

Cancer of the Pancreas— Actual 5, 10, and 20+ Year Survival: The Lucky and Fortunate Few



Avram M. Cooperman, MD^{a,*}, Howard Bruckner, MD^a,
Harry Snady, MD^a, Hillel Hammerman, MD^a, Andrew Fader, MD^a,
Michael Feld, MD^a, Frank Golier, MD^a, Tom Rush, MD^a,
Jerome Siegal, MD^a, Franklin Kasmin, MD^a, Seth Cohen, MD^a,
Michael G. Wayne, DO^a, Mazen E. Iskandar, MD^b,
Justin G. Steele, MD^a

KEYWORDS

- Cancer of the pancreas (CaP) • Pancreaticoduodenal resection (PDR)
- 5Fluorouracil, Streptozotocin, Cis-Platinum (FSP) • Chemoradiation therapy (CRT)
- Lead time bias, Selection bias, Length bias • Actual vs actuarial survival

KEY POINTS

- Cancer of the pancreas is an abysmal disease, increasing annually worldwide, and with dismal cure rates.
- Survival notwithstanding surgery remains the basis of therapy.
- Initial systemic treatment may improve selection, lower morbidity and improve survival.
- Since metastases exist before tumors are detected initial systemic therapy is indicated, and surgery in selective responders may be a more logical approach.
- Since 1986 a shared multidisciplinary approach has included initial multidrug chemo radiationtherapy at first in borderline resectable or regionally unresectable patients, and surgery after maximum response.
- In a 10 year period (1991–2000) 80/180 PDR's were for CaP and 17 (175) survived 5 + years, 15 ten plus years+ (15%) and 3, 20+ years (3%).
- Nearly half of the long term survivors were initially unresectable and had CRT before resection.
- Nearly 80% of the PDR's were done in a 50 bed community hospital in Dobbs Ferry NY, at a Center for Pancreatic and Biliary Surgery and care was provided by a multidisciplinary dedicated team.

Disclosure Statements: The authors have nothing to disclose.

^a The Pancreas, Biliary and Advanced Laparoscopy Center of New York, 305 Second Avenue, New York, NY 10003, USA; ^b Division of Surgical Oncology, Mount Sinai Beth Israel, New York, NY, USA

* Corresponding author.

E-mail address: avram.cooperman@gmail.com

Surg Clin N Am 98 (2018) 73–85

<https://doi.org/10.1016/j.suc.2017.09.007>

0039-6109/18/© 2017 Elsevier Inc. All rights reserved.

surgical.theclinics.com

INTRODUCTION

Cancer of the pancreas (CaP) is a dismal, uncommon, systemic malignancy. Although CaP is the twelfth most common malignancy and accounts for only 3% of all cancers, it is the 3-5th most common cause of cancer deaths worldwide and has the poorest survival of any solid cancer.¹⁻⁷ Significant gains in diagnosis by endoscopic and axial imaging, and by guided tissue sampling, facilitate accurate diagnosis. Selection of suitable candidates for resection is more objective and operative mortality has declined to less than 5%.^{6,8-11} All these advances are offset by the fact that the cure rate remains dismal and unchanged for 50 years.¹²⁻¹⁴ Systemic therapy may add 3 to 10 months to life and responses range from none to complete remission, with side effects of varying severity.¹⁵⁻¹⁷ These statistics aside, a few unpredictable CaP patients are fortunate and lucky to be long-term survivors or are cured.^{7-10,18-28}

This article updates an earlier experience of actual long-term survival of CaP in patients treated between 1991 to 2000, and reviewed the literature. Survival is expressed as actual, not projected, survival.⁷

UPDATED SERIES

Between May, 1991, and January 1, 2001, 180 pancreaticoduodenal resections (PDRs) were performed, including 80 for carcinoma of the pancreas (CaP). Seventy eight percent of operations were done at a 50-bed community hospital 18 miles from New York City (Table 1).⁷

OUTCOMES

There was 1 procedure-related death (0.55%), a cardiac event on the fifth postoperative day. For all patients, mean and median operative time was 150 minutes and mean hospital stay was 8 days. Blood was transfused during hospitalization in 14 (7%) operations, and a stage A pancreatic fistula developed in 6%, which closed spontaneously in all. The selection criteria for surgery and operative technique have been described.^{7,29-32}

OVERALL SURVIVAL

Seventeen patients survived 5 survived at least 5 years (21%), 15 at least ten years(19%), and 3 at least 20 years (4%) 2 of whom still survive. There were 3 groups. Group 1 had resection followed by adjuvant therapy (8), group 2 had resection and no additional therapy (1), and group 3 had chemotherapy (1) or chemoradiation therapy (7) followed by PDR (Table 2).

NEOADJUVANT THERAPY

Between 1984 and 1996, 346 patients with CaP were treated by 1 oncologist (HB). Of these, 168 had metastases or bulky local disease amenable to chemotherapy but not

Table 1 Demographics	
180 PDRs, 1994–2001	150 min operation time (180)
80 CaP (all adenocarcinoma), all PDR	8 d median hospitalization
62 PDR + adjuvant	7% blood tx
18 neoadjuvant + surgery	6% stage A pancreatic fistula
78% Dobb's Ferry Hospital	3 reoperations, 2 bleeding

Table 2 Current status years	
Living NED	17 4/12, 20 2/12, 23 4/12
Unknown status (NED last visit) ?	20 8/12, 14 5/12, 13 6/12, 15 1/12 13/7/12, 14 2/12.13
Died NED	12, 14 2/12, 15, 10 3/12, 11 1/12
Died of Mets	7, 9 10/12

radiation, 90 patients received adjuvant therapy after resection, and 88 unresectable patients were treated by chemoradiation therapy.³² Unresectability was determined at surgery in 52 and by axial imaging in 36. A positive biopsy of adenocarcinoma was obtained in all and confirmed in review.³³

CHEMORADIATION THERAPY

An initial 20 unresectable patients were part of a phase 2 study and the next 68 were included in this study. All were treated to maximum response. Chemoradiation therapy consisted of streptozotocin (350–500 mg/m2), cisplatin (100 mg/m2), and fluorouracil (1 g/m2). Radiation (5400 cGy) was split-course. The protocol was in-hospital Sunday to Friday, 1 week per month, and has been detailed.³³

SURGERY

Surgery-first, plus adjuvant therapy, was done in 62 PDRs. Surgery-last was considered in 22 out of 68 responders to neoadjuvant therapy. In 2 treatment toxicity and frailty precluded resection. Two underwent surgery elsewhere and died after complications. An initial 2 underwent surgery-last elsewhere and died after complications. The mean and median operative times for the 18 resected neoadjuvant subjects were 3 hours and 20 minutes and 3 hours. Two operations took more than 4 hours and the median and mean hospitalization was 13 and 16 days. Four were hospitalized for more than 20 days (21, 22, 29, and 32 days), including 3 with delayed gastric emptying after pylorus preservation (Table 1).⁷

OVERALL RESULTS

Tables 2 and 3 summarize overall survival and patient status as of April 2017. Seventeen survived at least 5 years, 15 at least 10 years, 9 at least 15 years and 3 at least 20 years. Five died with no evidence of disease (NED) and 7 were lost to follow-up, all NED (Table 2). Two developed second primary tumors, a lymphoma in the twentieth year (well in year 24) and a prostate cancer, which was fatal in year 15. Two others died of metastases in the seventh, and ninth year.

RESULTS OF NEOADJUVANT THERAPY

Eight of 15 who survived at least 10 years had neoadjuvant therapy. The 8 came from 68 neoadjuvant treated patients whereas the 9 whose initial treatment was surgery came from a much larger group of whom less than 10% were resectable. The 68 reported neoadjuvant patients were compared with 91 matched PDR-adjuvant therapy patients and there was a projected survival advantage for neoadjuvant therapy (23 vs 14 months), which increased to 33 months after resection. The difference would be more striking now given the 17 additional years of follow-up. Neoadjuvant therapy continued from 5–16 months (mean 11 months), until maximum tumor response. In

Table 3 Individual patient status			
Patient Initials	Date of Diagnosis (mo/y)	Date of Surgery	Status (mos)
PDR + ADJUVANT THERAPY			
TM	9/1994	—	D 144 NED
GM	9/1994	—	L 248 NED ?
AR	8/1996	—	L 173 NED ?
FW	7/1997	—	L 162 NED ?
RG	6/1998	—	L 181 NED ?
JR	11/1999	—	L 208 NED
RD	!2/2000	—	D 118 metastases
MH	9/2000	—	D 84 metastases
PDR NO ADJUVANT THERAPY			
FM	6/1995	—	L 163 NED ?
JP	1/1987	—	L 241 NED ?
NEOADJUVANT THERAPY + PDR			
NN	10/1990	5/1991	D 170 s primary
AK	9/1991	3/1992	L 170 NED ?
GS	10/1991	2/1992	L 280 NED
DD	8/1992	4/1993	L 156 NED ?
AB	7/1994	12/1994	D 180 NED
ES	11/1995	5/1996	D 123 NED
GF	2/1996	11/1996	D 133 NED
JS	2/1997	6/1998	L 242 NED

5 resected specimens, there was no residual gross or microscopic tumor, yet 3 patients died at 32, 32, and 19 months of metastases and 2 survived 10-plus years with NED.

DISCUSSION

Actual, not projected, 5 and 10 or more year survival from CaP is uncommon and the subject of several recent reports. The highest survival rates are from surgical databases and the lowest from population-based studies (Tables 4 and 5).^{7–11,18,28,34–42} The relative 1-year survival for CaP in England and Wales, 1971 to 1975, and 2005 to 2009, was 6% and 17.4% and the 5-year survival was 2% and 3.6%, respectively.^{4,21} Relative survival is the percent of patients with cancers surviving relative

Table 4 Population-based studies: CaP Patients - 5 year survival		
City, Country	Number of CaP Patients	5-y Survival (Estimated) (%)
Victoria, Australia	763	1.3
Shanghai, China	11,672	4.1
Norway	21,163	<3
San Francisco, CA, USA	1954	1.3
Sweden	4321	2.8
Finland	4922	0.6

Table 5
Actual 5-plus-year survival literature review

Institution	Number of Subjects	5-y Survival (%)	10-y Survival (%)	20-y Survival (%)
Manheim, Germany	53	13	8	—
Johns Hopkins	201	10	1	—
Dobbs Ferry, NY	80	21	19	4
Toronto	123	14.6	4	—
Amsterdam	160	4	—	—
Nagoya, Japan	182	4.3	—	—
Indiana University	226	4	—	—
Seoul, Korea	242	4	—	—
Mayo Clinic	357	17	6	—
France: Lyons, Nantes, and Strasbourg	302	10	3	—
Tampa, FL	149	8.5	—	—
Memorial Sloan Kettering Cancer Center, NY	618	12	5	—
MD Anderson Cancer Center	329	27	14	—
Massachusetts General Hospital, MA	499	19	10	—
Taipei, Taiwan	169	6.5	14	—
Athens, Greece	86	14	—	—
Osaka, Japan	147	12	—	—
Virginia Mason, Clinic	42	45	28	—
Madrid, Spain	128	7.0	—	—

to a healthy population. Relative 1-year survival reflects the stage of disease at diagnosis, whereas the 5-year statistics reflect survival after therapy. Although more cases were detected earlier, survival has not improved. Gudjonsson, in several publications, analyzed CaP and survival, and noted only 65 5-year survivors by 1978, 8 of whom were not resected.⁴³ By 1987, 5-year survivors had increased to 165, of whom 12 were not resected.^{44–46} By 2016, an estimated 2800 in 433,000 (<1%) CaP patients survived 5 years.^{24,26,27}

Before biliary stents were used to decompress jaundice and axial imaging was available, mortality rates exceeded 20%. Based on high mortality and morbidity rates after surgery, Crile,⁴⁷ in 1970, and Shapiro,⁴⁸ in 1975, questioned the value and wisdom of pancreatic resection. Eckstam⁴⁹ reported on a 10-year survivor in 1994 and cited 13 others in a literature review.⁴⁷

This study is among several in the last decade of actual survival of CaP. It is derived from carefully evaluated PDR subjects with CaP.^{27,30–36} The actual 5,10, and 20 year survival was 21%, 19% and 4%. The overall and individual survival is summarized in **Tables 2** and **3**. Seven were lost to follow up. All were NED at 13–20 years after treatment. Two of three 20 year survivors survive NED and 2 others are in years 18, and 19 NED. The longest survivor, now in year 24 since diagnosis had a small focus of tumor left on the superior mesenteric vein (SMV) and received additional radiation therapy. He developed lymphoma in year 20 and is NED in year 24. Another developed a fatal prostate cancer and died at 14 years, 2 months. Others have noted synchronous or metachronous second primary lesions in the same or other organ sites.^{50–53} This is

most unusual after CaP for an obvious reason: few survive long enough to develop a second primary lesion. The authors have noted a second primary pancreatic cancer after distal resection for a primary lesion, and have reported 3 synchronous, simultaneous lesions in the head of the pancreas (2 distinct adenocarcinomas and a neuroendocrine tumor).⁵¹ The present and overall status of each patient is summarized in [Tables 2](#) and [3](#). The incomplete follow-up of 7 patients is due to loss of data during transfer and storage of records, and changing computer systems. We make no projections about them and simply state the last contact with them, all of whom were NED after 10 years (see [Table 2](#)).

The unusual features in this series include: 78% of operations were done in a 50-bed community hospital, a high number of 5-year and 10-year survivors^{7,16} relative to the number of operations, a low recurrence rate after 5 years (2 out of 17), the development of second primary lesions in 2 patients, and nearly half the survivors had neoadjuvant therapy (8 out of 17, all of whom lived at least 10 years).^{7,28} The neoadjuvant group, was much smaller than the surgery-first adjuvant group who came from a much larger number of referred and screened patients.

TUMOR CHARACTERISTICS

Histologic features, lymph node status, tumor size, margin status, and vein involvement are considered important survival determinants.^{4,7,8,18–20,24,25,27,29} Common sense would suggest that patients with smaller, well-differentiated tumors, negative lymph nodes, and uninvolved resected margins fare better than those with large, poorly differentiated lesions with positive nodes, positive margins, and vein wall involvement. Yet these factors are irrelevant in predicting actual long-term survival.^{1,6,20} Nearly half of the 5-year and 10-year survivors were initially unresectable. One subject, JP, had a difficult postoperative course marked by portal vein thromboses and ascites from which she fully recovered. One year later she developed a malignant right pleural effusion. After drainage and pleurodesis with tetracycline, she remained disease-free an additional 19-plus years. Treated in 1987, before this study, she is cited to highlight the unpredictable pattern and unusual course of individual survivors.

SURGERY

Treatment was decided by multimodality specialists after review of all physiologic and diagnostic tests, and patient and family input. Of the operations, 78% were done at a 50-bed community hospital 18 miles outside New York City, suggesting that centers of specialization are independent of institution size and academic affiliations.^{7,28} The annual resectability rate for explored CaP patients was 93% to 98%. Survival for CaP should favor resected patients because of selection and lead-time bias. Smaller, less extensive, tumors; patients with fewer comorbid risk factors; and incidentally detected lesions, rather than surgery per se, may be the important survival determinants. Criteria for surgery should remain strict and selective because of the systemic nature of CaP. Four of the 17 survivors had pylorus preservation and 13 had distal gastric resection. The operative technique has constantly evolved since 1973 and now includes laparoscopic approaches.^{13,30,31} These technical modifications are important but do not affect tumor biology. The mean and median operative time was 150 minutes for primary resection and 30 to 40 minutes longer in the neoadjuvant patients. Blood transfusions during surgery or hospitalization (7%), and pancreatic fistula (6%), all type A were infrequent. Two of the long-term survivors presented with complete superior mesenteric vein obstruction, which cleared

with neoadjuvant therapy, suggesting vein obstruction could be caused by extrinsic compression and not tumor invasion. In both cases, the pancreas could be dissected from the vein. This began the authors' experience with skeletonization of the vein, which occurs when tumors abut the vein.³¹ A recent review of vein resection for PDR indicated 50% of vein resections showed no vein involvement and deeper invasion of the vein wall or arterial involvement represented incurable disease.^{54,55}

RECURRENCE AFTER TREATMENT

The low recurrence rate of 2 out of 17 subjects after 5 years may reflect a modest sample size or benefit of neoadjuvant therapy, which continued to maximum response. All 8 neoadjuvant 5-year survivors survived at least 10 years. Surgical tradition is difficult to change and neoadjuvant therapy has had a low impact on surgical practice for CaP. Surgery-last rather than surgery-first for CaP is logical. It precludes surgery when disease progresses during treatment; it ensures all patients receive systemic therapy, including the 20% to 40% whose postoperative morbidity excludes systemic therapy; it allows the results of treatment to be followed during therapy; and, most importantly, it may improve survival by killing microscopic systemic metastases.^{7,9,25} Neoadjuvant therapy has been an integral part of treatment of CaP at MD Anderson Cancer Center since 1990.^{9,25} From 1990 to 2002, 329 resected CaP subjects (77%) received neoadjuvant therapy and 91% received systemic therapy. Katz and colleagues¹⁴ reported an actual 5-year and 10-year survival of 27% (88 out of 329) and 14% (20 out of 145) of eligible subjects.⁹ Recurrence rates were 73% before 5 years but 8% after that. In their subsequent report survival is projected, but the use of chemotherapy-first continued in 3 out of 4 of subjects.²⁵ This is an important, well-formulated study with a high percentage of actual 5-year and 10-year survivors. Although vein resections were done in 1 out of 3 PDRs, the incidence of vein involvement was not stated. An updated MD Anderson experience correlated preoperative imaging and vein involvement, and indicated safe resection rates, but found that deeper vein wall involvement led to poorer survival.⁵⁵ Of 98 vein resections from 277 PDR subjects, 36% had no vein involvement and 17% had adventitial involvement. When greater than 180° vein involvement was present, tumor involvement exceeded 82% and survival was poor.⁵⁵ The senior surgeons (AMC) preference and experience supports teasing the pancreas from the lateral vein with a Freer vascular dissector and not resect the vein. "Skeletonization" of the vein has not compromised outcomes or resulted in local recurrence.³¹

LITERATURE REVIEW

Five and 10-year survival with CaP does not imply cure because of the likelihood of tumor recurrence after 5 years. A study from Memorial Sloan Kettering Cancer Center reported 75 of 618 (12%) resected CaP patients survived 5 years and 18 of 353 (5%) survived 10 or more years.¹⁸ The recurrence rate after 5 years was 19 out of 75 (26%), all of whom died in the year 6. Most deaths occurred in low-stage cancers (1a, 1b, and 2b). Only 20% of resected subjects received adjuvant therapy. A report from The Massachusetts General Hospital cited 499 CaP patients followed at least 5 years.¹⁸ Actual 5-year and 10-year survival was 19% (95 of 499) and 10% (33 of 329). Favorable factors included negative margins and negative nodes. However, 41% (39 out of 95) of survivors had positive nodes and 24% (23 out of 95) had positive margins. Twenty-three patients died after surviving 5 years, 12 of disease, 10 of unknown cause, and

1 unrelated to cancer. Several patients had recurrence after 10 years, 2 of whom had pulmonary resection for isolated lung metastases. Their conclusions: “prognosis is determined by tumor biology rather than clinicopathologic features.”⁸ Nearly 50% received adjuvant chemotherapy. Trede and colleagues^{11,12} report a long experience in Mannheim, Germany, with PDR and CaP dating to 1972. Of 130 PDR for CaP, there were 25 (19%) 5-year survivors. Six of 9 subjects with early cancers (<2-cm negative nodes and lymphatics) died of recurrence and the remaining 3 were well at 19, 42, and 65 months.^{11,12}

EXPRESSING SURVIVAL

In the last 15 years, more reports of actual 5-year survivors have been published suggesting longer patient survival. This has not improved the cure rate.^{6,13,14} Until recently, most reports were from large centers and were expressed as actuarial, not actual survival.^{21,22,46} Actuarial survival is an inaccurate and misleading projection of outcomes that fall short of reality. Short follow-up and patients lost to follow-up (censored patients) lessen the denominator of the equation: number of survivors to number of operations, and overstate survival. Actuarial survival may overestimate actual survival by 3-fold to 7-fold or as much as 20%. Gudjonsson cited a study in which 11 out of 200 (5%) CaP subjects survived 5 years, whereas the actuarial survival was 22%.^{21,22,27} In 1958, the actuarial method most commonly used was suggested by Kaplan and Meir⁵⁶ as a way of projecting survival when follow-up was incomplete. Today, centers have the capability to follow patients for 5, 10, and more years, longitudinal follow-ups expressing actual survival would be more accurate than multiple reports of the same patients projecting survival. Lead-time bias is an important factor that may explain the increase in actual 5-year survival but not cure. Lead-time bias favors patients with asymptomatic cancers detected earlier in development, which allows longer survival, than patients whose onset of cancer is the same but whose detection is delayed until symptomatic, which for CaP is often preterminal. This suggests the 10-year to 20-year span for pancreatic cancers from development to death provides an apparent longer survival for asymptomatic patients. Today, many CaPs are discovered in a preclinical stage, by axial imaging, in nonjaundiced patients with nonspecific symptoms. These tumors are detected earlier than 20-plus years ago, before axial scans, when jaundice and cancer cachexia (late symptoms) were common.⁵⁷ Earlier is not the same as early because latent metastases have occurred.⁵⁸ Depending on immune and defense mechanisms, metastases become evident months to years after the primary tumor is treated. Survival may seem longer for preclinical than symptomatic patients but the difference may be apparent, not real, and due to lead-time and selection bias. Because the percentage of resectable CaP cases has remained consistent at 10% to 20% for 5 decades, additional 5-year survivors represent earlier, but not early, detection.⁵⁹ This may explain the apparent increased survival but not cure.^{14,58}

Survival statistics may be misleading. At best 20% of CaP are resected, or 20 of 100 CaP. A 20% 5 year survival usually refers to resected patients since 80% of CaP are unresectable and very few survive 5 years. Thus the “20% survival” figure refers to only 4 patients (20% of 20 resections) and not 20.

SYSTEMIC THERAPY

Because pancreatic cancer is a systemic disease, logic and common sense hold that systemic therapy be given first, before rather than after surgery.^{7,9,25,33,60} Although the

value of chemotherapy in pancreatic and other cancers has been questioned, there are significant responses, even complete resolution.^{7,9,33} As personal therapy becomes available, outcomes may improve. Although the use of chemotherapy is not questioned, its benefits may be overestimated. Morgan, Ward, and Barton¹⁵ reviewed the contribution of cytotoxic chemotherapy to 5-year survival in 22 malignancies in the United States and Australia. The estimated overall benefits were 2.3% in Australia and 2.1% in the United States. For pancreatic cancer in which 5-year survival is less than 5%, it was difficult to determine a survival benefit.

LATENT OR DORMANT DISEASE

Some CaP patients are cured or improved after chemotherapy. Because the mean age for CaP is the mid-60s, the benefits of effective therapy have natural time limits. More than 80% metastasize and are viable but dormant, until they overcome or are overcome by host defenses.⁵⁷ The latent cells have properties of stem cells, express transcription factors, and slowly proliferate and have a high initial attrition rate.⁵⁸ Monocyte transported natural killer cells kill latent tumors and the protumor and anti-tumor actions of the immune system determine whether tumors will remain latent or lethal. Certainly, a few CaP patients are cured. Whether the surviving patients in this report will continue disease free and possibly cured is not known. Relative to most patients with treated CaP they are part of a fortunate and lucky few.

PERSONAL THOUGHTS

This study adapted a trial of neoadjuvant multidrug chemoradiation therapy for pancreatic cancer 30 years ago, believing that the mantra that pancreatic resection offers the only chance of cure was misleading and ignored the true outcomes of CaP. Patients may be misled and uninformed by a surgery-first approach and, if aware of morbidity, survival, and cure, might be receptive to other options. If the treatment of pancreatic cancer were a business model, it would have been scraped long ago and open-minded newer alternatives sought. For CaP, these include targeted therapy, neoadjuvant therapy, and prevention, all worthy of further exploration.

SUMMARY

Cure of pancreatic cancer is unlikely. A modest series is presented and followed for more than 10 years. Although the results compare favorably to other reports of actual survivors, nearly half had neoadjuvant therapy for initially unresectable lesions, and were treated to maximum response before consideration of surgery. Fifteen of 17 5-year survivors lived 10 or more years from diagnosis and 3 surpassed 20 years, 2 of whom are alive. Similar if not more impressive outcomes are reported from MD Anderson, at which chemotherapy before surgery has become their standard of care. A century of thinking that surgery is the only chance of cure should be replaced by the more accurate aphorism, surgery has little chance of cure. If surgery-first remains a standard, or traditional, approach, little change in outcome can be anticipated. An open-minded, less repetitive and more innovative approach is long overdue. Preventing pancreatic cancer should be everyone's first choice and effective therapy a distant second.⁵⁸

Between 1991 to 2000, the years of this study, patients were treated and followed at The Pancreas and Biliary Center at Dobbs Ferry Hospital, NY, where nearly all of the authors practiced, or consulted. Since then, physician affiliations have become more

diverse and include the Mount Sinai-affiliated institutions, Lenox Hill-Northwell Hospital, Dobbs Ferry Hospital, and Albert Einstein-Montefiore Hospitals.

ACKNOWLEDGMENTS

The authors acknowledge Ted Casper, MD and Charles Fishman, MD who provided expert critical and pulmonary care in the latter years of the study, and the extraordinary nursing staff at Dobbs Ferry Hospital who provided compassionate and superb care.

REFERENCES

1. Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review 1975-2010 NCI, Bethesda (MD).
2. Beger HG, Bettina R, Gansauge F, et al. Pancreatic cancer low survival rates. *Dtsch Arztebl Int* 2008;105:255-62.
3. Carpelan-Holmstrom M, Nording S, Pukkala E. Does anyone survive pancreatic ductal adenocarcinoma? A nationwide study reevaluating the data of the Finnish Cancer Registry. *Gut* 2005;54:385-7.
4. Office for national statistics, Cancer survival in England; Patients diagnosed 2005-2009 and followed up to 2010 LONDON, ONS 1959.
5. Gong Z, Holly EA, Paige M. Survival in population based pancreatic cancer patients; San Francisco Bay Area, 1995-1999. *Am J Epidemiol* 2011;174(12):1373-81.
6. Cooperman A. Pancreatic cancer: the bigger picture. *Surg Clin North Am* 2001;81:557-74.
7. Cooperman AM, Snady H, Bruckner H, et al. Long-term follow-up of twenty patients with adenocarcinoma of the pancreas: resection following combined modality therapy. *Surg Clin North Am* 2001;81:699-708.
8. Ferrone CR, Vanmarcke RP, Bloom JR, et al. Pancreatic ductal adenocarcinoma: long term survival does not equal cure. *Surgery* 2012;152:S43-9.
9. Katz MHG, Wang H, Fleming J, et al. Long term survival after multidisciplinary management of resected pancreatic adenocarcinoma. *Ann Surg Oncol* 2009;16:836-47.
10. Rocha F, Hashimoto Y, Traverso W, et al. Interferon-based adjuvant chemoradiation for resected pancreatic head cancer: long-term follow-up of the Virginia Mason protocol. *Ann Surg* 2016;263(2):376-84.
11. Trede M, Schwall G, Seeger HD. Survival after pancreaticoduodenectomy 118 consecutive resections without an operative mortality. *Ann Surg* 1990;211:447-58.
12. Trede M, Richter A, Wendel K. Personal observations, opinions, and approaches, to cancer of the pancreas and periampullary area. *Surg Clin North Am* 2001;81:595-611.
13. Cooperman A, Wayne M, Steele J. Editorial cancer of the pancreas (CaP) New thoughts, new approaches for the new year pancreatic disorders & therapy. ISSN: 2165-7992.
14. Luberice K, Downs D, Sadowitz B, et al. Has survival improved following resection for pancreatic adenocarcinoma? *Am J Surg* 2017;214(2):341-6.
15. Morgan GM, Ward R, Barton M. The contribution of cytotoxic chemotherapy to 5 year survival in adult malignancies. *Clin Oncol* 2004;16:549-69.
16. Wagman R, Grann A. Adjuvant therapy for pancreatic cancer: current treatment approaches and future challenges. *Surg Clin North Am* 2001;81:667-83.

17. Kozuch P, Petryk M, Evans A, et al. Therapy for regionally unresectable pancreatic cancer. *Surg Clin North Am* 2001;81:691–9.
18. Ferrone CR, Brennan M, Gonen M, et al. Pancreatic adenocarcinoma: the actual 5 year survivors. *J Gastrointest Surg* 2008;12:701–6.
19. Helm JF, Centeno BA, Coppola D, et al. Outcomes following resection of pancreatic adenocarcinoma: 20-year experience at a single institution. *Cancer Control* 2008;15(4):288–94.
20. Schnelltdorfer T, Ware AL, Sara MG, et al. Long term survival after pancreatoduodenectomy for pancreatic adenocarcinoma: is cure possible. *Ann Surg* 2008;247:456–62.
21. Riall TS, Cameron JL, Lillemoe KD. Resected periampullary adenocarcinoma: 5 year survivors and their 6-10 year follow up. *Surgery* 2006;140:764–72.
22. Yeo CJ, Cameron JL, Lillemoe KD. Pancreaticoduodenectomy for cancer of the head of the pancreas. *Ann Surg* 1995;221(6):721–33.
23. Cleary SP, Gryfe R, Guindi M. Prognostic factors in resected pancreatic adenocarcinoma: analyses of actual 5 year survivors. *J Am Coll Surg* 2004;198:722–31.
24. Perysinkas I, Avonitis S, Georgiadou D. Five-year actual survival after pancreatoduodenectomy for pancreatic head cancer. *ANZ J Surg* 2015;85(3):183–6.
25. Cloyd JM, Katz MH, Prakash L, et al. Pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. A 25 year single institution experience. *J Gastrointest Surg* 2017;21(1):164–74.
26. Duran H, Lelpe B, Diaz E, et al. Real 5 year survival after radical surgery for pancreatic carcinoma: can it be predicted with the usual prognostic factors. *JOP*.
27. Kuhlman KFD, deCastro SMM, Wesseling SG. Surgical treatment of pancreatic adenocarcinoma; actual survival and prognostic factors in 343 patients. *Eur J Cancer* 2004;40(4):549–58.
28. Kure S, Kaneko T, Takeda S. Analysis of long term survivors after surgical resection for invasive pancreatic cancer. *HPB (Oxford)* 2005;7:129–34.
29. Cooperman AM, Schwartz E, Fader A, et al. Safety, efficacy and cost of pancreaticoduodenal resection in a specialized center based at a community hospital. *Arch Surg* 1997;132:744–8.
30. Cooperman AM. Pancreaticoduodenal resection pearls, perils, pitfalls. *Surg Clin North Am* 2001;81(3):579–93.
31. Cooperman AM, Wayne M, Iskandar M. Steele Skeletonization in lieu of portal mesenteric vein resection during pancreaticoduodenal resection *J GI Research and Therapy* Vol 1 ;1;2016
32. Cooperman A, Fader A, Cushman B, et al. Surgery for cancer of the pancreas: will common sense become common practice. *Hematol Oncol Clin North Am* 2002;16(1):81–94.
33. Snady H, Bruckner H, Cooperman AM, et al. Survival advantage of combined chemoradiotherapy compared with resection as the initial treatment of patients with regional pancreatic carcinoma; an outcomes trial. *Cancer* 2000;89:314–37.
34. Lambe M, Elorante S, Wigertz A, et al. Pancreatic cancer; reporting and long term survival in Sweden. *Acta Oncol* 2011;50(8):1220–7.
35. Soreide K, Agnes B, Moller B, et al. Epidemiology of pancreatic cancer in Norway:trends in incidence, basis of diagnosis and survival 1965-2007. *Scand J Gastroenterol* 2010;45:82–92.
36. Luo J, Xiao L, Wu C, et al. The incidence and survival rate of population based pancreatic cancer patients: Shanghai cancer registry 2004-2009. *PLoS One* 2013;8(10):e76052.

37. Coleman MP, Babb P, Damiecki P, et al. Cancer survival trends in England and Wales 1971-1995. Deprivation and National Health Service regional series SMDS 61 London ONS 1959.
38. Speer AG, Thurfield VJ, Tom-Broors Y, et al. Pancreatic cancer: surgical management and outcomes after 6 years of follow-up. *Med J Aust* 2012;196(8):511-5.
39. Adham M, Jack D, Le Borgne JL. Long term survival (5-20 years) after pancreatectomy for pancreatic ductal adenocarcinoma: a series of 30 patients collected from 3 institutions. *Pancreas* 2008;37:352-7.
40. Kimura K, Amano R, Nakata B. Clinical and pathological features of five-year survivors after pancreatectomy for pancreatic adenocarcinoma. *World J Surg Oncol* 2014;12:350.
41. Cooperman AM, Bruckner HB, Siegal J, et al. Is pancreatic cancer curable by surgery alone? [abstract]. *Gastroenterology* 1994;110:4.
42. Gudjonsson BEM, Livstone EM, Spiro HM. Cancer of the pancreas diagnostic accuracy and survival statistics. *Cancer* 1978;42:2494-506.
43. Gudjonsson B. Cancer of the pancreas 50 years of surgery. *Cancer* 1987;60:2284-303.
44. Gudjonsson B. Pancreatic cancer: 80 years of surgery-percentage and repetitions. *HPB Surg* 2016;2016:6839687.
45. Gudjonsson B. Letter to the editor. *J Am Coll Surg* 1996;183:290-1.
46. Gudjonsson B. Carcinoma of the pancreas critical analyses of costs, results of resections, and the need for standardized reporting. *J Am Coll Surg* 1995;181(6):483-503.
47. Crile G Jr. The advantage of bypass operations over radical pancreaticoduodenectomy in the treatment of pancreatic carcinoma. *Surg Gynecol Obstet* 1970;130(6):1049-53.
48. Shapiro TM. Adenocarcinoma of the pancreas: a statistical analyses of biliary bypass vs Whipple resection in good risk patients. *Ann Surg* 1975;182(6):715-21.
49. Eckstam M. Survival 13 years after pancreatectomy for ductal adenocarcinoma of the head of the pancreas. *Wis Med J* 1994;93:266-9.
50. Grundman RT, Meyer F. Second primary malignancy among cancer survivorsepidemiology, prognosis and clinical relevance. *Zentralbl Chir* 2012;137(6):565-74 [in German].
51. Sastry A, Wayne M, Steele J, et al. Three separate synchronous, sporadic and separate periampullary and pancreatic tumors; more than a coincidence. *World J Surg Oncol* 2014;12:382.
52. Shen M, Boffetta P, Olsen J, et al. Pooled analysis of second primary pancreatic cancers. *Am J Epidemiol* 2006;163(6):502-11.
53. Akabai H, Shiomi H, Naka S. Resectable carcinoma developing in the remnant pancreas 7 years and 10 months after distal pancreatectomy for invasive ductal carcinoma of the pancreas. *World J Surg Oncol* 2014;12:224.
54. Barreto SG, Windsor JA. Justifying vein resection with pancreaticoduodenectomy. *Lancet Oncol* 2016;17:e118-24.
55. Tran C, Bao HS, Balanchander A, et al. Radiographic tumor vein interface as a predictor of intraoperative pathologic and oncologic outcomes in resected Borderline resected pancreas cancer. *J Gastrointest Surg* 2014;18(2):269-78.
56. Kaplan EI, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;457-81.
57. Pollard JW. Defining metastatic cell latency. *N Engl J Med* 2016;375(3):280-2.

58. [Ryan DR, Hong TS, Bardea TJ. Pancreatic adenocarcinoma. N Engl J Med 2014; 371:1039–49.](#)
59. Cooperman AM, Iskandar M, Wayne M, et al. Prevention and early detection of pancreatic cancer. Surg Clin North Am, in press.
60. [Chen SC, Shyr YM, Wang SE. Long term survival after pancreaticoduodenectomy for periampullary adenocarcinomas. HPB \(Oxford\) 2013;15:951–7.](#)