THE LARGEST WESTERN EXPERIENCE WITH HEPATOPANCREATODUODENECTOMY: LESSONS LEARNED WITH 35 CASES

A maior experiência ocidental com hepatopancreatoduodenectomia: lições aprendidas com 35 casos

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ABSTRACT - Background: Hepatopancreatoduodenectomy is one of the most complex abdominal operations mainly indicated in advanced biliary carcinoma. Aim: To present 10-year experience performing this operation in advanced malignant tumors. Methods: This is a retrospective descriptive study. From 2004 to 2014, 35 hepatopancreatoduodenectomies were performed in three different institutions. The most common indication was advanced biliary carcinoma in 24 patients (68.5%). Results: Eighteen patients had gallbladder cancer, eight Klatskin tumors, five neuroendocrine tumors with liver metastasis, one colorectal metastasis invading the pancreatic head, one intraductal papillary mucinous neoplasm with liver metastasis, one gastric cancer recurrence with liver involvement and one ocular melanoma with pancreatic head and right liver lobe metastasis. All patients were submitted to pancreatoduodenectomy with a liver resection as follows: eight right trisectionectomies, five right lobectomies, four left lobectomies, 18 central lobectomies (IVb, V and VIII). The overall mortality was 34.2% (12/35) and the overall morbidity rate was 97.4%. Conclusion: Very high mortality is seen when major liver resection is performed with pancreatoduodenectomy, including right lobectomy and trisectionectomy. Liver failure in combination with a pancreatic leak is invariably lethal. Efforts to ensure a remnant liver over 40-50% of the total liver volume are the key to obtain patient survival.

INTRODUCTION

Hepatopancreatoduodenectomy (HPD) is a highly complex abdominal operation mainly used to treat advanced biliary carcinoma that includes gallbladder cancer and perihilar cholangiocarcinoma. In the western countries, it is in known as a “Japanese operation”, and only few centers have developed interest in performing such major interventions in the treatment of very limited malignancies. Japanese specialized centers developed an enormous expertise in HPDs and delineated their role in treating advanced biliary carcinomas1,16,22.

Advances in imaging technology over the last decade led to early diagnosis of gastrointestinal tumors. Patients, who do not share that fortune, typically present with jaundice and vascular encasement. The gallbladder cancers disseminate to local and distant lymph nodes by a richly drained submucosal layer of the biliary tree, especially at the body of the gallbladder, and by veins through the gallbladder fossa to intrahepatic portal branches of segment IV, V and VIII. The perihilar cholangiocarcinoma usually grow radially and locally with fewer distant dissemination routes such as those seen in gallbladder carcinomas10.

Liver failure, pancreatic leakage and sepsis are the most catastrophic complications

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after HPDs. Prevention of these complications by systematic application of portal vein embolization, biliary drainage, bile replacement and preoperative nutritional optimization are of paramount importance.3

The aim of this study was to present the results with this complex procedure, which represent the largest Western experience.

METHODS

This study was approved by the Ethics Committee of the Rio de Janeiro Adventist Hospital, Rio de Janeiro, RJ, Brazil. From March 2004 to September of 2014, 35 consecutive HPDs were performed in three institutions in Brazil. A retrospective analysis was based on chart revision. Most of the patients had advanced biliary cancers (68.5%) and all cases were performed by an experimented senior surgeon.

Procedures

All procedures include major liver resections (at least three segments) and pancreateoduodenectomy. The surgical approach always started with the pancreateoduodenectomy followed by the liver resection, mainly because vascular reconstructions were frequently applied (48.5%) and because the liver transection becomes easier without the pancreateoduodenal block. For biliary cancer an en-block specimen was always preferred. Indications of HPD are detailed in Table 1.

TABLE 1 – Indications for hepatopancreateoduodenectomy

| Diagnosis                  | Indication                          | n   |
|----------------------------|-------------------------------------|-----|
| Gallbladder cancer (n=18)  | Periampullary lymph nodes metastasis| 4   |
|                            | Diffuse biliary infiltration        | 4   |
|                            | Duodenal/pancreatic invasion        | 10  |
| Klastin tumor (n=8)        | Distal bile duct infiltration       | 3   |
|                            | Direct pancreatic invasion          | 5   |
| Neuroendocrine tumors (n=5)| Duodenal invasion from recurrent cancer | 1 |
| Colorectal metastasis (n=1)| Liver metastasis and pancreatic tumor| 4   |
| Metastatic intraductal papillary | Recurred liver tumor with duodenal invasion | 1 |
| Mucinous neoplasm (n=1)    | Direct liver infiltration           | 1   |
| Metastatic melanoma (n=1)  | Metastatic ocular melanoma          | 1   |
| Gastric cancer recurrence (n=1)| Tumor invasion to liver and pancreatic head | 1 |

GBC=gallbladder cancer; NET=neuroendocrine tumor; Hilar CC=hilar cholangiocarcinoma

Were separated those patients who underwent pancreateico-duodenectomy with right hepatectomy (Group 1), right trisectionectomy (Group 2), left hepatectomy (Group 3) and central hepatectomy (Group 4). Reconstruction of the pancreatic stump was made by three different technics: 1) pancreateojejunostomy in seven cases; 2) pancreatico-gastrostomy in 17 cases, and 3) pancreatico-stump ligation in 11 cases. A standard Roux-en-Y reconstruction of the biliary tree was performed on all cases.

RESULTS

The overall 30-day mortality was 34.2% (12/35), independent of initial hospitalization time. Mortality was especially high in those patients who underwent major liver resections (Group 1 and 2 – Table 2). The most common causes of death were: liver failure as defined by Broek27, followed by abdominal sepsis related to pancreatic leakage, pneumonia, and renal failure. Groups 3 and 4 had lower complications rates and liver failure was not present in any of these patients. However, pancreatic leak was still a significant morbidity in this group.

TABLE 2 – Types of liver resections on hepatopancreatoduodenectomies

| Liver resections     | n  | Mortality (%) |
|----------------------|----|---------------|
| Right hepatectomy    | 8  | 5 (62.5%)     |
| (Group 1) 8          |    |               |
| Right trisectionectomy| 5  | 2 (40%)       |
| (Group 2) 5          |    |               |
| Left hepatectomy     | 4  | 0             |
| (Group 3) 4          |    |               |
| Central hepatectomy  | 18 | 5 (22.7%)     |
| (Group 4) 18         |    |               |

Twenty-three patients who survived the surgical intervention were discharged from the hospital, 11 cases were lost follow-up over the 10 years of this study. Twelve are alive with up to date follow-up (Table 3). Seven (20%) out the original cohort are alive and free of recurrence at the time of the writing of this report.

TABLE 3 - Patients follow-up

| Age/ Sex | Group Diagnosis | Recurrence | Year | Diagnosis | Recurrence | Alive | Cause of death | Survival |
|----------|-----------------|------------|------|-----------|------------|-------|----------------|----------|
| 66M      | 1               | GBC        | 2005 | No        | Yes        | NA    | 9 years        |          |
| 70F      | 2               | Melanoma   | 2006 | No        | Yes        | NA    | 8 years        |          |
| 63M      | 2               | Hilar CC   | 2006 | Yes       | No         | Recurrence | 39 months |          |
| 71F      | 3               | Hilar CC   | 2008 | No        | No         | Sepsis | 15 months     |          |
| 69M      | 4               | GBC        | 2008 | No        | Yes        | NA    | 6 years        |          |
| 59M      | 1               | GBC        | 2009 | Yes       | No         | Recurrence | 9 months |          |
| 61F      | 2               | GBC        | 2010 | Yes       | No         | 27 months |          |          |
| 52M      | 4               | GBC        | 2010 | Yes       | No         | Recurrence | 22 months |          |
| 56F      | 4               | GBC        | 2012 | Yes       | No         | NA    | 2 years        |          |
| 53F      | 4               | NET        | 2013 | Yes       | No         | NA    | 1 year         |          |
| 55M      | 3               | Gastric CA No | 2014 | Yes        | NA         | 1 year |          |          |
| 49F      | 4               | GBC        | 2014 | Yes       | No         | NA    | 6 months       |          |

GBC=gallbladder cancer; NET=neuroendocrine tumor; Hilar CC=hilar cholangiocarcinoma

DISCUSSION

HPD was introduced in Japan in the 70’s to treat advanced biliary carcinomas12,21,24. Japanese specialized surgeons have developed significant experience in the surgical management of patients with advanced hepatopancreatoduodenal cancer14,17,19,23. In the western hemisphere, very few groups are interested in reproducing this experience. So far, only Hemming et al.9 published a consisted report with HPD in the western countries. Nonetheless, a growing number of surgeons are engaged in developing more expertise with it in this decade. In the southern hemisphere, our groups have the largest HPD experience outside Japan.

Ebe et. al. define it as a multi-visceral resection combining a major liver resection and a pancreatoduodenectomy, which obtains an en-block specimen that encircles the entire extra-hepatic biliary system. In this study, all types of major liver resections with pancreatoduodenectomy performed simultaneously was called HPD1. In 1990’s Japanese reports with it, including Nimura’s initial series with 24 cases and 25% mortality, mainly by liver failure and sepsis20,21. Tsukada et al.20 reported seven HPDs with 29% mortality rate. Miyagawa et al.18 in 1996 published 0% mortality in seven cases and routine preoperative portal vein embolization. Shirai et al.24 in 1997 reported 17 cases in stage IV gallbladder cancer and the 5-years survival was 29% and those with R0 resection the 5-years survival was 50%. The authors learned from this series that HPD is a very complex operation and the combination of right lobectomy or right trisectionectomy has a high mortality.
rate and such procedures requires a mandatory portal vein embolization to ensure a liver remnant large enough to avoid liver dysfunction. Likewise, preoperative biliary drainage and bile replacement are also important tools to guarantee better clinical status. So the called “Nagoya’s protocol” appears to be instrumental in order to achieve lower postoperative mortality. The benefits of preoperative biliary drainage and bile re-infusion improving mitochondrial function, promoting adequate liver regeneration and also improving intestinal mucosa immunity to protect against bacterial translocation, has been well documented.

Ebata et al. reported that hepatic failure rates decreased from 56% to 14% after routine preoperative portal vein embolization. In the 2000’s, because portal vein embolization has been widely used in the preoperative management, a lower incidence of liver failure was observed and many reports with zero mortality following HPD. Interestingly, many studies showed a worse survival in gallbladder cancer when compared to cholangiocarcinomas. All this cumulative knowledge has encouraged many eastern surgeons to perform HPD in cholangiocarcinomas with very good results. Ebata et al. reported a 10-years survival of 32.1% with it for cholangiocarcinomas. Kawakita et al. and Miwa et al. also reported excellent 5-years survival for HPD in cholangiocarcinomas 52% and 64%, respectively. Wakai et al. in 2008 published 28 cases with perioperative mortality of 21%.

We acknowledge the weaknesses of this report where 11 patients (31.4%) were lost to follow-up. This is mainly related to the public health system in a very large country where patients need to travel long distances to get to specialized centers and many of those patients returned home were advanced medical care is scarce. Only 12 cases (34.2%) had long term follow-up in this series.

During 10-years period, many improvements and experience were collected in the management of biliary carcinoma by the partners of this study. Using the Nagoya’s team protocol refined our approach to HPD. All the complications observed in this period were the same observed by Japanese surgeons in the 90’s. The combination of right trisectionectomy right lobectomy with pancreateoduodenectomy is feasible but mandatory portal vein embolization is required to obtain good postoperative survival because our results suggest that mortality over 40% is seen in those patients who underwent HPD (Group 1 and 2). So, far long term survival (9-years) was observed only in one patient who underwent right trisectionectomy plus pancreateoduodenectomy and portal vein reconstruction for gallbladder cancer and two patients with complex central hepatectomies plus pancreateoduodenectomy are also free of tumors recurrence in this series. Another four patients are alive and free of disease but the follow-up interval is short.

CONCLUSION

HPD is a complex abdominal operation with a high mortality rate and a long learning curve. We emphasize that this operation should be limited to specialized centers with experience in liver transplantation background and advanced hepatobiliarypancreatic surgery. Aggressive preoperative management with biliary drainage and portal vein embolization are crucial maneuvers to obtain satisfactory results. The HPDs for gallbladder cancer is feasible but requires a careful patient selection.

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