

Ampullary tumours (ampullomas) in the elderly – an interdisciplinary problem

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Background & objectives: Ampullary cancer is one of the periampullary tumours with better prognosis, but relapses occur early in some patients. This study was carried out to assess whether pancreatoduodenectomy (PDE, Whipple operation) could be a safe therapeutic procedure for elderly patients with periampullary tumours.

Methods: Between 2005 and 2007, 19 patients (12 male, 7 female) aged over 65 yr (range 66 and 83 yr) with diagnosis of ampulloma were operated.

Results: Of the 19 patients, 6 underwent local surgical ampullectomy with reinsertion of ductus choledochus and Wirsungi's duct for benign or early cancer lesion and 13 underwent PDE (Whipple operation). Of these 13, only one was in T1 stage, one was in T4 stage, two patients were T3 and the rest in T2 stage. Lesion of lymphatic system had 40 per cent of patients in T2 stage and all in T3 and T4 stages. One patient died of pulmonary embolism several days after operation. Post-operative complications occurred in 3 cases: 1 patient with partial dehiscence of gastroenteroanastomosis – treated by conservative approach, 2 patients with dehiscence of pancreatojejunoanastomosis.

Interpretation & conclusions: Diagnosis and therapy of ampullary tumours is multimodal. With careful patient selection, PDE can be performed in elderly people (>65 yr) safely. The post-operative morbidity in this group is essentially influenced by their multi-morbidity.

Key words Multi-morbidity - old age - periampullary tumours - Whipple's operation

Ampullary tumours are benign or malignant tumours in the ampulla of Vater and periampullary region¹. These represent 1.5 per cent of GIT (gastrointestinal tract) tumours with incidence about 6/1 million per year. Blockage of ampulla leads to the development of obstructive jaundice; intermittent cholangitis, epigastric discomfort and weight loss². Frequently the patient underwent an endoscopy,

endosonography, contrast enhanced CT and endoscopic retrograde cholangiopancreatography (ERCP). Treatment possibilities include endoscopic ampullectomy, surgical transduodenal excision of tumours of the ampulla and pancreatoduodenectomy (PDE)³.

Prognosis depends on histological typing of the tumour and their clinical stage. Ampullary tumours

are associated with an excellent prognosis, and if the tumour is limited to the duodenal mucosa without any invasion into the adjacent pancreas then the five-year survival may be as high as 90 per cent^{4,5}. Prognosis for patients with carcinoma of papilla Vater is better than other periampullary tumours⁶. The overall survival after the Whipple operation for pancreatic adenocarcinoma is about 20 per cent at five years after surgery. Patients without spread of cancer into their lymph nodes may have up to 40 per cent survival⁷.

The present study was done to assess perioperative (local surgical ampullectomy and PDE) and short-term post-operative results as a safe therapeutic procedure for elderly patients with ampullary tumours and to evaluate feasibility and safety of more aggressive (*i.e.*, more surgical and thus possibly curative) approach in elderly patients (>65 yr) as elderly are known to have increased operative risk.

Material & Methods

A group of 19 consecutive patients with proven ampullary tumours underwent surgical intervention in the department of surgery, Faculty Hospital Brno, Czech Republic during 2005 and 2007. These patients were referred from gastroenterological department as not indicated for endoscopic solution. All the 19 patients were older than 65 yr (range 66 and 83 yr, mean age 74.5 \pm 5.5 yr). Of these, 12 were men and 7 women.

The study objective was focused exclusively on patients with ampullary tumours who underwent operative procedure. The patients who underwent only endoscopic treatment, or multi-morbid persons contraindicated for surgical therapy for severe medical condition and short life expectancy were not included.

The diagnosis was stated by means of duodenoscopy with biopsy (histology), ultrasound and CT examination of abdomen for finding dilated biliary tract or Wirsung's duct and also the invasion to adjacent organs (especially pancreas). Endosonography was done in 12 patients in order to assess infiltration of duodenal submucosa and adjacent area of ampulla and MRI was done in four patients. In 5 patients, duodenoscopy with ERCP was done and biopsy taken. All patients were examined to assess metastatic lesions in regional lymphatic nodules.

Data on pre-operative diagnosis and symptoms were analysed retrospectively. Data on the peri-operative course together with histological findings, staging, technique of the operation and the post-

operative course were collected prospectively since 2005.

All data were summarized using descriptive statistical technique, and chi-square test was used for comparing different groups.

Results

Of the 19 patients, 6 underwent local surgical ampullectomy with reinsertion of ductus choledochus and ductus Wirsung for benign or early cancer lesion.

Thirteen underwent PDE (proven cancer): one each was in T1, and T4 stage, two patients were T3 and the remaining in T2 stage. Lesions of lymphatic system occurred in 40 per cent of patients in T2 stage and all in T3 and T4 stages, and the difference was statistically significant ($P < 0.05$). The patient with T4 stage tumour died 9 months after the surgery. The patient in T2N2 stage has developed metachronous metastases 12 months after PDE. All other patients were alive and being followed up. One patient aged 83 yr stopped attending/coming to screening examinations in the 4th year after surgery.

Short term surgical results in the group of patients with PDE were as follows:- 1 revision 6 h after PDE because of haemoperitoneum caused by haemorrhage from mesocolon. One patient died of pulmonary embolism several days after his operation. Post-operative complications occurred in 3 cases: 1 patient with partial dehiscence of gastroenteroanastomosis - treated by conservative approach, 2 patients with dehiscence of pancreatojejunoanastomosis - first treated by conservative approach, followed by total pancreatectomy. Perioperative mortality was 0 per cent, perioperative morbidity after PDE 38.5 per cent. In all cases pylorus preserving PDE was done.

In 6 patients treated locally, the perioperative mortality was 0 per cent, perioperative morbidity - 15 per cent. Adenomas 5 times, carcinoma T2NXM0 once with local recurrence in 6 months with repeated haemorrhage. Selective embolism of tumour was used in this one patient. Survival time was 11 months.

Discussion

Carcinoma of Vater's ampulla is a relatively uncommon tumour^{8,9}. The incidence in a nonselected autopsy series has been reported to range from 0.028 to 0.040 per cent, accounting for 6 per cent of all periampullary tumours¹⁰. Qiao *et al*⁶ reported ampullary carcinomas accounting for approximately 0.2 per cent

of all tumours in the GIT. Three epithelial types can be found in this area springing either from the duodenal mucosa or from the bile duct or the pancreatic duct.

PDE is the traditional operative method for patients with ampullary adenocarcinoma^{4,11}. Outcomes of the patients undergoing surgical resection depend on various tumour specific factors (*e.g.*, primary tumour location, tumour size, status of resection margins and lymph node and other metastases), use of post-operative chemotherapy and radiation and other laboratory signs¹².

There are two main problems of ampullomas – their diagnosis and the stage estimation. Development of techniques of endoscopy revealed the necessity of the most precious and most complex pre-therapeutic examinations^{1,11}. The main problem at the time of examination of the ampullar adenoma is the necessity to distinguish the lesion from the carcinoma in which there is a threat of lymphatic nodules infiltration indicating PDE.

Our study on 13 patients with PDE confirmed the effectiveness of this therapy in older multi-morbid people. Di Giorgio *et al*¹⁰ showed tumour size, tumour grade, and tumour infiltration (lymph nodes, *etc.*) as significant factors for 5-year survival after PDE. Todoroki and group¹³ underlined the importance of pre-operative carcinoembryonic antigen level as predictor for surgical results.

Nowadays use of conventional, classical radiology is limited in diagnosis as well as in staging of tumours, thus raising the importance of endoscopic methods – duodenoscopy, endosonography and endoluminal miniprobe examination. Endosonography enables to visualize tumourous lesions of duct choledochus and Wirsung's duct. This examination should precede all therapeutic procedures. Endosonography is the essential examination for diagnosis of lesions over T1 and/or intracanalicular infiltrations – both of them being indications for PDE. Biliar endosonographic miniprobes enable to visualise duodenal submucosis and Oddi's sphincter (in 89-95%). MRI is used nowadays more for diagnosis of possible vascular variants during pre-operation examinations. Curative ampulectomy is indicated in intraepithelial adenomas and adenocarcinomas that do not extend to muscularis mucosae and do not infiltrate Oddi's sphincter¹⁴. This method was used in six patients in our study. The patient with carcinoma T2NXMO with local recurrence in 6 month was not able to undergo PDE because of his polymorbidity.

It is necessary to undergo following examinations before deciding for endoscopic therapy: (i) Duodenoscopy with biopsy (vegetative duodenal lesion x ulcerations far from papilla), (ii) Intraampullar lesions require endosonography and miniprobe endoscopic sphincterotomy with collection of histological samples. CT examination is useful for finding dilated biliary tract or ductus Wirsungi and also the invasion to adjacent organs (especially pancreas). Biliopancreatic endosonography differentiates safely intra-ampullar tumours: infiltration of submucosis of duodenum; infiltration of distal choledochus; metastatic lesions in regional lymphatic nodules (53-87%)¹.

MRI and helical CT may find ampullar carcinomas that invade pancreas. We used these examinations in all cases to assess the status. If the endoscopic result is unclear, then the most important method becomes endosonography.

Staging should enable to choose tumours with no risk of lymphatic lesion and thus suitable for local therapy^{1,11}. Studies using TNM (tumour, node, metastasis) classification³⁻⁵ show a risk of lymphatic lesion in T1 tumours from 0 to 20 per cent. D0 tumours are always N-, with rare lymphatic emboli and with 5-year survival of 100 per cent. D1 tumours have 30 per cent metastatic adenopathias with 5-year survival (65%). They are indicated for curative, local therapy. We used local resection of ampulla in 6 cases.

Surgical ampulectomy should be limited to patients with endocanalicular lesion¹⁴. It can thus be indicated in patients with ampullomas with endobiliar growth which account for 15 to 20 per cent of benign ampullomas.

Mortality of surgical ampulectomy is 0. Morbidity is about 15 per cent (pancreatitis, haemorrhage, fistula duodenalis, cholangitis). Recurrences are exceptional. We found similar results in the present study³.

PDE is indicated in patients with carcinomas that infiltrate submucosis and if the ampulectomy was not successful^{15,16}. It is indicated in patients with invasive adenocarcinomas that infiltrate duodenal submucosis and/or next tissue layers and in most endocrine tumours^{3,17}. PDE in ampullomas is characterised by high resectability, but there is a large number of post-operative pancreatic fistulas - up to 25 per cent. Mortality level lies between 1-5 per cent (in our set 0%), but the morbidity is high - about 40 per cent (in our set

38.5%). In patients with adenocarcinomas the 5-years survival lies between 60 to 70 per cent when there is no lymphatic lesion and 30 per cent if the lymphonodi are infiltrated^{1,8}.

Our results were similar to that of Hentati *et al*¹⁸ case report of 84-year old woman that age alone should not to be a contraindication for PDE. Radical resection of ampullary tumours is safe in correctly selected patients of advanced age, with morbidity and mortality rates approaching those observed in younger patients.

In conclusion, PDE is the treatment of choice not only for ampullary carcinoma but also for adenoma with high grade dysplasia also for elderly persons in good somatical status^{3,17}; for frail unfit persons¹⁹ with distant metastases or miscellaneous contraindications for surgery remains endoscopic sphincterotomy and stenting a valide alternative of palliative treatment.

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