Journal of Surgical Oncology 64:242–245 (1997)

Experience With Distal Bile Duct Cancers in U.S. Veterans Affairs Hospitals: 1987–1991

TERENCE P. WADE, MD,* CHANDRA N. PRASAD, MD, KATHERINE S. VIRGO, PhD, AND FRANK E. JOHNSON, MD
[1]Department of Surgery, John Cochran VA Medical Center, St. Louis, MO
[2]Department of Surgery, St. Louis University, St. Louis, MO

Background: Treatment selection and results were reviewed in a population with distal bile duct cancers.
Method: Cases of bile duct cancer were retrieved from computerized U.S. Department of Veterans Affairs records from 1987–1991.
Result: A total of 156 patients with distal bile duct cancers were recovered (34 resections, 37 operative bypasses, and 85 nonoperative biliary intubations). Mean survival after resection was 22 months, which was significantly higher than after biliary bypass (14 months) or intubation (11 months). Death rate within 30 days of resection, bypass, or intubation was 11%. Distal bile duct cancer had a much higher resectability rate (48%) than did pancreatic cancer (22%) and significantly longer mean survival by stage. Projected 5-year survival rate after resection was 21% for localized cancers, but no 3-year survivors were seen with nodal metastases regardless of treatment.
Conclusions: Resection increases survival in patients with distal bile duct cancer. Five-year survival was achieved only when patients when nodal or other metastases were absent; most resections do not result in cure and prolonged survival also can occur without resection.
J. Surg. Oncol. 64:242–245, 1997

KEY WORDS: **periampullary; pancreaticoduodenectomy; biliary bypass**

INTRODUCTION: HISTORY AND PROGNOSIS

Cancer of the distal common bile duct is a rare cause of obstructive jaundice. Pancreatic cancer is the most common periampullary malignancy that causes jaundice, and cancers of the ampulla of Vater comprise the majority of the remaining malignancies that produce bile duct obstruction. Duodenal and bile duct cancers account for a much smaller number of nonpancreatic periampullary malignancies, and each represent ~4% of all periampullary cancers [1,2].

These periampullary cancers of nonpancreatic origin, i.e., ampullary, bile duct, and duodenal (ABD) tumors, generally have a prognosis that is superior to pancreatic cancers in cure rate, mean duration of survival, and resectability rate [3]. Although most reported series are generally <20 patients, they generally suggest that patients with distal bile duct cancers fare more poorly than do those with other ABD cancers [1].

This study examines the treatment of primary periampullary bile duct adenocarcinoma from 1987 through 1991 in the national system of hospitals directed by the U.S. Department of Veterans Affairs (DVA) and compares mean survival and operative mortality after both curative resection and palliative treatments.

MATERIALS AND METHODS

The sources of data and methods of retrieval used to assemble these DVA computer records have been described in detail [4]. Admission data from all 159 DVA hospitals were compiled from DVA computerized datasets using codes from the *International Classification of Disease*, 9th ed., *Clinical Modification* (ICD-9-CM) [5]. The bile duct adenocarcinoma subset was isolated from the DVA computerized Patient Treatment

*Correspondence to: Department of Surgery, Box 15250, 3635 Vista Avenue, St. Louis, MO 63110-0250.
Accepted 19 December 1996

Files (PTF) by using the ICD-9-CM diagnostic code for bile duct adenocarcinoma (156.1).

The PTF data available in the bile duct adenocarcinoma subgroup included admission and discharge dates, condition at discharge, ICD-9-CM diagnostic codes for concomitant medical conditions treated during the admission, operations, procedures, complications, and demographic information. Institutional tumor registrars and medical record departments in DVA hospitals were contacted to request tumor staging information on these patients. This specific gross and histologic information from local tumor registrars' records superseded data derived from the PTF, and other pathologies (sarcoma, lymphoma, etc.) were eliminated. A central pathologic slide review was not conducted; the opinion of the local pathologist regarding anatomic site and depth of invasion were accepted.

Since the DVA operates both acute and domiciliary care facilities, the 30-day mortality rate was chosen as the measure of operative mortality because the frequent intrainstitutional transfers without discharge would invalidate in-hospital mortality calculations.

Information regarding mortality after hospital discharge is not recorded in the PTF but is available from the Beneficiary Identification and Record Location System (BIRLS), another computerized data set that contains records of all veterans whose beneficiaries applied for death benefits. The data of death was recorded for each veteran in whose name death benefits were requested. Whereas a recent comparison of mortality recording systems estimated that 80–89% of all veterans deaths are compiled by BIRLS [6], our own analysis of 1,637 patients who underwent palliative treatments for pancreatic cancer between 1987 and 1991 reported a documented death record in >92% of cases by December 15, 1992 [4]. This rate of retrieval improved to >98% by December 31, 1994, and thus validated the use of these computerized mortality records as a reliable means of followup. This percentage was calculated after submitting data on patients without BIRLS or PTF death records through the files of the U.S. Social Security Administration. In the present study, mortality data were updated to December 31, 1994, and patients without a death record from these four sources (PTF, BIRLS, Social Security or tumor registrar records) were assumed to be alive.

Patients were then placed in three groups using the most invasive intervention performed for treatment or palliation of their lesion: (1) resection, including pancreaticoduodenectomies and local resections, (2) operative bypass, consisting of an anastomosis between the common bile duct and small intestine, and (3) percutaneous or endoscopically placed biliary intubation without operation. TNM status was determined using the American Joint Committee on Cancer criteria from local pathology reports when available.

Because the ICD-9 coding system does not indicate the anatomic locations of bile duct cancers within the duct (proximal or proper hepatic bifurcation vs. distal or periampullary), the site of biliary obstruction in these patients was inferred from the procedure used to alleviate the obstruction. Thus patients with hepaticojejunostomy bypass procedures or bile duct excisions without ampullary or pancreatic resection were eliminated from the analysis to allow most patients with proximal biliary or Klatskin tumors to be excluded. However, nonoperative approaches to biliary tract intubation for the relief of biliary obstruction are identical whether applied to perihepatic or periampullary bile duct cancers, and thus the third group (endoscopic or transhepatic biliary intubation) necessarily includes patients with both proximal and distal cancers. This accounts for the disproportionally large number of biliary tract intubations reported here.

Mean survival of the various therapeutic groups and differences in survival were compared using analysis of variance (ANOVA). Categorical data were statistically analyzed with the Chi-square test, and projected 5-year survival rates were calculated using the Mantel-Haenszel method.

RESULTS

Between 1987 and 1991, DVA computer records yielded 156 patients with bile duct cancer using the ICD-9 code of 156.1; 34 resections and 37 operative bypasses were performed for distal bile duct cancers, plus 85 nonoperative biliary intubations with bile duct cancer. Over the same period, 1,752 patients had resection or biliary bypass for pancreatic cancer [4], and these patients with bile duct cancer were selected from 432 patients with ABD malignancies [7], excluding neuroendocrine and other rare cancers. When patients from these two contemporary DVA series [4,7] are compiled, bile duct carcinomas accounted for 8% of periampullary cancer resections (34 excised bile duct cancers / 252 Whipple resections + 44 total pancreatectomies for pancreatic cancer + total 135 ABD resections = 34/431 = 8%). The 156 distal bile duct cancers comprised 7% of this series of periampullary malignancies (156 bile duct cancers / 1,752 pancreatic + 432 total ABD tumors). This 7% incidence of periampullary bile duct cancer is almost twice the 4% frequency previously reported [1,2]. This might be explained by the inclusion in the present analysis of biliary malignancies from any level of the biliary tree that were treated with nonoperative intubation.

Mean survival duration in the 34 patients who underwent bile duct cancer resection was 22 months, significantly ($P = 0.005$) higher than the 14-month mean survival of 37 patients after operative bypass and 11 months in 85 patients after biliary intubation. The death rate of 11% within 30 days of the procedure was identical for resection, bypass, and intubation. Of patients undergoing resection, 14% were projected to be alive after 5 years,

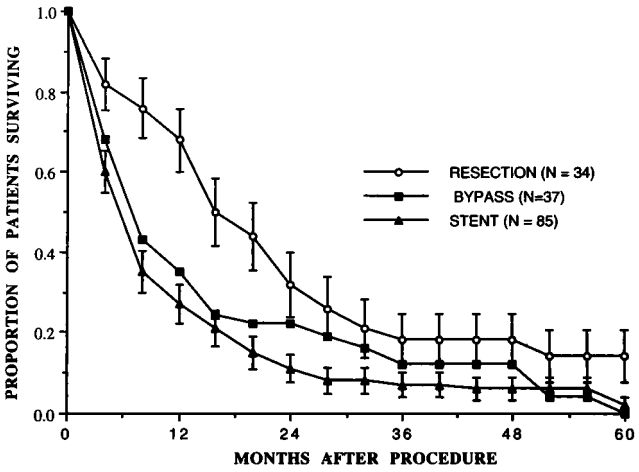

Fig. 1. Survival curves after resection, operative palliation, or biliary intubation of bile duct cancers are calculated by the Mantel-Haenszel method. Mean survival after resection is significantly longer than after palliative procedures ($P \leq 0.01$). Vertical bars indicate standard error of the mean. Computerized records documented the date of death in 95–96% of patients after palliative procedures, and in 85% of the resected patients.

but no patients treated without resection were 5-year survivors (Fig. 1).

Pathologic data allowing TNM staging was available from tumor registrars for 73 from the total of 156 patients. *With* resection, mean survival was 29 months in 13 patients with Stage I, II, or IV A distal bile duct cancers, who were grouped together and termed as ''localized'' tumors. Nine patients resected for Stage III (regional nodal involvement) distal bile duct cancers had a mean survival of 16 months, and three patients resected with Stage IV (metastatic) disease survived for an average of 18 months. *Without* resection, overall mean survival was significantly ($P = 0.01$) lower: 21 months in 21 patients with localized cancer, 7 months in eight patients with regional metastases, and 4 months in 19 patients with distant or peritoneal metastases (Table I).

The listed resections included 30 Whipple procedures, one total pancreatectomy, and three local or other resections. Complications were recorded in 18% of resected patients and sepsis, which occurred in 10%, was the most common problem. Sepsis, postoperative hemorrhage, and gastrointestinal bleeding each significantly increased the risk of 30-day mortality ($P \leq 0.01$, Chi square), but pneumonia, pancreatic fistula, or wound problems did not. No specific complication was associated with a significant decrease in mean survival. Twelve of 85 patients (14%) treated with biliary intubation alone required repeated invasive procedures, as did two patients after resection (6%) and one after bypass (3%).

Of patients with resected, localized cancers, 22% were predicted to survive for 5 years (Fig. 2), but no patient with regional or distant metastases survived for 3 years, regardless of treatment.

DISCUSSION

This large, recent series of patients with periampullary cancers in DVA hospitals has afforded a unique opportunity to analyze the results with different treatments for these frequent and virulent tumors. In addition, the national scope of the DVA and the wide diversity in hospital size and experience with these cancers has allowed us to illustrate the impact of many variables on surgical outcomes [8]. The large number of periampullary cancer patients in the DVA system has permitted more detailed analysis of rare locations such as the ampulla of Vater [9], periampullary duodenum [10], and common bile duct separately from tumors of the dominant site of origin, the pancreas. However, almost 15% of patients with a record of ABD cancer were not included in these three site-specific reviews, because there were conflicting or nonspecific sites of origin in their computer or pathologic records. As would be expected, the great majority of patients with tumors of unclear pathologic type had undergone palliative therapies.

When compared to the 1,964 veterans with pancreatic cancer treated in the DVA during the same period [4], distal bile duct cancer had a much higher resectability rate (48% = 34 resections / 34 + 37 bypasses) than did pancreatic cancer (22% = 327 resections / 327 + 1,180 bypasses), and dramatically longer mean survival by stage with similar operative morbidity and mortality rates. The projected 22% 5-year survival rate after resection of localized distal common bile duct cancer is equivalent to that of other ABD cancer subsets drawn from this DVA series, since projected 5-year survival was 21% with ampullary cancer and for periampullary duodenal cancer was 23%. Other smaller series [1,11,12] report that distal bile duct cancers have fewer long-term survivors after resection than do ampullary or duodenal cancers, but outcomes in the present series are similar to ampullary cancer, including the absence of 5-year survivors when lymph nodes were invaded by tumor.

The 30-day operative mortality rate of 11% after distal common bile duct cancer resection in DVA hospitals was lower than the 14% rate with ampullary cancers, but higher than the 6% rate with duodenal cancer resections. Similarly, operative mortality rates after bypass procedures ranged from 11–18% in these ABD tumor subsets; none of these variations in operative outcome by anatomic site were statistically significant.

This review emphasizes that distal bile duct cancer is a more favorable subtype of periampullary cancer than pancreatic cancer and that long-term results after resection are similar to those achieved in patients with ampullary or duodenal cancer. Resection can be performed safely and is associated with prolonged survival over palliative treatments. Patients with localized (lymph node negative) tumors may also survive over 3 years *without*

TABLE I. Mean Survival After Bile Duct Cancer Treatment by Stage Groups

	Resection		Biliary diversion		
	# Mo.	(# patients)	# Mo.	(# patients)	*P* value*
Localized (Stages I, II, IV A)	29	(13)	21	(21)	0.25
Regional (Stage III, node +)	16	(9)	7	(8)	0.07
Metastatic (Stage IV B)	18	(3)	4	(19)	0.001
Overall	23	(25)	12	(48)	0.01

*Comparing resection vs. diversion.

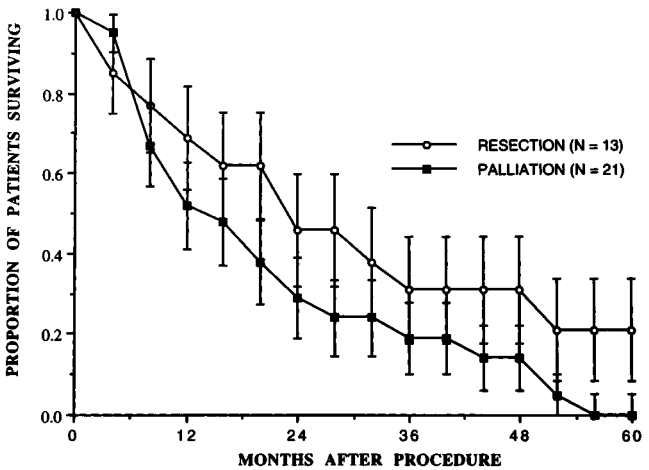

Fig. 2. Survival curves are displayed for distal bile duct cancers that do not involve lymph nodes (Stages I, II, IV A), calculated by the Mantel-Haenszel method. Vertical bars indicate standard error of the mean. Computerized records documented the date of death in 67% of patients who underwent resection for localized distal bile duct tumors and 96% of those undergoing palliative procedures for biliary cancers.

resection, but all patients had a death record within 3 years of initial treatment when lymph nodes were involved. Reports of operative results for periampullary cancer should include both patient stratification by tumor stage, and a contemporary comparison to palliative methods to avoid falsely overstating the value of resection. Central, blinded review of pathologic specimens is also important when claims of cure are made [13]. Since this tumor type is so uncommon, retrospective analyses such as the current one are likely to remain the primary source of information on outcomes after treatment.

We agree with Shyr [3] that resection of ABD cancers does not seem to be justified when nodal metastases are discovered at operation, with periampullary duodenal cancer a possible exception [10]. With nodal or distant metastasis from distal bile duct cancer, 5-year survivors after resection are rare (zero in this report) despite a longer mean survival than observed after palliative treatments. A proper assessment of the emotional and palliative value of treatments for periampullary cancers with lymph node involvement awaits an analysis that includes prospective measures of quality of life. Although 5-year survival was achieved in about one-quarter of resected patients without nodal or other metastases, most resections do not result in cure and prolonged survival is also seen for nonmetastatic tumors without resection.

ACKNOWLEDGMENTS

This work would not have been possible without the diligent, detailed work and ready co-operation of the tumor registrar personnel in the Department of Veterans Affairs hospitals across the United States, and their efforts are greatly appreciated.

REFERENCES

1. Michelassi F, Erroi F, Dawson PJ, et al.: Experience with 647 consecutive tumors of the duodenum, ampulla, head of the pancreas and distal common bile duct. Ann Surg 1989;210:544–556.
2. Klinkenbijl JHG, Schmitz PIM, Rombout PAR, et al.: Carcinoma of the pancreas and periampullary region: palliation versus cure. Br J Surg 1993;80:1575–1578.
3. Shyr Y, Su C, Lo S, et al.: Is pancreatoduodenectomy justified for periampullary cancers with regional lymph node involvement? Am Surg 1995;61:288–293.
4. Wade TP, Radford DM, Virgo KS, Johnson FE: Treatment of pancreatic adenocarcinoma in the U.S. veteran: Complications and outcomes. J Am Coll Surg 1994;179:38–48.
5. ''International Classification of Diseases, Clinical Modification (ICD-9-CM),'' 9th ed. Alexandria, VA: St. Anthony's, 1994.
6. Boyle CA, Decoufle P: National sources of vital status information: Extent of coverage and possible selectivity in reporting. Am J Epidemiol 1990;131:160–168.
7. Wade TP, Coplin MA, Virgo KS, Johnson FE: Periampullary cancer treatment in U.S. Department of Veterans Affairs hospitals 1987–1991. Surgery 1994;116:819–826.
8. Wade TP, El-Ghazzawy AG, Virgo KS, et al.: The Whipple resection for cancer in U.S. Department of Veterans Affairs hospitals. Ann Surg 1995;221:241–248.
9. El-Ghazzawy AG, Wade TP, Virgo KS, et al.: Recent experience with cancer of the ampulla of Vater in a national hospital group. Am Surg 1995;61:607–611.
10. Sexe RB, Wade TP, Virgo KS, et al.: Incidence and treatment of periampullary duodenal cancer in the U.S. Veteran patient population. Cancer 1996;77:251–254.
11. Andersen HB, Baden H, Bille Brahe NE, et al.: Pancreaticoduodenectomy for periampullary adenocarcinoma. J Am Coll Surg 1994;179:545–552.
12. Shyr Y, Su C, Wang H, et al.: Comparison of resectable and unresectable periampullary carcinomas. J Am Coll Surg 1994; 178:369–378.
13. Nitecki SS, Sarr MG, Colby TV, et al.: Long-term survival after resection for ductal adenocarcinoma of the pancreas: Is it really improving? Ann Surg 1995;221:59–66.