Surgical Treatment and Complications of Treating Pancreatic Tumor

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Pancreatic tumor is one with the worst prognosis of all cancers, and the tenth most frequent cancer in Europe, making the 3% of all cancers affecting both sexes. Most patients seek treatment when the disease is in its advanced stage and the level for possible resectability is low. Late presentation of the disease is responsible for the short survival period of 6 months and a five-year survival of 0.4 to 5% of patients. At the Clinic for Surgery in Tuzla during period from January 1st 1996, to January 1st 2011, a total of 127 resection surgeries were performed due to malignant tumors. The goal of this study was to show that adequate assessment of operability, proper surgical strategy and modern techniques of creating anastomoses reduces morbidity and mortality, results in fewer postoperative complications and contributes to better surgical results. In our study sample the most common place of tumor location was the head of pancreas, in 69 (59.7%) patients. Men develop this type of cancer more often than women in the ratio of 2:1, while the median age of patients was 62 years. We faced postoperative complications in 37 (29.1%) patients, pancreatic fistula being the most prevalent complication, occurring in 16 (12.6%) patients. Overall early and late postoperative mortality was observed in 12 (9.8%) patients. Conclusion: Patients with chronic and hereditary pancreatitis are at a higher risk for developing pancreatic cancer and should be screened for the purpose of early diagnosis. The staging of pancreatic cancer has improved, with the accuracy of 85-90%. Postoperative complications, morbidity, and mortality are significantly reduced (p<0.05) if the standardized operational procedure is applied and if modern techniques are used to create pancreaticojejunal anastomosis as the anastomosis carrying the highest risk. Key words: pancreatic cancer, resection surgery, complications.

1. INTRODUCTION
Pancreatic tumor is one with the worst prognosis of all cancers, and the tenth most frequent cancer in Europe, making the 3% of all cancers affecting both sexes. Most patients seek treatment when the disease is in an advanced stage and the level for possible resectability is low. Late presentation of the disease is responsible for the short survival period of 6 months and a five-year survival of 0.4 to 5% of patients. There is only 5-10% patients with a resectable tumor have an average rate of survival of 11-20 months and a five-year survival 7-25% of patients. However, almost all patients die within 7 years after surgery. Early diagnosis and surgical treatment may provide a chance to these patients. Risk factors include smoking, fat rich diet, carcinogens (azaserine, nitrogen), genetic predisposition, chronic pancreatitis, hereditary pancreatitis, pancreatic cancer in the family, cystic fibrosis, Peutz-Jeghers syndrome, breast cancer in the family, familial adenomatous polyposis while coffee has not been proven as a risk factor. The progression from normal ductal epithelium to an intraepithelial pancreatic neoplasia of a low grade (PanIN) and to a high grade of malignancy PanIN is connected with specific genetic changes. Early changes include Her-2/neu and K-ras mutations; intermediate changes include p16 mutations; changes connected with carcinoma in situ or early invasive carcinoma include p53, BRCA2 and DPC4 mutations. Symptoms of pancreatic cancer are weight loss in 92% of cases, jaundice 82%, pain 72%, dark urine 63%, light stool 62%, anorexia 64%, and nausea 37%, weakness 35%, vomiting 37%, and itching 24%. Conditions that are a contraindication for the resection of pancreas includes liver metastases (of any size), involvement of lymph nodes, peritoneal carcinomatosis, infiltration of transverse mesocolon, involvement of lymph nodes of the liver hilum. Conditions that are not a contraindication for the resection of pancreas includes liver metastases (of any size), involvement of lymph nodes, peritoneal carcinomatosis, infiltration of transverse mesocolon, involvement of lymph nodes of the liver hilum. Conditions that are not a contraindication for the resection of pancreas are the infiltration of duodenum
or gastric antrum, infiltration of peripancreatic lymph nodes, infiltration of lymph nodes along porta hepatis that can be removed by resection.

2. PATIENTS AND METHODS

Our study was conducted at the Clinical Centre Tuzla, Clinic for Surgery from January 1st 1996 to January 1st 2011 and involved 127 patients who underwent the resection surgery of the pancreas.

Our study did not include patients who had a palliative operation, distant metastases, liver cirrhosis, complicated portal hypertension, hereditary coagulopathy, primary and secondary diseases of extrahepatic bile ducts. We analyzed the obtained results by applying Chi-square, Student’s t-test and Kaplan-Meyer’s test. If the difference between the value of analyzed parameters was p<0.05, it is considered to be statistically significant.

Description of surgical procedures, preoperative and postoperative treatment

CDP with pylorus preserving technique was performed on 21 (16.53%) patients. Surgical approach of median laparotomy in 64 (50.40%) patients, laparotomy according to OTR (bilateral sub costal) in 63 (49.60%) patients. We used abdominal retractor with support on the soft tissues over the abdominal compression. Preoperatively, each patient signed a consent form for surgery and the same procedures for consent had been previously presented to the patients with explanation of potential complications. The form was approved by the Ethical Committee of the University Clinical Centre and the Service for Quality Control. Preoperative urinary catheter was placed in all cases, the venous catheter was placed (central venous catheter) and nasogastric tube. All patients were preoperatively treated by the application of isotonic intravenous fluid (0.90% NaCl, 5%) and substitution of blood derivatives; fresh frozen plasma (SSP), thrombocyte (TS) if the laboratory balance was deficient, in addition to preoperative application of antibiotic prophylaxis (third-generation cephalosporin). Preoperative preparation consists of the ultrasound examination of the abdomen, CT scan of the abdomen with contrast, chest X-ray, X-ray of the abdomen, electrocardiogram and complete laboratory tests. Tumor markers (CEA, AFP, CA 19.9) were determined preoperatively and postoperatively on the 15th day. We had a previously confirmed diagnosis for 58 (45.68%) patients. With the patients with pronounced icterus and previous endoscopic stent placement 41 (32.29%), the operative treatment was scheduled after the stabilization of the general condition and laboratory parameters (the level of bilirubin in the serum below 2mg/l) within 2-4 weeks. We have to repeat surgery in 16 (12.60%) patients with previously done biliodigestive anastomosis (choledochoduodenal) after the unsuccessful attempt of endoscopic stent placement. The operative technique of performing celiac duodenopancreatectomy with hemigastrectomy and pyloric preservation technique is a standard. The technique of creating pancreaticojejunal anastomosis is termino-lateral Blumgart’s method and polydioxanone absorbable monofilament suture 4-0 in one layer with previously placed prosthesis in the joint pancreatic duct in 29 (28.83%) patients. Creating hepaticejejunual anastomosis in one layer individually with the PDS polydioxanone absorbable monofilament suture 6-0 in 29 (28.83%) patients. In 98 (71.77%) patients, the pancreaticojejunal anastomosis was created by Safil suture, polyglycolic acid absorbable 3-0 in one layer and the hepaticejejunual anastomosis was created by prolene suture 4-0 by the technique of continuous suture. Prior to creating pancreaticojejunal anastomosis, we take sample from every patient and send it to bacteriology testing. We closed operative wounds with a continuous suture 2-0 polydioxanone in one layer and the skin with metal claps.

3. RESULTS:

The results of our study are preoperative procedures that include the diagnosis and assessment of resectability, patient’s general condition – ASA score, the level of tumor markers CA19-9, thromboembolism prophylaxis, antibiotic prophylaxis, correction of metabolic and nutritional disorders, the role of somatostatin, the role of preoperative biliary drainage, adequate analgesia, intraoperative conducted planned surgical strategy with a technique with minimal bleeding that does not require intraoperative transfusion, postoperative intensive monitoring (during the first 24 hours), nasogastric tube (extracted 12 hours after the extubation), abdominal drains (extracted within 3 days of the secretion is minimal), postoperative nutrition (enteral feeding by using nasogastric tube, probiotic-enriched), control of laboratory parameters, analgesia, early mobilization of the patient, vaccination of splenectomized patients (Streptococcus pneumonie and Hae-mophilus influenzae type B).

The localization of tumor is shown in Table 1.

<table>
<thead>
<tr>
<th>Localization of the tumor</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas head</td>
<td>69</td>
<td>59.78</td>
</tr>
<tr>
<td>Papilla Vateri</td>
<td>26</td>
<td>18.30</td>
</tr>
<tr>
<td>Distal part of choledocus</td>
<td>8</td>
<td>7.61</td>
</tr>
<tr>
<td>Entire pancreas</td>
<td>4</td>
<td>3.15</td>
</tr>
<tr>
<td>Pancreas body</td>
<td>3</td>
<td>2.71</td>
</tr>
<tr>
<td>Pancreas tail</td>
<td>9</td>
<td>7.61</td>
</tr>
</tbody>
</table>

The median age of patients was 62 (range 34-81). The types of resection surgery are shown in Table 2.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>no of pat.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac duodenopancreatectomy (CDP)</td>
<td>101</td>
<td>79.53</td>
</tr>
<tr>
<td>Total duodenopancreatectomy</td>
<td>4</td>
<td>3.15</td>
</tr>
<tr>
<td>Subtotal left pancreatectomy</td>
<td>4</td>
<td>3.15</td>
</tr>
<tr>
<td>Distal spleen-preserving pancreatectomy</td>
<td>10</td>
<td>7.87</td>
</tr>
<tr>
<td>CDP + subtotal stomach resection</td>
<td>4</td>
<td>3.15</td>
</tr>
<tr>
<td>CDP + right hemicolectomy</td>
<td>4</td>
<td>3.15</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Abdominal postoperative complications found in our sample are shown in Table 3.

The total number of intra-abdomi-
inal complications occurred in 37 (29.1%) patients and the most common complication was pancreatic fistula 15 (11.8%). Pancreatic fistula occurred in our sample in all cases as an early complication from 3 to 7 days. We treated it conservatively and successfully in 6 (4.7%) patients by adequate rehydration and enteral feeding with a regular cleaning of the surgical wound. All patients had a postoperative administration of sandostatin – 100 micrograms daily in two doses. Because of the impossibility of adequate cleaning by using conservative methods, we conducted a revision because of pancreatic fistula in 9 (7.1%) patients. Revision was conducted by a repeated relaparotomy, resection of pancreatic surface and jejunal convolutions, with a new anastomosis and external drainage of pancreatic duct by Witzell. We treated biliary fistula only conservatively according to a pattern adequate to a conservative treatment of a pancreatic fistula and all are cleaned within 6 weeks.

We treated abscess collections, as a result of accumulation of pancreatic or biliary secretion components, by placing a drainage catheter in the zone of abscess collection and by administrating of broad-spectrum antibiotics after antibiogram confirmation. We want to emphasize that there is a statistically significant lower number of abdominal complications when we use Blumgart’s technique of creating pancreaticojejunal anastomosis with suture PDS 4-0 and hepaticojejunal anastomosis by individual sutures PDS 6-0 in one layer (p<0.02). In our sample we showed that there is a statistically significant difference in a number of patients with a better gastrointestinal function (p<0.05) and a lower incidence of marginal ulcer (p<0.01) after the application of PPPD (pylorus preserving pancreatic duodenectomy). A statistically significant difference in our series is related to oncologic adequacy and delayed gastric emptying (p<0.05) with patients after standard cephalic pancreatic duodenectomy. Out of late abdominal complications we emphasize bleeding from the marginal ulcer on the gastrojejunal anastomosis in 2 (1.5%) patients whom we treated operatively after unsuccessful control of bleeding by endoscopic procedures. The operative treatment consisted of an additional resection of stomach and of a part of a jejunal convolution with establishing new anastomosis in one layer.

We treated extra abdominal complications related to thrombosis preoperatively and postoperatively by administrating low molecular heparin, pleural effusion was treated by thoracic puncture. The patient with pulmonary embolism had an intensive monitoring and therapy in the intensive care unit. The reasons for postoperative mortality with patients after the resection of pancreas are shown in Table 5.

The dominant pathohistological diagnosis in our sample is adenocarcinoma in 112 (88.2%) patients. Among other types of tumors in our sample, there were metastatic pancreatic tumors (tail) in the primary cancer of rectum 3 (2.6%), breast cancer (body and tail) 2 (1.6%), solid pseudo papillary tumor 4 (3.1%), serous cystic neoplasms 2 (1.6%), intraductal papillary mucinous neoplasm (IPNM) 4 (3.1%) patients. Intraoperative blood transfusion and immediately after the operation (within 72 hours) was 240-760ml.

4. DISCUSSION:

Good prognostic factors for pancreas resection as a result of malignity include negative margins of resection, the absence of metastases in lymph nodes, good or moderate tumor differentiation, tumor smaller than 2 cm in diameter, the absence of perineural and vascular invasion. Poor prognostic signs are DNA aneuploidy, inactivation of suppressor genes (p16, p53, DPC4). On the basis of previous experience it can be stated that there are no indications for routine stenting of all patients with icterus because of the of the pancreatic head cancer.

Endoscopic stenting of papilla Vateri can be justified in a smaller number of patients who have cholangitis and a high level of damage of the liver function as well as with patients who for whatever reasons cannot undergo surgery immediately after the tumor of the head of pancreas is diagnosed. It is to be expected that in the following period the controlled prospective studies will clearly define criteria for selective application of both the internal endoscopic biliary drainage and external biliary drainage. Incidence of pancreatic fistula (10-25%) and sepsis and bleeding that result in mortality when patients are not sufficiently postoperatively prepared and when patients have early postoperative complications reaches the level between 20 and 40%.

Fourth classifications of postoperative pancreatic fistula in the sample of 242 patients with celiac duodenopancreatectomy are shown in Table 6.
Knowing this classification is extremely important to be able to correctly note a complication and apply an adequate treatment. Important factors for creating pancreatic anastomosis are firmness of pancreatic tissue, type of pancreatic disease, width of pancreatic duct, operative technique, patient’s age, associated diseases, and icterus.

Prevention of pancreatic fistula includes the choice of adequate anastomosis, stent of the pancreatic duct, somatostatin. It is unclear whether pancreaticogastrostomy changes the endocrine function of pancreas and whether it is preserved in the same way as with pancreaticojejunal anastomosis. The incidence with pancreaticojejunal anastomosis is bigger than with pancreaticogastrostomy and both techniques have an acceptable rate of fistulas with expected pancreaticojejunal anastomosis. The incidence of postoperative complications, lower percentage of complications, a lower mortality and morbidity rate. Concomitant chemo radiotherapy in treatment of adenocarcinoma of pancreas is applied as neoadjuvant (often with border resected tumors), adjuvant and for locally advanced disease without proved metastasis. In spite of constant research and discoveries of new chemotherapeutics, neoadjuvant chemo radiotherapy did not succeed to significantly increase the number of resectable tumors.

On the other hand, new diagnostic methods managed to increase to a certain extent the number of those patients who are potentially curable by surgical treatment, in addition to adjuvant chemo radiotherapy.

REFERENCES