

Case report

INITIAL EXPERIENCE WITH HEPATOPANCREATODUODENECTOMY IN NORTH MACEDONIA: CASE SERIES AND LITERATURE REVIEW

ИНИЦИЈАЛНО ИСКУСТВО СО ХЕПАТОПАНКРЕАТОДУОДЕНЕКТОМИЈА ВО СЕВЕРНА МАКЕДОНИЈА: СЕРИЈА НА СЛУЧАИ И ПРЕГЛЕД НА ЛИТЕРАТУРА

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Abstract

Introduction. Hepatopancreatoduodenectomy (HPD) is one of most complex abdominal surgical procedures, consisted of hepatic resection and pancreatoduodenectomy. Although associated with high morbidity and mortality, in selected group of patients it remains the only curative option for advanced biliary tract malignancies.

Methods. We retrospectively reviewed four consecutive patients who had undergone HPD between 2023 and 2025 at a tertiary center in North Macedonia. Clinical, operative, and histopathological outcomes were analyzed.

Results. Two patients had advanced gallbladder carcinoma and perihilar cholangiocarcinoma with multiorgan involvement, the third had high-grade gallbladder neoplasia, and the fourth suffered inflammatory biliary disease with severe liver infiltration, abscesses and complex fistula. Extended hepatopancreatoduodenectomy with major hepatectomy, pancreatoduodenectomy, colectomy, lymphadenectomy, and vascular reconstruction was performed in selected cases. R0 resection was achieved in 3 patients, while R1 resection in 1 patient. Perioperative mortality occurred in one case (25%) due to massive pulmonary embolism. The remaining three patients had uneventful postoperative recovery.

Conclusion. HPD remains a high-risk procedure requiring strict patient selection and multidisciplinary expertise. Acceptable outcomes and improved overall survival may be achieved even in low-volume centers, although results remain inferior to high-volume institutions.

Keywords: Hepatopancreatoduodenectomy; hepatobiliary surgery; gallbladder cancer; cholangiocarcinoma; complex abdominal surgery; cholecystoduodenal fistula.

Апстракт

Вовед. Хепатопанкреатодуоденектомија (ХПД) е една од најсложените абдоминални хируршки процедури, која се состои од ресекција на црниот дроб и панкреатодуоденектомија. Иако е поврзана со висок морбидитет и морталитет, кај избрана група пациенти таа останува единствената куративна опција за напреднати малигни тумори на билијарниот тракт.

Методи. Ретроспективно анализиравме четири последователни пациенти кои беа подложени на ХПД помеѓу 2023 и 2025 година во терцијарен центар во Северна Македонија. Анализирани беа клинички, оперативни и хистопатолошки исходи.

Резултати. Двајца пациенти имаа напреден карцином на жолчното кесе и перихиларен холангиокарцином со мултиорганска инволвираност, третиот имаше неоплазија на жолчното кесе од висок степен, а четвртиот страдал од воспалителна билијарна болест со тешка инфилтрација на црниот дроб, апсцеси и комплексна фистула. Проширена хепатопанкреатодуоденектомија (ХПД) со масивна хепатектомија, панкреатодуоденектомија, колектомија, лимфаденектомија и васкуларна реконструкција беше извршена кај избрани случаи. R0 ресекција беше постигната кај 3 пациенти, додека R1 ресекција беше добиена кај 1 пациент. Периоперативна смртност се манифестираше со еден случај (25%) поради масивна белодробна емболија. Останатите три пациенти имаа постоперативно закрепнување без несакани настани.

Заклучок. ХПД останува процедура со висок ризик што бара строг избор на пациенти и мултидисциплинарна експертиза. Прифатливи исходи и подобро вкупно преживување може да се постигнат дури и во центри со мал обрт на случаи, иако резултатите остануваат инфериорни во однос на институциите со голем обрт на случаи.

Клучни зборови: Хепатопанкреатодуоденектомија; хепатобилијарна хирургија; карцином на жолчното кесе;

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холангиокарцином; комплексна абдоминална хирургија, Холецистодуоденална фистула.

Introduction

Hepatopancreatoduodenectomy (HPD) is recognized as one of the most complex and challenging procedures in hepatobiliary and pancreatic surgery, involving simultaneous resection of the liver and pancreas, and high level of surgical expertise is imposed. HPD was first reported by Takasaki *et al.* in 1980, initially in the context of gallbladder cancer. Subsequently, the procedure gained wider application in the management of hilar cholangiocarcinomas and gallbladder carcinoma. However, it is well-documented that when major hepatectomy is performed with simultaneous pancreatoduodenectomy, the risks associated with the intervention, including perioperative morbidity and mortality, increase exponentially [1]. In the past, HPD was a rarely performed procedure due to significant technical difficulties and high risk of complications. With the advance of the surgical techniques, perioperative care, and obtained careful selection of patients, HPD is nowadays considered a safe procedure in developed countries [2-6]. Primary indications for HPD are advanced malignancies of the gallbladder and biliary tract with extension into the pancreas, or pancreatic malignancies with infiltration into the perihilar region of the liver. The goal of this challenging intervention is to achieve negative tumor margins (R0 resection), and to relieve jaundice. Therefore, improved survival and increasing the likelihood of a cancer-free state is expected [7,8]. The outcomes of HPD are highly dependent on patient selection, center experience, and surgical volume. Most available data are derived from high-volume centers, whereas evidence from low-volume institutions remains limited [9].

The ambiguity regarding the outcomes may also be related to differences in the definitions of HPD. In Japan and other Asian centers, HPD is defined as a procedure consisting of hepatectomy, complete resection of the biliary trunk and pancreaticoduodenectomy. On the other hand, in western countries HPD is considered any surgery containing hepatectomy and pancreaticoduodenectomy [10].

The aim of this study was to present the first series of HPD in North Macedonia and to compare the results with other centers, with consideration of the odds leading to improvement.

Material and methods

This study included a series of four patients who had undergone surgery at the University Clinic for Digestive Surgery in Skopje, Macedonia, during the period between 2023 and 2025. The inclusion criteria were patients who underwent both hepatectomy and pancreato-

duodenectomy in the same operative session. The study enrolled patients diagnosed with perihilar cancer infiltrating the hepatoduodenal ligament downhill beyond the head of the pancreas, as well as patients with gallbladder cancer invading the liver and with infiltration toward the pancreas and duodenum. Data were collected retrospectively by reviewing patient medical charts, laboratory examination results, and documentation from the electronic medical record system. Collected data included clinical history, surgical treatment, laboratory findings, postoperative histopathological staging and postoperative course.

Case series

Case 1

A 68-year-old woman which was previously operated for jaundice, cholangitis, and a cholecystoduodenal fistula was presented to our clinic. Postoperative histopathological finding reported intracholecystic papillary neoplasm (ICPN), with mucinous malignancy. She was admitted for definitive radical surgical treatment for malignancy. Exploration revealed a dense tumor mass with extensive adhesions involving the gallbladder bed in the liver, duodenum, and right colon. Therefore, a radical HPD was performed, with liver resection of IVb and V segmentectomy (figure 1). Due to tumor abutment and supposed colon infiltration, a colectomy was undertaken. Standard lymphadenectomy was performed for the mucinous neoplasm. Reconstruction included pancreaticojejunostomy, hepaticojejunostomy, gastrojejunostomy, and ileotransverse anastomosis. The postoperative course was uneventful, and the patient was discharged in stable condition on the 8th postoperative day.



Fig. 1. Resected en bloc specimen following hepatopancreatoduodenectomy, including partial hepatectomy, pancreaticoduodenectomy, duodenum, and involved bowel segments

Case 2

A 52-year-old woman was admitted due to gallbladder tumor infiltrating the duodenum and right colonic flexure. Intraoperatively, the tumor was associated with a large cholecystoduodenal fistula with defect of the duodenal wall (figure 2). Cholelithiasis, cholangitis, an intrahepatic abscess, and tumor mass penetration in the segment IV and V were also revealed. The patient underwent HPD, Whipple procedure including limited anatomical hepatectomy of segments IVB and V, right colonic flexure and transverse colon resection with colo-colic anastomosis. Due to predicted gallbladder carcinoma, lymphadenectomy was also performed. Reconstruction consisted of pancreaticojejunostomy, hepaticojejunostomy, gastrojejunostomy, and Braun enteroenterostomy.

The postoperative course was uneventful, and the patient was discharged on postoperative day 10 in good general condition. Histopathological examination demonstrated chronic inflammatory biliary disease with coralliform cholelithiasis, big fistula with vast defect on the duodenal wall. In addition, chronic abscess-forming cholecystitis, chronic suppurative cholangitis, and cholangiolithiasis without evidence of malignancy were identified.

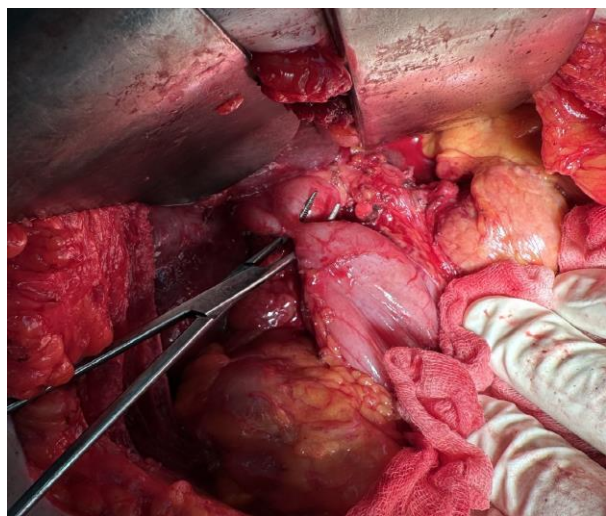


Fig. 2. Intraoperative photograph showing cholecystoduodenal fistula caused by advanced inflammatory gallbladder disease with dense adhesions and duodenal wall destruction

Case 3

A 72-year-old male patient was admitted with obstructive jaundice caused by advanced perihilar cholangiocarcinoma (Klatskin tumor type IIIc) with longitudinal extension toward the ampulla of Vater. The patient had previously undergone biliary stenting for decompression of the biliary tract.

Intraoperative exploration revealed a large tumor extending from the hepatic hilum to the ampulla of Vater. An anatomic variation of the right hepatic artery

originating from the superior mesenteric artery was also identified.

The patient underwent exploratory laparotomy followed by HPD, extended left hepatectomy, hepaticojejunostomy with the right hepatic duct, pancreaticojejunostomy, gastrojejunostomy, enteroenterostomy, and systematic regional D3 lymphadenectomy (figure 3).

Histopathological examination demonstrated a moderately differentiated adenocarcinoma (G2) of the common bile duct involving both the extrahepatic and intrapancreatic portions of the biliary duct.

Postoperatively, the patient was transferred to the intensive care unit. Unfortunately, on postoperative day 3, the patient died due to pulmonary embolism and cardiac failure.

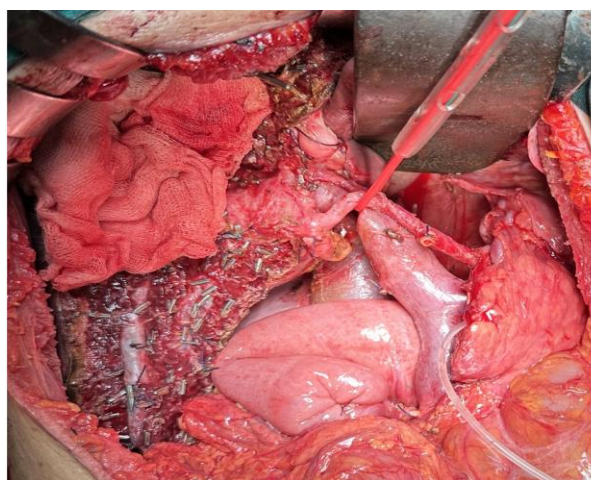


Fig. 3. Intraoperative appearance after extended left hepatectomy during hepatopancreatoduodenectomy for advanced perihilar cholangiocarcinoma (Klatskin tumor)

Case 4

A 72-year-old male patient with a previous history of radical cholecystectomy and limited staging lymphadenectomy for gallbladder carcinoma was admitted for treatment of a recurrent disease. Preoperative imaging evaluation demonstrated recurrent tumor involvement of liver segment V, as well as hepatic duct confluence. Radiological preoperative staging exposed regional lymph node metastases, pancreatic infiltration and infiltration of the anterior wall of the inferior vena cava. The patient had previously undergone ERCP with placement of a pancreatic duct stent and a self-expanding metallic stent (SEMS) due to biliary obstruction and recurrent cholangitis.

Intraoperative exploration revealed massive intra-abdominal adhesions and recurrent tumor involving liver segment V, the hepatoduodenal ligament, duodenum, biliary tree, and pancreatic head. After extensive adhesiolysis, operability was confirmed and radical HPD was performed. The procedure included anatomic resection of liver segments IVb and V with partial resection of segment VI, hepaticojejunostomy, exten-

sive pancreaticoduodenectomy-Whipple procedure, hemigastrectomy, proximal jejunal resection, omentectomy, and extended D2+ regional lymphadenectomy (figure 4). Due to tumor infiltration of the inferior vena cava, partial resection of the anterior wall of inferior vena cava was done.

Histopathological examination demonstrated recurrent mucin-producing adenocarcinoma originating from the gallbladder with local extension into the hepatic parenchyma, hepatoduodenal ligament, pancreatic head, and duodenal wall with infiltration of the ampulla of Vater. However, amid the infiltration of the right aberrant hepatic artery by the recurrent tumor, the postoperative pathological TNM exposed R1 resection status. The operative and postoperative course was uneventful. The patient was discharged in good general condition on postoperative day 12.

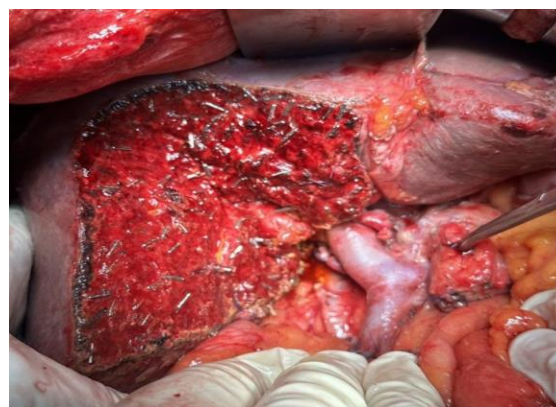


Fig. 4. Intraoperative appearance after partial hepatectomy during hepatopancreatoduodenectomy for recurrent gallbladder carcinoma

Table 1. Patients included in this study

Case	Age/ Sex	Histopathology	Procedure	Postoperative Hospital Stay	Marg in status (R0/ R1)	Overall Survival / Disease- Free Survival	Operative time (min)	Blood loss / Transfusion (mL)	Bile leak	POPF
	69yo/F	Intracholecystic papillary mucinous neoplasm with high-grade dysplasia	HPD – Seg. IVb/V hepatectomy	8 d	R0	22 months DFS alive	645	450 / 300	No	Grade B
	52yo/F	Chronic inflammatory biliary disease, no malignancy	HPD – Seg. IVb,V, VIII partial hepatectomy	10 d	R0	30 months alive	840	500 / 1100	No	Biochemical leak
	72yo/M	Moderately differentiated adenocarcinoma of the CBD	HPD – Extended left hepatectomy	POD 3 death	R0	Death POD 3	930	1850 / 1300	N/A	N/A
	73yo/M	Recurrent mucinous adenocarcinoma of the gallbladder	HPD – Seg. IVb/V hepatectomy	12 d	R1	8 months OS/ 4 months DFS	620	500 / 300	No	Biochemical leak

Discussion

So far HPD has not been established as a standard procedure by protocols for treatment malignancy of the liver, pancreas and biliary system. Some centers consider it an appropriate treatment for advanced biliary malignant diseases, and even metastatic diseases, such as cholangiocarcinomas or pancreatic malignancies. Also, HPD has been reported for certain benign diseases, in which it could be the only plausible therapeutic solution. Thus, combined hepatolithiasis with extrahepatic bile duct adenoma demand HPD in order to obtain feasible solution of the patient's status. In our

study, three of the patients experienced malignant diseases, while one patient was submitted to HDP due to severe inflammatory tumor, associated with liver abscesses, liver necrosis, pericholecystic abscess, and massive cholecystoduodenal fistula with wide defect of the duodenal wall [10,11].

Morbidity in our series included transitory pancreatic biochemical leakage in two patients, and POPF grade B in one patient (25%), grade I Clavien-Dindo. No biliary fistula occurred in our series. All three patients recovered after conservative treatment, without the need for surgery, or radiologically-guided interventions. On the other hand, mortality consisted of one fatal

outcome or 25% on the third postoperative day, caused by pulmonary thromboembolism, and classified as Clavien-Dindo grade V. The morbidity rate is comparable to that reported in high-volume centers, where morbidity may reach 58%, while mortality rate appears higher. In our opinion, this may be explained by the small series and insufficiently strict selection, which included a patient with a concomitant cardiac disorder [7-14]. Another important issue is the achievement of radical curative resection for the malignant disease, R0 resection. R1/R0 is one of the most influencing factor on overall survival (OS) and disease-free survival (DFS). In our series, one patient underwent R1 resection (free margin less than 1 mm), 25%, due to radial tumor growth, invading the right hepatic artery for the future liver remnant. This artery was aberrant, emerging from the superior mesenteric artery (SMA). Comparison with other studies and results from other referent centers reveals comparable results of R1/R0 ratio, which we believe may be improved with increased turnover in our center [8,9,14,15].

The least favorable outcomes in our series were observed in patients with OS and DFS for biliary carcinoma. The patient who underwent HPD for gallbladder carcinoma had OS of 8 months, DFS of 4 months. The explanation may be the presence of an R1 radial resection margin involving the right hepatic artery. On the other hand, the patient with intracholecystic papillary neoplasm has remained disease-free 22 months to date. Further improvement in outcomes for these patients may be expected with increased turnover, and earlier preoperative diagnosis, particularly in patients with gall bladder carcinoma [12,13].

Blood loss and blood transfusion is another issue which deserves particular attention. Blood transfusion is commonly recognized as a high-risk factor during extensive surgery for either malignant or benign diseases. In our patients with HPJ, blood loss and transfusion were comparable to other high-volume centers for HPB surgery. However, advanced surgical technique and skills, high-volume turnover, sophisticated accessory devices should decrease transfusion as much as possible. Regretfully, the highest volume of blood transfusion in our series was associated with the patient who experienced a fatal perioperative outcome [16,17].

Conclusion

Finally, we believe that HDP may offer meaningful benefits for these patients, despite the significantly higher rate of perioperative morbidity and mortality. The ambiguity regarding HPD, in our opinion, is supported by concerns related to unsatisfactory final outcome, including OS and DFS, weighted against the estimated perioperative morbidity and mortality. We can conclude that the best strategy for desired outco-

mes in these patients includes their referral to high-volume centers, careful and strict selection of the target population, and significant improvements in the early diagnosis of the disease.

Conflict of interests: None declared.

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