Definition and Management of Borderline Resectable Pancreatic Cancer

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KEYWORDS
• Borderline resectable pancreatic cancer • Definitions • Management
• Pancreatic ductal adenocarcinoma

KEY POINTS
• Pretreatment evaluation of patients can aid in accurate communication and treatment planning for patients with borderline resectable pancreatic cancer; many patients have technically resectable tumors but are not adequate candidates for surgery.
• Imaging using contrast-enhanced computed tomography is necessary to stage the patient and evaluate extrapancreatic extent of the primary tumor.
• Even though small variations in the definition of borderline resectable tumors exist, the surgeon remains responsible for the complete and safe resection of the primary tumor.
• Safe surgical resection requires detailed preoperative knowledge of pertinent vascular anatomy, careful retroperitoneal dissection, and vascular isolation before vascular resection if necessary.

INTRODUCTION
Recent genetic studies have shown that initial clinical evaluation of pancreatic ductal adenocarcinoma (PDAC) occurs very late in the natural history of the disease,1 because only 10% to 20% of patients present with surgically resectable disease.2–5

Nevertheless, the possibility of a potentially curative surgical resection provides a powerful impetus toward surgical resection of all possible patients. The impetus must be governed by the discipline and insight necessary to perform a safe and oncologically effective pancreatic resection, which is just one part of a multidisciplinary effort engineered to achieve long-term patient survival.

Over the last several decades, particularly at high-volume centers, the postoperative mortality following pancreaticoduodenectomy (PD) has decreased from 30% to 1%.6 However, despite these advances in surgical safety, patients with PDAC have...
not benefited from improved long-term survival when surgery is used as initial therapy. Furthermore, despite multiple trials showing a survival benefit with adjuvant therapy, to up 47% of patients treated with up-front surgical resection fail to receive any adjuvant therapy, usually because of delayed postoperative recovery or early disease recurrence. These pitfalls of surgery as primary therapy are amplified in borderline resectable (BR) patients for whom careful staging, meticulous patient evaluation, and preoperative therapy are necessary to identify the subset of patients most likely to benefit from the aggressive surgical procedures necessary for complete surgical resection.

IDENTIFICATION OF BORDERLINE RESECTABLE PATIENTS

Any patients with PDAC evaluated by a pancreatic surgeon may require a high-risk surgical procedure that offers the only chance of cure. A new diagnosis of PDAC is often made in patients with multiple underlying medical conditions of variable significance with respect to the risks of pancreatectomy. This high-stakes clinical scenario mandates that the surgeon uses an organized approach to ensure a thorough and efficient initial evaluation. The anatomic relationship of the tumor and critical vessels as determined by a pancreas protocol computed tomography (CT) scan is of crucial significance, but other nonanatomic factors must also be evaluated, such as suspicion for extrapancreatic disease, comorbidities, and functional status. Using this approach, the whole patient and not just tumors are classified as potentially resectable or borderline candidates for surgical resection of the primary tumor.

Our center has developed a systematic approach in which all patients with localized PDAC receive a physical examination, a review of laboratory studies, and radiographic imaging as part of a comprehensive evaluation in a surgical clinic. These data are then collated using a system denoted by the acronym ABC in which A refers to tumor anatomic considerations for surgery, B to cancer biology or stage; and C to patient condition or performance status and fitness for surgery (Fig. 1). In the course of treatment planning and communication across our multidisciplinary care team, patients are classified as clinically resectable (CR) or BR using the common nomenclature BR-A, BR-B, or BR-C. BR-A patients have no major comorbidities, no clinical findings that are suspicious for extrapancreatic disease, and meet anatomic imaging criteria for a BR tumor, as outlined later. BR-B patients have no major comorbidities or anatomic imaging criteria for a borderline resectable tumor, and have clinical findings suspicious for extrapancreatic disease: (1) indeterminate liver lesions, (2) serum carbohydrate antigen 19-9 (CA19-9) level greater than or equal to 1000 U/mL in the setting of a normal bilirubin level, or (3) biopsy-proven involvement of regional lymph nodes. BR-C patients are advanced in age (≥80 years old) or possess severe comorbidities requiring extensive evaluation or optimization, or depressed performance status (Eastern Cooperative Oncology Group [ECOG] ≥2). They may or may not have clinical findings suspicious for extrapancreatic disease.

In practice, the fitness of each patient for pancreatic surgery is evaluated first (see Fig. 1). Patients who are too frail for surgery secondary to uncorrectable comorbidities do not need to undergo extensive evaluation for surgical resection or consideration for preoperative therapy because surgical resection will not be the end result. These patients can therefore be efficiently triaged for palliative therapy or supportive care. If the patient is not currently fit for surgery, but has a potentially reversible condition, then medical optimization or prehabilitation during preoperative therapy is the goal. These patients are referred to as BR-C and are generally older (median age, 75 years) with a higher ECOG status (44% ECOG 2) usually secondary to
Fig. 1. Initial evaluation and categorization of patients with pancreatic adenocarcinoma. CA19-9, carbohydrate antigen 19-9; Chemo, chemotherapy; XRT, X-ray therapy.
cardiopulmonary disease (63%). If the patient is fit for surgery, biological staging is next. Evidence of distant metastases on radiographic imaging is a contraindication to resection, but in many cases there are suspicious radiographic findings, but not diagnostic for distant metastatic disease. These patients are termed BR-B and receive chemotherapy followed by restaging. Similarly, patients with a high CA19-9 level (1,000 U/mL) even with negative imaging are considered BR-B and receive chemotherapy followed by restaging. In addition, local anatomic factors related to the primary tumor are considered in patients who are without metastases and are fit for surgery, which necessitates careful review of radiographic image using standard anatomic criteria designed to categorize tumors as resectable, borderline, or locally advanced. Patients who are fit for surgery with no evidence or suspicion of metastases and borderline tumors are considered BR-A, and usually receive chemotherapy plus or minus chemoradiation and restaging before proceeding with surgical resection.

Clinical application of this approach to the initial evaluation identifies that at least 50% of patients have borderline clinical features. When treated preoperatively, only 37% of BR-C patients can be expected to undergo resection, whereas the others fail to reach surgical resection because of poor performance status (31%) or interval identification of metastatic disease (26%). BR-C patients who undergo resection experienced a median survival of 38.6 months versus 13.3 months \( P = .02 \) for those not receiving surgery. Roughly 46% of BR-B patients receive surgical resection after preoperative therapy and an equal portion (46%) have distant metastases precluding surgery. The loss of performance status is uncommon (4.9%) in BR-B patients. Resection conferred a 33-month median survival versus 11.8 months in those patients unable to proceed to resection \( P<.001 \). Of note, local progression was rarely observed during preoperative therapy in either BR-B or BR-C patients (2.6%)\(^{15,16}\) (Fig. 2). Management of patients with BR type A is considered later.

**IMAGING**

All patients with apparent localized disease are evaluated with a contrast-enhanced CT scan, which provides essential information about the presence of regional or distant metastases and the site and local extent of the primary tumor. This evaluation allows the surgeon to determine whether the patient has a resectable tumor and the likelihood of achieving a margin-negative resection. Multidetector row CT is the

![Fig. 2](image-url)  
**Fig. 2.** Typical distribution of outcomes for patients with type BR-B and type BR-C treated with preoperative therapy. Identification of distant metastases or poor performance status (PS) is most common in patients with BR-B or BR-C, respectively.
most widely used staging modality for pancreas cancer and a workhorse for new patient evaluation. When performed and interpreted correctly, it provides valuable staging for both distant and regional metastases as well as local extrapancreatic extension of the primary tumor to adjacent critical vascular structures. The National Comprehensive Cancer Network (NCCN) recommends that all patients with suspicion for PDAC have a dedicated pancreas protocol CT scan as part of the initial evaluation (Version 2.2015). At MD Anderson Cancer Center (MDACC), a pancreas protocol CT scan uses water as a negative oral contrast agent and starts with precontrast imaging from the dome of the liver extending caudally to include the entire liver reconstructed to 2.5-mm slice thickness. Next, 125 mL of iodinated contrast is administered intravenously at a rate of 3 to 5 mL/s. The pancreas phase/arterial phase uses bolus tracking and images are obtained 10 seconds after a Hounsfield unit value of 100 is reached in the aorta at the level at the celiac axis from the dome of the liver to the iliac crests. Images for the portal venous phase are obtained at a 20-second delay from the pancreas phase. Hepatic metastases are usually best visualized on the portal venous phase. Delayed images are obtained 15 seconds after the portal venous phase. The images are reconstructed to 2.5-mm slice thickness for imaging review and at 0.625-mm or 1.25-mm slice thickness to create coronal and sagittal reformatted images.

The primary pancreatic tumor is best seen on the pancreas phase of the CT scan and is usually a hypodense mass, because the surrounding normal pancreatic parenchyma enhances. The pancreas phase/arterial phase illuminates the branches of the celiac axis and superior mesenteric artery (SMA), enabling clinicians to identify important arterial anatomy variants and discern whether the tumor has any arterial involvement. As many as 40% to 45% of patients have variants of normal hepatic arterial anatomy, which are of vital importance to appreciate on preoperative imaging because these variants can affect operative planning. A replaced or accessory right hepatic artery is present in up to 15% of patients, and most commonly arises from the SMA and courses posterior to the pancreas and posterolateral to the bile duct. An additional 2.5% of patients have a replaced common hepatic artery (CHA) that arises from the SMA and follows a similar path to a replaced or accessory right hepatic artery. The superior mesenteric vein (SMV) and portal vein (PV) are best evaluated on the portal venous phase. The initial staging CT scan has 94% sensitivity and 84% specificity for determining vascular involvement, and the surgeon should carefully note the tumor-vein interface, vein contour, and/or deformity; there are multiple classification schemes that predict venous involvement based on imaging characteristics and these should be used for operative planning. In addition, the surgeon should identify the location and relationship of the gastroepiploic vein, colic veins, inferior mesenteric vein (IMV), and jejunal/ileal branches of the SMV because these have variable courses and the drainage pattern directly affects the surgical options for reconstruction of the SMV-PV confluence, which can be expected in more than 40% of cases. Terminology that describes vascular involvement has become standardized and is reviewed in detail later. Vascular involvement of less than or equal to 180° of the circumference of the vessel is termed abutment. Vascular involvement greater than 180° of the circumference of the vessel is termed encasement. Properly staging patients and determining potential vascular involvement is a cornerstone of treatment planning and its importance cannot be overstated.

DEFINITIONS OF RESECTABILITY

As patient assessment, imaging, and multidisciplinary treatment techniques for patients with localized PDAC were refined in the late 1990s, it became evident that
this patient group included a spectrum of primary tumor types from removable to unresectable. To allow common classification, the multidisciplinary team at MDACC developed imaging criteria that are still in use that define CR tumors by (1) absence of extrapancreatic disease; (2) clear tissue plane between the tumor and the celiac axis, hepatic artery, and SMA; (3) a patent SMV-PV confluence, abutment, or encasement is allowed as long as the vessel is patent.\textsuperscript{4,16,25} Locally advanced (LA) tumors are defined by (1) encasement of the celiac axis; (2) encasement of the hepatic artery with no options for vascular reconstruction; (3) encasement of the SMA greater than 180°; (4) occlusion of the SMV-PV confluence with no options for vascular reconstruction.\textsuperscript{4,16,25} Patients who were classified as CR based on these imaging criteria were likely candidates for an R0 resection, whereas patients with LA tumors were unlikely to respond to chemotherapy and/or chemoradiation to a degree that would allow surgical resection; however, improved response to systemic therapy is occurring more frequently and has allowed patients with advanced tumors to undergo resection.

At present, NCCN defines resectable PDAC as a tumor with no contact of celiac axis, SMA, or CHA, and no contact with the SMV-PV or less than or equal to 180° contact without vein contour irregularity (Version 2.2015). LA PDAC of the head/uncinate process is a tumor that contacts the SMA greater than 180°, the celiac axis greater than 180°, the first jejunal SMA branch, the most proximal draining jejunal vein, or has unreconstructable SMV-PV involvement or occlusion. Tumors of the body/tail are LA when there is contact of greater than 180° with the SMA or celiac axis, contact with the aorta, or unreconstructable SMV-PV involvement or occlusion (Version 2.2015).

In 2001, Mehta and colleagues\textsuperscript{26} described a group of marginally resectable patients who were treated with chemoradiation preoperatively in order to downstage the tumor and increase the likelihood of a margin-negative resection. Marginally resectable was defined as a tumor in which the perivascular fat plane was absent over 180° of the SMA, SMV, or PV and persisted for a length greater than 1 cm.\textsuperscript{26} The NCCN adopted the term BR in 2006 to describe patients with localized tumors who blurred the distinction between CR and LA tumors. These patients were thought to be at higher risk of a margin-positive resection if up-front surgery was used; thus the NCCN suggested the use of preoperative therapy.

Over the last several years, several groups developed specific radiographic features to define BR PDAC. At MDACC, the imaging criteria used to define a BR tumor are (1) abutment of the celiac axis; (2) abutment of the hepatic artery or short-segment encasement; (3) abutment of the SMA less than or equal to 180°; (4) short-segment occlusion of the SMV-PV confluence amenable to resection and reconstruction.\textsuperscript{4,16,25} The American Hepato-Pancreato-Biliary Association (AHPBA), the Society of Surgical Oncology (SSO), and the Society for Surgery of the Alimentary Tract (SSAT) define BR PDAC as tumors with no abutment or encasement of the celiac axis, short-segment abutment or encasement of the CHA amenable to reconstruction, abutment less than 180° of the SMA, or abutment with or without impingement or narrowing of the SMV-PV or encasement with or without occlusion with suitable vein proximal and distal to allow resection and reconstruction.\textsuperscript{27,28} The difference between the MDACC and AHPBA/SSO/SSAT definitions depends on the extent of SMV-PV involvement that differentiates BR from resectable tumors. The NCCN definition for BR PDAC has changed multiple times over the years, but currently includes tumors of the head/uncinate process that contact the CHA without extension to the celiac axis or the hepatic artery bifurcation, contact less than or equal to 180° of the SMA, contact greater than 180° of the SMV or PV, contact less than or equal to 180° with a contour irregularity or thrombosis of the SMV-PV with suitable vessel proximal and distal that
allows venous resection and reconstruction, or contact with inferior vena cava. Tumors of the body/tail are classified as BR when there is contact of less than or equal to 180° with the celiac axis or contact of greater than 180° with the celiac axis without involvement of the aorta and an intact and uninvolved gastroduodenal artery (Version 2.2015) (Table 1).

A current multi-institutional treatment trial investigating preoperative FOLFIRINOX (folinic acid, fluorouracil, irinotecan, oxaliplatin) and chemoradiation defines BR PDAC as radiographically localized tumors with 1 or more of the following: (1) an interface between the tumor and SMV-PV of greater than or equal to 180°, (2) short-segment occlusion of the SMV-PV with normal vein above and below that is amenable to resection and reconstruction, (3) short-segment interface between the tumor and hepatic artery with normal artery proximal and distal that is amenable to resection and reconstruction, (4) interface between the celiac axis or the SMA less than 180°.29

Although no consensus definition for BR has been reached, common themes can be appreciated. All BR criteria include statements regarding the ability or inability of the surgeon to reconstruct the SMV-PV or the hepatic artery involved with tumor. These statements imply that anatomic resectability depends heavily on the judgment and experience of the surgeon. The importance of this expertise cannot be overemphasized. In contrast, another common theme of borderline criteria is the exclusion of tumors involving greater than 180° of the SMA: a practice largely derived from the concept that tumor involvement of the nerves and periadventitial tissue reflects an aggressive tumor biology that likely cannot be overcome through surgical technique alone.

**MANAGEMENT**

Despite differences in definitions of BR PDAC, there is agreement that these patients are at a higher risk for margin-positive resection, and that preoperative therapy is prudent. Since initially described by Rich and Evans30 in 1995, the potential benefits of preoperative therapy have been itemized and include (1) early treatment of

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<td><strong>CA</strong></td>
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<td><strong>CHA</strong></td>
<td>Abutment of short-segment encasement</td>
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<td><strong>SMA</strong></td>
<td>Abutment &lt;180°</td>
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<td><strong>SMV/PV</strong></td>
<td>Short-segment occlusion amenable to resection and reconstruction</td>
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*Abbreviations: CA, celiac axis; CH, common hepatic artery; SMA, superior mesenteric artery; SMV/PV, superior mesenteric vein/portal vein.*
micrometastatic disease; (2) higher proportion of patients receiving multimodal therapy; (3) select patients with localized disease and more favorable tumor biology, who are most likely to benefit from surgical resection; (4) increased likelihood of an R0 resection; and (5) smaller radiation fields with well-oxygenated tissue. At MDACC, all patients with BR PDAC receive chemotherapy, chemoradiation, or both before surgical resection. Chemotherapy regimens have continued to evolve over the years; currently, most patients receive either gemcitabine with nab-paclitaxel or FOLFIRINOX. External beam radiation therapy is used and consists of 50.5 Gy delivered in 28 fractions or 30 Gy in 10 fractions with a concomitant radiosensitizing dose of 5-fluorouracil, gemcitabine, or capecitabine. The most common treatment sequence for BR PDAC is 2 to 4 months of chemotherapy, followed by chemoradiation, and a 6-week treatment break before surgical resection. Patients are typically restaged every 2 months. Patients only undergo surgical resection if the operating surgeon and multidisciplinary treatment group reach consensus that pancreatectomy will safely achieve an R0 resection and provide a reasonable chance for cure.

Restaging should include a pancreas protocol CT scan and measurement of CA19-9. Katz and colleagues evaluated the radiographic response, using response evaluation criteria in solid tumors (RECIST) criteria, of 129 patients with BR PDAC after completion of preoperative therapy (Fig. 3). The preoperative therapy consisted of gemcitabine-based chemotherapy followed by chemoradiation (30 Gy or 50.4 Gy) or chemoradiation alone. One-hundred and twenty-two patients completed therapy and were restaged, 84 (69%) had stable disease, 15 (12%) had a partial response, 23 (19%) had progressive disease (development of metastases, n = 21; primary tumor growth, n = 2), and no patient had a complete response. All patients were classified by the MDACC and AHPBA/SSO/SSAT definitions, and only 1 patient was downstaged, whereas approximately 80% remained at the same stage and 20% were upstaged.

**Fig. 3.** Outcomes after preoperative therapy for 129 patients with borderline tumor criteria classified by AHPBA/SSO/SSAT and MDACC criteria. Regardless of criteria, local downstaging or progression is uncommon. After initial staging, 5 patients did not return for restaging for unclear reasons, possibly a decline in PS. BLR, borderline resectable; Cx, chemotherapy; CXRT, chemoradiation; LA, locally advanced; LP, local progression; PR, potentially resectable; PS, performance status.
The main purpose of a restaging CT scan is to rule out disease progression, not necessarily to look for downstaging. Donahue and colleagues\textsuperscript{32} reported a series of patients with BR and LA pancreaticobiliary malignancies who were treated with preoperative chemotherapy and were restaged with CT/MRI imaging, which only had a 71% sensitivity and 58% specificity for vascular involvement after completion of preoperative therapy.\textsuperscript{32} Ferrone and colleagues\textsuperscript{33} reported a series of patients with BR and LA PDAC treated with preoperative FOLFIRINOX with or without radiation therapy, and 30% were deemed resectable on posttreatment imaging. Most patients were still classified as LA (48%) and BR (22%), because there were no clear fat planes around the critical vascular structures. Nonetheless, an R0 resection was achieved in 92% of the patients.\textsuperscript{33} Current cross-sectional imaging does not differentiate viable tumor from fibrosis.

Another important data point to consider during a restaging visit is the CA19-9 level. Tzeng and colleagues\textsuperscript{34} compared pretreatment and posttreatment CA19-9 levels in patients with BR PDAC. All patients had a pretreatment CA19-9 level greater than or equal to 40 U/mL and a total bilirubin level less than or equal to 2 mg/dL. A decline in CA19-9 level was seen in 116 (82%) patients and 47 (33%) had normalization of CA19-9. Posttreatment CA19-9 level was a predictor of failure to undergo pancreatectomy. Normalization of CA19-9 level was associated with improved median overall survival in resected (38 vs 26 months, \(P<.02\)) and unresected patients (15 vs 11 months, \(P = .02\)).\textsuperscript{34} After completion of preoperative chemotherapy/chemoradiation, patients without evidence of radiographic disease progression and a decrease in CA19-9 level should undergo attempted surgical resection, if medically fit for an operation.

The application of these management approaches is described in a recent report in which 160 patients with BR PDAC (BR-A 84, BR-B 44, BR-C 32) were followed prospectively. One-hundred and twenty-five (78%) patients completed induction therapy and a restaging evaluation. Forty-three patients were determined to not be surgical candidates: poor performance status (n = 10), distant disease progression (n = 16), and unresectable local-regional disease (n = 17). Seventy-nine patients were taken to the operating room, 9 were found to have radiographically occult distant metastases, 4 had LA disease, and the other 66 underwent a grossly complete resection of the primary tumor; 53% of the patients underwent restaging. Most underwent a PD (86%), 27% required an SMV-PV resection, and an additional 3% required a hepatic artery resection. An R0 resection was achieved in 94% of the patients, 4 patients had microscopically positive margins (2 SMA, 1 pancreatic duct, 1 bile duct). Twenty-six (39%) patients had nodal metastases. A partial or complete pathologic response (<50% remaining viable tumor cells) was seen in 56% of patients, and 4 patients (6%) had a complete pathologic response. Considering the cohort of 160 patients, 41% of patients underwent resection; the resection rates for BR-A, BR-B, and BR-C were 38%, 50%, and 38%, respectively. The median overall survival for the cohort was 18 months, with a 5-year survival of 18%. For the 66 patients who completed all therapy, the median survival was 40 months with a 5-year survival of 36%.\textsuperscript{16} Together, these prospective data provide support for planned and ongoing single-institution and multi-institutional prospective studies evaluating this multidisciplinary approach for patients with BR PDAC.

**SURGICAL TECHNIQUE**

Once the decision to perform surgical resection is reached, the surgeon must adhere to certain principles necessary for safe and oncologically effective pancreatectomy, so that the patient has a chance for cure. There are several variables associated
with improved patient survival after up-front surgical resection of localized PDAC. These variables include smaller tumor diameter, histologic grade (well differentiated or moderate differentiation), absence of lymph node metastases, negative surgical margins, and receipt of adjuvant therapy. Although many of these variables are outside a surgeon’s control, pathologically negative margins and a patient’s ability to receive therapy after surgery are heavily influenced by surgical technique and postoperative morbidities. However, in large series, up to 42% of patients underwent a margin-positive PD. A recent rapid autopsy series of patients with localized PDAC showed that 80% of patients treated with up-front surgical resection died with local recurrence, and 15% died of local recurrence alone. Of note, 5 of 6 patients who underwent a positive-margin PD recurred locally. A positive margin pancreatectomy should be viewed as a failure of patient selection, treatment strategy, and/or surgical technique. Routine use of planned segmental resection of the SMV-PV during PD was initially described in 1996 as a safe method of achieving negative margins when the primary tumor and SMV-PV interface were obliterated. Importantly, no difference in tumor biology or cancer-related outcome were observed suggesting that loss of the dissection plane between tumor and SMV-PV is an anatomic consequence more than an indicator of aggressive tumor biology.

Performing a PD for a BR-A tumor requires a high level of technical expertise. The principles of oncologic and vascular surgery must simultaneously be applied in order to achieve the following surgical objectives:
1. Maintenance of hepatic artery blood flow
2. Exposure and meticulous dissection of the SMA
3. Preservation of portal venous flow from the stomach, spleen, and intestines, while minimizing the risk of sinistral portal hypertension

Tumor encasement of the SMV-PV confluence is challenging, because it limits the exposure of the proximal SMA. During a procedure without vascular involvement, after the SMV-PV is freed from the pancreas and uncinate process, the venous confluence is retracted to the patient’s left, so the proximal SMA can be exposed; this maneuver is not possible when there is encasement of the SMV-PV. When the SMV-PV is encased, division of the splenic vein allows retraction of the SMV-PV to the patient’s right. Next, the periadventitial plane on the SMA is accessed sharply caudal to the tumor and followed cephalad to the proximal portion of the SMA. After division of the remainder of the retroperitoneal tissues, the tumor and specimen are attached by only the SMV-PV confluence. After obtaining proximal and distal vascular control and heparinizing the patient, the vein is resected at a level to ensure negative margins but also being cognizant to preserve as much vein as possible. Portal venous flow can be restored with a primary venous anastomosis, vein patch, or internal jugular interposition, depending on the defect after venous resection. Resection of infiltrating tumors commonly requires ligation of the 3 main veins that drain the stomach: the coronary, right gastric, and right gastroepiploic veins. Venous outflow from the stomach can be comprised, especially after splenic vein ligation. If the IMV drains directly into the SMV, then we perform a splenorenal shunt to prevent sinistral hypertension. If the IMV drains into the splenic vein, then we do not perform a shunt, and rely on retrograde flow through the IMV. Arterial resection can be necessary for tumors in the head of the pancreas that extend cephalad along the gastroduodenal artery to involve the common or proper hepatic arteries. In addition, an aberrant right hepatic artery or CHA arising from the SMA can easily be involved by a tumor in the head. The same principals discussed earlier for venous resection apply to arterial resection. After arterial resection, hepatic artery flow is restored with a saphenous vein interposition graft or polytetrafluoroethylene graft.
The SMA margin is the margin that is most frequently positive after a PD.\textsuperscript{40,41} As previously mentioned, the Johns Hopkins rapid autopsy series revealed that 80\% of patients had evidence of local recurrence, and 15\% had isolated local recurrence.\textsuperscript{35} This finding highlights the importance of adherence to the surgical principals outlined earlier. Katz and colleagues\textsuperscript{42} evaluated recurrence patterns in 194 patients with CR and BR PDAC with respect to the use of preoperative chemoradiation and SMA margin status. Fifteen (8\%) patients had an R1 resection; the SMA margin was the most commonly involved margin. An additional 40 (22\%) patients had a negative margin, but the margin distance was less than or equal to 1 mm. Patients who received preoperative chemoradiation had longer SMA margin distances ($P < .01$). Patients who underwent up-front surgical resection and had an SMA margin distance less than or equal to 1 mm had the highest overall (82\%), locoregional (36\%), and distant (50\%) recurrence rates. CT scan overestimated the distance between the cancer and the SMA in 73\% of cases. Liu and colleagues\textsuperscript{43} found that the SMA margin distance is an independent predictor of both disease-free and overall survival in patients with PDAC treated with preoperative therapy. Adherence to meticulous surgical technique with periadvential SMA dissection and preoperative chemoradiation should be used to maximize the SMA margin (Fig. 4).

**SUMMARY**

Patients with BR PDAC represent a heterogeneous group of patients at high risk of regional and distant recurrence after therapy. The first step is to evaluate, accurately identify, and stage, so that a treatment plan can be derived accordingly for each patient. A multidisciplinary approach using preoperative chemotherapy and/or chemoradiation is necessary to select patients who are most likely to benefit from pancreatectomy. In the patients receiving surgery, a safe and oncologically sound resection of the primary tumor is achieved through meticulous retroperitoneal dissection and vascular resection if necessary. Postoperative recovery that allows additional systemic therapy provides patients with the greatest opportunity for long-term survival.
REFERENCES


