Results of surgical treatment of carcinoma of papilla of Vater

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Key words: ampulla of Vater; carcinoma; surgery; survival rates.

Summary. Adenocarcinoma is the most common malignant tumor of the ampulla, but in general, it is still rare. Therefore, these tumors are difficult to study, and most reports are of retrospective design. To evaluate immediate postoperative and long-term results, we have collected data prospectively in a specially created database on 21 consecutive patients with adenocarcinoma of the papilla of Vater, operated on at the Department of Surgery, Kaunas University of Medicine Hospital. All patients have undergone classical or pylorus-preserving pancreatoduodenectomy.

Postoperative mortality was 4.8% and overall morbidity – 28.6%. Pancreas-associated morbidity was 14.3% in the series.

Actuarial 3-year survival among our patients was 89%.

Stage I–II patients with T1–T2 and/or N negative tumors had significantly better 3-year survival when compared with stage III–IV patients, T3–T4 and/or N positive tumors. Patients with highly or moderately differentiated tumors (G1, G2) survived better than patients with poor cell differentiation (G3), though significant difference was not achieved.

Results are satisfactory in terms of overall postoperative morbidity and mortality. Long-term survival pattern concerning T, N, and G status corresponds with other reports in literature, while the 3-year survival results are promising and speaks in favor of our surgical strategy.

Introduction

The anatomy of the ampulla of Vater is very complex. It consists of three different epithelia (bile duct, pancreatic duct, and duodenum). Adenomas are considered as precancerous lesions, and they usually occur in the fifth-sixth decade of life. There is evidence supporting adenoma-carcinoma sequence of neoplastic lesions of ampulla of Vater (1–3). The frequency of malignant lesion in an adenoma of the papilla is about 26% (4). In postmortem studies, carcinomas of papilla of Vater have been reported in 0.2% of cases (5).

Through increased use of endoscopy, ampullary tumors are more frequently recognized. Differentiation of adenocarcinoma of the pancreas from ampullary tumors is also important considering better prognosis for long-term survival in the latter group. It is generally agreed that adenocarcinoma of papilla of Vater should be removed by partial pancreatoduodenectomy, whereas local ampullectomy with local lymphadenectomy should be reserved for pTIs and pT1N0M0G1 or G2 tumors (4).

Adenocarcinoma is the most common malignant tumor of the ampulla, but in general, it is still rare. That is why these tumors are very difficult to study, and most reports considering ampullary tumors are of retrospective design.

To evaluate immediate postoperative as well as long-term results, we have collected data prospectively in a specially created database on 21 consecutive patients with adenocarcinoma of the papilla of Vater who had been operated on at the Department of Surgery, Kaunas University of Medicine Hospital. We have evaluated preoperative clinical data, pathology reports, tumor stage according to the International Union Against Cancer (UICC), postoperative morbidity, mortality, and long-term follow-up results.

Patients and methods

Between January 1, 1999, and May 30, 2003, 21 patients with adenocarcinoma of the papilla of Vater were operated on. In this group, 5 patients were male and 16 were female. The median age of all studied patients was 66 years (interquartile range 62–72). The median age of men was 72 years (interquartile range 66–73), and the median age of women was 66 years (interquartile range 59.5–70.5). Stage I and stage II tumors were predominant in female patients but without statistical difference (Table 1).
Surgical techniques

All 21 patients underwent major resection for malignant disease – Whipple procedure or pylorus-preserving partial pancreatoduodenectomy. The lymph-node dissection in all cases was performed in pursuance of D2 extent as it is performed in case of adenocarcinoma of the head of the pancreas.

Definition of surgical principles

Radical pancreatoduodenectomy was defined at our department as a resection of the head of the pancreas, duodenectomy, and a resection of the initial segment of jejunum; lymph node dissection, including anterior and posterior lymph nodes of the pancreatic head, supraduodenal, common and proper hepatic artery, hepatoduodenal ligament, and lymph nodes to the right of the superior mesenteric artery; cholecystectomy with an en-block resection of the common bile duct; retroportal, retropancreatic fatty tissue dissection plus dissection of lymph-nodes from the interaortocaval space with following reconstruction using the first jejunal loop, end-to-side pancreaticojejunostomy, end-to-side hepaticojejunostomy without internal stents or other intraluminal decompressing or draining devices (6).

Whipple procedure consisted of Billroth II resection of the stomach with sequential retrocolic gastroenteroanastomosis. Additional Braun entero-enteroanastomosis was never applied.

Pylorus-preserving panreaticoduodenectomy (PPPD) consisted of the resection of duodenum approximately 3 cm below pylorus and sequential end-to-side duodenojejunal anastomosis in front and above the transverse colon using one-layer running fine (4/0 or 5/0) resorbable monofilament suture. Thus, the latter anastomosis is being located in some distance from pancreaticojejunosotomy with a flap of omentum interposed between the two.

R0 and R1 resections were defined as stated elsewhere (4). Definitions of pancreas-related morbidity were described by our group earlier (7).

Statistical analysis

Data were expressed as median and interquartile range. Survival analysis was performed by the method of Kaplan-Meier. Differences in survival rates between patient subsets were compared by log-rank test. Significance was accepted at the 5% level.

Results

Twenty-one patients with malignant tumor of the papilla of Vater had undergone radical pancreatoduodenectomy, and 61.9% (13 of the 21 patients) of them were older than 65 years of age. Median serum bilirubin level of the cohort at presentation was 79 μmol/L (range 10–271 μmol/L). Of them, 57.1% (12 of the 21 patients) were not jaundiced, whereas 42.9% (9 of the 21) of patients presented with serum bilirubin level exceeding 100 μmol/L. In 4 of these patients, preoperative biliary drainage was performed because of excessive serum bilirubin level and markedly impaired cardiac function, requiring medical management prior to surgery. All these patients were aged more than 65 years.

Diagnostic tests performed were contrast-enhanced CT scan and endoscopic retrograde cholangiopancreatography (ERCP) with multiple biopsies before surgery. Final pathology report stated that the diagnosis in all 21 patients was adenocarcinoma of the papilla of Vater (Table 2). According to pTNM stages (UICC, 1997), there were 4 (19.1%) stage I, 10 (47.6%) stage II, 5 (23.8%) stage III, and 2 (9.5%) stage IV patients. Distribution of patients according to cell differentiation is presented in Table 3. In 28.6% of cases (6 of 21 patients), lymph nodes were involved (pN1). In 19 (90.5%) patients, pylorus-preserving pancreatoduodenectomy was performed and R0 resection was accomplished.

Two patients in stage IV have undergone standard Whipple procedure. In one of these patients, partial pancreatoduodenectomy was classified as R1 resection, and was confirmed by postoperative pathology report as showing malignant cell invasion into retroperitoneal tissues at the plane of resection.
The median number of lymph nodes procured during lymphadenectomy was 17. Among the patients who underwent radical pancreatoduodenectomy, none presented with distant metastases at surgery. None of the patients have received postoperative chemotherapy.

Postoperative mortality after pancreatoduodenectomy was 4.8% (1 of the 21 patients). The overall morbidity rate was 28.6%. Pancreas-associated morbidity (pancreatic fistula and peripancreatic sepsis) was 14.3%. Relaparotomy was needed in 2 (9.5%) patients due to intraabdominal hemorrhage. We observed a low rate of delayed gastric emptying postoperatively (1 of 21 patients, 4.8%).

The median follow-up of patients after radical pancreatoduodenectomy because of ampullary tumor was 21.1 months, ranging from 6.3 to 55 months. The overall 3-year actuarial survival among the patients with carcinoma of papilla of Vater was 89%. A 3-year actuarial survival among the patients with the stage I and stage II disease was 100%. Patients diagnosed with stage III and IV disease had an actuarial 3-year survival of 67%, the difference between groups being significant, P=0.046 (Fig. 1). We tested 3-year survival according to T (tumor) classification, grouping T1 and T2.

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**Table 2. Tumor (T) classification in patients with ampullary carcinoma**

| Tumor classification | Number of patients (%) | Node involvement (negative/positive) |
|----------------------|------------------------|--------------------------------------|
| T1                   | 4 (19)                 | 4/0                                  |
| T2                   | 9 (42.9)               | 8/1                                  |
| T3                   | 6 (28.6)               | 2/4                                  |
| T4                   | 2 (9.5)                | 1/1                                  |

**Table 3. Distribution of patients according to cell differentiation (G)**

| Cell differentiation | Number of patients | %   |
|----------------------|--------------------|-----|
| G1                   | 3                  | 14.2|
| G2                   | 9                  | 42.9|
| G3                   | 9                  | 42.9|

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**Fig. 1.** Three-year survival between the patients with stage I and stage II tumor was significantly different (P=0.046) when compared with stage III and stage IV cancer patients.
Grouping patients according to N (node) value to positive (N1) and negative (N0) showed significant differences (P=0.024) (Fig. 3). Patients who had ampullary tumors with high or moderate differentiation of cells (G1 and G2) experienced slightly better survival than the patients with poorly differentiated tumors (G3); however, significant difference was not achieved (P=0.132) (Fig. 4). Establishing gender differences, our data show that overall 3-year survival was higher in women who underwent radical pancreateoduodenectomy for ampullary cancer than in men, though not significantly (93% vs. 75%, respectively; P=0.28) (Fig. 5).

**Discussion**

Ampullary cancer has the best resectability rate and the best prognosis among periampullary cancers. It can be explained by earlier presentation because of anatomic location of tumor and in part by different biological aggressiveness with regard to pancreatic adenocarcinoma. Carcinoma of the ampulla exhibits differences in macroscopic growth pattern showing lower frequency of local infiltration, vascular or neural invasion when compared to pancreatic adenocarcinoma (8). More extensive use of endoscopic retrograde cholangiopancreatography also contributed to earlier and more precise diagnosis of this particular tumor. Though magnetic resonance cholangiopancreatography (MRCP) may take over the diagnostic role of ERCP, direct visualization of the papilla and possibility to obtain multiple biopsies under direct visual control remains unsurpassed.

Pancreateoduodenectomy is the procedure of choice in case of cancer of papilla of Vater though still bearing 2% to 5% mortality and substantial morbidity of 30–40%.

Our data show similar results. The grounds of delayed gastric emptying are still debated, and few hypotheses have been proposed (9–12). Quite a low rate of delayed gastric emptying in our series might be attributed to the pattern of reconstruction of gastrointestinal tract.

Some authors have been advocating a local ex-
Fig. 3. Grouping the patients according to N (node) value to positive (N1) and negative (N0) showed significant difference (P=0.024)

Fig. 4. Patients who had ampullary tumors with high or moderate differentiation of cells (G1 and G2) survived better than patients with poor cell differentiation (G3), though significant difference was not achieved (P=0.132)
Fig. 5. Overall 3-year survival was higher in women who underwent radical pancreatoduodenectomy for ampullary cancer than in men though significant difference was not achieved (P=0.28)
evidence confirming more extensive lymph node dissection translates directly into prolonged survival for patients with periampullary tumors (27).

**Conclusion**

We find our results satisfactory in terms of overall postoperative morbidity and mortality. The lower rate of delayed gastric emptying may be attributed to the pattern of gastrointestinal tract reconstruction and meticulous surgical technique. Long-term survival pattern concerning T, N, and G status corresponds with other reports in literature, while the 3-year survival results are promising and speaks in favor of our surgical strategy.

**Didžiojo dvylkapirštės žarnos spenelio karcinomos chirurginio gydymo rezultatai**

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**Raktažodžiai:** didysis dvylkapirštės žarnos spenelis, vėžys, chirurginis gydymas, išgyvenimas.

**Santrauka.** Adenokarcinoma yra dažniausias dvylkapirštės žarnos didžiojo spenelio piktybinis navikas, tačiau kitų pyktybinį naviką atžvilgiu tai yra retas navikas. Tai apsunkina šių navikų tyriminės, o publikuojami moksliniai darbai dažniausiai yra retrospektyviojo pobūdžio. Siekiant išanalizuoti anksčyviusius ir vėlyvuosius gydymo rezultatus, mes savo sukurtoje duomenų bazėje prospektyviai surinkome duomenis 21 ligonio, operuoto Kauno medicinos universiteto klinikų Chirurgijos skyriuje dėl *papilla Vateri* adenokarcinomos. Visisimo ligoniams buvo atlikta pankreatoduodeninė rezekcija.

Pooperacinių mirštumamų buvo 4,8 proc. Komplikacijų radosi 28,6 proc. atvejų, dėl kasos pažeidimo radosi 14,3 proc. komplikacijų. Apskaičiuotas trejų metų išgyvenimas – 89 proc.

Ligoniai, įsirėg. I ir II stadijos vėžui, kurių navikas buvo klasifikuojamas T1 ir T2 kategorijomis ir (ar) buvo nepažeisti limfmazgai (N0), išgyveno žmogui ilgiau nei ligoniai, įsirėg. III–IV stadijos vėžui, kurių navikas buvo klasifikuotas T3 ar T4 ir (ar) buvo pažeisti limfmazgai (N1). Ligoniai, kurių navikų ląstelės buvo gerai ar vidutiniškai diferencijuotos (G1 ar G2), išgyveno ilgiau nei ligoniai, kurių navikai buvo diferencijuoti (G3), tačiau reikšmingo išgyvenimo skirtumo nenustatėme.

Anksčyvieji (pooperacinių mirštumamų, komplikacijų) ir vėlyvieji (trejų metų išgyvenimas) dvylkapirštės žarnos didžiojo spenelio adenokarcinomos chirurginio gydymo rezultatai yra patenkinami. Išgyvenimo priklausomumo nuo naviko stadijos ir navikų charakterizuojančių kategorijų (T, N, G) tendencijos atitinka kitų autorių publikuotus analogiškus duomenis. Bendrasis trejų metų išgyvenimas po chirurginė operacijos nuo karcinomos apibrėžtas optimistiskai ir rodo mūsų gydymo strategijos pagrįstumą.

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