ORIGINAL ARTICLE

CONTENTS

Comparison of the clinical effectiveness of hepaticojejunostomy and self-expanding metal stents for bypassing the bile ducts in patients with unresectable pancreatic head cancer complicated by obstructive jaundice

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ABSTRACT

Aim: To improve treatment outcomes of patients with unresectable pancreatic head cancer complicated by obstructive jaundice by improving the tactics and techniques of surgical interventions.

Materials and Methods: Depending on the treatment tactics, patients were randomised to the main group (53 people) or the comparison group (54 people). The results of correction of obstructive jaundice by Roux-en-Y end to side hepaticojejunostomy (main group) and common bile duct prosthetics with self-expanding metal stents (comparison group) were compared.

Results: The use of self-expanding metal stents for internal drainage of the biliary system compared to hepaticojejunostomy operations reduced the incidence of postoperative complications by 29.9% ($\chi2=13.7$, 95% CI 14.38-44.08, $p=0.0002$) and mortality by 7.5% ($\chi2=4.16$, 95% CI -0.05-17.79, $p=0.04$). Within 8-10 months after biliary stenting, 11.1% (6/54) of patients developed recurrent jaundice and cholangitis, and another 7.4% (4/54) of patients developed duodenal stenosis with a tumour. These complications led to repeated hospitalisation and biliary restentation in 4 (7.4%) cases, and duodenal stenting by self-expanding metal stents in 4 (7.4%) patients.

Conclusions: The choice of biliodigestive shunting method should be selected depending on the expected survival time of patients. If the prognosis of survival is up to 8 months, it is advisable to perform prosthetics of the common bile duct with self-expanding metal stents, if more than 8 months, it is advisable to perform hepaticojejunal anastomosis with prophylactic gastrojejunal anastomosis.

KEY WORDS: pancreatic head cancer, obstructive jaundice, cancerous pancreatitis

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INTRODUCTION

Due to late diagnosis, up to 80% of patients with pancreatic head cancer (PHC) undergo only palliative surgical treatment aimed at eliminating complications such as obstructive jaundice and impaired gastric evacuation [1, 2]. Correction of biliary obstruction is performed by biliodigestive bypass or transpapillary stenting of the common bile duct with self-expanding metal stents (SEMS). The use of SEMS is characterised by a lower number of postoperative complications, lower mortality and shorter hospital stay [3]. However, due to the high efficiency of modern polychemotherapy regimens, the life expectancy of patients after palliative interventions has increased from 9 to 12-16 months. During this period, biliodigestive shunts retain their drainage function, and SEMS can be bypassed by the tumour, bile acid salts, and bacterial biofilms. As a result, recurrent jaundice and cholangitis develop, requiring repeated hospitalisations and reconstructive interventions [4, 5].

AIM

To improve the outcome of treatment of patients with unresectable pancreatic head cancer complicated by obstructive jaundice by improving the tactics and techniques of surgical treatment.

MATERIALS AND METHODS

The randomised prospective study included 107 patients with locally advanced and unresectable pancreatic head cancer without signs of duodenal obstruction treated at the clinics of the Department of Surgery #2 of the Bogomolets National Medical University in

2016-2022. Exclusion criteria were: verified duodenal obstruction, liver gate cancer, carcinomatosis. Pancreatic head cancer was verified in accordance with the recommendations of the European Society for Medical Oncology (ESMO, 2019, 2022), the National Comprehensive Cancer Network (NCCN, 2015-2022) and the classification of the American Joint Committee on Cancer (AJCC, editions VI, VII, VIII, 2002-2017). Based on these documents, the patients were diagnosed with stage III-IV pancreatic head cancer. In all patients, the cancer was histologically identified as ductal adenocarcinoma (WHO, 2000). The resectability of pancreatic head tumours was determined based on comparisons of clinical, laboratory and radiological examination data, according to the NCCN (2019-2022) and ESMO (2019, 2022) guidelines.

Depending on the treatment tactics, patients were randomised to the main group (53 people) or the comparison group (54 people). At the time of hospitalisation, patients in both groups did not differ significantly in age and gender characteristics, hyperbilirubinemia, indications for surgical treatment, comorbidities, and histological characteristics of tumors ($p>0.05$) (Table 1).

It is important to note that patients in both groups were elderly or senile and all had comorbidities (from one to three diseases).

Patients in the main group underwent correction of obstructive jaundice by biliodigestive bypass using the Roux-en-Y end to side hepaticojejunostomy technique with a 50 cm Roux limb. A prophylactic side-to-side gastrojejunostomy was performed in all patients. Patients in the comparison group underwent transpapillary stenting of the common bile duct with SEMS after endoscopic retrograde cholangiopancreatography. The decision to perform endoscopic stenting vs. surgery was based on the suggestion of our interdisciplinary discussion with due regard to the patient's general health status, and the cancer staging. In addition, all options of palliative treatment were extensively discussed with the patient. Boston Scientific WallSTENT Biliary Uncovered 10mm-60mm stents were used. In cases of duodenal stenosis, HANAROSTENT Duodenum/Pylorus NDSL20-140-230 stents were used. Histological diagnoses were confirmed intraoperatively.

After surgical treatment in the study groups, the incidence of postoperative complications, mortality and survival were analysed. Postoperative mortality and morbidity were recorded according to the "Accordion Severity Grading System of Surgical Complications" by Steven M. Strasberg, 2009, which is a variant of the Clavien-Dindo scale (1992, 2004, 2018) [6, 7]. Additionally, the duration of stent functioning without recurrence of mechanical jaundice and/or cholangitis and the frequency and timing of duodenal stenosis were analysed in patients of the comparison group.

STATISTICS

The normality of data distribution was determined by the Shapiro-Wilk test. The difference between the groups was determined using Student's t test for independent samples in the case of parametric and Kruskal-Wallis test in the case of nonparametric data distribution. Differences in sample distribution were assessed using the $\chi 2$ test criterion. Differences between indicators were considered significant at $p<0.05$. Statistical analysis was performed using Statistica 10 (Serial Number: STA999K347150-W) and MEDCALC® (open access Internet resource, https://www.medcalc.org/calc/). Median survival time (together with 95% CI) was calculated via the Kaplan-Meier method and the data were analyzed by means of the log-rank test.

RESULTS

In a comparative analysis of the results of surgical treatment of patients, the specific weight of postoperative complications in patients of the main group was 37.3% versus 7.4% in the comparison group ($\chi 2=13.7$, 95% CI 14.38-44.08, $p=0.0002$) (Table 2).

Among the patients in the main group, complications developed in 20 (37.7%) patients, in 14 (26.4%) patients they were classified as Grade I-III (Minor complications: postoperative wound suppuration, gastrostasis, urinary retention), in 6 (11.3%) patients - as Grade IV-VI (Major complications: hepaticojejunoanastomosis suture failure, acute liver failure, myocardial infarction, pulmonary thrombosis). In the comparison group, complications (cholangitis) were observed in 4 (7.4%) patients and were classified as Grade II and required only pharmacological treatment. The mortality rate among patients in the intervention group was 7.5% (4/53), and there were no deaths in the comparison group ($\chi 2=4.16$, 95% CI -0.05-17.79, $p=0.04$). It is important to note that complications in the comparison group were mild and were effectively managed with pharmaceuticals. All re-hospitalisations within 90 days after surgery occurred among patients in the main group (6 patients, 11.3%) ($\chi 2=6.4$, 95% CI 2.33-22.55, $p=0.01$). Of these patients, 2 (3.8%) were readmitted for percutaneous abdominal drainage, 2 (3.8%) for intravenous antibiotic therapy for cholangitis, and 2 (3.8%) for nonspecific hypogastric pain due to urinary tract infection.

Out of 4 (7.5%) in-hospital deaths (30 days after surgery), all deaths occurred among patients in the main group and were due to the development of the

Table 1. Demographic characteristics and serum bilirubin content at the time of hospitalization in the studied groups

Indexes	Main group (n=53)	Comparison group (n=54)	p
Median age (years)	67.3±5.4	68.1±4.9	0.42
Sex			
men	34 (64%)	32 (59.2%)	0.61
women	19 (36%)	22 (40.8%)	0.61
Bilirubin content in blood serum, μmol/l	204.4±49.3	216±38.1	0.17
Indication for palliative surgery			
Tumor locally advanced	53 (100%)	54 (100%)	–
Liver metastasis	12 (22.6%)	15 (27.8%)	0.53
Peritoneal metastasis	2 (3.8%)	3 (5.6%)	0.66
Histological diagnosis	Pancreatic adenocarcinoma 53 (100%)	Pancreatic adenocarcinoma 54 (100%)	–
Comorbidities			
Hypertension	53 (100%)	53 (98.1%)	0.31
Diabetes mellitus	19 (35.8%)	16 (30.2%)	0.53
COPD	2 (3.8%)	2 (3.7%)	0.97
CVA	3 (5.6%)	2 (3.7%)	0.64
IHD	27 (50.9%)	29 (53.7%)	0.77

Abbreviations: COPD – chronic obstructive pulmonary disease; CVA – cerebrovascular accident; IHD – ischemic heart disease.

Table 2. Post-operative complications and outcomes

Indexes	Main group (n=53)	Comparison group (n=54)	p
Surgical complications (Accordion Severity Grading System scale, ASGS)			
Total number of complications	20 (37.3%)	4 (7.4%)	0.0002
Grade I	8 (15.1%)	–	0.002
Grade II	4 (7.5%)	4 (7.4%)	0.98
Grade III	2 (3.8%)	–	0.15
Grade IV	2 (3.8%)	–	0.15
Grade V	–	–	–
Grade VI	4 (7.5%)	–	0.04
Management of complications			
Surgical revision of hepaticojejunostomy	2 (3.8%)	–	0.15
Radiological procedures	4 (7.5%)	–	0.04
Intravenous antibiotics	4 (7.5%)	4 (7.4%)	0.98
Hospital stay (days)	14 ±2,1	3 ±0,8	<0.0001
Hospital readmission with 90 days	6 (11.3%)	–	0.01
In hospital-mortality	4 (7,5%)	–	0.04

following complications: acute liver failure, myocardial infarction, thromboembolism of the pulmonary artery, abdominal sepsis.

After surgical correction of obstructive jaundice, according to the recommendations of the chemotherapist, 51.7% (28/49) of patients in the main and 66.7% (36/54) of patients in the comparison group received adjuvant chemotherapy. The time to start chemotherapy was not different (42±9.8 days vs. 39±6.7 days) in the study groups (p=0.06). Overall, the survival rate of patients in the main group was 8.5±1.7 (range 6-11) months versus 7.9±1.9 (range 5-10) months for patients in the experimental group, with no significant difference in survival between the two groups (p=0.08). However, among the 21 patients in the experimental group and 18 patients in the comparison group who did not receive chemotherapy, the survival rate was 7.5±0.6 and 6.8±0.7 months, respectively. After surgical correction of jaundice, chemotherapy treatment of 28 out of 49 patients in the main group and 36 out of 54

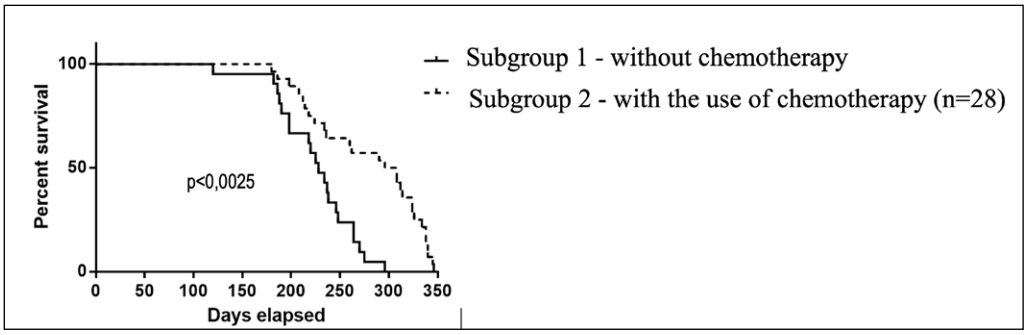

Fig. 1. Survival of patients in the main group depending on chemotherapy.

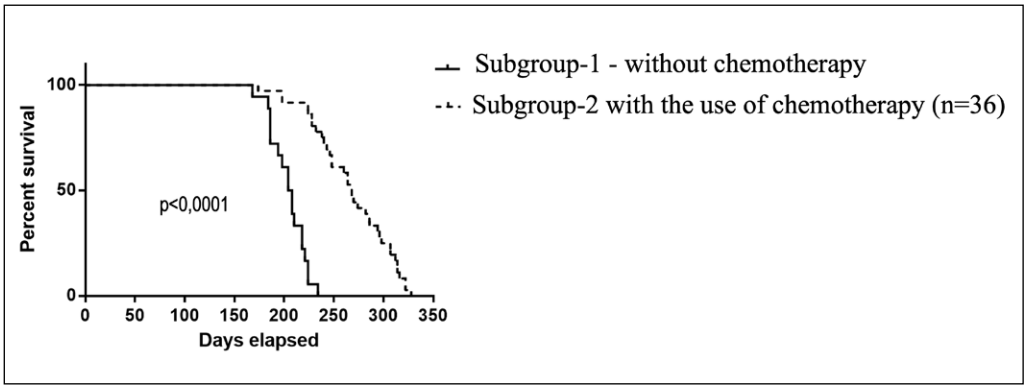

Fig. 2. Survival of patients in the comparison group depending on chemotherapy.

patients in the comparison group ensured survival in the main group and the comparison group of 9.3±0.98 and 8.9±0.81 months, respectively. Thus, chemotherapy treatment contributed to an increase in survival by 24.0% (p=0.007) of patients in the main group and by 30.8% (p=0.01) of patients in the comparison group. All patients in both groups were under medical supervision until death. The survival rates of patients in the two groups, depending on the method of correction of obstructive jaundice and chemotherapy, are shown in Figures 1 and 2.

When analysing the results of treatment of patients in both groups in the period from 4 to 11 months after surgical correction of jaundice, it was found that during this period biliodigestive and gastrojejunal shunts in patients of the main group functioned without complications. However, in 6 (11.1%) patients who underwent SEMS biliary prosthesis, recurrent jaundice and cholangitis developed in the period from 8 to 10 months after stenting. In these cases, 4 patients underwent biliary system replacement, and in 2 cases, jaundice and cholangitis were eliminated by endoscopic stent rehabilitation and antibiotic therapy, taking into account the sensitivity of the bile microflora to antibiotics. In another 4 (7.4%) patients in the comparison group, the course of the disease was complicated by nausea, vomiting, a feeling of heaviness in the epigastrium, and progression of cachexia. According to the results of fluoroscopy and fibrogastroduodenoscopy, patients were diagnosed with duodenal stenosis due to a tumour of the pancreatic head. This complication was eliminated by duodenal stenting with duodenal SEMS. No complications were observed after the procedure, and the evacuation of gastric contents was restored.

DISCUSSION

Meta-analyses of other studies show that surgical bypass is associated with a higher rate of postoperative complications and mortality, but some authors report that in the long-term postoperative period, the incidence of jaundice recurrence in patients after surgical bypass is lower [8, 9]. At the same time, the issues of postoperative outcomes in the correction of jaundice with the use of modern SEMS models and the latest chemotherapy protocols remain unclear. Our study demonstrates that the use of SEMS is associated with a 29.9% reduction in the incidence of early postoperative complications ($\chi2$=13.7, 95% CI 14.38-44.08, p=0.0002) and a 7.5% reduction in mortality ($\chi2$=4.16, 95% CI -0.05-17.79, p=0.04) compared to surgical bypass. At the same time, Ying-bin Liu (2020), Beger H.G., Büchler M.W. (2023) report that SEMS effectively drain the biliary system for 6 months, and later, due to obstruction of the stent by a tumour, salts, bacterial films, recurrent jaundice and cholangitis may develop [2]. Therefore,

it becomes clear that patients whose life expectancy after jaundice correction exceeds 8 months should be given preference for biliary bypass surgery. In 2020, Fabian et al. published a meta-analysis comparing palliative double stenting for malignant duodenal and biliary obstruction with surgical double bypass [10, 11]. The clinical success of endoscopic biliary stenting was higher than that of surgical bypass, and double stenting was associated with fewer complications but more frequent need for reintervention than surgical bypass. The recurrence rate of jaundice in surgical patients was consistently lower than in stented patients [12].

Our study demonstrated that, taking into account medical indications and contraindications (comorbidities, multiorgan dysfunction/insufficiency), adjuvant chemotherapy could be performed in 57.1% of patients in the main group and 66.7% of patients in the comparison group. As a result, the survival rate of patients in the main and comparison groups increased by 24.0% and 30.8%, respectively. At the same time, no recurrence of jaundice and cholangitis was observed among the patients in the main group and there were no signs of impaired gastric evacuation. At the same time, in the SEMS group, in the period from 8 to 10 months after stenting, 6 (11.1%) patients developed recurrent jaundice and cholangitis, and another 4 (7.4%) patients developed duodenal stenosis by a tumour. These complications of the late postoperative period led to re-hospitalisation of 10 (18.5%) patients, intensive care and biliary system replacement in 4 (7.4%) patients and duodenal stenting with duodenal SEMS in 4 (7.4%) patients. No complications were observed after these procedures. The results obtained are in line with the results of the meta-analysis of five randomised controlled trials by Scheufele F. and Friess H. (2018), which showed that surgical bypass is associated with a reduction in recurrence of jaundice compared to biliary stent placement [13].

The results of the study show that the two analysed treatment strategies are successful. Surgical bypass, compared to SEMS placement, ensures no recurrence of jaundice and no development of duodenal obstruction in the long-term postoperative period. The use of SEMS demonstrates better results in the early postoperative period, but more than 8 months after stent placement, 18.5% of patients develop complications: recurrent jaundice with cholangitis or duodenal obstruction. An important factor in the choice of surgical treatment technology is the selection of an effective palliative polychemotherapy regimen. Currently, there is a debate in the literature about the individual choice of chemotherapy protocols, as there is no biomarker that can predict its effectiveness. However, the experience of the study shows that if the cancer tumour is sensitive to the drugs of the chosen polychemotherapy regimen, survival can increase up to 12 months, and then the value of surgical bypass, given its better long-term results, becomes relevant.

CONCLUSIONS

The use of self-expanding metal stents for internal drainage of the biliary system compared to hepaticojejunostomy operations reduced the incidence of postoperative complications by 29.9% ($\chi2=13.7$, 95% CI 14.38-44.08, p=0.0002) and mortality by 7.5% ($\chi2=4.16$, 95% CI -0.05-17.79, p=0.04).

Within 8-10 months after biliary stenting, 11.1% (6/54) of patients developed recurrent jaundice and cholangitis, and another 7.4% (4/54) of patients developed duodenal stenosis with a tumour. These complications led to repeated hospitalisation and biliary restentation in 4 (7.4%) cases, and duodenal stenting by self-expanding metal stents in 4 (7.4%) patients.

The choice of biliodigestive shunting method should be selected depending on the expected survival time of patients. If the prognosis of survival is up to 8 months, it is advisable to perform prosthetics of the common bile duct with self-expanding metal stents, if more than 8 months, it is advisable to perform hepaticojejunal anastomosis with prophylactic gastrojejunal anastomosis.

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CONFLICT OF INTEREST
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