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Adenocarcinoma of the Ampulla of Vater

A 28-Year Experience

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Objective
The aims of this study were to review the experience with adenocarcinoma of the ampulla of Vater at The Johns Hopkins Hospital and to determine what factors influenced the long-term outcome in these patients.

Summary Background Data
Adenocarcinoma of the ampulla of Vater is the second most common periampullary malignancy. However, most series have relatively small numbers. As a result, analysis of factors influencing outcome has been limited.

Methods
From 1969 to 1996, 120 patients with adenocarcinoma of the ampulla of Vater were managed at The Johns Hopkins Hospital. Clinical, operative, and pathologic factors were correlated with morbidity and long-term survival. Factors influencing outcome were evaluated by univariate and multivariate analyses.

Results
Resection was performed in 106 patients (88%), and 105 of these patients (99%) underwent either pancreatoduodenal resection (n = 103) or total pancreatectomy (n = 2). Resection rate increased from 62% in the 1970s to 82% in the 1980s to 96% in the 1990s ($p < 0.05$). Overall mortality after resection was 3.8% with no mortality in the 45 consecutive patients resected in the past 5 years. Morbidity also decreased significantly ($p < 0.05$) from 70% before to 38% after December 1992. Five-year survival for resected patients was 38%. Factors favorably influencing long-term outcome were resection ($p < 0.001$), no perioperative blood transfusions ($p < 0.05$), negative lymph node status ($p = 0.05$), and moderate or well-differentiated tumors ($p < 0.05$). In a multivariate analysis, the best predictor of prolonged survival was absence of intraoperative transfusion ($p = 0.06$, relative risk = 1.90, 95% confidence limits = 0.95–3.78).

Conclusions
Compared to carcinoma of the pancreas, carcinoma of the ampulla of Vater has a higher resectability rate and a better prognosis. Early diagnosis is important because lymph node

status influences survival. Careful operative dissection and avoidance of transfusions also improves long-term survival.

William Stewart Halsted[1] described the first successful surgical resection of an adenocarcinoma of the ampulla of Vater in 1899. He performed a local resection of the lesion with reimplantation of the bile and pancreatic ducts. However, the patient expired 6 months after surgery. At autopsy "it was found that the carcinoma had recurred in the head of the pancreas and duodenum . . .". Controversy continues today regarding the indications for local resection of these cancers as opposed to pancreatoduodenectomy. Moreover, the factors influencing long-term survival have not been well defined.

Carcinoma of the ampulla of Vater is the second most common periampullary malignancy.[2] In most series, the resectability rate is higher and the prognosis is better when carcinomas of the ampulla are compared to other periampullary pancreatic cancers.[3] However, reported series of ampullary carcinomas usually contain relatively small numbers of patients, making definitive conclusions difficult. Therefore, the aims of this analysis were to review the experience with adenocarcinoma of the ampulla of Vater at The Johns Hopkins Hospital over a 28-year period and to determine what factors influence the outcome in these patients.

METHODS

Patient Population

Between March 1969 and April 1996, 120 patients with adenocarcinoma of the ampulla of Vater were managed at The Johns Hopkins Hospital. Patients were included in this review if pathologic examination results of a resected specimen showed a tissue diagnosis of adenocarcinoma of the ampulla of Vater or endoscopic biopsy specimen results confirmed a diagnosis of ampullary adenocarcinoma in the setting of inoperable tumor. Patients with a villous adenoma of the ampulla, ampullary stenosis, carcinoid tumors, or other rare tumors of the ampulla were excluded. In instances where a question existed regarding differentiation of a duodenal, distal bile duct, or pancreatic cancer from an ampullary carcinoma, pathologic rereview was undertaken for final categorization.

Data on age, gender, and race of the patients are presented in Table 1. The mean age of the 120 patients was 65 years (range, 34–90 years). Fifty-six (47%) were female, and 64 (53%) were male. One hundred (83%) were white, 14 (12%) were black, and six (5%) were Asian. Of the 120 patients, 106 (88%) were resected, 9 (8%) were managed without surgery but with endoscopic or percutaneous stents, and 5 (4%) were explored and bypassed. No significant differences in age, gender, or race were noted between the resected and unresected patients.

Associated symptoms also are listed in Table 1. History of jaundice (71%), weight loss (61%), and abdominal or back pain (46%) were the most common symptoms. No statistically significant differences were noted between the resected and unresected patients with respect to presentation. Associated illnesses also are presented in Table 1. Hypertension (30%) and a history of smoking (30%) were most common, whereas diabetes mellitus was found in 17% of patients. Presentation with acute pancreatitis was uncommon (5%) but was significantly more common in unresected than in resected patients (28% *vs.* 2%, $p < 0.05$). Twenty-two patients (18%) had a history of biliary tract surgery, including 8 (7%) with a simple cholecystectomy. Nine other patients underwent cholecystectomy along with a biliary bypass procedure (six), local excision of the tumor (two), or transduodenal sphincteroplasty (one).

Laboratory Data

Laboratory data at presentation are outlined in Table 2. Only a minority of patients were anemic, had an elevated leukocyte count, or an increased serum glucose. Hyperbilirubinemia was the most common abnormality, being present in 51% of patients. An elevated serum amylase was observed in 30% of the patients. Hypoalbuminemia occurred in 28%. The only difference between resected and unresected patients was that unresected patients were more likely to have an elevated aspartate aminotransferase ($p < 0.05$).

Radiologic Evaluation

A computed tomography scan was performed in 88% of the patients and in 95% of the resected patients. An example of a typical computed tomography scan is shown in Figure 1. An angiogram was performed in 65% of the patients, including 71% of the resected patients. Most patients had either an endoscopic retrograde cholangiopancreatography (54%) or a percutaneous transhepatic cholangiogram (48%). The results of cholangiograms performed in a patient at the time of cholecystectomy and 6

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Table 1. PATIENT POPULATION

	Resected (N = 106)	Unresected (N = 14)	All Patients (N = 120)
Mean age (yr)	66	64	65
Gender (% patients)			
Female	48	36	47
Race (% patients)			
White	87	57	83
Black	8	43	12
Symptoms (% patients)			
Jaundice	73	80	71
Weight loss	52	60	61
Abdominal/back pain	42	75	46
Nausea	23	63	26
Fever	12	13	13
Pruritis	13	38	16
Gastrointestinal bleeding	5	22	7
Associated illnesses (% patients)			
Hypertension	31	21	30
Smoking	30	28	30
Diabetes mellitus	15	28	17
Heavy alcohol use	16	14	16
Coronary artery disease	13	7	12
Acute pancreatitis	2	28*	5

* $p < 0.05$ *vs.* resected.

months later when the patient became jaundiced are shown in Figures 2A and 2B. An endoprosthesis was placed in 32% of the patients, including 34% of the resected and 20% of the unresected patients.

Procedures

Data with respect to the procedures performed are presented in Table 3. As mentioned above, 106 patients (88%) had their tumor resected, 9 (8%) were managed without surgery with stents, and 5 (4%) were explored and bypassed. The number of patients resected and the resection rate increased significantly ($p < 0.05$) by decade (Fig. 3). Among the resected patients, 105 underwent pancreatoduodenectomy. Two of these 105 patients were managed initially with local resection but subsequently required reoperation. In 85 (81%), the pylorus was preserved, whereas in 20 (19%), an antrectomy was performed. A partial pancreatectomy was performed in

Table 2. LABORATORY DATA

	Resected (N = 106) (%)	Unresected (N = 14) (%)	All Patients (N = 120) (%)
Hematocrit <35%	32	66	34
WBC >10,000 mm^3	16	0	14
Glucose >150 mg/dL	20	42	22
Bilirubin >1.1 mg/dL	48	75	51
AST >100 IU/L	22	83*	27
ALT >100 IU/L	16	20	17
Alkaline phosphatase >300 IU/L	31	71	35
Amylase >100 U/L	28	50	30
Albumin <3.5 g/dL	27	28	28

WBC = white blood cell; AST = aspartate aminotransferase; ALT = alanine aminotransferase.
* $p < 0.05$ *vs.* resected.

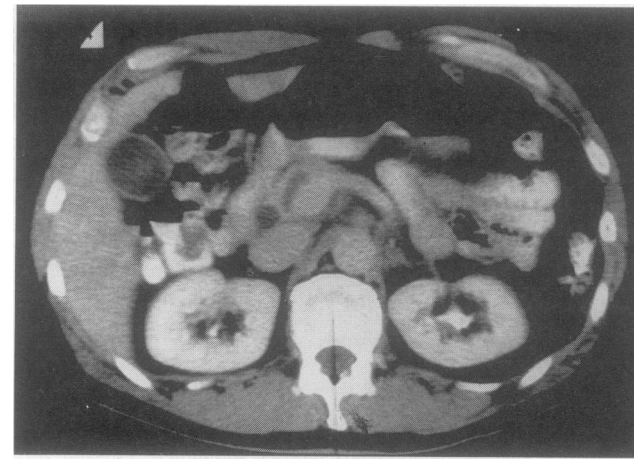

Figure 1. Computerized tomogram of a patient with an ampullary carcinoma. Note the dilated bile duct and pancreatic duct with no mass or vascular encasement.

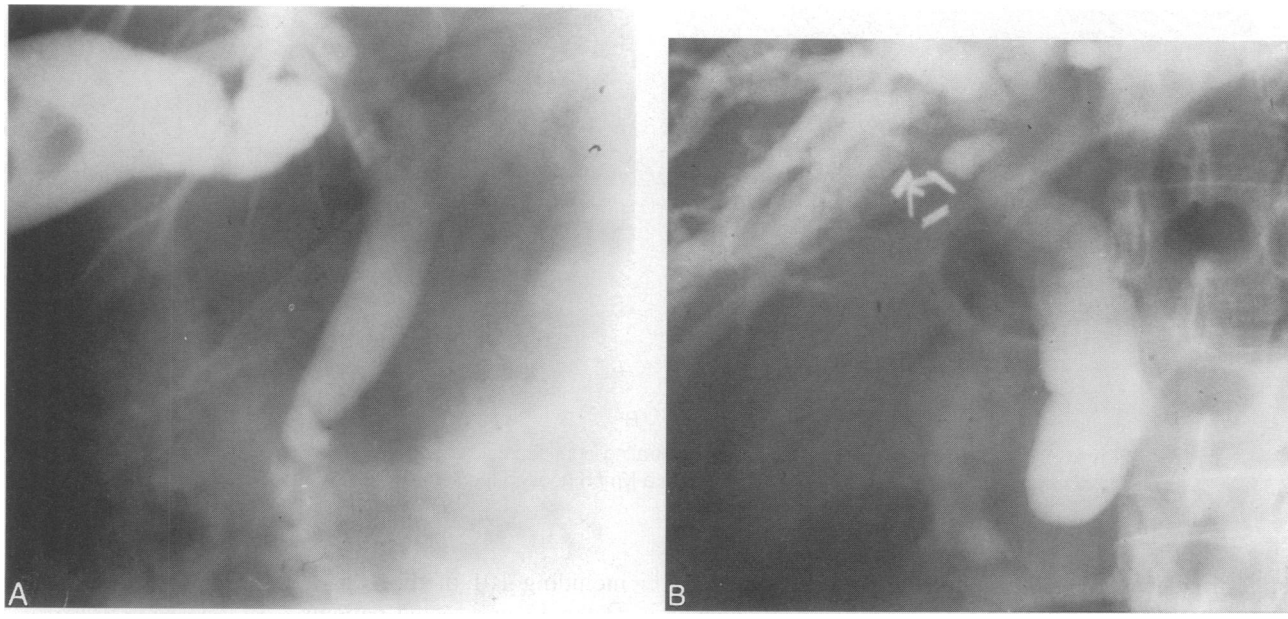

Figure 2. (A) Operative cholangiogram at the time of cholecystectomy. Note the dilated bile duct and ampullary abnormality. (B) Transhepatic cholangiogram 6 months later when the patient became jaundiced and was found to have an ampullary carcinoma.

103 patients (98%), whereas a total pancreatectomy was required in only 2 patients (2%). Reconstruction of the pancreatic remnant was done by pancreatojejunostomy in 85 patients (83%) and by pancreatogastrostomy in 18 patients (17%). Data with respect to operative time, blood loss, and transfusions for patients undergoing pancreatic resection in the 1980s and 1990s are presented in Table 4. Although operative time and blood loss did not change significantly, fewer transfusions ($p < 0.05$) were given in the 1990s. One patient was managed successfully with local resection. Resection was not performed in 14 patients because of liver metastases (n = 3), superior mesenteric vein obstruction (n = 1), or increased risk due to associated illness.

Pathologic Evaluation

All specimens were reviewed to confirm the diagnosis, tumor size, lymph node status, degree of differentiation, and margin status. Typical histologic findings are presented in Figures 4A and 4B. The average tumor size was 2.4 cm. Lymph nodes were positive in 41 of 105 patients (39%). The tumors were classified as well differentiated in 13%, moderately differentiated in 68%, and poorly differentiated in 19%. Margins were positive in only 2 (1 bile duct and 1 pancreatic duct) of the 105 pancreatic resections.

Table 3. PROCEDURES

	No. (%) of Patients
Resection	106 (88)
Pancreatoduodenectomy	105 (99)
Pylorus preseving	85 (81)
Antrectomy	20 (19)
Partial pancreatectomy	103 (98)
Total pancreatectomy	2 (2)
Local	1 (1)
Stents	9 (8)
Bypass	5 (4)

Complications

A pancreatic fistula was defined as drainage of more than 50 mL of amylase-rich fluid per day from the operatively placed drains on or after postoperative day 10. Delayed gastric emptying was defined as the need for

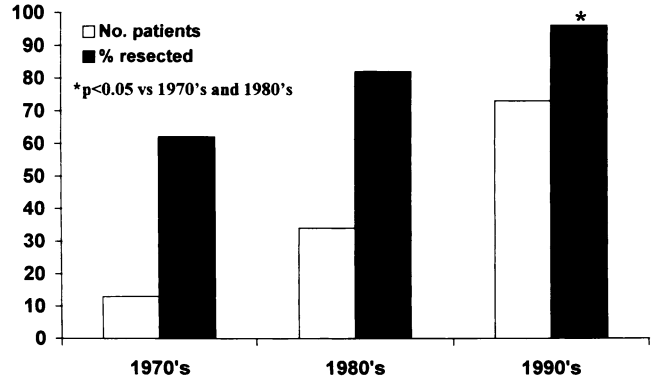

Figure 3. Number of patients resected and resection rate by decade.

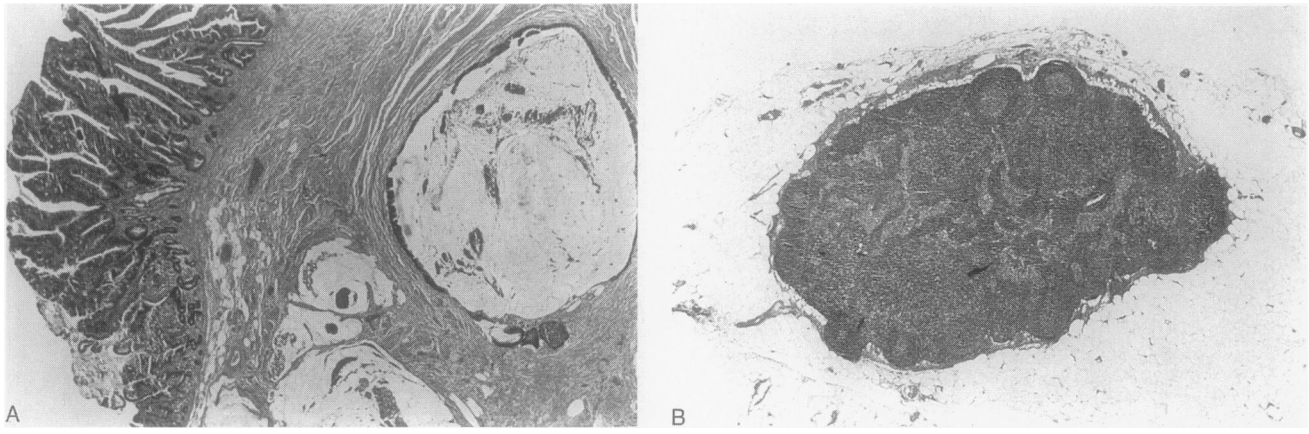

Figure 4. (A) Photomicrograph of *in situ* and infiltrating adenocarcinoma of the ampulla of Vater. (B) Photomicrograph of metastatic adenocarcinoma in a lymph node in the same patient.

nasogastric decompression beyond the 10th postoperative day as well as 3 other criteria as described previously.[4] A wound infection was defined as the presence of pus in a wound that required opening and grew bacteria. These and other complications have been defined similarly in previous publications from this institution.[2,4]

Adjuvant Therapy

Chemotherapy or radiation therapy was not offered to most patients before 1990. As a result, only 17 recently resected patients received chemoradiation (n = 13), radiation alone (n = 3), or chemotherapy alone (n = 1). Similarly, only two unresected patients received radiation, and only one received chemotherapy.

Follow-Up

Follow-up was obtained by patient contact, review of hospital and physician records, and by the United States Social Security Administration contact. Data on hospital morbidity were available on 97 (87%) of the 111 patients undergoing surgical exploration. Follow-up regarding survival was available on 114 (95%) of the 120 patients, including 101 of the 106 resected (95%) and 13 (93%) of the 14 unresected patients.

Statistical Analysis

Comparisons between groups were evaluated by Student's t test or by chi square analysis as appropriate. Kaplan–Meier statistics were used to compare survival data by the log–rank test. Cox proportional hazard methodology was used to perform the multivariate analysis. Values with a p value of 0.05 or less were considered statistically significant.

RESULTS

Morbidity and Mortality

One or more complications occurred in 49 resected patients for an overall morbidity rate of 47% (Table 5). The most common complication was pancreatic fistula, which occurred in 23 patients (25%). The incidence of

Table 4. OPERATIVE TIME, BLOOD LOSS, AND TRANSFUSIONS

	1980s (N = 28)	1990s (N = 70)
Operative time (min)	448	421
Blood loss (mL)	686	653
Transfusions (units)	1.5	0.62*

* $p < 0.05$ *vs.* 1980s.

Table 5. MORBIDITY AND MORTALITY

Complication	No. (%) of Patients
Pancreatic fistula	23 (25)
Delayed gastric emptying	16 (17)
Wound infection	13 (14)
Abdominal abscess	9 (10)
Pancreatitis	6 (7)
Cholangitis	6 (7)
Bleeding	6 (7)
Bile leak	5 (5)
Overall morbidity	49 (47)
Death	4 (3.8)

Table 6. AMPULLARY CANCER SURVIVAL

	Survival		Year		
	Mean (mo)	Median (mo)	1 (%)	3 (%)	5 (%)
Resected	60*	46	81	55	38*
Unresected	10	5	29	10	0
No transfusion	69†	>60	85	63	53†
Transfusion	44	45	72	52	30
Lymph node negative	69‡	52	84	66	43‡
Lymph node positive	40	24	77	36	31
Moderately or well differentiated	69§	52	85	58	49§
Poorly differentiated	17	16	59	18	18

* $p < 0.001$ *vs.* unresected.
† $p < 0.05$ *vs.* tranfusion.
‡ $p < 0.05$ *vs.* positive lymph node.
§ $p < 0.01$ *vs.* poorly differentiated.

this problem did not vary significantly between the 1980s (25%) and the 1990s (28%). Delayed gastric emptying developed in 16 patients (17%). Endoscopy was required for evaluation or balloon dilation in 6 (35%) of these 16 patients. Gastric emptying improved before discharge in all patients. Wound infection occurred in 13 patients (14%). Reoperations were performed for major complications in six patients (6%). Since December 1992, overall morbidity has decreased significantly ($p < 0.05$) from 70% to 38%.

Four postoperative deaths (3.6%) occurred in the 111 patients who were explored. All four deaths (3.8%) occurred among the 105 patients undergoing pancreatoduodenectomy. Two deaths resulted from intra-abdominal hemorrhage in patients with pancreatic fistulas. One death was the result of a pulmonary embolism, and one was caused by multiple organ dysfunction syndrome. All four deaths occurred in patients operated on before 1992. Thus, mortality was 6.6% among 61 patients resected before 1992 and 0% in the most recent 45 patients.

Hospital Stay

The mean length of hospitalization after surgery was 22 days, and the median was 17 days. Since December 1992, mean postoperative hospital stay has decreased significantly ($p < 0.01$) to 20 days. Similarly, median postoperative hospital stay has decreased from 24 days before to 15 days after December 1992.

Survival

Survival for all patients is presented in Table 6 and Figure 5. For unresectable patients, median and actuarial 5-year survivals were only 5 months and 0%, respectively (Fig. 5A). In comparison, for resected patients, median and actuarial 5-year survivals were 46 months and 38%, respectively ($p < 0.001$). The effect of blood loss on survival almost reached statistical significance ($p = 0.052$) with greater blood loss correlating with decreased survival. Conversely, blood transfusion adversely did affect survival (Table 4, Fig. 5B). Five-year survivals were 53% without and 30% with transfusion ($p = 0.05$). Tumor size did not affect survival, but lymph node status (Table 4, Fig. 5C) and tumor differentiation (Table 4, Fig. 5D) were both significant factors in long-term survival. Adjuvant therapy had no discernible influence on survival, but the number of patients treated was small. In addition, survival did not change significantly by decade. When the multivariate analysis was performed using blood loss, blood transfusions, lymph node status, and tumor differentiation, none of these factors were significant. However, among these, the best predictor of improved survival was absence of intraoperative blood transfusion ($p = 0.06$, relative risk 1.90, 95% confidence interval = 0.97–3.78).

DISCUSSION

Adenocarcinoma of the ampulla of Vater is the second most common periampullary adenocarcinoma, representing 21% of patients undergoing Whipple resection in a previous series from this institution.[2] Previous reports suggest that these patients can expect a better chance of survival after resection compared to those with adenocarcinoma of the pancreatic head. In fact, this tumor has been called "the most curable of all carcinomas of the upper gastrointestinal tract."[5] However, reported series are small, and the treatment of periampullary cancer has evolved significantly in recent decades. The current series of 120 patients over 28 years represents the largest single

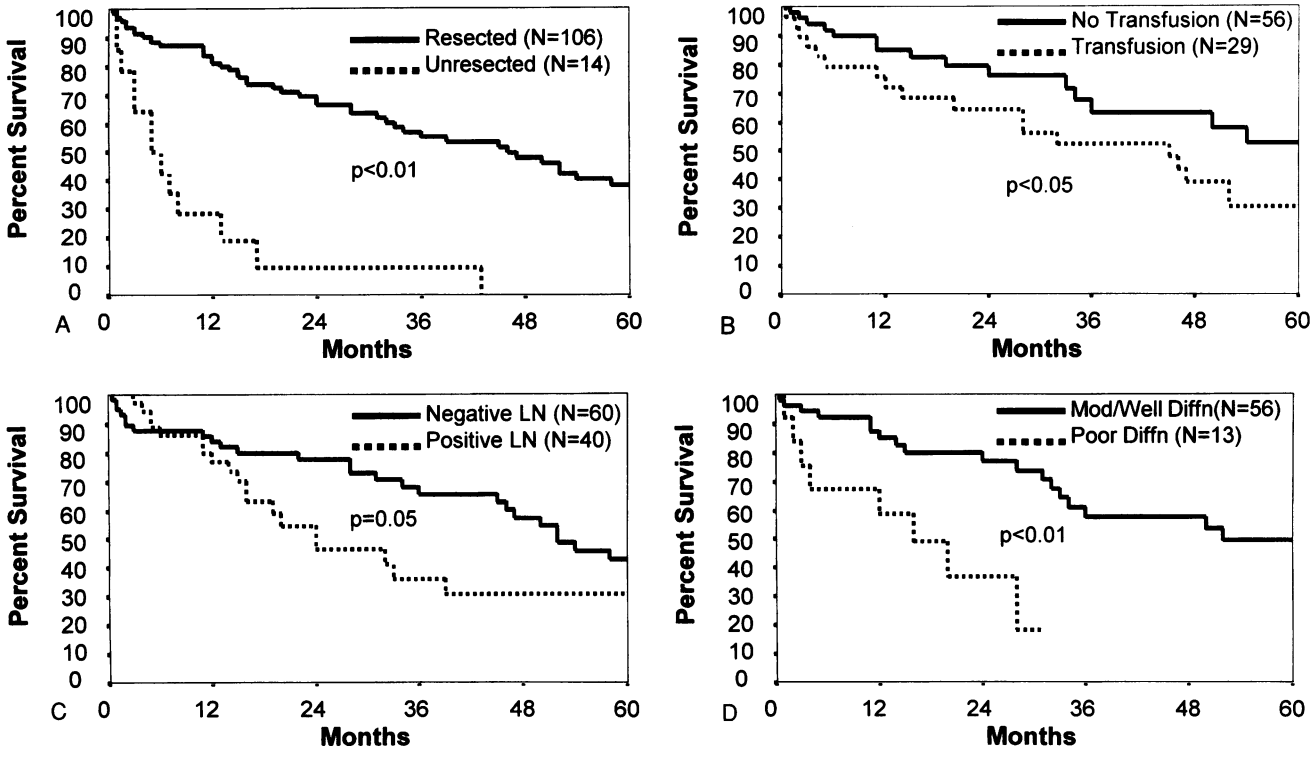

Figure 5. (A) Influence of resection on outcome for ampullary carcinoma. (B) Influence of blood transfusion on outcome for ampullary carcinoma. (C) Influence of lymph node status on outcome for ampullary carcinoma. (D) Influence of tumor differentiation on outcome for ampullary carcinoma.

institution experience with adenocarcinoma of the ampulla. In this report, the resectability rate was 88%; hospital mortality was 3.8%, and the 5-year survival was 38% in the resected patients. Resectability, negative lymph nodes, moderate or well-differentiated histology, and the absence of intraoperative blood transfusion all favored prolonged survival. Overall morbidity and hospital stay levels have fallen since 1992, and all four postoperative deaths occurred before 1992.

The largest series of ampullary adenocarcinoma published to date is a multicenter series reporting on 459 patients collected from 57 institutions between 1949 and 1974.[6] In that series, 77% of patients were resectable with an operative mortality of 17%, and the 5-year survival was only 6%. Another multicenter series, from the Veterans Administration Hospitals,[7] reported 123 patients, 64 (52%) of whom were resected successfully. Monson et al.[8] from the Mayo Clinic reported 104 patients with a 5-year survival of 34%. A single center series from The Netherlands[9] reported an 8-year experience with 67 pancreatic resections in patients with ampullary adenocarcinoma. Hospital mortality was 9%, and the overall 5-year survival was 50%.

Matory et al.[10] from the Memorial–Sloan Kettering Cancer Center reported that resection was performed in 57 (83%) of 69 patients with carcinoma of the ampulla of Vater. Only resectability favored improved outcome, and the 5-year survival was 40%. Similarly, Walsh et al.[11] from the University of Michigan reported a series of 51 patients where resectability favored survival. Forty-four (86%) were resected, but 5-year survival was only 16%. Willet et al.[12] from the Massachusetts General Hospital reported 41 patients. Five-year survival was 55% among 29 patients undergoing pancreatoduodenectomy. Another single center series from Italy[13] reported a 19-year experience with 36 patients, 31 (86%) of whom underwent resection. The 5-year survival was 56% in this series. Factors found to improve the chance of survival included tumor stage, lymph node status, and degree of differentiation in the lesion.

The current series reports an overall morbidity rate for resected patients of 47% with the most common complication (25%) being pancreatic fistula. Our strict definition of a fistula as 50 mL or more of amylase-rich fluid at 10 days after surgery may be more stringent than other published series. However, this incidence is higher than the 11.7% incidence reported for all pancreatoduodenectomies at Johns Hopkins by Yeo et al.[14] using the same definition in a prospective randomized trial comparing pancreaticojejunostomy to pancreaticogastrostomy. In

that study, multivariate analysis found that duodenal and ampullary pathology were risk factors for pancreatic fistula. The specific risk of a soft gland as a causative agent in fistula formation was addressed specifically in a series of 35 ampullary adenocarcinoma patients reported by Hayes et al.[5] They concluded that leakage "strongly correlated with the quality of the pancreatic remnant." Ten patients with evidence of obstructive pancreatitis experienced no leaks, whereas in 21 patients with a normal pancreas, the leak rate was 43% ($p < 0.05$).

Chronic pancreatitis may occur less often from adenocarcinoma of the ampulla of Vater than from pancreatic cancer. Biliary obstruction occurs with ampullary carcinomas, but in most patients, pancreatic juice still can decompress through the duct of Wirsung. Thus, in the current series, 73% of those resected had a history of jaundice, but only 2% had a history of acute pancreatitis. Interestingly, patients eventually found to be unresectable were more likely (28%) to present with acute pancreatitis ($p < 0.05$).

The overall hospital mortality for this group of patients with ampullary carcinoma (3.8%) treated over a 28-year period is similar to that of the Johns Hopkins series of patients with pancreatic cancer (5%) during this same period.[15] In both series, hospital mortality is lower in recent years than early in the series. The reduction in mortality after the Whipple procedure for ampullary adenocarcinoma (0% since 1992) also reflects the institutional trend for all resections.[16] This trend is attributed to careful preoperative patient evaluation, better anesthesia and critical care, and specialization.[17] The Johns, Hopkins mortality rate appears to be acceptably low compared to that of other series of resections for ampullary carcinoma where mortality ranges from 3% to 10%.[7,9,13,18–20]

Adenocarcinoma of the ampulla is considered by some to have the best survival potential of the periampullary adenocarcinomas. The results presented for this series confirm this impression with a 5-year actuarial survival of 38% in resected patients. These results are similar to most other large series where 5-year survival ranges from 34% to 45%.[8,9,12,18,20,21] Conversely, 5-year survivals as low as 21%[7] and as high as 50% to 56% have been reported.[9,13,22] However, in comparison to pancreatic cancer, ampullary adenocarcinoma indeed has a better prognosis. Some authors have suggested that the high survival rates reported for patients with ampullary carcinomas may be because of short follow-up, exclusion of postoperative deaths, and inclusion of early cancers.[8] The current series, however, is large and spans 28 years providing for long follow-up.

The current study shows, for the first time, that intraoperative blood transfusions are a significant factor affecting long-term survival in patients undergoing resection for adenocarcinoma of the ampulla of Vater. This observation also has been the case in reports from this institution evaluating survival after pancreatoduodenectomy for pancreatic adenocarcinoma.[15,23] In the first report, patients receiving fewer than 2 units of blood survived a median of 24.7 months, compared to 10.2 months for those receiving more than 2 units of blood.[23] In the more recent multivariate analysis of patients with pancreatic cancer, tumor biology was more important than blood transfusions. However, in the multivariate analysis of the current series of ampullary tumors, blood transfusions were more important than was tumor biology. Thus, our current practice is to perform a careful operation with minimal blood loss and to avoid transfusion therapy unless absolutely necessary.

The presence or absence of positive lymph nodes and the degree of tumor differentiation both were important factors affecting survival in the current series. Several authors have found that tumor-positive lymph nodes adversely affect outcome.[8,13,24–26] However, reports from Amsterdam and Memorial–Sloan Kettering have not confirmed this observation, perhaps because these series are smaller.[9,10] Both Sperti et al.[13] from Italy and Yamagushi and Nishihara[27] from Japan also have found that the degree of tumor differentiation is important. Conversely, Allema et al.[9] from The Netherlands did not find that the degree of differentiation was as important as was neural invasion.

The presence of a small tumor of the ampulla of Vater has presented a temptation to both gastroenterologists and surgeons to be satisfied with a local resection. In some cases, these lesions are benign or premalignant polyps that can be controlled adequately in this manner. However, once the specimen has been identified as containing carcinoma, a decision must be made regarding the adequacy of local resection *versus* the increased operative risk of pancreatoduodenectomy.

Rattner et al.[28] have proposed criteria regarding the acceptability of local resection for neoplasms of the ampulla. Their criteria for ampullectomy (local resection) consisted of benign lesions smaller than 3 cm, small neuroendocrine tumors, and T1 carcinomas (tumor limited to the mucosa) of the ampulla. However, the presence of a genetic "field effect" such as occurs in patients with familial adenomatous polyposis mitigates toward radical resection. They also concluded that size, duration of symptoms, or jaundice can not predict malignancy reliably. Iwama et al.[29] from Japan suggested that indications for local resection in patients with familial adenomatous polyposis include severe atypia or carcinoma *in situ,* no jaundice, no bile duct dilatation, and age older than 35 years. With local resection, the duodenal wall submucosa and muscularis are preserved. Therefore, endoscopic ultrasound is important in determining depth of invasion before surgery.[30]

Reports from Italy,[13] Duke,[31] and Lahey Clinic[32] all

suggest that the recurrence rate after local resection is high. In the Italian series, tumors recurred in three of five patients.[13] At Duke, six of eight tumors recurred after local resection.[9] At the Lakey Clinic, one of two cancers and three of nine villous tumors eventually required a pancreatoduodenectomy.[32]

In the current series, three patients were treated initially with local resection. After full pathologic evaluation, one patient went on to "completion" pancreatoduodenectomy in a few days. Another patient recurred after 18 months and then underwent a pancreatoduodenectomy. Both are long-term survivors (greater than 5 years). The remaining patient appeared to be resected adequately by local means, and pancreatoduodenectomy was not performed despite the presence of carcinoma. This small subgroup of patients confirms that local resection has a limited role in carefully selected patients.

Adjuvant chemotherapy has been applied more frequently in the recent decade after extirpative therapy. As data have accumulated regarding the benefit of adjuvant therapy for other gastrointestinal malignancies, some groups have given adjuvant chemotherapy or radiation therapy to patients with ampullary carcinoma. Bakkevold and Kambestad[24] have suggested that chemotherapy may be helpful. However, Willet[12] and associates from the Massachusetts General Hospital found no benefit for radiation therapy. Recent data from Johns Hopkins suggest that adjuvant chemoradiation may be helpful in patients with pancreatic cancer.[15] However, the number of patients with ampullary carcinoma treated with chemoradiation is too small to draw any conclusions.

This series shows evolution over 3 decades in the therapy and results after treatment of adenocarcinoma of the ampulla of Vater. Although the overall resectability rate for the series was 88%, this rate has risen from 62% in the 1970s to 82% in the 1980s to 96% in the 1990s. Factors contributing to this rise may include more careful screening of surgical candidates or increased aggressiveness of the surgical approach. Data regarding blood loss and transfusion were not available for the 1970s, but when the 1980s were compared with the 1990s, the blood loss was not significantly different. However, the number of erythrocyte transfusions per patient decreased from an average 1.5 units in the 1980s to 0.62 unit in the 1990s. In addition, the length of stay, morbidity, and mortality also have all dropped since 1992. Despite these improvements, long-term survival after resection has remained the same in each decade. This difference from our recent report in patients with pancreatic cancer[14] may be because of a less dramatic change in hospital mortality and limited use of adjuvant therapy.

This series presents a large single institution experience with adenocarcinoma of the ampulla of Vater, the second most common periampullary neoplasm. Adenocarcinoma of the ampulla has a higher resectability rate and a better long-term survival rate than does ductal pancreatic cancer. Survival was better in those patients whose tumor could be resected, those receiving no blood transfusions, those with negative lymph nodes, and those with moderate or well-differentiated histology. Morbidity, mortality, and length of stay have decreased since 1992. Thus, this study affirms the appropriateness of an aggressive approach to ampullary adenocarcinoma and, by extension, to all periampullary adenocarcinomas because a definitive tissue diagnosis often can be determined only after careful pathologic evaluation of the resected specimen.

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DISCUSSION

DR. R. SCOTT JONES (Charlottesville, Virginia): First, I want to thank all the authors, and particularly Dr. Mark Talamini for inviting me to comment on this splendid paper. As everyone realizes, this work, this series, and its analysis and presentation really set the standard for the management of this disorder, ampullary carcinoma.

I would like to make one comment and ask one question. The comment is that the authors have shown vividly that this disease has a very high resectability rate and a very low mortality rate. And the diagnosis can be made preoperatively fairly accurately.

Dr. Pitt, in his presentation, mentioned that as surgeons, we usually do not completely control the preoperative evaluation of patients such as this, and preoperative management up to a certain point. But I would like to suggest that we generally do too much in terms of evaluation of these patients. On the basis of the data presented about resectability, I would suggest that we had a jaundiced patient whose history and laboratory data suggested obstructive jaundice. We did an ultrasound examination that demonstrated distal bile duct obstruction, no mass in the liver, and no mass in the pancreas. That clearly should be an indication for endoscopy.

In that case, if the endoscopist saw ampullary lesion and performed a biopsy, you have a diagnosis of adenocarcinoma of the ampulla of vater, and you probably don't need any more tests, assuming the patient is fit and is not septic. You could spare some of this other workup.

There are a couple of points that are worth comment. It is possible I have been confused a time or two about a patient who had carcinoma of the pancreas invading the duodenum, but I would suggest a careful review of that situation, even an ultrasound would probably reveal that.

In the discussion, I hope the authors will comment on my suggestion about streamlining the workup. There is one other point, and that is the arteriogram. It has been used in staging. Dr. Pitt, in his presentation, mentioned that spiral computed tomography has decreased the need for the arteriogram. You could say you need an arteriogram to reveal the hepatic artery anatomy. But I suspect, I know, that the surgeons at Hopkins can determine in a matter of minutes whether or not there is a replaced or an accessory hepatic artery, so that argument fades into the background.

The second thing I wanted to ask about is something we ponder: the role of radiation as adjuvant therapy in patients who have ampullary carcinoma. We now have available trials in pancreatic cancer that show adjuvant therapy increases survival. And, to my knowledge, we do not have such information for ampullary carcinoma. This question comes up, and I would like to ask the authors to comment and share their thoughts with us about if and when adjuvant therapy is indicated in patients with carcinoma of the ampulla of vater.

I would like to close my comments by thanking the group at Johns Hopkins Hospital for their leadership, their scientific approach, and their excellent clinical studies that really show the way for the rest of us to understand how to manage these patients.

Thank you very much.

DR. MURRAY F. BRENNAN (New York, New York):

Mr. Chairman, Members, and Guests. I, too, would like to thank the authors for providing me a copy of the manuscript and asking me to comment on this paper.

Operations on the pancreas for malignancy receive far more attention than they statistically deserve. I am beginning to worry that operations on the pancreas achieving status is an indicator of some kind of surgical manhood.

Perhaps most worrisome, that reflects most on the personality and the insecurities of people such as myself and, indeed — can I say it? — our distinguished president, who talk and write about such subjects.

In preparation for this commentary, I gathered our own results