

EXTENSIVE GASTROPANCREATODUODENAL RESECTIONS IN THE TREATMENT OF DUCTAL CARCINOMA OF THE HEAD OF PANCREAS

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The aim of the investigation is to estimate short- and long-term results of the treatment of ductal adenocarcinoma of the head of pancreas after conventional and extensive pancreatoduodenal resection.

Materials and methods. There were performed total 27 conventional and 27 extensive interventions. The groups under study were comparable by sex, age, and the degree of tumour differentiation. Mean time of surgery, the volume of blood loss and hemotransfusion, the frequency of postoperative complications, and mortality did not differ significantly.

Results. After extensive pancreatoduodenal resection, local recurrence occurred significantly more rarely (7.4 versus 33.3% after conventional surgery). Broadened lymphadenectomy in ductal adenocarcinoma of the head of pancreas did not lead to the increase of postoperative complications, mortality and overall survival. In the meantime, extensive gastropancreatoduodenal resection enables to decrease significantly recurrence rate.

Key words: extensive gastropancreatoduodenal resections, ductal carcinoma of the head of pancreas.

Pancreatic cancer amounts up to 15% of malignant tumours of gastrointestinal tract diagnosed in Russia annually, and is the sixth cause of death from oncological diseases [1]. Mortality in Russia is 13000 cases per year [2, 3]. Three-year survival rate in cancer of the head of pancreas after radical surgery is from 0 to 41% that is reliant on tumour differentiation degree, stage of the disease, metastasis in lymph nodes, involvement of great vessels in the tumour, using different options of adjuvant chemotherapy [1, 4]. Poor results of standard operative therapy of ductal adenocarcinoma (DA) of pancreas are responsible for the search of new approaches. One of the ways of improvement of surgical results is considered to be the introduction of extended gastropancreatoduodenal resections (GPDR) into practice [5–7].

Randomized studies have shown an extended lymphadenectomy in GPDR not to increase the frequency of postoperative complications and mortality, yet have no significant effect on survival rate. However, the volume of the studies carried out has appeared to be inadequate for making decision on the question, therefore, further researches on the estimation of the impact of extension of surgery volume on survival rate continue to be relevant [8–12].

Materials and Methods. From June 2006 to December 2011 in Privolzhsky District Medical Centre of Federal Medico-Biological Agency of Russia (Nizhny Novgorod, Russia) there were performed 54 GPDR for DA of the head of pancreas, it amounting to 40.4% of the total GPDR performed over the period in the clinic, and 52% of GPDR for malignant periampullary tumours. Standard GPDR was performed in 27 patients (19 male and 8 female) aging from 40 to 78 years, average age being 59.2±7.8 yrs. These patients composed the 1st group. Extended GPDR was performed in 27 patients (17 male and 10 female — the 2nd group), ageing from 51 to 74 yrs, average age — 61.3±9.8 yrs. According to clinic protocol, bilirubin level being above 100 μmol/l, on admission, all the patients were performed biliary ducts decompression: in the 1st group — 16 patients, in the 2nd group — 14 (percutaneous transhepatic biliary ducts drainage controlled by ultrasound was preferable).

The volume of the operations performed was according to the recommendations of S. Pedrazzoli et al. [8].

Standard GPDR included the transection of pancreas in the area of isthmus, within 1 cm to the determined tumour margin, cholecystectomy, and the transection of common hepatic duct, hemigastrectomy, and antrumectomy. Pylorus-

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saving operations were not performed for oncological reasons. Small intestine was transected 20–25 cm below the ligament of Treitz. There were dissected lymph nodes on the right side of hepatoduodenal ligament: upper and lower lymph nodes of common hepatic duct and lymph nodes around the cystic duct (12b1, 12b2, 12c), posterior pancreaticoduodenal (13a, 13b), and lymph nodes of the right side of superior mesenteric artery (SMA) from its beginning near aorta up to the level of inferior pancreaticoduodenal artery (14a, 14b), anterior pancreaticoduodenal nodes (17a and 17b), lymph nodes (8a) of anterior-superior part of the common hepatic artery (Fig. 1).

In extended GPDR the volume of a standard operation was completed by the transection of pancreas to the left of superior mesenteric vein, nearly at the “entry” of splenic artery into pancreatic parenchyma, by complete resection of Gerota fascia behind the head and more extended regional lymphadenectomy with complete skeletization of common and propria hepatic artery, arterial trunk and the right semi-circle of SMA, additional lymphadenectomy from aorto-caval area from crura of diaphragm to bifurcation of aorta. Thus, there were resected the lymph nodes of the following groups: 8a, 8p, 9, 12a1, a2, 12b1, b2, 12c, 12p1, p2, 12h, as well as the areas of superior mesenteric artery (14a-d), anterior lateral surface of aorta and inferior vena cava (16a2, 16b1) together with Gerota fascia (Fig. 2).

Intraoperatively, in all the patients there was assessed the margin of pancreatic resection macroscopically, and in tumour growth suspected, the body of pancreas was additionally dissected.

The anastomoses were formed successively on an enteric loop put into the window of mesocolon: pancreatojejunal anastomosis (PJA), hepaticojejunal anastomosis (HJA), and gastrojejunal anastomosis. PJA was formed in two ways: on Wirsung-stoma drainage (Fig. 3), the duct diameter being up to 2 mm, and “juicy” gland (in standard GPDR — in 22, in extended — in 11), or there was formed direct PJA (Fig. 4), when precisely Wirsung duct with serous-muscular intestinal layer was anastomosed (in standard GPDR — in 5, in extended — in 16).



Fig. 1. Standard gastropancreatoduodenal resection. Marginal excision of the right semi-circle of portal vein. The view of operative field

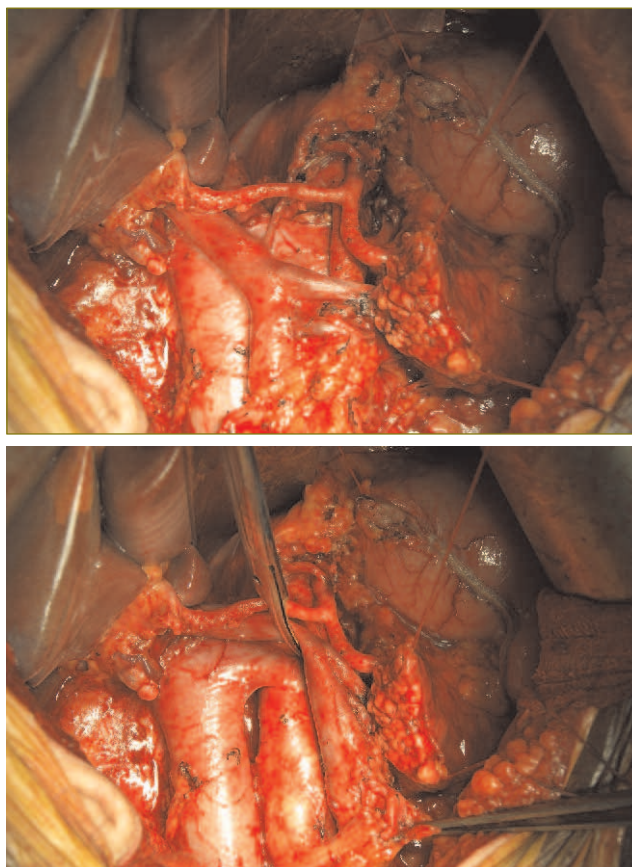


Fig. 2. Extended gastropancreatoduodenal resection. The view of operative field (the volume of lymph dissection is in the text)

Common hepatic duct was stitched in jejunum by “end-to-side”, single-layer anastomosis by a continuous suture without framework drainage. It should be noted that since 2011, in GPDR all enteric and ductal anastomoses have been performed using a single-layer, continuous stitch that significantly saves the time of reconstruction period of the operation. According to clinic protocol, for early enteral feeding, naso-intestinal feeding tube was used. Naso-intestinal feeding was started 6 h after the operation using semi-elemental mixture for enteral feeding, at a speed of 25 ml/h on the first day. Motility having appeared, there were used standard balanced mixtures, the volume of them being increased up to a patient’s daily energy requirement calculated according to Harris-Benedict equation.

Currently, the application of reparative surgeries on great vessels of hepatoduodenal area (portal and superior mesenteric veins, hepatic and superior mesenteric arteries) are considered as significant factor of increasing tumour resectability [13]. When portal and superior mesenteric veins were infiltrated by the tumour, circular or marginal excisions were performed (Fig. 1, 5, 6). In cases when angioplasty by self-tissues was impossible, the preference was given to synthetic prostheses GORE-TEX (USA), 14 or 16 mm. 5 patients (18.5%) from the group of standard GPDR underwent the procedure, one patient was performed the resection of the right hepatic artery with end-to-end anastomosis due to anatomical peculiarities of the right hepatic artery going from the superior mesenteric

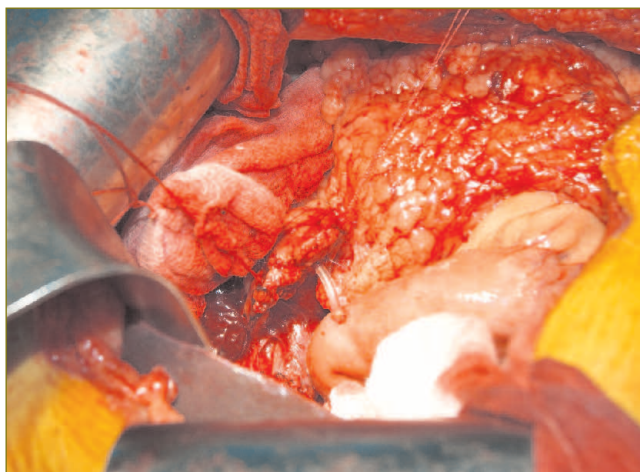


Fig. 3. Formation of pancreatojejunal anastomosis on external Wirsung-stoma drainage

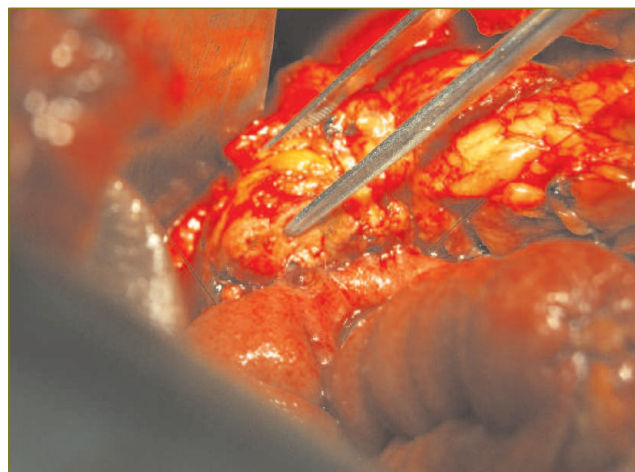


Fig. 4. Precision formation of direct pancreatojejunal anastomosis

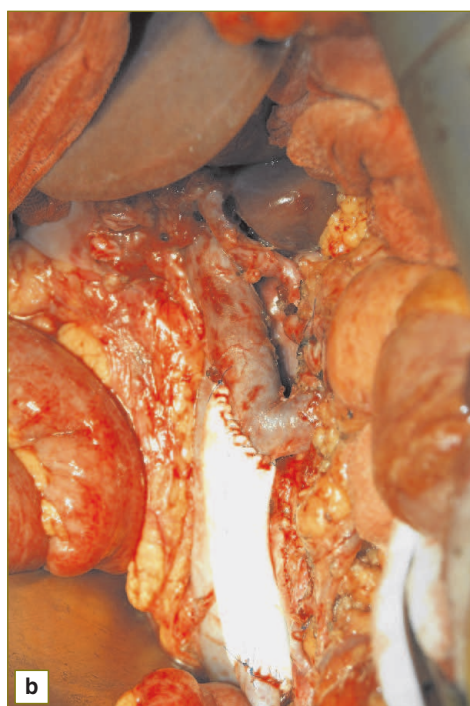
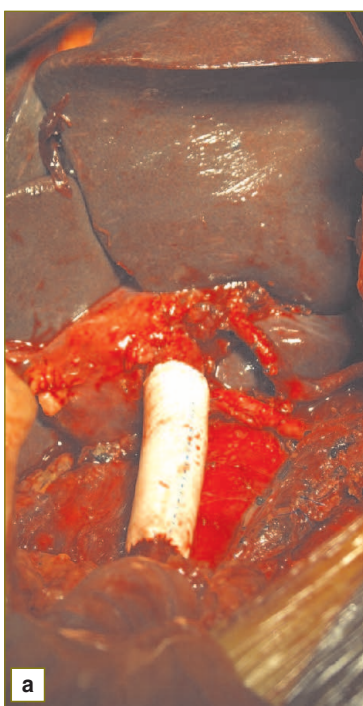


Fig. 5. Replacement of portal vein (a), superior mesenteric vein (b) by synthetic GORE-TEX prostheses

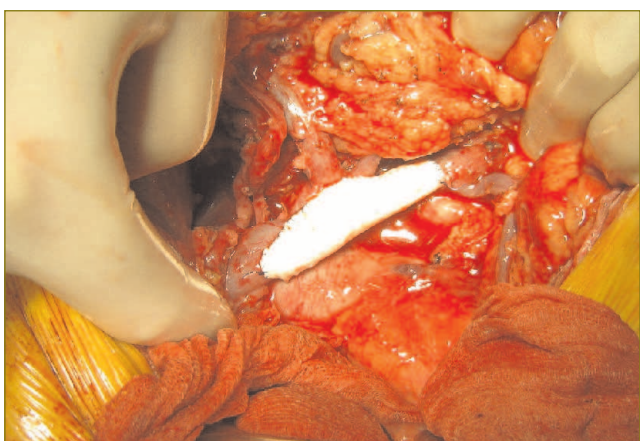


Fig. 6. Variant of portal vein replacement by synthetic GORE-TEX prostheses with venous ducts saving

artery. The rest of the patients underwent the resection of portal vein and (or) superior mesenteric vein (See Fig. 3, 4). In the group of extended GPDR, vascular resection was performed in 13 patients (48%). The efficiency of angioplasty was controlled by intraoperative Doppler ultrasound. Postoperative thrombosis was revealed in one female patient 18 h after the surgery. Thrombectomy with blood flow restoration was successfully performed. No thrombi of prostheses were found.

Postoperative lethality was considered as a patient's death during the present hospitalization.

For statistical data processing there was used Statistica 6.0. Student t-test was used to reveal the differences between the groups in case of normal distribution, otherwise χ^2 criterion. The differences were considered to be statistically significant in $p < 0.05$. Survival rate was calculated using Kaplan–Meier method [14].

Results and Discussion. In both groups of patients comparable by age and sex, there were revealed no statistically significant differences between the groups in the volume of intraoperative blood loss. An average time of extended GPDR was 4.8 h that exceeded timing of standard GPDR by 48 min (See the Table). The increase of the timing of surgery was explained by extended lymph nodes dissection.

Postoperative complication rate in the group of standard operations was 37%, and in the group of extended — 41% (the difference in complication rate is statistically insignificant). The main complications in GPDR resulting in lethal outcomes and disability of patients are the dehiscence of pancreatojejunal and hepaticojejunal anastomoses. PJA dehiscence was determined based on the criteria of International Study Group on Pancreatic Fistula. In our study it was proved only in B and C classes, and dehiscence in A class was not clinically significant. PJA dehiscence in the 1st group was diagnosed in 2 patients (7.4%). In both patients anastomosis was formed on external wirsungostomy drainage (See Fig. 3). There were no complications found in the 2nd group. Currently, we have given up external wirsungostomy giving preference to direct pancreatojejunal anastomoses with precision (x2.5) stitching in pancreatic duct in the opening in enteric wall (See Fig. 4). No dehiscence of these anastomoses were detected that can be explained by experience accumulation by clinic.

Literature data on pancreatojejunal anastomosis performance are rather contradictory. So, Patrick Pessaux et al. [15] report that if the diameter of Wirsung duct was up to 3 mm, they formed PJA on wirsungostomy drainage. The anastomosis dehiscence rate was 26%, while in direct PJA it was diagnosed in 42%. Other researchers report of even greater rate of PJA dehiscence in extended operations. Moreover, the advantages of pancreatogastroanastomoses over PJA regarding the dehiscence development (dehiscence rate being 12.3 and 11.1% respectively) were not confirmed [16–18].

HJA dehiscence in our study was registered in 2 patients in the group of standard operations and was 7.4%. In the group of extended surgeries it was diagnosed in 2 patients. The management of HJA dehiscence was in early additional seal of anastomosis, and if impossible the aspiration drainage of the anastomosis zone using drainage foamed rubber system of V.A.Solovyov. We succeeded in managing all the revealed HJA dehiscences.

In extended GPDR there were described such complications as lymphorrhea and secretory diarrhea related to a great volume of lymph node dissection [19]. In our study 1 patient (3.7%) in the 2nd group had prolonged lymphorrhea (more than 300 ml a day within 2 weeks), and 2 patients in the 1st group. Lymphorrhea self-stopped by 14–16 day. Prolonged secretory diarrhea (up to 3 weeks) in the group of extended GPDR was found in 28% of patients.

Two patients in the group of extended GPDR had clinically significant gastrostasis. We attribute it to the resection of antral part of the stomach with pylorus. On the other hand, M.Kawai et al. [20] report that distal

The results of standard and extended gastropancreatoduodenal resection

Parameter	GPDR	
	Standard (n=27)	Extended (n=22)
Timing of surgery, min	243±24	288±32
Average number of lymph nodes dissected, abs. number	10	21
Metastases in lymph nodes, %	14.8	37
Distant metastases in lymph nodes, %	Not dissected	18.5
Resection of great vessels, abs. number, %	5/18.5	13/48
Complication rate, %	37	41
Relaparotomy rate, %	18.5	7.4
Frequency of lethal outcomes, abs. number, %	2 (7.4)	0 (0)
Local recurrence rate in long-term periods, %	33.3	7.4

gastrectomy does not lead to the disturbance of gastric transit, and 6 months after the operation nutrition status of patients who have undergone classical Whipple operation is no different from that of the patients after pylorus-saving operations.

The main factor having an effect on patient longevity after GPDR is the maximally total resection of tumour tissue. In 4 patients from our study there was growth along the border of pancreas resection, and on receiving histologic conclusion, two of them underwent extirpation of pancreas stump. Within 3 months both patients died from progressing metabolic disorders. The other two patients were performed adjuvant chemotherapy. Mean lifetime after performed adjuvant chemotherapy was 13 months.

Extended GPDR was suggested in the late XX c. to reduce local recurrence rate. There have been carried out many researches to compare the results of standard and extended GPDR with various substantiation degrees. S. Pedrazzoli et al. [8] do not report of statistically significant differences in life expectancy of the patients in both groups that is likely to be explained by insignificant difference in the number of removable lymph nodes. In the research of C.J. Yeo et al. [9] one- and five-year survival rates after standard surgery were 75 and 13%, and after extended — 73 and 29%. Only 15% of operated patients were shown to have metastatic involvement of lymph nodes that can explain such insignificant differences in patients' survival. Y. Nimura et al. [10] have not noticed the differences in one- and three-year survival rates of patients after standard and extended GPDR either.

In order to increase the survival values of patients with adenocarcinoma of the head of pancreas, there have been suggested more aggressive approaches to operative treatment such as total pancreatectomy, maximally extended lymph nodes dissection, resection of great vessels. Afterwards, in total pancreatectomy, lifetime was stated not to increase significantly compared to extended GPDR, the number of complications and lethality

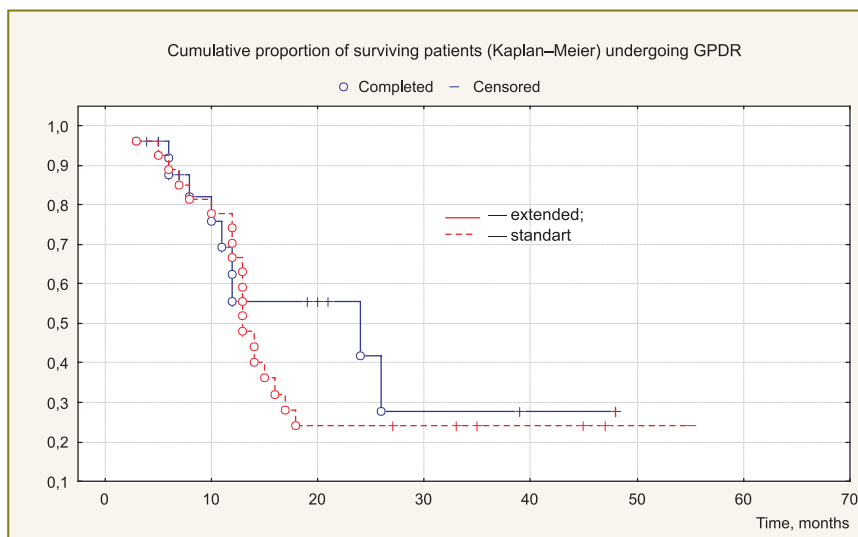


Fig. 7. Survival rate of patients after standard and extended GPDR

increasing, and the quality of life is significantly worsening [20–24].

In extended GPDR there were removed, on average, 21 lymph nodes, in standard — 10. Metastases in lymph nodes were revealed in the patients of the 1st group in 14.8% of cases, while in the 2nd group — in 37% of cases. And in the patients of the 2nd group metastases in distant lymph nodes were confirmed in 18.5% of patients.

One-year survival after a standard GPDR was 71.2%, the median survival being 13 months, while after extended GPDR — 69.1%, the median survival being 24 months (Fig. 7), the difference of the results is statistically insignificant. Local recurrence within the period of 12 months was observed in 33.3% of cases after standard GPDR, and in 7.4% of cases — after extended GPDR.

Postoperative lethality in the 1st group was 7.4% (2 patients), in the 2nd group — 0%. One of the fatal cases was resulted from acute heart failure developed as a result of acute myocardial infarction, another by reason of intraabdominal erosive hemorrhage, as a result of PJA dehiscence. In the group of extended GPDR there was performed none relaparotomy, and in the group of standard GPDR, relaparotomies were required in five cases.

The obtained results testify that the increase of GPDR volume due to the expansion of lymphadenectomy, greater resection of the body of pancreas do not lead to the increase of perioperative lethality and the postoperative complication rate. And long-term results of extended GPDR inspire optimism.

Conclusion. Extended gastropancreatoduodenal resections in ductal adenocarcinoma of the head of pancreas have the advantages over standard operations in terms of prevention of local recurrence development in operated patients. They do not result in significant increase of postoperative recurrence rate and operation duration. The chief factors of the prevention of life threatening complications of gastropancreatoduodenal resections such as dehiscence of hepaticojejunal and pancreatojejunal anastomoses are the experience of a clinic in performing these operations, refusal of framework drainage of ducts, precision technique of their formation.

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