroma.

It is the most common tumor in the pancreas, accounting for 85–90% of all pancreatic neoplasms. The majority (approximately 75%) arise in the head of the pancreas, mainly in the upper half, less commonly in the uncinate process, 15–20% in the body, and 5–10% in the pancreatic tail.

Ductal adenocarcinomas are firm and poorly defined masses. Hemorrhage and necrosis are uncommon, while microcystic areas may be present.

The pancreas is anatomically divided into three main parts: head, body, and tail. The head of the pancreas includes the neck (anterior to the superior mesenteric vein and the portal vein) and the uncinate process. The boundary between the head and body of the pancreas is the left margin of the superior mesenteric and portal vein. Body and tail of the pancreas are collectively referred to as distal pancreas; the boundary between body and tail is the line dividing the distal pancreas into two equal halves.

Given the different characteristics of lymphvascular and neural stream and the distinctive relationship with the contiguous organs, tumors originating from each portion of the pancreas display a peculiar behavior in terms of local invasion.

The identification of such specific patterns of tumor spread in relation to the site of origin within the gland is of paramount importance in guiding surgical decision-making as regards both the assessment of resectability and the definition of the optimal extension of the resection.

6.1.4 Staging

The evaluation of the extent of local invasion is fundamental for tumor staging, in order to identify patients who are eligible for resection with curative intent. The preferred staging system for pancreatic cancers is the tumor-node-metastasis (TNM) system of the combined American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC). In this classification, the characteristics of local aggressiveness are taken into account both in the evaluation of the T and N parameters (Tables 6.1 and 6.2).

6.1.5 Treatment

Treatment of pancreatic cancer depends on the stage of the disease, dividing patients with resectable, locally advanced (unresectable) or metastatic disease.

Table 6.1 TNM staging for pancreatic carcinoma

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to the pancreas, ≤2 cm in greatest dimension
T2	Tumor limited to the pancreas, >2 cm in greatest dimension
T3	Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
T4	Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

Table 6.2 Stage grouping for pancreatic cancer

Stage	
0	Tis, N0, M0
IA	T1, N0, M0
IB	T2, N0, M0
IIA	T3, N0, M0
IIB	T1-3, N1, M0
III	T4, Any N, M0
IV	Any T, Any N, M1

Patients with resectable cancer should undergo upfront surgery; depending on tumor location, this can be pancreaticoduodenectomy, distal pancreatectomy, or total pancreatectomy.

Chemotherapy may be used in neoadjuvant regimens, for adjuvant postoperative therapy, or as a single treatment in metastatic patients.

Medical treatment of metastatic pancreatic cancer is based on both FOLFIRINOX [4] and administration of gemcitabine and nabpaclitaxel [5].

Performance status, assessment of comorbidities, and presence of biliary stents are the main criteria for the choice of treatment.

6.1.6 Prognosis

Overall 5-year survival rate is 7.2%, ranging from 27.1% for localized disease to 2.4% for metastatic disease (Tables 6.3 and 6.4).

Table 6.3 5-Year observed survival rate (%)

Stage	5-Year observed survival rate (%)
IA	14
IB	12
IIA	7
IIB	5
III	3
IV	1

Table 6.4 5-Year relative survival (%) for 2005–2011 (SEER Cancer Statistic Review)

Stage at diagnosis	Both sexes	Males	Females
All stages	7.2	7.0	7.3
Localized	27.1	27.0	27.0
Regional	10.7	11.1	10.3
Distant	2.4	2.4	2.5
Unstaged	4.4	5.0	4.0

6.2 Patterns of Local Spread

6.2.1 Introduction

Besides its well-known metastatic aptitude, pancreatic ductal adenocarcinoma (PDAC) is characterized by a striking tendency for loco-regional dissemination. Local extension of the tumor is determined by multiple factors, reflecting both the peculiar biology of the cancer cells and the complexity of the anatomical location of the pancreas. The dense network of nerves, blood vessels, and lymphatic vessels surrounding the gland constitutes the optimal basis for tumor's local infiltration and involvement of adjacent organs that often occurs.

When the tumor is located mainly in the head of the pancreas, vascular invasion often occurs in the portal/superior mesenteric axis (Fig. 6.1a). Conversely, when the tumor is located in the body and tail of the pancreas, it generally infiltrates the celiac trunk and/or the splenic vessels [6] (Fig. 6.1b).

Occasionally, local invasion may also involve the inferior vena cava (especially for tumors arising in the pancreatic head) or, rarely, the aorta (tumors of the pancreatic head or body). The degree of vascular involvement is a fundamental parameter in cancer staging, and vascular invasion is the main determinant of local resectability [7].

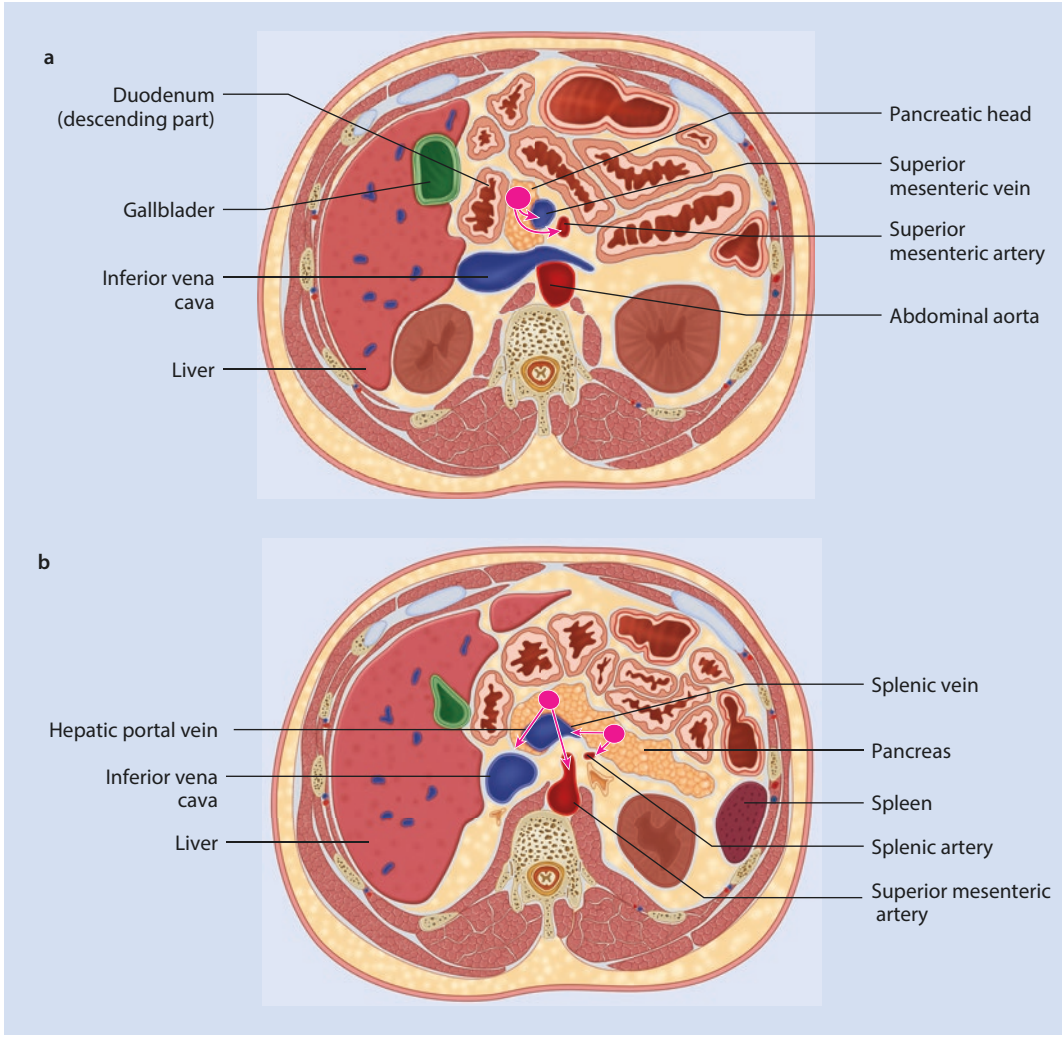

Fig. 6.1 Anatomy and spread patterns to the vessels for tumors in the pancreatic head **a** and body/tail **b**

6.3 Vessel Infiltration and Resectability

Given the absence of distant metastases, a tumor is considered resectable when clear fat planes can be identified around the celiac axis, hepatic artery, and superior mesenteric artery, and there is no radiologic evidence of superior mesenteric vein or portal vein distortion (Fig. 6.2).

The term "borderline resectable pancreatic cancer" (BRPC) is commonly used to describe tumors involving the porto-mesenteric or arterial axis, that is, an intermediate stage between straightforwardly resectable and technically unresectable disease.

The concept of borderline resectable itself is continuously evolving, in relation with the improvement of operative techniques and the deepening of the knowledge on the impact of vascular resections in terms of morbidity, mortality, and long-term survival.

As such, in the latest version of the NCCN guidelines (2015.2) the definition of BRPC has been reformulated (Table 6.5) and slight differences from the ISGPS consensus statement [8] have been introduced.

The definition of unresectability is related to the location of the primary tumor (Table 6.6).

For all tumor sites, tumors are considered unresectable if there are distant metastases, or LN metastases beyond the field of resection.

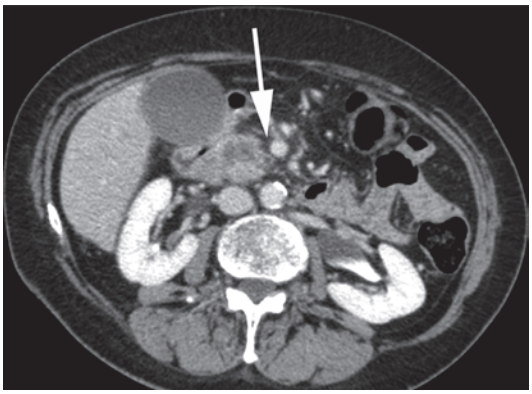

Fig. 6.2 Resectable tumor, a fat plane is seen between the tumor and the mesenteric vessels (*arrow*)

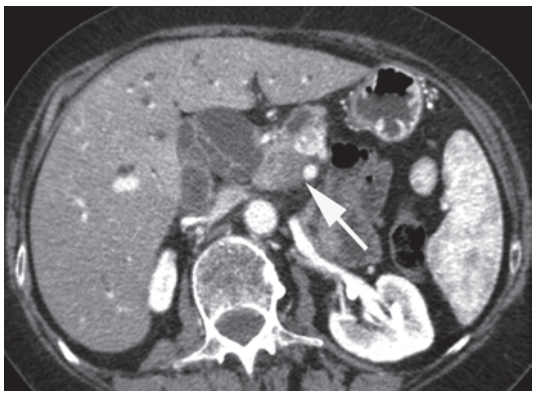

Fig. 6.3 180° encasement of the SMA (*arrow*)—borderline resectable pancreatic cancer (BRPC)

Table 6.5 2015 NCCN guidelines, definition of BRPC tumors

Tumors in the head/uncinate process	Contact with the common hepatic artery without extension to celiac axis or hepatic artery bifurcation, allowing for safe and complete resection/reconstruction
	Tumor contact with the SMA ≤180° (Fig. 6.3)
	Presence of variant anatomy, and the presence/degree of tumor contact should be noted because it may affect surgical planning
Distal tumors	Contact with celiac axis of ≤180°
	Contact with celiac axis of >180° without involvement of the aorta and with intact and uninvolved gastroduodenal artery
All locations	Contact with SMV or PV of >180°, contact of ≤180° with contour irregularity or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement, allowing for safe and complete resection/reconstruction (Fig. 6.4)
	Contact with the inferior vena cava

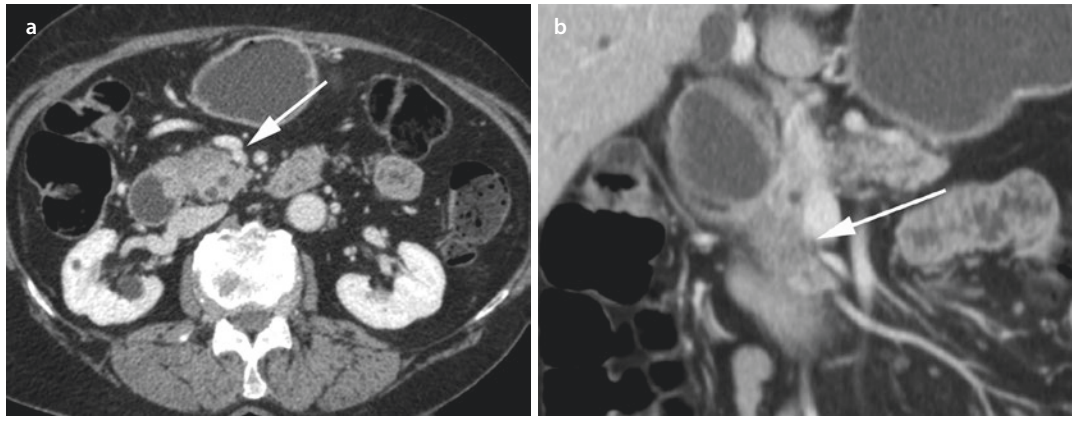

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Fig. 6.4 Axial **a** and coronal **b** CT images show a short contact between tumor and SMV (*arrow* in **a** and **b**), therefore defining a BRPC

Table 6.6 Definition of unresectability

Tumor site	Criteria for unresectability
Head of pancreas	>180° superior mesenteric artery encasement, any celiac abutment (Fig. 6.5)
	Non-reconstructable superior mesenteric/portal vein occlusion (Figs. 6.6, 6.7, and 6.8)
	Aortic or inferior vena cava invasion or encasement
Body of pancreas	Superior mesenteric artery or celiac encasement >180° (Fig. 6.9)
	Non-reconstructable superior mesenteric/portal vein occlusion
	Aortic invasion or encasement
Tail of pancreas	Superior mesenteric artery or celiac encasement >180°
For all sites	Distant metastases (Figs. 6.10 and 6.11)
	Metastases to lymph nodes beyond the field of resection

Tumors in the head of the pancreas are considered straightforwardly unresectable if the superior mesenteric artery is encased for more than 180°, if there is any abutment of the celiac axis, if there is invasion of the aorta or the inferior vena cava, or if there is a non-reconstructable occlusion of the superior mesenteric vein or the portal vein.

Tumors in the body of the pancreas are considered unresectable if there is encasement for more than 180° of the celiac axis or the superior mesenteric vein, invasion or encasement of the aorta, or a non-reconstructable occlusion of the superior mesenteric vein or the portal vein.

Tumors in the tail of the pancreas are unresectable when they encase for >180° the celiac axis or the superior mesenteric artery.

6.3.1 Splenic Vessels Infiltration

Splenic vessels constitute a relatively frequent site of local invasion by tumors arising in the distal pancreas: the rate of splenic artery and vein invasion in resected PDAC is reported around 20–30% and 50%, respectively [6, 9].

Surgical resection is commonly performed if infiltration of both the splenic vein and artery (T3 category) is present.

Retrospective studies on patients undergoing distal pancreatectomy [6, 9] have demonstrated that splenic artery infiltration is an independent predictor of survival, while splenic vein invasion is not. This might be explained based on anatomic considerations: the splenic artery courses a few millimeters outside the pancreas, whereas the splenic vein runs within the gland (Fig. 6.12). Arterial invasion could therefore represent an indicator of extrapancreatic tumor spread. In addition, given that pancreatic cancer is known to metastasize via the axonal flow, the dense network of nerves that surrounds the splenic artery could facilitate tumor progression upstream to the celiac plexus, leading to adverse prognosis.

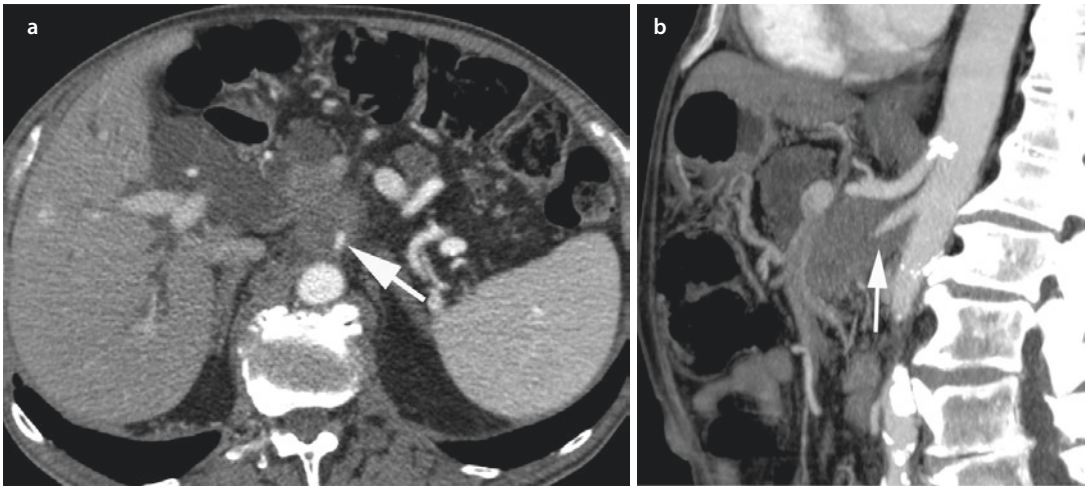

Fig. 6.5 Axial **a** and sagittal **b** CT images show encasement of the SMA (*arrow* in **a** and **b**) and involvement of the retroperitoneal fat, defining this tumor as unresectable

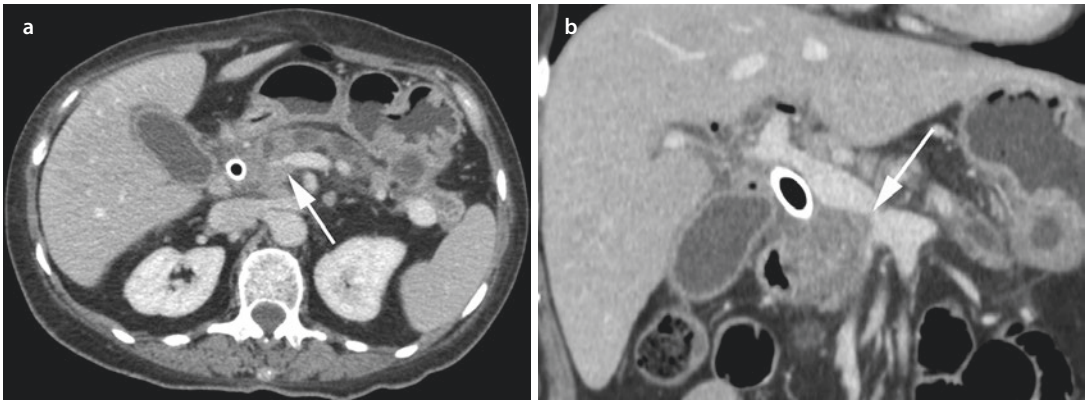

Fig. 6.6 Axial **a** and coronal **b** CT images show a non-reconstructable infiltration of the porto-mesenteric confluence (*arrow* in **a** and **b**)

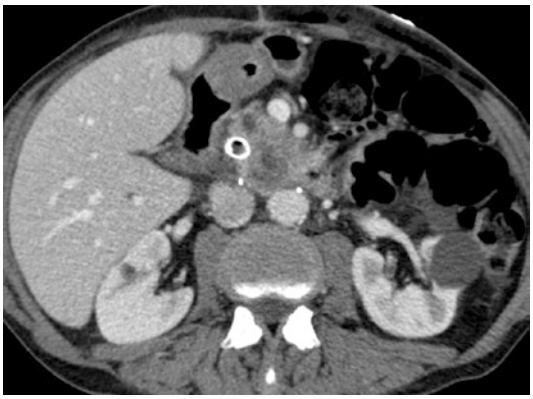

Fig. 6.7 Invasion of the SMA, SMV, and retroperitoneal fat

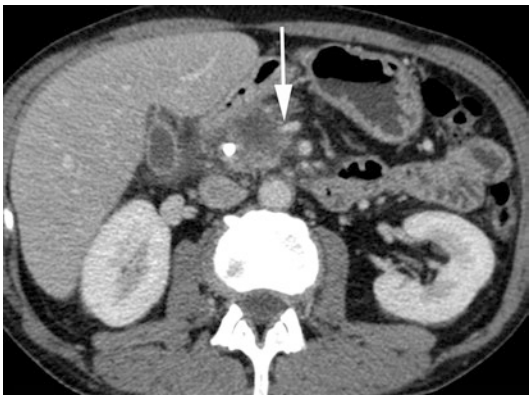

Fig. 6.8 Teardrop mesenteric vein (*arrow*), sign of infiltration of the SMV

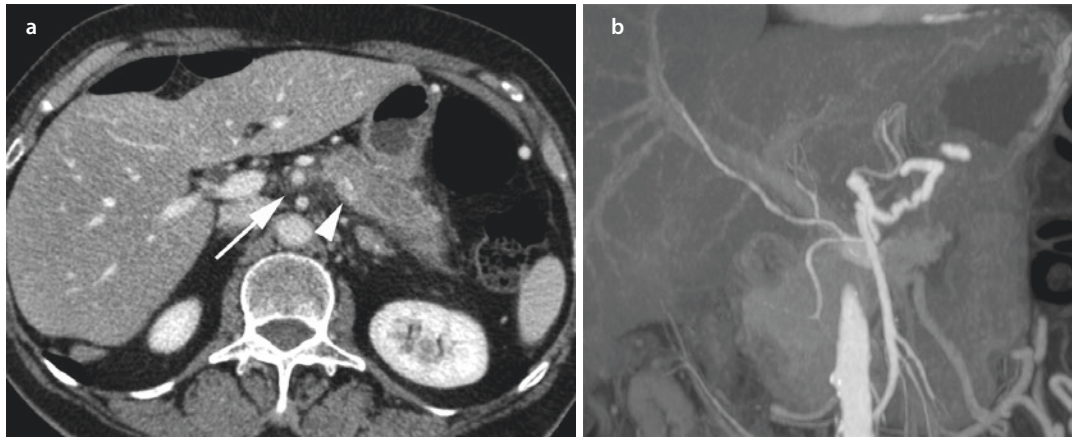

Fig. 6.9 Axial **a** and coronal MIP **b** CT images show infiltration of the splenic vessels (*arrowhead* in **a**) and encasement of the celiac axis >180° (*arrow* in **a**), which makes this tumor unresectable

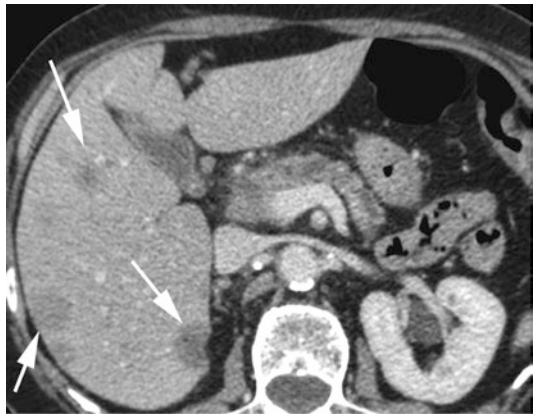

Fig. 6.10 Liver metastases (*arrows*)

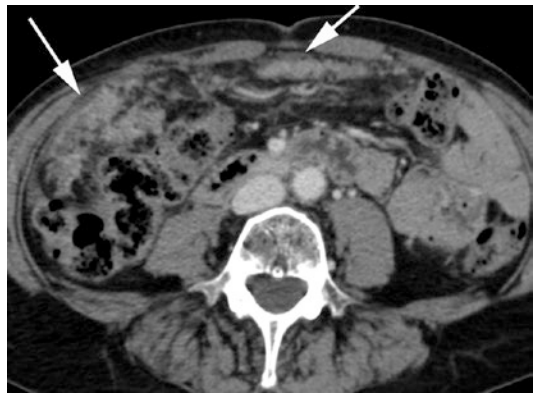

Fig. 6.11 Peritoneal metastases (*arrows*)

It should be therefore noted that—even if a radical resection can be achieved safely from a surgical standpoint—splenic artery involvement

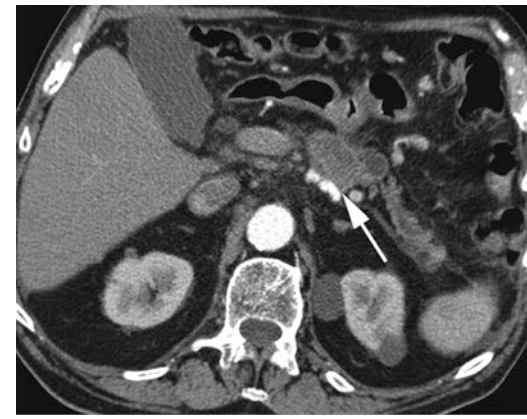

Fig. 6.12 Infiltration of the splenic artery—the tumor is technically resectable; note how the tumor extends dorsally outside the pancreas to reach the artery (*arrow*)

implies more aggressive tumor biology affecting patient prognosis.

6.4 Involvement of Adjacent Organs

Adjacent organs can be involved by direct tumor invasion. The pattern of local extension depends on the site of origin of the tumor.

- Head of pancreas
  Invasion of adjacent structures such as the duodenum and the biliary tract constitutes a relatively frequent finding on pancreaticoduodenectomy specimens. Occasionally, tumors originating in the pancreatic head

may also involve: colon (right or transverse), transverse mesocolon, small bowel, right kidney and adrenal gland, liver, gallbladder, and diaphragmatic crura.

- Distal pancreas
  Tumors arising in the body or tail of the pancreas can involve the spleen, stomach, colon (transverse or left), transverse mesocolon, small bowel, left kidney and adrenal gland, ligament of Treitz, spine, liver, diaphragmatic crura, and diaphragm.

The ISGPS has provided detailed descriptions of the organs resected during standard pancreaticoduodenectomy and distal pancreatectomy [10]. Every additional resection is considered an extended procedure.

Standard pancreaticoduodenectomy:

- Head of the pancreas and uncinate process
- Duodenum and first segment of jejunum
- Common bile duct and gallbladder
- Lymphadenectomy
- Sometimes pylorus and/or antrum of stomach
- Sometimes elements of the transverse mesocolon exclusive of relevant vasculature (e.g., limited soft tissue contiguous to the tumor but not including the colon itself)

Standard distal pancreatectomy:

- Body and/or tail of the pancreas
- Spleen, including splenic vessels
- Lymphadenectomy
- Sometimes fascia of Gerota
- Sometimes elements of the transverse mesocolon exclusive of relevant vasculature (e.g., limited soft tissue contiguous to the tumor but not including the colon itself)

In the absence of distant metastases, the involvement of adjacent organs does not constitute per se a criterion for non-resectability as far as an extended free-margin tumor resection can be safely performed.

6.5 Lymph Node Involvement

Lymph node metastases have been reported in 60–90% of patients with resected PDAC [11] and lymph node staging is considered one of the strongest prognostic factors after the resection [12].

The precise identification of the specific sequence of lymph node invasion and its correlation with patient survival would be of great value in clinical practice, potentially allowing a better selection of patients undergoing upfront surgery rather than neoadjuvant therapy, and affecting the definition of the optimal extension of lymphadenectomy during resection. The detailed pattern of lymph nodal spread is however difficult to outline, due to the complexity of the anatomical connections between the different lymphatic routes. In addition to this, we must consider the current limitations of even state-of-the-art imaging in the detection of LN metastases. Size-based criteria have been shown to be inadequate for the detection of LN metastases.

Lymph nodes within the pancreatic draining nodal basin are classified into different stations according to the nomenclature proposed by the Japanese Pancreas Society [13]. This nomenclature has reached international acceptance and its use has been also recommended by the latest Consensus Statement of the International Study Group on Pancreatic Surgery [14].

6.5.1 Anatomical Aspects: Tumors of the Pancreatic Head

According to the reports and on the basis of the previous findings of radioisotope and dye injection studies in normal pancreas samples [15–18], two main routes of lymphatic drainage from the pancreatic head were identified (Fig. 6.13):

- The superior part of the head appears to drain to lymph nodes around the celiac axis via the lymph nodes that surround the common hepatic artery.
- The remainder of the head is postulated to drain to lymph nodes around the superior mesenteric artery up to para-aortic lymph nodes.

A more recent study, however, has shown that pancreatic cancer can frequently spread to distant LNs via multiple lymphatic drainage basins without a dominant sentinel location [19].

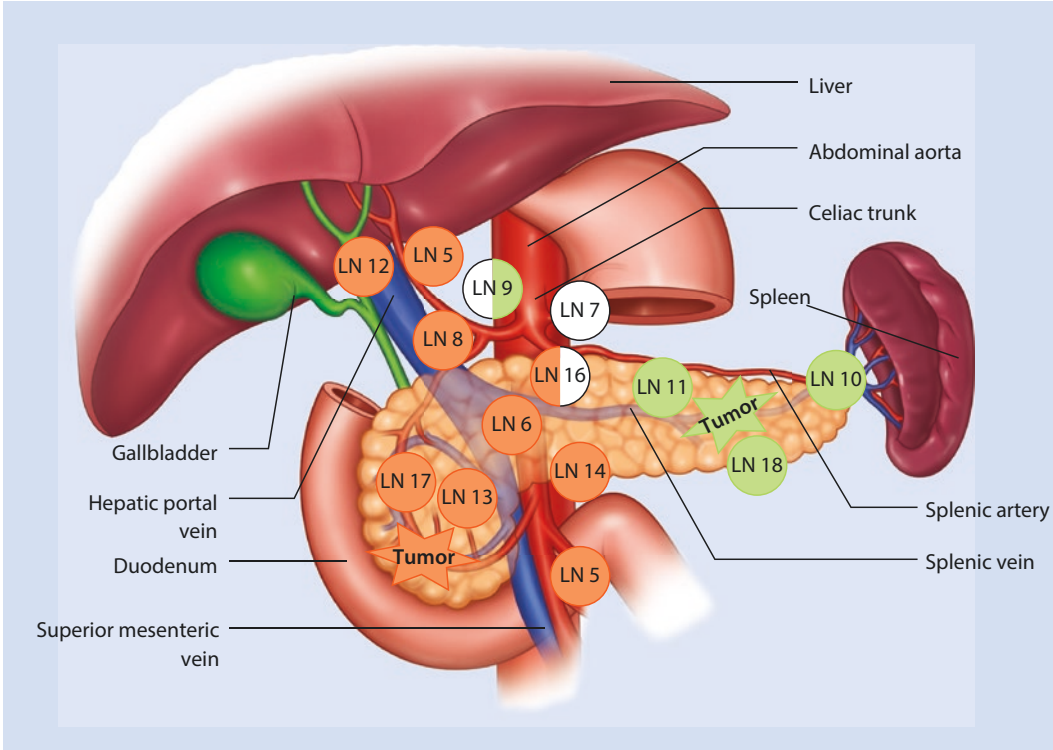

Fig. 6.13 Distribution of lymphatic metastases to lymph node stations from tumors in the pancreatic head (*orange*) and tail (*green*). *LN* Lymph Node Station

6.5.2 The Uncinate Process: A Ventral Enclave in the Dorsal Pancreas

During embryological development, the pancreas arises from the fusion of two independent primordia: the smaller ventral bud forms the caudal part of the pancreatic head and uncinate process, whereas the cephalic part of the pancreatic head, as well as the body and tail, are derived from the larger dorsal bud.

Pancreaticoduodenectomy is generally performed in a similar manner irrespective of the origin of the embryological segment. However, on the basis of their different embryological origins, pancreatic cancers arising in the head and in the uncinate process may actually display peculiar tendencies in local spreading. This fascinating field and its surgical implications have been explored by Japanese authors.

Kitagawa et al. [20] noticed that the lymphatic spread pattern of head PDAC could be attributed to tumor location and speculated that this phenomenon was correlated with the embryological structure of pancreas. The authors showed an exclusive pattern of lymph nodal metastases that was limited to station 8 (along the hepatic artery) and 12 (hepatoduodenal ligament) for tumors almost entirely confined to the dorsal pancreas, and to station 14 (superior mesenteric artery) for tumors almost entirely confined to the ventral pancreas (uncinate process). However, in the case of cancers extending into both domains the lymph node metastases were distributed widely in areas along the superior mesenteric artery, common hepatic artery, and the hepatoduodenal ligament. These results indicate that lymphatic spread of the embryological ventral and dorsal domains of pancreas head carcinomas may be independent of each other even after the fusion of these domains. On this basis, the authors concluded that in order to achieve radical resection during pancreaticoduodenectomy the specific site of lymph node dissection should be guided by the tumor location.

These results were not completely confirmed by the more recent study by Okamura [21], which showed somewhat various and not exclusive lymph nodal metastasis patterns like those of Kitagawa,

but confirmed some differences in loco-regional dissemination for pancreatic head tumors arising from the two different primordia. The authors indeed highlighted a significantly higher rate of lymph vessel invasion and of LN station 15 (lymph nodes along the middle colic artery) involvement for tumors arising in the dorsal pancreas, whereas the rate of perineural invasion tended to be higher in tumors arising from the ventral bud.

Comparable findings were reported for patterns of perineural invasion according to the site of origin of the tumor [22], reinforcing the idea that the spread pattern of pancreatic ductal adenocarcinoma of the head and of the uncinate process may differ on the basis of their different embryological development.

Anyway there is currently no evidence supporting the application of different surgical procedures during pancreaticoduodenectomy for tumors arising from the dorsal and ventral pancreas, and further studies are needed to clarify the field.

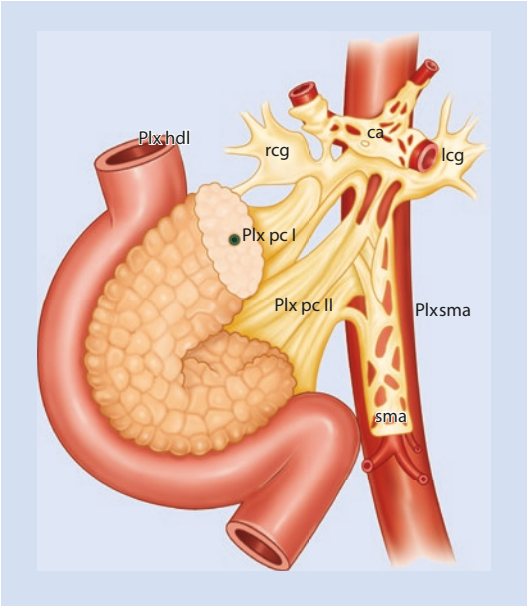

Fig. 6.14 Extrapancreatic nerve plexus

6.5.3 Anatomical Aspects: Tumors of the Distal Pancreas

Based on the anatomical study by Deki and Sato [23], two major lymphatic routes were initially identified in the left half of the pancreas: one follows the splenic blood vessels and the other accompanies the inferior pancreatic artery. By way of these routes, lymphatics from the left half of the pancreas flow into the nodes situated on the left side of the origins of the celiac trunk and superior mesenteric artery (Fig. 6.13).

Early studies [24] suggested a high metastatic rate in lymph nodes along the splenic artery (50%) and the inferior body (35%), around the common hepatic artery (25%) and the para-aortic lymph nodes (20%).

Subsequent studies [25] described quite a different pattern of nodal involvement by distal cancers, with a high metastatic incidence along the splenic artery, superior mesenteric artery, aorta and celiac trunk, and a relatively low incidence on the inferior pancreatic body and around the common hepatic artery.

The important role of stations 11 (splenic artery) and 14 (superior mesenteric artery) as metastatic sites was further confirmed by subsequent studies [26, 27] but a clear route of lymph nodal spreading could not be identified.

Indeed, as pointed out by Fernandez Cruz [28] lymphatic spread of tumors arising in the distal pancreas seems to be less continuous and somewhat "scattered" in comparison with head tumors: through the splenic artery route, these cancers appear to disseminate widely to the retroperitoneum, the para-aortic region, and to other peripancreatic lymph nodes (Fig. 6.14).

6.5.4 Surgical Implications

Despite the recognized prognostic importance of LN variables, the optimal extent of lymphadenectomy during pancreatic resection with radical intent for PDAC is still debated [12].

The performance of extended lymphadenectomy during pancreaticoduodenectomy has not been recommended in clinical practice [14]. However, the interpretation of the current evidence is somewhat hampered by the lack of a common definition of standard lymphadenectomy, preventing comparison of different studies.

As concerns tumors arising in the distal pancreas, studies on lymphadenectomy during left-sided pancreatectomy are scarce. On the basis of the Japanese histopathological studies on the distribution of metastatic lymph nodes, extended lymphadenectomy (including the para-aortic,

celiac, and superior mesenteric lymph nodes) has been proposed in order to improve patient prognosis. However, no study could provide evidence on a survival benefit related to such extended lymphadenectomy and the optimal extension of lymph nodal retrieval remains unclear.

6.6 Extrapancreatic Nerve Plexus Invasion

Pancreatic ductal adenocarcinoma shows a striking tendency for perineural invasion both within and beyond the pancreas. Perineural invasion and extrapancreatic nerve plexus infiltration are recognized as significant prognostic factors in pancreatic carcinoma [22, 29]. However, because of the complexity of the anatomical structures around the pancreas, the patterns of spread of carcinoma through the neural stream are difficult to define in details.

Extrapancreatic nerve plexus have been first categorized by Japanese investigators in the 1950s [30]. This classification has been further refined and finally endorsed by the Japanese Pancreas Society, which identifies (Fig. 6.14):

- PL Ph I: Pancreatic head plexus I originates from the right celiac ganglia and enters the superior medial margin of the uncinate process.
- PL Ph II: Pancreatic head plexus II originates from the superior mesenteric plexus and runs as a wide band along the entire length of the medial margin of the uncinate process.
- PL sma: Superior mesenteric arterial plexus.
- PL hdl: Plexus within the hepatoduodenal ligament.
- PL ce: Celiac plexus.
- PL cha: Common hepatic artery plexus.
- PL sp: Splenic plexus.

Head tumors display a more complex spreading pattern, depending on the specific location of the tumor within the pancreatic head. In particular, two main patterns of neural invasion by head PDAC have been identified, in close relationship with the embryological development of the pancreas.

Pathological studies [22] on pancreaticoduodenectomy specimens showed a significant correlation between the tumor location considering the two pancreatic primordia and the site of extrapancreatic nerve plexus infiltration (Fig. 6.15):

- Cancers almost entirely confined to the ventral pancreas extended through the pancreatic head nerve plexus (PL ph1 and PL ph2) to the superior mesenteric nerve plexus (PL sma) (Fig. 6.16).
- Tumors almost entirely confined to the dorsal pancreas tended to involve the neural

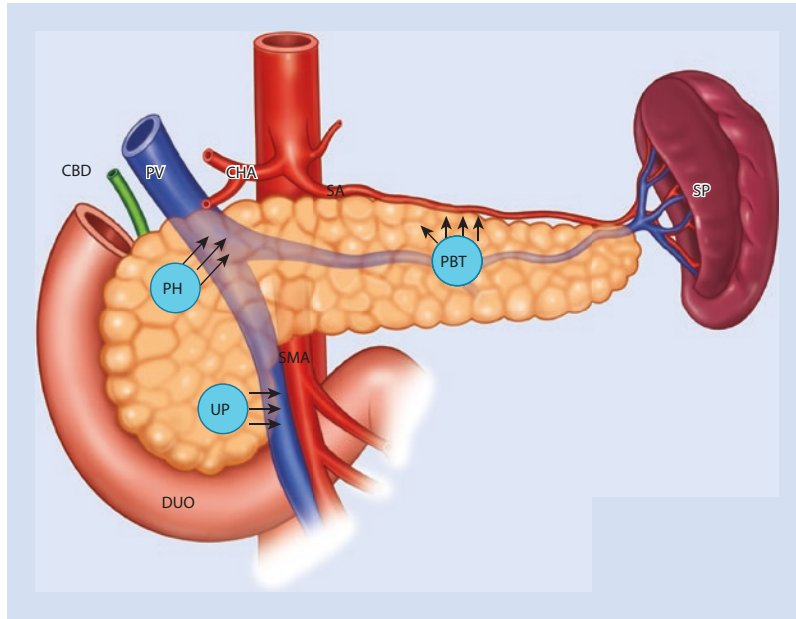

Fig. 6.15 Different routes of perineural invasion for tumors in the pancreatic head (*PH*), uncinate process (*UP*), and body/tail (*PBT*)

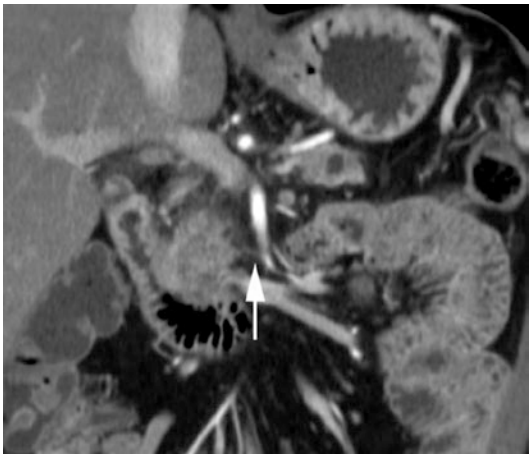

Fig. 6.16 Coronal CT image shows a hypoattenuating tumor in the pancreatic head and spiculations (*arrow*) in the adipose tissue between the pancreatic head and the superior mesenteric artery, consistent with perineural invasion (confirmed at pathology)

plexus around the common hepatic artery (PL cha) and the hepatoduodenal ligament (PL hdl).

In patients with carcinoma of the body and tail of the pancreas, the splenic plexus is the most frequent site of invasion [24]. In addition, a second route of neural invasion has been proposed [31], directly leading to the celiac ganglion via a distinct nerve trunk, which runs independently of blood vessels.

6.6.1 Surgical Implications

While the splenic ganglion is easily removed during distal pancreatectomy, the optimal extent of neural clearance during pancreaticoduodenectomy for pancreatic cancer is still debated. Extended extrapancreatic neural plexus dissection has been advocated, especially by Japanese authors [32], in order to obtain oncologically negative resections and better survival outcomes.

RCTs comparing outcomes of standard and extended lymph node resection failed to show any survival advantages in comparison with standard resections and were frequently associated with intractable diarrhea [33–37].

Coherently, in the recent ISGPS Guidelines [14] circumferential clearance of the lymph nodes and neural plexus around the superior mesenteric artery has not been recommended, and only tissue at the right side of the superior mesenteric artery has been included in the definition of standard resection.

6.7 Metastatic Spread

The liver is the primary site for hematogenous metastatic spread from the pancreas. The location of the primary tumor influences the distribution of metastases within the liver: tumors located in the body–tail of the pancreas, especially when splenic vein invasion is present, tend to metastasize to the left lobe of the liver more than tumors located in the head of the pancreas [38]. This has been hypothesized to be due to the streamline phenomenon, i.e., the dual blood flow in the portal trunk to the liver: the blood flow from the superior mesenteric vein follows preferentially the right portal trunk to the right lobe of the liver (Fig. 6.17). The blood flow from the splenic vein together with the inferior mesenteric vein follows the left side of the portal trunk to the left portal vein and the left lobe of the liver and, because of the smaller caliber of the left portal vein, also enters into the right branch of the portal vein. Therefore, the right lobe of the liver receives the majority of the blood flow, even from the splenic vein.

This streamline phenomenon, already well demonstrated by portal venography studies, can be explained with the shortness of the portal trunk, the smoother angle between the superior mesenteric vein and the right portal vein, and the larger caliber of the right portal vein.

Other less common sites for hematogenous metastases include, in approximate order of frequency, the lungs, adrenals, kidneys, bones, brain, and skin. For dissemination to these sites, no differences have been reported based on the location of the primary tumor.

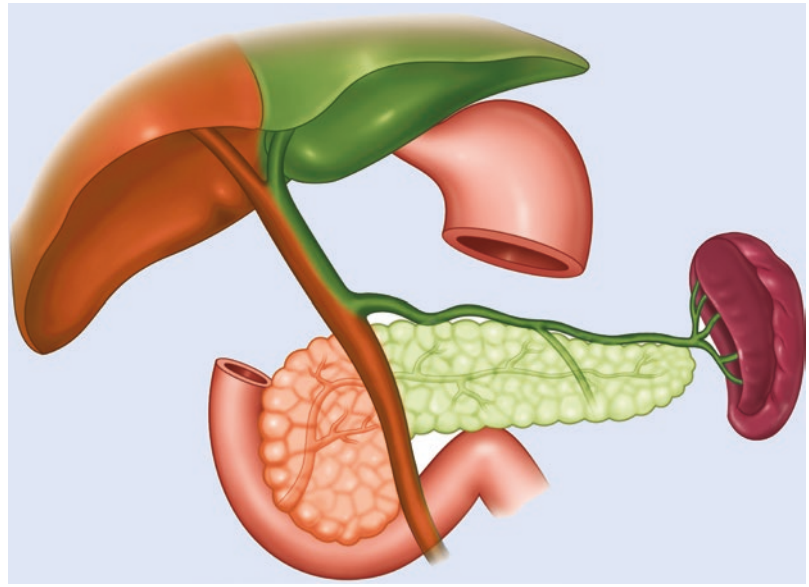

Fig. 6.17 Distribution of hematogenous metastases to the liver according to the streamline phenomenon theory

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