ORIGINAL ARTICLE – CONSENSUS REPORT: RESECTABLE AND BORDERLINE RESECTABLE PANCREAS CANCER

Surgical Treatment of Resectable and Borderline Resectable Pancreas Cancer: Expert Consensus Statement

Douglas B. Evans, MD[1], Michael B. Farnell, MD[2], Keith D. Lillemoe, MD[3], Charles Vollmer Jr, MD[4], Steven M. Strasberg, MD[5], and Richard D. Schulick, MD[6]

[1]Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX; [2]Division of Gastroenterologic and General Surgery, Mayo Clinic, Rochester, MN; [3]Department of Surgery, Indiana University School of Medicine, Indianapolis, IN; [4]Department of Surgery, Beth Israel Deaconess Medical Center, Boston, MA; [5]Department of Surgery, Washington University School of Medicine, St. Louis, MO; [6]Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD

LYMPHADENECTOMY: STANDARD OR EXTENDED?

The regional pancreatectomy first described by Fortner in 1973 was complex and not adopted by Western pancreatic surgeons.[1] In contrast, Japanese surgeons were influenced by Fortner's concept of extended lymph node dissection and soft-tissue clearance for resectable pancreatic head cancer. The rationale for a more extensive procedure was based on the observation that standard Whipple resection does not encompass nodal groups often involved with microscopic disease,[2–7] and that many patients frequently experienced local recurrence after resection.[8]

In the 1980s, several Japanese surgeons reported survival rates after pancreatic head resection superior to those achieved in the Western hemisphere. These reports were criticized because of the use of historical controls and lack of randomization.[2,5,8–13] These studies prompted surgical groups in the Western hemisphere to embark upon prospective, randomized trials addressing the question of more extensive operation for patients with pancreatic head cancer.

In the last decade, the results of four prospective and randomized trials comparing standard lymphadenectomy to pancreaticoduodenectomy with extended lymphadenectomy have been published (Table 1). Two of the studies were multi-institutional, one from Japan and the other from Italy.[14,15] Adjuvant therapy was not employed. The two studies in the United States were from single large institutions: Johns Hopkins and Mayo Clinic.[16–20] Adjuvant therapy was used for the majority in both of these studies. Three of the trials included only patients with adenocarcinoma of the head of the pancreas,[14,15,20] while in the Hopkins study, patients with ampullary, distal bile duct, and duodenal adenocarcinoma were included.[16] Extended lymphadenectomy was performed en bloc in the two multi-institutional studies[14,15] and sequentially in the two U.S. trials,[16,20] and the extent of lymph node and soft tissue clearance was similar in three studies.[14,15,20] The lymphadenectomy performed by the Hopkins group was not as extensive as in the other three trials.[16] These four studies concluded that the performance of an extended lymph node dissection added, on average, between 25 min and 2 h of operating time, carried similar morbidity and mortality as a standard lymphadenectomy, and conferred no improved long-term survival.

Pawlik et al. proposed a mathematical model in an attempt to calculate the number of patients that would

TABLE 1 Prospective randomized trials of pancreaticoduodenectomy with standard versus extended lymphadenectomy for pancreatic head adenocarcinoma

	No. patients	Node dissection	R_0	No. nodes harvested	Patients with positive N_2 nodes (%)	Morbidity	Mortality (%)	Adjuvant therapy	Quality of life	Actuarial survival
Pedrazzoli et al.[14]		En bloc	75%	$P < 0.03$	NA	Same		No	NA	4 year, NS
PD	40			13.3			5			12%
PD/ELND	41			19.8			5			6%
Yeo et al.[16–19]		Sequential	90%	$P = 0.001$	15%	LOS, DGE, fistula, wound infection		Yes	Validated tool, no change, mean 2 year	5 year, NS
PD	81			17			3.7			10%
PD/ELND	82			28.5			2.5			25%
Nimura et al.[15]		En bloc	NA		NA	Transfusion, diarrhea		No	No validated tool	3 year, NS
PD	51			13			0			28.5%
PD/ELND	50			40			2			16%
Farnell et al.[20]		Sequential	79%	$P < 0.01$	29%	Transfusion, diarrhea, bowel control		Yes	Validated tool, poorer at 4 mo	5 year, NS
PD	38			15			0			16.5
PD/ELND	34			36			3			16.4

pancreaticoduodenectomy Standard pancreaticoduodenectomy, *LOS* length of stay, *pancreaticoduodenectomy /ELND* pancreaticoduodenectomy with extended lymphadenectomy, *DGE* delayed gastric emptying, R_0 margin negative resection, *mo* months, *QOL* quality of life, *NS* not significant, *NA* not available

benefit from extended lymphadenectomy for adenocarcinoma of the head of the pancreas.[21] Three assumptions were made: extended lymphadenectomy would benefit only patients (1) with N_2 disease (lymph node stations not harvested with standard lymphadenectomy but removed with the extended lymphadenectomy), (2) those in whom pancreaticoduodenectomy was accomplished with negative margins (R_0), and (3) those without evidence of distant metastatic disease (M_0). Based on review of 158 patients in whom information regarding the status of second-echelon lymph nodes was available, the authors were able to assign percentages to each of the three categories (M_0 5%, N_2 disease 10%, R_0 resection 80%). It is noteworthy that 70% of the 158 patients received neoadjuvant therapy that may have decreased the percentage of patients with N_2 disease. Based on these data and the above assumptions, Pawlik et al. calculated that only 1 in 250 patients would benefit from extended lymphadenectomy.[21]

The quality of life following operation was analyzed to varying extents in all four randomized controlled trials. In two of the trials,[18,20] validated instruments were used to assess postoperative quality of life; in two[14,15] the incidence of severe postoperative diarrhea was reported. In none of the four studies was the incidence of diabetes preoperatively and postoperatively addressed, and in only one was the need for pancreatic enzyme replacement evaluated.[18] The data from these four trials suggest that severe diarrhea may occur postoperatively from circumferential dissection of the nerve plexus around the superior mesenteric artery (SMA) and that diarrhea improves within the first postoperative year.

Recent evidence suggest that the optimal number of lymph nodes to be examined following standard pancreaticoduodenectomy should be greater than or equal to 15.[22] In the four trials reviewed herein, the mean lymph node harvest in the standard lymphadenectomy group ranged from 13 to 17. While the mean number of lymph nodes removed in these four studies is commendable, as many as half of the patients may have had insufficient lymph nodes removed to optimize staging. Accordingly, both the surgical and pathology teams should endeavor to remove and analyze adequate lymph nodes to avoid stage migration effect.

Consensus Statement

1. Data from four prospective, randomized controlled trials involving a total of 424 patients suggest that extended lymphadenectomy confers no survival advantage over standard lymphadenectomy and may be associated with compromised quality of life, particularly in the early postoperative period. Pancreaticoduodenectomy with standard lymphadenectomy should be the operation of choice for patients with ductal adenocarcinoma of the head of the pancreas.

2. Cooperation between both the operating surgeon and the surgical pathologist should ensure analysis of a sufficient number of lymph nodes to optimize staging.

VASCULAR RESECTION AS PART OF PANCREATICODUODENECTOMY FOR PANCREAS CANCER

Portal vein (PV) resection at the time of pancreaticoduodenectomy was initially performed in an attempt to improve survival duration by performing an en bloc resection of the pancreas and surrounding structures.[23] This concept was popularized by Fortner in 1973 when he proposed "regional pancreatectomy," which involved the systematic resection of major peripancreatic vascular structures together with wide soft tissue clearance.[1] Contrary to the beliefs of Fortner and others, radical or extended pancreaticoduodenectomy has not been demonstrated to confer a survival benefit.[17] Most physicians and many surgeons assume that the negative experience with regional pancreatectomy also applies to patients with isolated tumor extension to involve a short segment of the superior mesenteric vein (SMV) or PV; in such patients the only factor preventing complete tumor resection is the area of venous involvement. Because of this, patients with suspected isolated tumor involvement of the SMV, PV, or SMV-PV confluence (by computed tomography [CT] or at the time of laparotomy) are often classified as having locally advanced, stage III pancreatic cancer. Patients with stage III disease have a median survival of 10–12 months, far inferior to the survival duration of 2 years demonstrated for patients with isolated venous involvement treated with vascular resection and reconstruction at the time of pancreaticoduodenectomy.[24–26]

Vascular resection and reconstruction at the time of pancreaticoduodenectomy remains controversial because of:

- The complexity of the operative procedure (when venous or arterial resection and reconstruction is added to pancreaticoduodenectomy), the limited experience of many surgeons (with the technical aspects of vascular surgery), and the potential for increased perioperative death and major morbidity.

- The aggressive natural history of pancreatic adenocarcinoma, which results in a short survival for most patients, even those who undergo a potentially curative R0 pancreaticoduodenectomy. This causes most physicians/surgeons to want to minimize perioperative risk.

- The poor quality of the published data that examines vascular resection as a prognostic factor for survival duration. This is largely due to the lack of standardized

pathologic evaluation and reporting of the pancreaticoduodenectomy specimen.

The concern regarding safety of venous resection during pancreaticoduodenectomy when the procedure is performed in high-volume centers is unjustified. Morbidity and mortality rates are similar with or without venous resection in properly selected patients and at high-volume centers. Technical advances such as the "SMA first technique" have added to the safety of venous resection. Importantly, recent data suggest that the survival duration of patients who undergo venous resection and reconstruction is not different from those who undergo standard pancreaticoduodenectomy when an R0/R1 resection is performed.[25,26] Therefore, predictably, the population of patients who have venous invasion and who might still have a R0/R1 resection, but do not, are being denied the same opportunity for cure as those who do not have venous invasion.

The difficulty in data acquisition and analysis is largely due to the failure to implement surgical and pathology quality control that is necessary to determine the presence or absence of a gross and microscopic complete resection. Such data are not available in many reports of venous resection at the time of pancreaticoduodenectomy (Table 2).[25,27–41] In the absence of prospective evaluation of the SMA margin (also referred to as retroperitoneal, uncinate, mesenteric margin), reports of venous resection during pancreaticoduodenectomy are impossible to interpret. Stated otherwise, failure may be attributed to ineffectiveness of venous resection for venous invasion when in fact it is caused by a positive margin elsewhere on the specimen.

When venous involvement is an unexpected finding at the time of pancreaticoduodenectomy, surgeons may attempt to separate the SMV-PV confluence from the pancreatic head. When this maneuver is unsuccessful, the surgeon is left with either a grossly positive margin or an inadvertent venotomy. Venous injury often results in uncontrolled hemorrhage and the necessity for rapid removal of the tumor without proper attention to the SMA dissection; it is easy to appreciate how such cases may result in an R2 resection. Therefore, studies that retrospectively examine the presence or absence of vascular resection as a prognostic factor for survival should include only those patients who have undergone a complete gross resection (R0 or R1). Patients who have undergone an R2 resection have persistent disease that will largely determine their survival duration. It is inappropriate to include such patients in an analysis of prognostic factors predictive of survival duration under the assumption that they have undergone complete tumor removal. The current (Sixth) edition of the AJCC Staging Manual emphasizes the importance of the R designation in all pathology reports. The surgeon must document (in the operative dictation) the presence or absence of a complete gross resection at the time of pancreaticoduodenectomy.[42]

In contrast to tumor-artery abutment, which can be accurately interpreted on good-quality CT imaging, tumor abutment of the lateral or posterolateral wall of the SMV or the SMV-PV confluence: (1) does not always imply tumor adherence and (2) even when tumor adherence is present, it may not always be appreciated on preoperative imaging. However, subtle deformity of the vein wall at the tumor interface often indicates tumor adherence and may only be appreciated if the CT images are performed with a venous phase of contrast enhancement and are accurately interpreted. This deformity is usually on the right wall of the vein and is

TABLE 2 Reports of pancreaticoduodenectomy with venous resection	First author (year)	No. patients	% Operative mortality	Median survival (mo)	No. positive margin (%)
	Al-Haddad[27] (2007)	22	0	NA	NA
	Riediger[28] (2006)	53	4	NA	16 (31)
	Carrere[29] (2006)	45	4.4	15	8 (18)
	Tseng[25] (2004)	141	2.1	23.4	24/110 (22)
	Poon[30] (2004)	12	0	19.5	1 (8)
	Capussotti[31] (2003)	22	0	NA	5/6 (83)[a]
	Howard[32] (2003)	13	8	13	3 (23)
	Shibata[33] (2001)	28	4	NA	8 (29)
	Van Geenen[34] (2001)[b]	34	0	14	20 (59)
	Bachellier[35] (2001)	21	3.2	12	8 (38)
	Launois[36] (1999)[b]	14	0	5	7 (50)
NA Not available/not reported	Roder[37] (1996)	22	0	8	15 (68)
[a] RP/SMA margin assessed in six of 22 patients	Harrison[38] (1996)	42	5	13	10 (24)
	Yeo[39] (1995)	10	NA	NA	NA
[b] Referenced in recently published NCCN guideline manuscript[42]	Trede[40] (1990)	12	0	NA	NA
	Sindelar[41] (1989)	20	20	12	NA

often manifested as straightening or "beaking" of the wall of the PV/SMV whose contour on cross-sectional imaging is normally round and symmetrical. Therefore, because of the limited experience of many surgeons with venous resection and reconstruction and the inability to consistently determine the presence or absence of tumor adherence/invasion preoperatively, current practice guidelines have failed to make a clear recommendation on the use of SMV or PV resection at the time of pancreaticoduodenectomy.[43] This, is so despite the inclusion of tumor-vein abutment and even minimal deformity in the definition of a resectable tumor.[43]

In summary, vascular resection and reconstruction at the time of pancreaticoduodenectomy adds an additional level of complexity to an already lengthy operation associated with significant morbidity and occasional mortality. However, the need for vascular resection probably does not impact survival duration if a complete resection (R0/R1) has been performed.

Consensus Statement

1. Pancreaticoduodenectomy with vein resection and reconstruction is the standard of practice for pancreatic adenocarcinomas, locally involving the PV/SMV, providing that adequate inflow and outflow veins are present, the tumor does not involve the SMA or HA, and a R0/R1 resection is reasonably expected.
2. Whipple specimens should be inked, examined, and reported by techniques in conformity with College of American Pathologists (CAP) or American Joint Committee on Cancer (AJCC) guidelines. Manuscripts that assess vascular (usually venous) resection as a prognostic factor for survival must include a system for the assessment of R status. This would include a clear description by the surgeon (in the operative report) of the presence or absence of gross residual disease, and a pathology report which conforms to CAP or AJCC guidelines.
3. Patients with pancreatic adenocarcinomas without distant metastases should be evaluated in institutions capable of and experienced in resection and reconstruction of major mesenteric veins.
4. Whipple procedures for pancreatic adenocarcinoma should be performed in institutions capable of and experienced in resection and reconstruction of major mesenteric veins.

MARGIN DEFINITION, ASSESSMENT, AND PROGNOSTIC SIGNIFICANCE

Margins in pancreatic cancer resection procedures occur at planes where the specimen is separated from surrounding structures or where the pancreas or bowel are divided. These include duodenal/gastric, common bile duct, proximal jejunal, and pancreatic neck transection margins, as well as margins measured "radially" or "tangentially" (anterior and posterior pancreatic surfaces).[42] The most important margin is the plane of abutment of the uncinate process with the SMA. Unlike other margins such as the posterior margin where a buffer of fat and areolar tissue lie between the pancreas and the margin, the uncinate process of the pancreas directly contacts the SMA as well as the neural and lymphatic plexus associated with the celiac trunk.[26,44] This margin is variously referred to as the uncinate, posterior pancreatic, mesenteric, or retroperitoneal margin. It should be referred to by the more appropriately descriptive term "SMA margin."

Margins can be described clinically and pathologically by R status, where R represents the degree of residual disease.[42] R0 means there is neither gross, nor microscopic evidence of cancer at the margin. R1 indicates grossly negative, but microscopically positive disease at the margin. Finally, R2 indicates that gross tumor remains. There is a paucity of detailed literature regarding margins and their influence on survival following pancreatic resections.[45,46] Most papers indicate total numbers or percentage of positive margin cases, yet do not provide R status by margin site.[47] Nor is the influence of the distance of the margin from edge of the tumor well understood.

Accordingly, some investigators have proposed standardization of the process of margin evaluation. This begins in the preoperative period with expert evaluation of the relationship between the tumor and with critical vasculature using high-quality imaging such as dual-phase CT with three-dimensional (3D) reconstruction. A major goal of this evaluation is to eliminate R2 resections prior to surgery. Next, the margins of resected specimens need to be properly oriented by the surgeon and the specimen inked by the pathologist or by the surgeon in the presence of a pathologist. Most importantly, the SMA margin should be evaluated using perpendicular, rather than en face, sampling which should lead to greater specificity, but possibly less sensitivity. It is critical that the surgeon and pathologist reconcile the R status collaboratively in the postoperative period. These principles have been nicely delineated in the current AJCC cancer staging manual (Sixth Edition).[42]

Clinical Impact of Positive Margins

Overall, positive margin rates are reported to range between 15% and 85% and, when present, these are regularly predictive of decreased survival.[26,46,48] Unfortunately, in many papers R2 and R1 margin results are lumped, making determination of the individual effect on survival of each of these outcomes is difficult. The SMA margin is most frequently involved (up to 85% of all positive margins). Increased blood loss and large tumor size are predictive of positive margins.[26] Outcomes of these historical series

indicate that any positive margin will have a survival equivalent to patients with palliative procedures alone.[46] However, the most contemporary series (in the setting of regular multimodality therapy, and no R2 resections) shows R1 resection median survival as high as 22 months. This differed significantly from 28 months for R0 resections, but R status did not predict survival on multivariate analysis.[26]

Surgical Technique

The effect of surgical technique on margin positivity has not been rigorously studied. Meticulous dissection of the pancreatic parenchyma off the adventitia of the SMA is advocated, but is not always practically possible.[26,44] Procedures have been proposed to minimize positive margins in body and tail tumors (RAMPS), and en bloc resection of adjacent organs to achieve positive margins is also appropriate.[49,50] Numerous devices are available to help the surgeon with transection of the pancreas, but none have been rigorously evaluated and none show superiority over the conventional clamp-and-ligate technique. Many surgeons perform frozen section analysis intraoperatively routinely; however, the utility of this practice is undefined in the literature, except in the specific circumstance of intraductal papillary mucinous neoplasm (IPMN).[51,52] Obtaining such analysis at the neck and bile duct transection points would seem appropriate in that further tissue may be resected to achieve a clean margin, if positive. However, this is practically not possible on the SMA margin where the artery provides the absolute boundary.

Cases with concomitant vein resection may have higher rates of positive margins, especially at the SMA margin, if the patients are not carefully selected. Venous wall invasion occurs up to two-thirds of the time when a decision is made to resect vein. However, despite these findings, on multivariate analysis survival is driven not by the positive margin, but rather by the larger tumor size encountered in these cases.[25] It is quite possible that vein resection may, in fact, decrease margin positivity, by facilitating a more controlled tumor resection off of the veins. Pylorus-preserving resection has been shown to have equivalent rates of margin positivity when compared to classical Whipple's resections, and extended lymphadenectomy procedures, likewise, are not superior in achieving clean margins.[17,53] On the other hand, a surgeon's experience appears to improve performance in this metric, with a threshold of >60 cases executed showing superior outcomes.[54]

Effect of Multimodality Oncologic Therapy

It is possible that combined multimodality (chemo/radiation) therapy may have a positive biologic effect on a positive margin.[26,55] The use of preoperative "neoadjuvant"

chemoradiation therapy has been studied in this regard and appears to provide lower rates of positive margins, although this does not necessarily equate to improved survival.[47] Similarly, focal "boosts" of adjuvant radiation to the positive resection margin may be beneficial.

Consensus Statement

1. Nomenclature regarding margins in pancreaticoduodenectomy should be should be standardized. Currently it is vague, confusing, and imprecise. The margin of the pancreas with the SMA should be termed "the SMA margin."
2. Pathologic assessment of margins is poorly standardized and inconsistently reported.
3. Whipple specimens should be inked, examined, and reported by techniques in conformity with CAP or AJCC guidelines. Manuscripts that assess vascular (usually venous) resection as a prognostic factor for survival must include a system for the assessment of R status. This would include a clear description by the surgeon (in the operative report) of the presence or absence of gross residual disease, and a pathology report that conforms to CAP or AJCC guidelines.
4. The utility of routine intraoperative frozen-section analysis should be determined by carefully planned studies.
5. Safe achievement of an R0 margin is the main surgical objectives of pancreaticoduodenectomy as it is great importance for extended survival. The SMA margin is the most important driver of this outcome.
6. The impact of a microscopically positive (R1) resection on ultimate clinical outcome is uncertain. Multimodality therapy may "recover" a R1 margin and improve survival to that similar to R0 resections.

PALLIATIVE PANCREATICODUODENECTOMY: DEFINITION AND INDICATIONS

Stedman's Medical Dictionary defines a palliative procedure as a "therapy that relieves symptoms, but does not cure the disease." It also defines a pancreaticoduodenectomy as "excision of all or part of the pancreas together with the duodenum." Putting these two terms together would imply that a palliative pancreaticoduodenectomy would be a pancreatic head resection that would alleviate symptoms, but would not cure the patient. Since the reported 5- and 10-year survival following pancreaticoduodenectomy for pancreatic ductal adenocarcinoma are less than 20% and 15%, respectively, one could argue that for the vast majority of patients undergoing this procedure for pancreatic cancer, palliation is the ultimate outcome.[56] Yet for most pancreatic surgeons, cure is the intent for each and every pancreaticoduodenectomy undertaken.

How does a pancreaticoduodenectomy intended for cure become a palliative procedure? In part this is based on the surgeon's inability to obtain an R0 resection. In most cases it requires an aggressive surgeon, confident in his or her ability, who is willing to persist in dissection and "burn the bridges" that ultimately requires a pancreaticoduodenectomy despite a high likelihood of a microscopic (R1) and sometimes even a grossly positive (R2) margin.

Is such an aggressive attitude appropriate? To determine the benefit, one must analyze the benefits of palliative pancreaticoduodenectomy versus either palliative surgery such as biliary and/or gastric bypass. These in turn should also be compared with endoscopic palliative techniques. Comparisons should include perioperative morbidity and mortality, long-term survival (even though the operation is not considered curative), and finally quality of life.

Unfortunately such studies are difficult to identify. In 1996, the Johns Hopkins group described a series of 64 consecutive patients undergoing pancreaticoduodenectomy with either gross or microscopically positive surgical margins—a so-called "palliative pancreaticoduodenectomy."[57] This group was compared with 62 consecutive patients who were found at laparotomy to be unresectable due to local invasion, but without metastatic disease. The two groups were similar with respect to age, gender, race, and presenting symptoms. The hospital mortality rate was identical in both groups (1.6%). Fifty-eight percent of the patients undergoing pancreaticoduodenectomy had an uncomplicated postoperative course compared with 68% of patients undergoing palliative bypass (not significant). The length of postoperative stay after pancreaticoduodenectomy was significantly longer than patients undergoing palliative bypass. The actuarial survival (Kaplan–Meier) was significantly improved in patients undergoing pancreaticoduodenectomy ($P < 0.02$). A formal quality-of-life assessment was not performed; however, 7 of the 62 patients (11%) discharged from the hospital after pancreaticoduodenectomy were readmitted to a hospital before their death, while 12 of 61 patients (20%) who did not undergo resection required a hospital readmission. No patient in the pancreaticoduodenectomy group required reoperation, while 3 patients undergoing palliative bypass required reoperation. This study concluded that selective use of "palliative pancreaticoduodenectomy" in patients with pancreatic cancer and residual local disease might be an appropriate option in selected high-volume centers.

A similar analysis has been reported by Reinders and colleagues showing comparable perioperative results and improved survival when patients undergoing microscopically positive margin Whipple resections were compared with patients undergoing palliative bypass.[58] A follow-up study from that institution confirmed their early results and demonstrated that patients undergoing "palliative"

resection spent a lower percentage of their overall survival time outside of the hospital than patients undergoing bypass.[59] In contrast Schniewind and colleagues showed that "palliative" resection patients had a trend to higher perioperative morbidity and mortality with significantly longer postoperative hospital stay.[60] In their analysis, palliative pancreaticoduodenectomy was not associated with improved long-term survival. These authors performed a validated quality–of-life analysis of all patients that also showed nonsignificant trend to a poorer quality of life after resection. Finally, a prospective randomized trial performed in Japan compared pancreatic resection with no surgery and chemoradiation in patients with locally advanced nonmetastatic pancreatic cancer.[61] In this study, 1-year (62% vs. 32%, $P = 0.05$) and mean survival time (>17 vs. 11 months, $P < 0.03$) were improved with surgery. There were no differences in quality-of-life scores between the two groups.

In conclusion, the quality of surgical imaging has improved markedly over the last decade, resulting in the better preoperative staging of patients with pancreatic cancer. Yet it is still only at laparotomy that the experienced pancreatic surgeon can definitely determine resectability for many patients. Thorough, complete dissection is necessary to make the final determination of resectability that in many cases may require the surgeon to complete steps that "burn the bridge" and mandate performing a pancreaticoduodenectomy, only to be left with either microscopic or grossly positive margins. Although these procedures are generally initiated with the intent of curative (R0) resection, it appears that the resulting palliative resection can be performed with satisfactory perioperative results and improved survival when compared with palliative bypass procedures. The limited analyses available would suggest that quality of life is comparable and perhaps resection decreases the need for hospitalization after discharge.

Consensus Statement

1. Although the goal for surgical treatment of pancreatic cancer is to complete an R0 resection, this is not accomplished in a substantial proportion (30%) of patients even at major centers.
2. An aggressive approach by an experienced pancreatic surgeon is appropriate in order to achieve an R0 resection, knowing that some will end up with R1 and even R2 resections.
3. Some studies demonstrate that a margin positive resection in this setting may yield a survival and quality-of-life advantage compared with standard surgical bypass without increasing perioperative morbidity or mortality.

4. There is no role for "palliative resection" of pancreatic cancer in the setting of metastatic or preoperatively apparent locally extensive disease.

REFERENCES

1. Fortner JG. Regional resection of cancer of the pancreas: a new surgical approach. *Surgery*. 1973;73:307–20.
2. Takahashi S, Ogata Y, Miyazaki H, Maeda D, Murai S, Yamataka K, et al. Aggressive surgery for pancreatic duct cell cancer: feasibility, validity, limitations. *World J Surg*. 1995;19: 653–9; discussion 60.
3. Cubilla AL, Fortner J, Fitzgerald PJ. Lymph node involvement in carcinoma of the head of the pancreas area. *Cancer*. 1978;41: 880–7.
4. Reber HA, Ashley SW, McFadden D. Curative treatment for pancreatic neoplasms. Radical resection. *Surg Clin North Am*. 1995;75 905–12.
5. Satake K, Nishiwaki H, Yokomatsu H, Kawazoe Y, Kim K, Haku A, et al. Surgical curability and prognosis for standard versus extended resection for T1 carcinoma of the pancreas. *Surg Gynecol Obstet*. 1992;175:259–65.
6. Kayahara M, Nagakawa T, Ueno K, Ohta T, Tsukioka Y, Miyazaki I. Surgical strategy for carcinoma of the pancreas head area based on clinicopathologic analysis of nodal involvement and plexus invasion. *Surgery*. 1995;117:616–23.
7. Liu CD, Slice LW, Balasubramaniam A, Walsh JH, Newton TR, Saxton RE, et al. Y2 receptors decrease human pancreatic cancer growth and intracellular cyclic adenosine monophosphate levels. *Surgery*. 1995;118: 229–35; discussion 35–6.
8. Ishikawa O, Ohhigashi H, Sasaki Y, Kabuto T, Fukuda I, Furukawa H, et al. Practical usefulness of lymphatic and connective tissue clearance for the carcinoma of the pancreas head. *Ann Surg*. 1988;208:215–20.
9. Manabe T, Ohshio G, Baba N, Miyashita T, Asano N, Tamura K, et al. Radical pancreatectomy for ductal cell carcinoma of the head of the pancreas. *Cancer*. 1989;64:1132–7.
10. Tsuchiya R, Oribe T, Noda T. Size of the tumor and other factors influencing prognosis of carcinoma of the head of the pancreas. *Am J Gastroenterol*. 1985;80:459–62.
11. Tsuchiya R, Eto T, Tsunoda T. Radical resection of pancreatic and periampullary neoplasms. Pancreatoduodenectomy. In: Braasch J, Tompkins R, eds. *Surgical disease of the biliary tract and pancreas. Multidisciplinary management*. St. Louis: Mosby, 1994: 570–87.
12. Hirata K, Sato T, Mukaiya M, Yamashiro K, Kimura M, Sasaki K, et al. Results of 1001 pancreatic resections for invasive ductal adenocarcinoma of the pancreas. *Arch Surg*. 1997;132:771–6; discussion 7.
13. Ishikawa O, Ohigashi H, Sasaki Y, Kabuto T, Furukawa H, Nakamori S, et al. Practical grouping of positive lymph nodes in pancreatic head cancer treated by an extended pancreatectomy. *Surgery*. 1997;121:244–9.
14. Pedrazzoli S, DiCarlo V, Dionigi R, Mosca F, Pederzoli P, Pasquali C, et al. Standard versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical treatment of adenocarcinoma of the head of the pancreas: a multicenter, prospective, randomized study. Lymphadenectomy Study Group. *Ann Surg*. 1998;228:508–17.
15. Nimura Y, Nagino M, Kato H, Miyagawa S, Yamaguchi A, Kinoshita T, et al. Regional vs extended lymph node dissection in radical pancreaticoduodenectomy for pancreatic cancer. A multicenter randomized controlled trial. *HPB*. 2004;6:2 (abstract).

16. Yeo CJ, Cameron JL, Sohn TA, Coleman J, Sauter PK, Hruban RH, et al. Pancreaticoduodenectomy with or without extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma: comparison of morbidity and mortality and short-term outcome. *Ann Surg*. 1999;229:613–22; discussion 22–4.
17. Yeo CJ, Cameron JL, Lillemoe KD, Sohn TA, Campbell KA, Sauter PK, et al. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. *Ann Surg*. 2002; 236:355–66; discussion 66–8.
18. Nguyen TC, Sohn TA, Cameron JL, Lillemoe KD, Campbell KA, Coleman J, et al. Standard vs. radical pancreaticoduodenectomy for periampullary adenocarcinoma: a prospective, randomized trial evaluating quality of life in pancreaticoduodenectomy survivors. *J Gastrointest Surg*. 2003;7:1–9; discussion 11.
19. Riall TS, Cameron JL, Lillemoe KD, Campbell KA, Sauter PK, Coleman J, et al. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma—part 3: update on 5-year survival. *J Gastrointest Surg*. 2005;9:1191–204; discussion 204–6.
20. Farnell MB, Pearson RK, Sarr MG, DiMagno EP, Burgart LJ, Dahl TR, et al. A prospective randomized trial comparing standard pancreatoduodenectomy with pancreatoduodenectomy with extended lymphadenectomy in resectable pancreatic head adenocarcinoma. *Surgery*. 2005;138:618–28; discussion 28–30.
21. Pawlik TM, Abdalla EK, Barnett CC, Ahmad SA, Cleary KR, Vauthey JN, et al. Feasibility of a randomized trial of extended lymphadenectomy for pancreatic cancer. *Arch Surg*. 2005;140: 584–9; discussion 9–91.
22. Tomlinson JS, Jain S, Bentrem DJ, Sekeris EG, Maggard MA, Hines OJ, et al. Accuracy of staging node-negative pancreas cancer: a potential quality measure. *Arch Surg*. 2007;142:767–23; discussion 73–4.
23. Asada S, Itaya H, Nakamura K, Isohashi T, Masuoka S. Radical pancreatoduodenectomy and portal vein resection. Report of two successful cases with transplantation of portal vein. *Arch Surg*. 1963;87:609–13.
24. Wolff R, Crane C, Li D, Abbruzzese J, Evans D. Neoplasms of the exocrine pancreas. In: Kufe D, Bast R, Hait W, Hong WK, Pollock RE, Weichselbaum RR, et al., eds. *Holland-Frei Cancer Medicine*. Ontario: B.C. Decker, Inc., 2006:1331–58.
25. Tseng JF, Raut CP, Lee JE, Pisters PW, Vauthey JN, Abdalla EK, et al. Pancreaticoduodenectomy with vascular resection: margin status and survival duration. *J Gastrointest Surg*. 2004;8:935–49; discussion 49–50.
26. Raut CP, Tseng JF, Sun CC, Wang H, Wolff RA, Crane CH, et al. Impact of resection status on pattern of failure and survival after pancreaticoduodenectomy for pancreatic adenocarcinoma. *Ann Surg*. 2007;246:52–60.
27. Al-Haddad M, Martin JK, Nguyen J, Pungpapong S, Raimondo M, Woodward T, et al. Vascular resection and reconstruction for pancreatic malignancy: a single center survival study. *J Gastrointest Surg*. 2007;11:1168–74.
28. Riediger H, Makowiec F, Fischer E, Adam U, Hopt UT. Postoperative morbidity and long-term survival after pancreaticoduodenectomy with superior mesenterico-portal vein resection. *J Gastrointest Surg*. 2006;10:1106–15.
29. Carrere N, Sauvanet A, Goere D, Kianmanesh R, Vullierme MP, Couvelard A, et al. Pancreaticoduodenectomy with mesentericoportal vein resection for adenocarcinoma of the pancreatic head. *World J Surg*. 2006;30:1526–35.
30. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK, et al. Pancreaticoduodenectomy with en bloc portal vein resection for pancreatic carcinoma with suspected portal vein involvement. *World J Surg*. 2004;28:602–8.

31. Capussotti L, Massucco P, Ribero D, Vigano L, Muratore A, Calgaro M. Extended lymphadenectomy and vein resection for pancreatic head cancer: outcomes and implications for therapy. *Arch Surg*. 2003;138:1316–22.

32. Howard TJ, Villanustre N, Moore SA, DeWitt J, LeBlanc J, Maglinte D, et al. Efficacy of venous reconstruction in patients with adenocarcinoma of the pancreatic head. *J Gastrointest Surg*. 2003;7:1089–95.

33. Shibata C, Kobari M, Tsuchiya T, Arai K, Anzai R, Takahashi M, et al. Pancreatectomy combined with superior mesenteric-portal vein resection for adenocarcinoma in pancreas. *World J Surg*. 2001;25:1002–5.

34. van Geenen RC, ten Kate FJ, de Wit LT, van Gulik TM, Obertop H, Gouma DJ. Segmental resection and wedge excision of the portal or superior mesenteric vein during pancreatoduodenectomy. *Surgery*. 2001;129:158–63.

35. Bachellier P, Nakano H, Oussoultzoglou PD, Weber JC, Boudjema K, Wolf PD, et al. Is pancreaticoduodenectomy with mesentericoportal venous resection safe and worthwhile? *Am J Surg*. 2001;182:120–9.

36. Launois B, Stasik C, Bardaxoglou E, Meunier B, Campion JP, Greco L, et al. Who benefits from portal vein resection during pancreaticoduodenectomy for pancreatic cancer? *World J Surg*. 1999;23:926–9.

37. Roder JD, Stein HJ, Siewert JR. Carcinoma of the periampullary region: who benefits from portal vein resection? *Am J Surg*. 1996;171:170–4; discussion 4–5.

38. Harrison LE, Klimstra DS, Brennan MF. Isolated portal vein involvement in pancreatic adenocarcinoma. A contraindication for resection? *Ann Surg*. 1996;224:342–7; discussion 7–9.

39. Yeo CJ, Cameron JL, Lillemoe KD, Sitzmann JV, Hruban RH, Goodman SN, et al. Pancreaticoduodenectomy for cancer of the head of the pancreas. 201 patients. *Ann Surg*. 1995;221:721–31; discussion 31–3.

40. Trede M, Schwall G, Saeger HD. Survival after pancreatoduodenectomy. 118 consecutive resections without an operative mortality. *Ann Surg*. 1990;211:447–58.

41. Sindelar WF. Clinical experience with regional pancreatectomy for adenocarcinoma of the pancreas. *Arch Surg*. 1989;124:127–32.

42. Exocrine Pancreas. In: Greene F, Page D, Fleming I, Fritz AG, Balch CM, Haller DG, et al., eds. *AJCC Cancer Staging Manual*. New York: Springer-Verlag, 2002:157–64.

43. Tempero M, Arnoletti JP, Ben-Josef E, Bhargava P, Casper ES, Kim P, et al. Pancreatic adenocarcinoma. Clinical Practice Guidelines in Oncology. *J Natl Compr Cancer Netw*. 2007;5:998–1033.

44. Howard TJ, Krug JE, Yu J, Zyromski NJ, Schmidt CM, Jacobson LE, et al. A margin-negative R0 resection accomplished with minimal postoperative complications is the surgeon's contribution to long-term survival in pancreatic cancer. *J Gastrointest Surg*. 2006;10:1338–45; discussion 45–6.

45. Wagner M, Redaelli C, Lietz M, Seiler CA, Friess H, Buchler MW. Curative resection is the single most important factor determining outcome in patients with pancreatic adenocarcinoma. *Br J Surg*. 2004;91:586–94.

46. Forrest JF, Longmire WP, Jr. Carcinoma of the pancreas and periampullary region. *Ann Surg*. 1979;189:129–38.

47. Pingpank JF, Hoffman JP, Ross EA, Cooper HS, Meropol NJ, Freedman G, et al. Effect of preoperative chemoradiotherapy on surgical margin status of resected adenocarcinoma of the head of the pancreas. *J Gastrointest Surg*. 2001;5:121–30.

48. Sohn TA, Yeo CJ, Cameron JL, Koniaris L, Kaushal S, Abrams RA, et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg*. 2000;4:567–79.

49. Strasberg SM, Drebin JA, Linehan D. Radical antegrade modular pancreatosplenectomy. *Surgery*. 2003;133:521–7.

50. Christein JD, Kendrick ML, Iqbal CW, Nagorney DM, Farnell MB. Distal pancreatectomy for resectable adenocarcinoma of the body and tail of the pancreas. *J Gastrointest Surg*. 2005;9:922–7.

51. Cioc AM, Ellison EC, Proca DM, Lucas JG, Frankel WL. Frozen section diagnosis of pancreatic lesions. *Arch Pathol Lab Med*. 2002;126:1169–73.

52. Raut CP, Cleary KR, Staerkel GA, Abbruzzese JL, Wolff RA, Lee JH, et al. Intraductal papillary mucinous neoplasms of the pancreas: effect of invasion and pancreatic margin status on recurrence and survival. *Ann Surg Oncol*. 2006;13:582–94.

53. Tran KT, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW, et al. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. *Ann Surg*. 2004;240:738–45.

54. Tseng JF, Pisters PW, Lee JE, Wang H, Gomez HF, Sun CC, et al. The learning curve in pancreatic surgery. *Surgery*. 2007;141:456–63. Corrected and republished in: *Surgery* 2007;141:694–701.

55. Butturini G, Stocken DD, Wente MN, Jeekel H, Klinkenbijl JH, Bakkevold KE, et al. Influence of resection margins and treatment on survival in patients with pancreatic cancer: meta-analysis of randomized controlled trials. *Arch Surg*. 2008;143:75–83; discussion.

56. Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: a single-institution experience. *J Gastrointest Surg*. 2006;10:1199–210; discussion 210–1.

57. Lillemoe KD, Cameron JL, Yeo CJ, Sohn TA, Nakeeb A, Sauter PK, et al. Pancreaticoduodenectomy. Does it have a role in the palliation of pancreatic cancer? *Ann Surg*. 1996;223:718–25; discussion 25–8.

58. Reinders ME, Allema JH, van Gulik TM, Karsten TM, de Wit LT, Verbeek PC, et al. Outcome of microscopically nonradical, subtotal pancreaticoduodenectomy (Whipple's resection) for treatment of pancreatic head tumors. *World J Surg*. 1995;19:410–5; discussion 4–5.

59. Kuhlmann K, de Castro S, van Heek T, Busch O, van Gulik T, Obertop H, et al. Microscopically incomplete resection offers acceptable palliation in pancreatic cancer. *Surgery*. 2006;139:188–96.

60. Schniewind B, Bestmann B, Kurdow R, Tepel J, Henne-Bruns D, Faendrich F, et al. Bypass surgery versus palliative pancreaticoduodenectomy in patients with advanced ductal adenocarcinoma of the pancreatic head, with an emphasis on quality of life analyses. *Ann Surg Oncol*. 2006;13:1403–11.

61. Imamura M, Doi R, Imaizumi T, Funakoshi A, Wakasugi H, Sunamura M, et al. A randomized multicenter trial comparing resection and radiochemotherapy for resectable locally invasive pancreatic cancer. *Surgery*. 2004;136:1003–11.