Adenocarcinoma of the Ampulla of Vater

Diagnosis and Treatment

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Fifty-one patients underwent operation for adenocarcinoma of the ampulla of Vater. Seven patients underwent palliative bypass, with an operative mortality of 28.6%; 44 additional patients underwent potentially curative pancreaticoduodenal resection (PDR), with an operative mortality of 15.9%. Postoperative complications occurred in 63% of patients. Postoperative gastrointestinal bleeding was observed in 11 of 44 patients who underwent PDR (25%). Although anastomotic ulcers (AU) were directly implicated in five cases (45%), the 12% incidence of AU-related bleeding among 33 patients who underwent PDR without truncal vagotomy (TV) was not significantly different from the 9% incidence observed in 11 patients who underwent PDR plus TV. However, performance of TV appeared to result in a higher incidence of postoperative pulmonary complications. Five patients who underwent curative resection survived for five years (11%). Only one of seven patients who underwent palliative bypass survived three years (14%), and none survived to five years. Acceptable survival rates following resectional therapy warrant an aggressive approach to this tumor. Further, our experience suggests that TV may increase postoperative patient morbidity without actually providing any protection from anastomotic ulceration.

WHIPPLE AND CO-WORKERS in 1935 described a two-stage resectional procedure for carcinoma of the ampulla of Vater.[1] Since that time enthusiasm for radical extirpation or pancreaticoduodenectomy has varied. Warren et al. have suggested that increased five-year survival rates and reduced operative mortality justify an aggressive surgical approach.[2] On the other hand, Crile has reported improved survival and reduced postoperative mortality in patients undergoing palliative bypass alone.[3]

In the last decade, methods of diagnosis have changed dramatically. Such modalities as ultrasonography, endoscopic retrograde cholangiopancreatography (ERCP), computerized axial tomography (CAT), and selective arteriography have generally replaced barium contrast studies in terms of diagnostic sensitivity and specificity.[4]

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These newer diagnostic techniques may aid in the early differentiation of ampullary from pancreatic head carcinomas, lesions with similar clinical presentations yet quite different clinical courses.[5-8] This study reviews a 22-year experience with adenocarcinoma of the ampulla of Vater at the University of Michigan Medical Center and affiliated hospitals. The diagnostic efficacy of ultrasonography, ERCP, arteriography, and CAT scanning, as well as the relationship of preoperative laboratory studies, tumor size, and known metastases to ultimate patient prognosis following operation, has been analyzed.

Materials and Methods

From 1957 through 1979, 51 patients with adenocarcinoma of the ampulla of Vater documented by gross and microscopic examination of resected specimens underwent operation at the University of Michigan Medical Center and affiliated hospitals. Follow-up information was complete through 1980 or to the time of the patient's death. The autopsy data from 25 patients who died during the course of the study have been included.

Duration of symptoms was calculated from date of onset as determined by the patient to date of initial evaluation. Positive physical findings were those evident at the time of admission. Laboratory values were included when first abnormal or when values peaked prior to operation. X-ray examinations were reported as normal, abnormal, or diagnostic. Such studies were considered diagnostic when the radiologist's evaluation suggested a malignant neoplasm as the most likely cause of roentgenographic abnormalities. The accuracy of the surgeon's initial assessment of the site of tumor origin

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was determined by comparison of operative notes and the pathologist's evaluation of the resected specimen. The location and number of lymph nodes involved with tumor were determined by histologic examination. Operative deaths were defined as those deaths that occurred prior to or within 30 days of discharge from the hospital.

Two-way cross tabulations were used to compare results in separate but comparable populations. Maximum likelihood, chi-square, and Fisher exact probability tests were applied separately to each tabulation. Significance was established only when p values less than 0.05 were achieved for all three tests.

Results

Of the 51 patients with adenocarcinoma of the ampulla of Vater, 27 were men and 24 were women. The mean patient age was 58.6 years, with a range of 25 to 82 years. There was no significant age or sex predilection.

Jaundice was the most common presenting symptom and was exhibited by 82% of patients at the time of admission. Dyspepsia, malaise, and anorexia occurred less frequently, in 15–30% of patients. Constitutional symptoms in general preceded the onset of clinical jaundice by several months. The most common presenting symptoms and signs are listed in order of decreasing frequency in Table 1.

Scleral or cutaneous icterus was the most common abnormality noted on physical examination. Other abnormal physical findings, in order of decreasing frequency, included weight loss (51%), hepatomegaly (31%), hemacult positive stool (16%), and the presence of an abdominal mass (10%). None of the patients exhibited a palpable gallbladder at the time of evaluation.

Five hundred one laboratory tests were run on 51 patients. Of these, 280 (56%) were abnormal (Table 2). Alkaline phosphatase and bilirubin levels were four and eight times above normal mean values, respectively. Anemia was noted in nearly two thirds of patients, but the relatively small variance of hematocrit values from normal mean values suggested that it was not severe. Prothrombin time was abnormal in 59% of patients. All remaining coagulation parameters were normal.

Nine diagnostic modalities were used in this study with varying success (Table 3). Barium contrast studies of the upper gastrointestinal tract, including hypotonic duodenography, were normal in 39% of cases. Ultrasonography, which was used in assessing seven patients, suggested solid mass lesions in the area of the pancreatic head or ampulla in three instances. False-negative results were obtained in 29% of cases. Selective arteriography was used in ten patients. All of these studies were considered abnormal, but only eight demonstrated angiographic features typical of malignant neoplasms. The ampulla was visualized endoscopically and thought to be abnormal in six patients. Biopsies in three of these patients were positive for adenocarcinoma. Biopsies in the remaining three patients were diagnosed initially as benign periampullary ulcers. These patients were later proven to have ampullary malignancies. Computerized axial tomography was obtained in only two cases but successfully demonstrated periampullary mass lesions in both instances.

TABLE 1. *Presenting Signs and Symptoms*

Symptom	Per Cent of Patients	Median Day of Occurrence Prior to Admission
Jaundice	82.3	30
Pruritis	49.0	30
Abdominal pain	37.2	90
Nausea	33.3	90
Anorexia	31.4	90
Malaise	29.4	150
Vomiting	27.4	30
Dyspepsia	13.4	365
Melena	11.8	30

Fifty-one patients underwent operation (Table 4). Of these, 28 had undergone previous exploration and biliary drainage. Four of the latter group of patients had also undergone limited local resection, as well as exploration and biopsy. Twenty-three patients underwent a single operative procedure. No initial attempt at curative resection was made at this institution if the preoperative level of serum bilirubin exceeded 10 mg/dl. Pancreaticoduodenal resection was performed using previously described surgical techniques.[9]

During each operation an attempt was made by the responsible surgeon to assess the site of origin of the tumor. The surgeon's impression was confirmed or re-

TABLE 2. *Laboratory Studies*

Test	Number of Tests	Per Cent Abnormal	× Normal Mean Value
SGPT	35	85.7	4.3
SGOT	42	73.8	2.8
Hematocrit	47	68.3	0.9
Alkaline phosphatase[1]	50	66.0	4.3
Bilirubin total serum	50	64.0	8.6
Hemoglobin	44	64.6	0.9
LDH	29	62.1	2.9
Prothrombin time	41	58.5	0.85
Albumin	31	48.4	0.8
Fasting blood sugar	38	44.7	1.3
Total protein	39	23.1	0.95
Amylase	32	15.6	0.9
Globulin	23	0	1.5
Total tests	501	56	

TABLE 3. *Diagnostic Procedures*

Procedure	Number of Cases	Per Cent Normal	Per Cent Abnormal	Per Cent Diagnostic
CAT scan	2	0.0	100.0	100.0
Selective arteriography	10	0.0	100.0	80.0
IVC	4	0.0	100.0	75.0
Gastroduodenoscopy	6	0.0	100.0	50.0
ERCP	6	0.0	100.0	50.0
Ultrasonography	7	28.6	71.4	42.9
UGI	33	39.4	60.6	27.3
Barium enema	13	84.6	15.4	0.0
Liver scan	8	75.0	25.0	0.0

futed by pathologic examination of the resected specimen. Clinical judgment was correct in 29 instances, for an overall accuracy rate of 66%. Incorrect assessments were made in the remaining 13 cases.

Seven of 44 patients who underwent PDR died, for an operative mortality of 16%. Of these, 33 patients underwent resection alone, and 11 patients underwent resection plus TV. The operative mortality among patients who underwent palliative bypass was not significantly different from that of patients who underwent potentially curative resections (Table 5).

The complication rates in patients who underwent pancreaticoduodenectomy alone vs. those who underwent PDR with TV were 57.6% and 81.8%, respectively (PNS). However, the frequency of pulmonary and biliary complications varied in relation to the type of operation performed (Table 6). Pneumonia occurred more frequently in patients who underwent vagotomy in addition to PDR than in those who underwent resection alone. A subsequent analysis of possible contributing factors such as prolonged operating time, increased intraoperative blood loss, and an increased incidence of intra-abdominal sepsis failed to demonstrate any significant differences between these two groups of patients. Ascending cholangitis occurred only in patients who had undergone palliative bypass. Morbidity and mortality did not vary according to the type of operation performed when patients were grouped by age, duration of symptoms, weight loss, severity of jaundice, and/or preoperative levels of serum proteins.

TABLE 4. *Operative Therapy*

Operative Therapy	
Primary procedure	18
Prior exploration and biopsy	1
Prior exploration and biliary drainage	22
Prior exploration, biliary drainage, and local resection	3
Total	44
Biliary Bypass	
Primary procedure	5
Prior exploration and biliary drainage	1
Prior local resection and biliary drainage	1
Total	7

Among patients who underwent PDR, postoperative gastrointestinal hemorrhage was observed in 11. The sources of bleeding, documented either endoscopically or at reoperation, included erosive gastritis in five cases and anastomotic ulcerations (AU) in five other cases. No specific source of bleeding was identified in the remaining patient. Anastomotic ulcers were observed from ten days to four years following operation, but 80% of these lesions were demonstrated within three months of operation. The 12% incidence of AU-related gastrointestinal bleeding among 33 patients who underwent resection alone was not significantly different from the 9% incidence observed in 11 patients who underwent resection plus TV.

Forty-four resected specimens were available for pathologic examination. The mean diameter of the resected lesions was 2.1 cm, with a range of 0.75 to 8.0 cm. Among patients who underwent curative resection, tumor size did not correlate with operative morbidity or mortality. Lymph node metastases were demonstrated in 16 (36.4%) resected specimens. Neither operative morbidity nor mortality was altered by the presence or number of lymph nodes involved by tumor.

The five-year survival rates of patients who underwent resection vs. palliative bypass are illustrated in Figure 1. Cumulative survival rates at one, three, and five years for 44 patients who underwent resection were 67%, 26%, and 16%, respectively. In contrast, there were no five-year survivors among the group of seven patients who underwent palliative bypass only. All of the latter patients eventually died of carcinoma. Similarly, 24 of 32 patients (75%) who died within five years of a curative resection succumbed to recurrent tumor. One additional patient died of unrelated causes. The cause of death could not be determined in the seven remaining patients. Length of survival among patients who underwent curative resection was not affected significantly by tumor size or by the presence and number of involved lymph nodes at the time of resection.

Ten of 37 patients (27%) who survived a curative resection developed late postoperative gastrointestinal problems. Four patients complained of intractable diarrhea, eight patients experienced weight loss of greater than 10 kg, and nine additional patients were affected with persistent abdominal pain.

Discussion

There appears to be no age or sex predilection among patients with adenocarcinoma of the ampulla of Vater in this or other clinical series.[2,5,8] Although there was a tendency for males to outnumber females, only Warren, Fish, and Beall determined this difference to be significant.[2,10,11] In this as in other studies, ampullary

TABLE 5. *Morbidity and Mortality*

Operation	Number of Patients	Per Cent Morbidity	Per Cent Mortality
Pancreaticoduodenectomy alone	33	57.6	12.1
Pancreaticoduodenectomy with vagotomy	11	81.8	27.3
Bypass	7	57.1	28.6

adenocarcinoma occurred most frequently between the ages of 55 and 65 years.

Nonspecific abdominal complaints have been reported as the earliest appearing symptoms in patients with ampullary adenocarcinoma.[7,12,13] This was also true among our 51 patients. Jaundice occurred in 30% of the patients in the present series. This sign most commonly caused our patients to seek medical attention. Similar occurrence rates were documented previously by others[7,15,16] A palpable gallbladder has been reported in 13–65% of patients with ampullary adenocarcinoma. However, none of the 51 patients in the present series exhibited this finding at the time of examination. The absence of a palpable gallbladder in our patients may have been due to earlier diagnosis as compared with that of previous reports. Perhaps more likely, this observation was due to the significant number (n = 23) of patients who had undergone biliary decompression prior to admission to our institution.

Many authors have emphasized the clinical association of occult blood in the stool and jaundice in patients with periampullary neoplasms[9–10,15,17]; some have gone so far as to suggest that these findings are specific for periampullary neoplasms.[15,18] In our series, however, only 15.7% of jaundiced patients were found to have hemacult positive stools. This incidence may be artificially high since many patients had undergone previous exploration and biliary decompression. Jaundice and hemacult positive stools have been reported not only in patients with ampullary carcinoma, but also in patients with biliary lithiasis, acute alcoholic hepatitis, and hemobilia as well.[19–24]

The classic findings of anemia and obstructive jaundice occur with regularity in patients with adenocarcinoma of the ampulla of Vater.[7,13,15,17] Pancreatic endocrine and exocrine functions, as evaluated by glucose tolerance tests and serum amylase levels, are usually normal.[11,13,25] In contrast to the findings of Gilsdorf and Spanos, no relationship existed in the present series between specific laboratory abnormalities and postoperative morbidity or mortality.[26] It is important to note, however, that curative resections were not undertaken unless the preoperative serum bilirubin was below 10 mg/dl.

Hypotonic duodenography has been a traditional method of diagnosis in patients with obstructive jaundice.[27,28] Among the patients in the present study, 50–80% of the contrast studies of the upper gastrointestinal tract were abnormal. Unfortunately, falsely normal studies occurred in 40% of cases; although sensitive, hypotonic duodenography lacks specificity, an observation that has been demonstrated in other series as well.[15,25,28] Initial experience with selective visceral arteriography in patients with suspected ampullary carcinoma is less extensive than that with contrast radiography, but it is encouraging.[28,29] In the present series, arteriography was abnormal in 100% of cases and was diagnostic of periampullary mass lesions in 80% of cases. Ultrasound, which clearly is a safe and useful noninvasive technique in the evaluation of jaundiced patients, failed to delineate a mass in four of seven patients with documented periampullary lesions. This lack of specificity may have been due in part to the small size of some of the ampullary lesions noted at the

TABLE 6. *Complications*

Complication	Pancreaticoduodenectomy alone (n = 33)	Pancreaticoduodenectomy with Vagotomy (n = 11)	Bypass (n = 7)
Wound infection	18.2%	9.1%	14.3%
Abdominal abscess	15.2%	27.3%	14.3%
GI hemorrhage	24.0%	18.0%	14.3%
Septicemia	12.1%	18.2%	14.3%
Pneumonia	3.0%	36.4%	14.3%
Marginal ulcer	12.1%	9.1%	0.0%
Pleural effusion	6.1%	9.1%	0.0%
Renal failure	0.0%	9.1%	14.3%
Ascending cholangitis	0.0%	0.0%	28.6%
Bile peritonitis	0.0%	9.1%	0.0%
Pulmonary embolus	3.0%	0.0%	0.0%
Average	7.6%	12.0%	10.4%

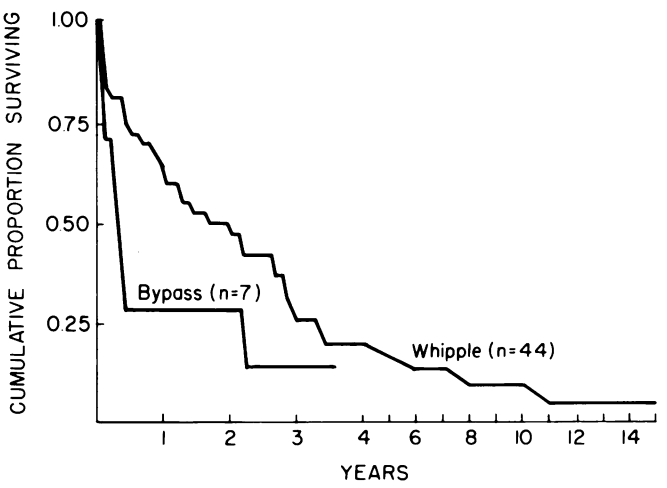

FIG. 1. Cumulative survival rates of patients with adenocarcinoma of the ampulla of Vater who underwent radical pancreaticoduodenal resection vs. palliative biliary and/or enteric bypass.

time of operation. Warren and Hoffman have observed previously that fiberoptic duodenoscopy and duct radiography cannot be depended upon to diagnose ampullary neoplasms reliably.[4] These modalities were accurate in 50% of patients studied. However, ampullary neoplasms were diagnosed incorrectly as benign ampullary ulcers in 25% of our patients who underwent endoscopy and biopsy. This high incidence of misleading histologic diagnoses contrasts sharply with the experience of Braasch and Camer, who strongly advocate these diagnostic techniques.[25] Computerized axial tomography was used in only two patients but was diagnostic in each. Our results echo similar reports, which describe the excellent diagnostic accuracy of CAT in the jaundiced patients.[30,31]

Five-year survival rates of 6–40% have been reported in patients undergoing curative resection for ampullary adenocarcinoma.[4,5,8,14,15,16,18,25,32,33] Five patients (11%) in our series survived five years. This comparatively low five-year survival rate may be explained by the greater number of curative resections (86%) attempted in this than in other series. Only one patient in this series who underwent palliative bypass survived for three years, and no patients so treated survived to five years. Operative mortality was similar whether the patient underwent curative resection or palliative bypass. Patients who underwent bypass procedures generally had locally extensive or metastatic disease that precluded safe resection. Improved patient selection clearly plays an important role in any effort to improve survival rates among patients with ampullary adenocarcinoma. Resectional therapy in our hands was not associated with an increase in morbidity or mortality. Crile's experience, however, suggests that bypass is preferable to resection because of lower mortality and morbidity. Data from the present study do not support Crile's observations. The significant opportunity for prolonged patient survival without increased risk of attendant complications emphasizes the importance of resectional therapy among these patients. An aggressive approach to these lesions has indeed been advocated by other investigators as well.[3,18,31,32]

Intraoperative differentiation of pancreatic from ampullary carcinomas can be difficult and at times impossible. Warren cited a 10% incidence of incorrect intraoperative assessment of the site of tumor origin in his series.[2] The 34% incidence in the present series, although higher than that described by Warren, did not alter therapy and simply serves to underscore the difficulties in differentiation that may be encountered at laparotomy.

Scott and Grant recently reported an association between postoperative anastomotic ulceration and decreased survival in patients undergoing pancreaticoduodenectomy without vagotomy.[35,36] The development of anastomotic ulcerations following operation in our series did not appear to decrease survival significantly. The high incidence (36%) of this complication reported by Scott among patients undergoing pancreaticoduodenal resection with vagotomy differs from the 9% incidence observed in the present series. Similar low incidences have been reported in other series as well.[7,15,16,36] In this study, the addition of TV to pancreaticoduodenectomy did not decrease the frequency or severity of postoperative gastric complications (ulceration and/or bleeding). However, vagotomy plus resection appeared to result in an increased incidence of postoperative pulmonary complications. Disparities in patient age, operative blood loss, and duration of the operative procedure could not be identified as factors that may have contributed to this difference. Our experience suggests that TV may increase postoperative patient morbidity without actually providing any protection from AU.

Warren and others have reported increased survival rates among patients without nodal metastases who undergo curative resection.[4,6,17,33] In the present series, 16 of 44 resected specimens showed histologic evidence of nodal involvement. However, the presence and/or number of nodes involved with carcinoma did not appear to alter patient survival.

Evaluation of the patient with symptoms of weight loss and mild but persistent gastrointestinal distress should include ultrasonography and/or computerized tomography. These noninvasive techniques may be useful in evaluating the presence of a small pancreatic mass and may help to define the status of the biliary ductal system. Duodenoscopy and duct radiography may be of additional value to determine the etiology of the biliary obstruction. It is important to note, however, that a negative endoscopic biopsy of the ampulla should be viewed with suspicion in such a patient. Selective visceral arteriography may be necessary to define normal and variant fore and midgut arterial anatomy, to provide differential diagnostic information regarding tumor vascularity, and to aid in establishing resectability prior to operation.

Obstructive jaundice resulting from carcinoma of the ampulla of Vater warrants aggressive surgical therapy. If the level of serum bilirubin does not exceed 10 mg/dl, single-stage resection and primary reconstruction should be considered. However, if the total serum bilirubin exceeds 10 mg/dl, preliminary biliary decompression should be undertaken. This can be accomplished most easily by the percutaneous or intraoperative placement of a catheter in the biliary duct system. Pancreaticoduodenectomy remains the therapeutic procedure of choice in patients with ampullary adenocarci-

noma and no evidence of distant metastases. Resection, as opposed to palliative bypass, offers the greatest opportunity for cure at no apparent increased risk to the patient.

References

1. Whipple AD, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg 1935; 102:763–779.
2. Warren KW, Veidenheimer MC, Pratt HS. Pancreaticoduodenectomy for periampullary cancer. Surg Clin North Am 1967; 47:639–645.
3. Crile G, Isbister WH, Hawk WA. Carcinoma of the ampulla of Vater and the terminal bile and pancreatic ducts. Surg Gynecol Obstet 1970; 131:1052–1054.
4. Warren KW, Hoffman G. Changing patterns in surgery of the pancreas. Surg Clin North Am 1976; 56:615–629.
5. Forrest JF, Longmire WP Jr. Carcinoma of the pancreas and periampullary region. Ann Surg 1979; 189:129–138.
6. Sato T, Saitoh Y, Noto N, Matsuno S. Follow up studies of radical resection for pancreaticoduodenal cancer. Ann Surg 1977; 186:581–588.
7. Cattell RB, Warren KW, Au FTC. Periampullary carcinomas. Surg Clin North Am 1959; 39:781–798.
8. Coutsoftides T, MacDonald J, Shibata HR. Carcinoma of the pancreas and periampullary region. Ann Surg 1977; 186:730–733.
9. Child CG III, Frey CF. Pancreaticoduodenectomy. Surg Clin North Am 1966; 46:1201–1213.
10. Fish JC, Cleveland BR. Pancreaticoduodenectomy for peri-ampullary carcinoma. Ann Surg 1964; 159:469–476.
11. Beall MS, Dyer HA, Stephenson HE. Disappointments in the management of patients with malignancy of pancreas, duodenum, and common bile duct. Arch Surg 1970; 101:461–465.
12. Longmire WP Jr, Shaffey OA. Certain factors influencing survival after pancreaticoduodenal resection of carcinoma. Am J Surg 1966; 111:8–12.
13. Monge JJ, Dockerty MB, Wollaeger EE, et al. Clinicopathologic observations on radical pancreaticoduodenal resection for peripapillary carcinoma. Surg Gynecol Obstet 1964; 118:275–283.
14. Miller EM, Dockerty MB, Wallaeger EE, Waugh JE. Carcinoma of the region of the papilla of Vater. Surg Gynecol Obstet 1951; 92:172–182.
15. Wise L, Pizzimbono C, Dehner LP. Periampullary cancer. Am J Surg 1976; 131:141–148.
16. Warren KW, Cattell RB, Blackburn JP, Nora PF. A long-term appraisal of pancreaticoduodenal resection for peri-ampullary carcinoma. Ann Surg 1962; 155:653–662.
17. Makipour H, Cooperman A, Danzi JT, Farmer RG. Carcinoma of the ampulla of Vater. Ann Surg 1976; 183:341–344.
18. Crane JM, Gobbel WB Jr. Surgical experience with malignant tumors of the ampulla of Vater and duodenum. Surg Gynecol Obstet 1973; 137:937–940.
19. Nauyn B. Klinik du Cholelithiasis. Leipzig, 1892.
20. Green J, Mistilis S, Schiff L. Acute alcoholic hepatitis. Arch Intern Med 1963; 112:67–79.
21. Gad P. Okkult blodning ver galdesten. Nord Med 1862; 68:1069–1072.
22. Sandbloom P, Mirkoutch V. Minor hemobilia. Ann Surg 1979; 190:254–264.
23. Demeulenaere L; Van Waes L. Clinical aspects of alcoholic hepatitis. Acta Gastroenterol Belg 1977; 40:261–270.
24. Mihas AA, Doos WG, Spenney JG. Alcoholic hepatitis. J Chronic Dis 1978; 31:461–472.
25. Braasch JW, Camer SJ. Periampullary carcinoma. Med Clin North Am 1975; 59:309–314.
26. Gilsdorf RB, Spanos P. Factors influencing morbidity and mortality in pancreaticoduodenectomy. Ann Surg 1977; 177:332–337.
27. Poppel MH. Roentgen Manifestations of Pancreatic Disease. Springfield, IL: Charles C Thomas, 1951.
28. Eaton SB, Fleischili DJ, Pollard JJ, et al. Comparison of current radiologic approaches to the diagnosis of pancreatic disease. N Engl J Med 1968; 279:389–396.
29. Sata T, Saitoh Y, Koyama K, Watanabe K. Preoperative determination of operability in carcinomas of the pancreas and the periampullary region. Ann Surg 1968; 168:876–886.
30. Levitt RG, Sagel SS, Stanley RJ, Jost RG. Accuracy of computerized tomography of the liver and biliary tract. Radiology 1977; 124:123–128.
31. Havrilla TR, Haaga JR, Alfidi RJ, Reich NE. Computerized tomography and obstructive biliary disease. Am J Radiol 1977; 128:765–768.
32. Monge JJ, Judd ES, Gage RP. Radical pancreaticoduodenectomy. Ann Surg 1964; 160:711–722.
33. Warren KW, Choe DS, Plaza J, Relihan M. Results of radical resection for periampullary cancer. Ann Surg 1975; 181:534–540.
34. Nakase A, Matsumoto Y, Uchida K, Honjo I. Surgical treatment of cancer of the pancreas and the periampullary region. Ann Surg 1977; 185:52–57.
35. Scott HW Jr, Dean RH, Parker T, Avant G. The role of vagotomy in pancreaticoduodenectomy. Ann Surg 1980; 191:688–696.
36. Grant CS, Van Heerden JA. Anastomotic ulceration following subtotal and total pancreatectomy. Ann Surg 1979; 190:1–5.