Management of Localized Pancreatic Cancer

Current Treatment and Challenges

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Preface

For over three decades, the survival for patients with pancreatic cancer has been stagnant, and the lack of progress offered little hope for patients afflicted with this disease. However, recent improvements in our understanding of tumor biology have impacted our clinical management of the disease. Moving away from a Halstedian approach to cancer management has allowed for more innovative approaches to treatment sequencing, which has in turn resulted in dramatic improvements in overall survival for patients with localized disease. Similarly, there has been an evolution in our understanding of the management of advanced pancreatic cancer as well. Along with a movement away from single-drug regimens towards multi-drug therapies, there is a growing appreciation of the impact of specific somatic and germline mutations on chemotherapeutic sensitivity. As with other solid tumors, the fundamental understanding of the genetic predeterminants of the disease continues to evolve to allow us to better understand disease subtypes and develop a tailored approach for each. These changes have ushered in a new age of hope for patients and their families.

We have created this handbook as a resource for the practicing clinician. The authors represent a diverse group of experts who have endeavored to provide a practical evaluation of the available data and provide insights into the complexities of multimodality management of pancreatic cancer. We are indebted to the exceptional contributions of the authors and reflect their ongoing commitment to the advancement of care for this disease.

We are at an exciting time where clinical medicine and translational science are converging to allow for unprecedented advancements in the care of cancer patients. We look forward to future developments in the area of pancreatic cancer to build upon our current successes and catapult us into a new era of discovery.

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The Future of Multidisciplinary Care in Pancreatic Cancer

1

Susan Tsai and Douglas B. Evans

Introduction

Over the past two decades, cancer care has evolved from a physician-specific approach, in which cancer care providers existed in relative isolation and interacted with other specialists when their expertise in the management of the cancer patient had been exhausted, to a disease-specific approach, whereby multidisciplinary teams of physicians converge to develop and coordinate a care plan for each individual patient at the time of diagnosis. Such care teams have developed to facilitate patient-centered care. Intended consequences of multidisciplinary care have included improved patient and physician communication, coordination of care (whether the treatments are intended to be in series or parallel), and reduced fragmentation of services as patients move from one treatment modality to the next. There is now clear evidence that multidisciplinary care is associated with better clinical and process outcomes for cancer patients, decreased time from diagnosis to start of treatment, and improved patient survival [1, 2]. Current multidisciplinary pancreatic cancer teams frequently including medical oncologists, radiation oncologists, and surgeons, as well as abdominal imaging specialists, pathologists, gastroenterologists with expertise in advanced endoscopy, and genetic counselors, who collectively are able to select the best treatment options for each patient. As our understanding of the interaction between host (patient) factors and tumor biology/natural history has evolved, the management of pancreatic cancer has shifted away from a physician specialty-centric approach to one that focuses on all aspects of patient care, often including the sequential delivery of oncologic therapies. In the very near future (and right now at some larger centers to include our own), the limitation of available treatments may be dictated by patient factors, and multidisciplinary teams will need to expand to include the expertise of dietitians, psychologists, endocrine specialists, and geriatric specialists to fully realize a patient-centered care model (Fig. 1.1).

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Moving Beyond a Physician (Specialty)-Centric Approach

Patients with pancreatic cancer have historically been treated with up-front surgical resection, likely influenced by the Halstedian paradigm of

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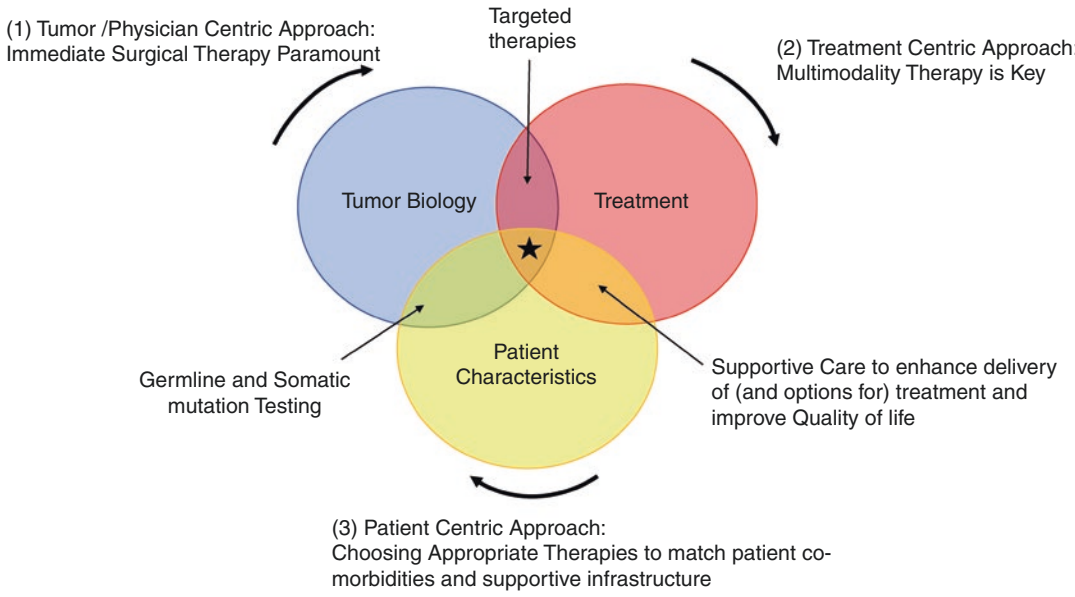

Fig. 1.1 Interrelationship of tumor-, treatment-, and patient-specific factors in the management of pancreatic cancer

cancer progression, whereby cancer spreads from the primary tumor to regional lymph nodes and only afterward to distant sites. Following such reasoning, surgical extirpation of a localized tumor would prevent cancer dissemination and metastatic tumor progression. However, decades of surgical experience have demonstrated that surgical resection alone, even with the addition of adjuvant therapy, provides a limited median survival benefit of only 20–24 months for patients with localized pancreatic cancer [3]. Indeed, the vast majority of patients with presumed localized pancreatic cancer succumb to metastatic disease after a curative-intent surgery [4]. Despite the optimization of surgical technique and perioperative management over the past three decades, little progress has been made to improve the limited survival of patients with localized pancreatic cancer who receive surgery [5, 6]. The development of metachronous distant tumor metastases in the majority of patients for whom local-regional tumor control was achieved, supports an alternative paradigm of cancer progression, whereby systemic metastases may be present even in the absence of radiographic or pathologic (node negative) evidence of disease. This hypothesis, first proposed by Bernard Fisher as an alternative to the Halstedian theory of cancer, was developed from observations in the laboratory involving tumor metastasis in animal models of breast cancer. In pancreatic cancer, preclinical models of genetically engineered mice also support the hypothesis that pancreatic cancer has a proclivity for early metastases, which can occur before a visible tumor may be present in the pancreas [7]. As such, there is an evolving recognition that pancreatic cancer is a systemic disease at the time of diagnosis, even among patients with apparent localized disease, and "a chance to cut" is not necessarily a chance to cure [8, 9].

For patients with localized pancreatic cancer who undergo a margin negative (R0) resection, most will experience disease recurrence, and the overall median survival is approximately 20 months [5]. Most notably, within 6 months of successful surgery, up to 60% of patients who underwent curative-intent surgery have already experienced disease relapse, as reported in the CONKO-001 trial [10]. Therefore, radiographically occult micrometastatic disease may be present in the majority of patients with pancreatic cancer at the time of diagnosis. The benefit of adjuvant systemic therapy was first demonstrated in the CONKO-001 trial, which compared

adjuvant gemcitabine to observation in patients with resected pancreatic cancer. This study reported a median overall survival of 22.8 months with gemcitabine as compared to 20.2 months in the observation (surgery alone) group [3]. More recently, the ESPAC4 trial, which compared adjuvant gemcitabine to adjuvant gemcitabine and capecitabine, demonstrated a median overall survival of 25.5 months and 28.0 months, for the two arms, respectively [11]. It is important to note that the modest benefit of adjuvant therapy appears to be stage independent, further supporting the hypothesis that metastatic disease progression occurs early (regardless of nodal status) in this disease.

Although universally recommended, the feasibility of delivering adjuvant therapy to patients with pancreatic cancer in the postoperative setting remains problematic. Approximately 50% of patients will fail to receive any adjuvant therapy following pancreatectomy due to surgery-associated complications, delayed recovery, or failure to return to an adequate baseline performance status acceptable for systemic therapy [12, 13]. Indeed, one of the problems with the interpretation of adjuvant therapy trials is the selection bias introduced by the trial design itself. In order to be enrolled in a trial of adjuvant therapy for operable pancreatic cancer, patients must survive the operation, recover within 2–3 months, have no evidence of early disease recurrence, and have a performance status acceptable for the delivery of systemic therapy. As the toxicity profile of planned adjuvant therapy increases, the selection bias is further exaggerated. This was recently demonstrated in the PRODIGE trial reported at the ASCO 2018 where patients in the control arm (adjuvant gemcitabine) had a median survival of 35 months compared to 26 months (with the same treatment) in ESPAC4 [14]. The selection bias was likely due to the fact that the experimental arm (in PRODIGE) involved adjuvant mFOLFIRINOX – medical oncologists knew that patients would need to be particularly robust to handle this treatment after a pancreatectomy. While those who received mFOLFIRINOX experienced a very favorable survival duration, this lucky subset may represent only a tiny percentage of all patients who undergo a pancreatectomy for pancreatic cancer. Acknowledging that surgery alone is an insufficient therapy to achieve long-term disease control and understanding that surgical resection may unintentionally impede the delivery of future systemic therapies, treatment sequencing which specifically relies on the delivery of adjuvant therapy has been called into question. Commitment to a surgery-first approach may be attractive to surgeons and rewards technical proficiency with respect to local disease management, but does not provide a treatment strategy which reliably delivers systemic therapy for a disease which many clinicians and scientists now agree is distinguished by early metastatic disease.

Era of Neoadjuvant Therapy: Adopting a Patient-Centric Approach

In light of the limitations of a surgery-first approach for patients with localized pancreatic cancer, a logical alternative is to deliver preoperative (neoadjuvant) therapy before surgery. Advantages of a neoadjuvant strategy include (1) early treatment of presumed micrometastatic disease, (2) the ability to minimize stage misclassification by providing a time interval during which indeterminate lesions (that may be metastases) can be better characterized through serial radiographic imaging, and (3) theoretical efficacy of radiation in a non-hypoxic environment. Initial neoadjuvant trials required additional expertise in the management of patients with pancreatic cancer to include the talent of abdominal radiologists, advanced endoscopists, and cytopathologists. First, since treatment would precede an operation, it was necessary to develop a clinical (as opposed to pathological) staging system in order to provide an objective, CT-based anatomic staging system which could assess the efficacy of a therapeutic intervention. When such assessments are performed over serial time points, they provide important insights into tumor biology, response to therapy, and more accurately predict the utility of surgical resection. Second, a tissue diagnosis was required prior to treatment, which

historically necessitated percutaneous biopsy with the incumbent risk of peritoneal seeding. This risk could be abrogated with an endoscopic approach. This would require the expertise of an advanced endoscopist to obtain the sample and a cytopathologist to interpret the specimen. Currently, tissue diagnoses can be obtained in almost all patients using endoscopic ultrasound-guided fine needle aspiration, and associated procedural complications are very rare. Finally, patients with tumors in the head of the pancreas frequently require decompression of biliary obstruction with endobiliary stenting. Stent-related morbidities, including cholangitis due to stent occlusion during neoadjuvant therapy, occur in up to 15% of patients and require prompt recognition [15]. However, the use of metal endobiliary stents rather than polyethylene (plastic) stents has reduced stent-related complications [16]. With these issues addressed, neoadjuvant therapy could be implemented in patients with localized pancreatic cancer.

In the early experience with neoadjuvant therapy, approximately 30% of patients with localized PDAC developed metastatic disease progression after a short course of neoadjuvant therapy [17, 18]. Importantly, the patients who were able to complete all intended neoadjuvant therapy and surgery experienced median overall survivals up to 44 months [17, 19, 20]. Such survival durations far exceeded that of a surgery-first approach and suggested that multimodality neoadjuvant therapy may be more effective at eradicating micrometastatic disease than adjuvant therapy; indeed, the sequencing of therapies may matter and effect the host-tumor relationship and tumor response. These early successes spurred an intense debate regarding the optimal treatment sequencing for patients with pancreatic cancer, due to the lack of level III evidence to support a survival benefit. More recently, the PREOPANC trial randomized patients with resectable and borderline resectable pancreatic cancer to either upfront surgical resection followed by adjuvant gemcitabine or preoperative gemcitabine-based chemoradiation, surgery, and adjuvant gemcitabine [21]. An intention to treat analysis demonstrated an improved overall survival among patients treated with perioperative therapy as compared to a surgery-first approach ($p = 0.07$). In addition, a planned subset analysis of just patients who underwent resection demonstrated that the patients who received a perioperative/neoadjuvant approach had a significantly greater overall survival than patients who received upfront surgical resection (42.2 vs. 16.8, $p < 0.001$).

As acceptance of neoadjuvant treatment grows, additional efforts have been directed at improving outcomes for the proportion of patients who develop metastatic disease progression during neoadjuvant therapy. Such disease progression, which occurs despite the receipt of systemic therapy, is due to chemotherapeutic resistance and may be potentially prevented by administering a more effective first-line chemotherapeutic agents. We recently reported the first neoadjuvant trail utilizing molecular profiling to guide chemotherapeutic selection in patients with localized pancreatic cancer [22]. Among 130 patients, 82% of patients were able to complete all intended neoadjuvant therapy and surgery, including 92% of patients with resectable disease and 74% of patients with borderline resectable disease. Because of the increased proportion of patients who were able to complete all intended therapy, the median overall survival of *all* 130 patients was 38 months, and the median overall survival for the 107 patients who completed all intended neoadjuvant therapy and surgery was 45 months [17, 18]. These encouraging findings suggest that real-time prospective molecular profiling may allow for optimal selection of neoadjuvant therapy for patients with localized pancreatic cancer. In the future, an approach which leverages both tumor-specific and treatment-specific approaches and capitalizes on the growing availability of molecular techniques will be needed to guide targeted therapies.

Future of Multidisciplinary Care: Incorporating a Patient-Centric Approach

Tremendous efforts are underway to better understand pancreatic cancer biology and to guide the treatment selection for all patients. Gone are the

days of a one-size-fits-all approach to this disease, and the last frontier may be the ability to best predict and meet the needs of each individual patient. This will require improved understanding of individual patent characteristics (immunity and physiologic reserve), refinement of treatment monitoring, innovative approaches to treatment delivery, and improved supportive care. The most compelling example of this is the recent recommendation to include germline genetic testing for all patients with pancreatic cancer [23]. This change occurred as a result of recent studies which demonstrated that approximately 5–10% of patients with pancreatic cancer have disease-associated germline mutations which may not be reliably identified through personal and family history [24]. The identification of BRCA2, BRCA1, PALB2, and MMR gene mutations has important therapeutic implications. This is the first step towards a standardized approach to incorporate individual patient characteristics into multidisciplinary care.

Current neoadjuvant therapy is generally delivered as a prescriptive therapy, where patients are required to undergo multiple therapies in sequence. There is a lack of consensus around what the most effective treatment regimen may be, with controversy regarding the type of systemic therapy delivered, the utilization of radiation therapy, and the plan, if any, for additional adjuvant therapy [25]. It is important to note that neoadjuvant therapy was first conceived in an effort to accurately identify those patients who would evidence disease progression during/after neoadjuvant therapy and thereby avoid the morbidity of surgery, when an operation would provide no clinical benefit. Therefore, the historic threshold for proceeding with surgery after neoadjuvant therapy has been the absence of disease progression rather than the presence of a treatment response. In fact, the primary tumor may not significantly change following neoadjuvant therapy, and occult micrometastases, even if unresponsive to induction therapy, may still not be radiographically apparent at the time of preoperative restaging. The inability to accurately assess response to neoadjuvant therapy, as distinct from disease stabilization, is likely responsible for the early postoperative recurrence seen in some patients who have received neoadjuvant therapy. There is growing evidence that normalization of CA19-9 levels in response to neoadjuvant therapy is an important prognostic marker [26]. Novel clinical trials which prioritize changes in CA19-9 to guide adaptive modification of neoadjuvant treatment over prescriptive, static regimens are ongoing (NCT03322995).

As with other solid tumors, an evolution in treatment sequencing to include total neoadjuvant therapy may also occur in pancreatic cancer. With more extended neoadjuvant therapies, cumulative toxicities are inevitable. As therapies are increasingly tailored to each patient's tumor, it will be equally important that treatment sequencing be tailored to each patient, including patients of all ages, with a variety of medical comorbidities, and with family/social infrastructure varying from robust to unfortunate. It is unrealistic to assume that all patients can tolerate all therapies. In anticipation of the need for increased supportive care, multidisciplinary teams will need to expand to include the expertise of dietitians, psychologists, endocrine specialists, and geriatric specialists to fully realize a patient-centered care model.

Conclusions

The next decade will witness an intense focus on the many new therapeutic options available for patients with pancreatic cancer. For such patients, they will realize this opportunity only if they have been properly cared for at the time of diagnosis – to include accurate staging, tumor biopsy, endobiliary stenting, diabetes management, and genetic counseling. This will require the expertise that exists at a high-volume cancer center (to accurately stage and prepare the patient for treatment, to include review of clinical trial options). Pressure applied to physicians to keep patients in "their system" for the entire continuum of diagnosis and treatment, rather than offer them referral to a center who can do it better, should be discouraged. As we are entering a new era of physician employment, we will face new

challenges in inter-system collaboration, and patients may get caught in the middle. For every million population, there are only 150 patients with pancreatic cancer. It is unrealistic to think that all hospital systems will have the physician expertise and breadth of services needed to develop complex treatment recommendations for patients with pancreatic cancer. Physicians in competing health systems must work together to find that sweat spot for optimal patient care wherein patients receive the expertise of the regional high-volume center and the convenience and compassion of their local physicians. Working together for the good of the patient may be as challenging as finding the optimal therapy.

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2 Clinical Staging of Pancreatic Cancer with MDCT and MRI

Naveen M. Kulkarni

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in the United States, with an overall 5-year survival rate of only 7%, when accounting for all stages [1–4]. The poor prognosis of pancreatic cancer relates to its propensity to infiltrate critical vascular and neural structures near the pancreas and is associated with an aggressive disease biology with early metastatic spread, particularly to the liver and peritoneum (Fig. 2.1). As a result, approximately, 40–50% of patients who are considered to have localized, operable pancreatic cancer will have a microscopically positive (R1) resection after surgery [5]. Patients with incomplete/margin positive resection [residual microscopic (R1) or residual macroscopic (R2)] have survival rates similar to patients with metastatic disease, and hence, would not benefit from surgery [6–9]. Cross-sectional imaging plays an essential role in the clinical staging of pancreatic cancer and assists in allocating patients into the appropriate management group.

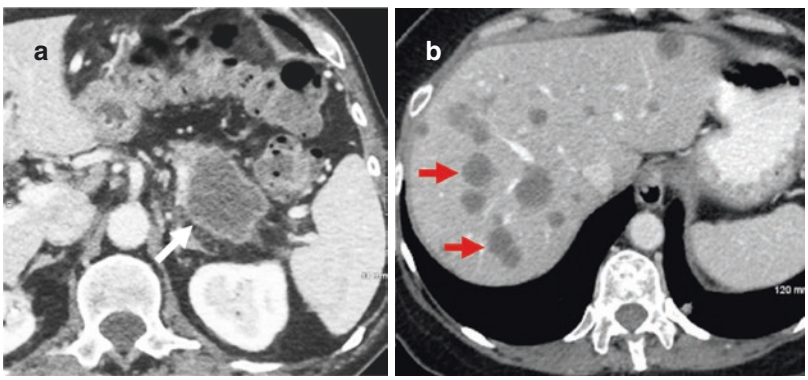

Fig. 2.1 Metastatic pancreatic cancer at presentation. (**a**, **b**) Portal venous phase axial MDCT images through the pancreatic tail and liver shows large pancreatic tail mass (white arrow) and multiple liver metastases (red arrows)

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Staging and Resectability

To understand the clinical significance of cross-sectional imaging in the management of pancreatic cancer, it is important to be familiar with the staging system/resectability criteria for pancreatic cancer. Multiple staging systems from a variety of different societies and institutions have been described [10–14]. The American Joint Committee on Cancer (AJCC) TNM staging has been used to characterize the pathologic stage of pancreatic cancer. This system assesses the status of the primary tumor (T), lymph nodes (N), and metastases (M) with an aim to define tumor stages and provide prognosis based on gross *pathologic* characteristics [15]. With the advent of neoadjuvant therapies for pancreatic cancer, alternative staging systems were developed based on *preoperative* clinical parameters to more accurately categorize the probability of surgical resection based on anatomic factors an the ability to achieve a complete surgical resection, to include the extent of peripancreatic and perivascular invasion. This classification of tumor-mesenteric vessel relationship is a critical component in surgical planning and is not addressed in the AJCC staging system. In order to define the resectability status of pancreatic cancer, additional classification systems have been described. Depending on the tumor location, relationship with peripancreatic vessels, and presence/absence of metastatic disease, published guidelines generally agree on four clinical stages: (1) resectable, (2) borderline resectable, (3) locally advanced [unresectable], and (4) metastatic [unresectable]. Although there is a close agreement on what constitutes resectable and unresectable (locally advanced and metastatic) disease, the definition of borderline resectable disease is more variable (Table 2.1) [16]. Differences in surgical experience, as well as imaging practices and interpretation, contribute to these varying definitions of borderline resectable category. Patients with borderline resectable disease were previously considered as poor candidates for resection; but with improved neoadjuvant therapy, there is growing consensus to offer surgery as a part of multimodality therapy [10, 14]. Irrespective of the classification system used, cross-sectional imaging provides the most objective means to preoperatively stage the pancreatic cancer.

Table 2.1 Definitions of resectability between different classification systems [10–14]

Stage	Anatomy	MCW	NCCN (2017)	MDACC	AHPBA/SSO/SSAT
Resectable	Artery (CA, SMA, or HA)	No involvement	No involvement	No involvement	No involvement
	Vein (SMV, PV, or SMV-PV confluence)	• No involvement • If involved, ≤50% circumference narrowing of vein	• No involvement • ≤180° contact without vein contour irregularity	• No involvement • Abutment (provided vein is patent)	No involvement

Table 2.1 (continued)

Stage	Anatomy		MCW		NCCN (2017)	MDACC	AHPBA/SSO/SSAT
Borderline resectable	Artery	CA	Abutment		• Abutment • Encasement [no involvement of aorta and GDA]	Abutment	Uninvolved
		SMA	Abutment		Abutment	Abutment	Abutment
		HA	Short segment abutment/encasement without involving CA or HA bifurcation		Contact without extension to CA or HA bifurcation	Abutment or short segment encasement	Abutment or short segment encasement
	Vein (SMV, PV, or SMV-PV confluence)		>50% narrowing[a]		• Contact >180°[a] • Contact ≤180° with contour irregularity or thrombosis of vein[a] • Contact with IVC	• Abutment with impingement and narrowing[a] • Segmental venous occlusion[a]	Abutment, encasement, or short segment occlusion[a]
Locally advanced	Artery		Type A	Type B	Encasement of CA, SMA and HA without options for reconstruction		
		CA	Encasement but no extension to aorta[b]	Encasement and extension to aorta			
		SMA	Encasement (>180° but ≤270°)	>270° encasement			
		HA	Encasement and extension to CA[b]	Encasement with extension beyond bifurcation of proper HA			
	Vein (SMV, PV, or SMV-PV confluence)		Occlusion without options for reconstruction				
Metastatic	Evidence of peritoneal and distant metastases						

Abutment is defined as ≤180° contact with vessel and encasement indicates >180° involvement
MCW Medical College of Wisconsin, *NCCN* National Comprehensive Cancer Network, *MDACC* MD Anderson Cancer Center, *AHPBA* American Hepato-Pancreato-Biliary Association, *SSAT* Society for Surgery of the Alimentary Tract, *SSO* Society for Surgical Oncology
CA celiac axis, *SMA* superior mesenteric artery, *HA* hepatic artery, *GDA* gastroduodenal artery, *SMV* superior mesenteric vein, *PV* portal vein
[a]Amenable for safe and complete resection and venous reconstruction
[b]Amenable for celiac resection (with or without reconstruction)

Cross-Sectional Imaging Techniques

During the initial evaluation of patients with pancreatic cancer, obtaining a high-quality cross-sectional imaging is one of the most important components of the workup. A pancreatic mass can be seen on abdominal ultrasound and routine contrast-enhanced computed tomography (CT) may be performed for the evaluation of abdominal pain or sometimes is detected as an incidental

finding. However, these studies are not adequate for the staging of pancreatic cancer. A dedicated pancreatic protocol performed as a biphasic technique and scan parameters optimized for detection and staging is essential [17, 18].

Multidetector Computed Tomograph (MDCT)

When pancreatic pathology is suspected, a biphase pancreatic CT protocol should be performed on multidetector scanner (64-detector row or greater is preferred). Neutral oral contrast such as water is used to distend stomach and duodenum to provide optimal visibility of periampullary and pancreatic head pathology (Fig. 2.2). Positive oral contrast should be avoided as it obscures the periampullary region and could impair the visibility of subtle pancreatic head abnormalities secondary to beam-hardening artifacts from contrast pooling within the stomach and duodenum. This also interferes with three-dimensional (3-D) CT post-processing. Multi-phase pancreatic CT is done with rapid injection of intravenous nonionic iodinated contrast (3–5 mL/s). Rapidly injected contrast bolus causes intense pancreatic enhancement enabling distinction of a hypovascular cancer (as is characteristic of pancreatic cancer) from the enhancing normal pancreas. The first part of biphasic pancreatic protocol is acquired during the pancreatic (late arterial) phase, approximately 40–50 seconds after the start of contrast injection. The latter hepatic (portal venous) phase optimizes enhancement of the liver and portomesenteric vasculature and is typically acquired 65–75 seconds after contrast injection. For the pancreatic phase, upper abdomen, including the pancreas is scanned, and the hepatic phase should include entire abdomen and pelvis (Table 2.2) [19–23].

The MDCT images are acquired using thin collimation (0.5–0.6 mm thickness) in a relatively short and comfortable breath hold time to obtain motion-free images. With new MDCT scanners, isotropic volume acquisition (identical resolution in all three planes) allows generation of high-quality multiplanar and curved-planar reformatted images, and 3-D reconstruction of mesenteric vessels [maximum intensity projection (MIP) and volume rendering (VR)] which provides an excellent view of vascular anatomy (Fig. 2.3) and tumor-vessel relationship. Three-D reconstructions offer certain unique advantages over the axial image: (1) better display of tumor encasement/abutment of vessels which may not be seen in the standard axial plane, (2) 2-D and

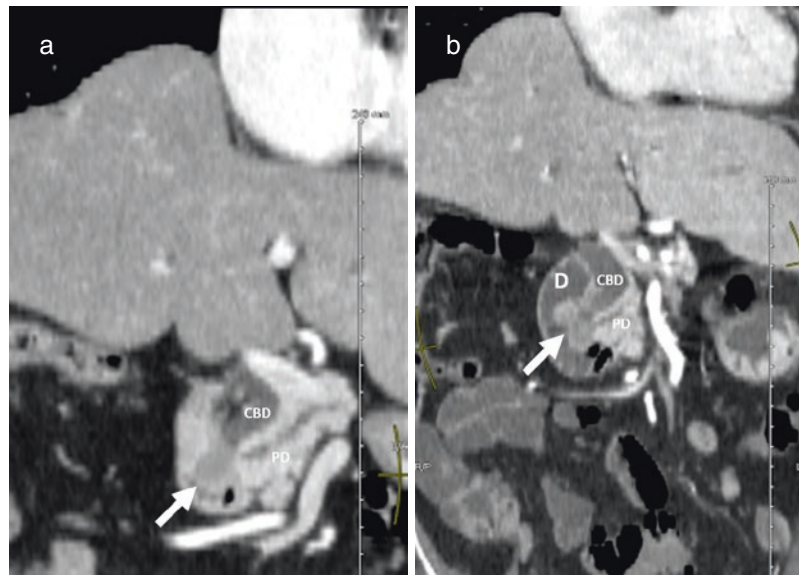

Fig. 2.2 Ampullary tumor on two different studies from the same patient (acquired 4 weeks apart). (**a**) Oblique coronal image from routine contrast-enhanced MDCT shows dilated common bile duct and pancreatic duct and suspected periampullary tumor (white arrow). (**b**) Repeat dual-phase pancreatic MDCT with neutral oral contrast (water) resulted in sufficient duodenum (D) distension confirming bilobed ampullary tumor (white arrow)

Table 2.2 MDCT protocol for evaluation of pancreatic adenocarcinoma [11, 20]

Parameters	Technical aspects	Comments
Scan type and acquisition	Multidetector row CT with thinnest possible section thickness	Scanner with 64-slice or greater is preferred
Oral contrast	Neutral agent (water) should be used	Positive oral contrast can limit assessment of periampullary region and pancreatic head
Contrast-enhanced phases and acquisition timing	Pancreatic phase: 40–50 s Portal venous phase: 65–70 s (Iodinate contrast agent with high iodine content, >300 mg I/ml at injection rate of 3–5 ml/s is preferred)	Pancreatic phase is ideal for assessment of primary tumor and portal venous phase for evaluating metastases
Standard reconstructions	Axial: 2–5 mm thickness MPR (Coronal and sagittal): 2–3 mm	May vary between institutions
Additional reconstructions	MIP, VR, oblique MPR, and CPR (These are always reviewed in conjunction with standard reconstructions)	MIP & VR: for vascular maps Oblique MPR and CPR: to view structures like blood vessel or pancreatic duct which lie or course in a nonstandard plane

MPR multiplanar reformats, *MIP* maximum intensity projection, *VR* volume rendered, *CPR* curved planar reformats

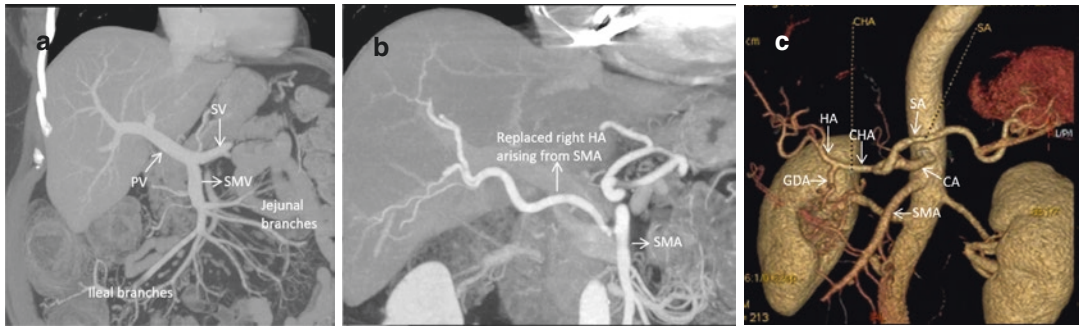

Fig. 2.3 Different post-processing tools to display 3-D anatomy of central mesenteric vasculature relevant to pancreatic imaging. (**a**) Normal coronal maximum intensity projection (MIP) of mesenteric venous systems. (**b**) Coronal MIP shows replaced right HA arising from the SMA. (**c**) Normal volume rendered (VR) image displays important peripancreatic arteries. (PV portal vein, SV splenic vein, SA splenic artery, SMV superior mesenteric vein, SMA superior mesenteric artery, CA celiac axis, CHA common hepatic artery, HA hepatic artery, GDA gastroduodenal artery)

3-D views of variations to mesenteric arterial anatomy and length of vascular involvement, and (3) perineural spread of the tumor [24–28].

The pancreatic phase maximizes the detection of a pancreatic cancer and allows for characterization of the tumor to nearby arterial structures, whereas the hepatic phase is ideal for detecting liver, peritoneal, and lymph node metastases, as well as tumor involvement of venous structures (Figs. 2.1 and 2.4). The visibility of pancreatic cancer is enhanced due to its hypoattenuating appearance on the background of enhancing normal pancreas; this is seen in approximately 90–95% of patients on the pancreatic phase (Fig. 2.4). Often, secondary findings like contour deformity and/or dilatation of either the pancreatic or common bile duct or both (the "double-duct sign") can be seen (Fig. 2.5). 3-D curved-planar reformatted images along the length of the pancreas can better outline subtle degree of dilated pancreatic duct to localize site of obstruction when pancreatic mass is radiographically occult. Such secondary signs are useful in localizing isoattenuating pancreatic cancer