TWELVE YEARS OF EXPERIENCE USING CHOLECYSTOJEJUNAL BY-PASS FOR PALLIATIVE TREATMENT OF ADVANCED PANCREATIC CANCER

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ABSTRACT – Background: The cholecystojejunal bypass is an important resource to treat obstructive jaundice due to advanced pancreatic cancer. Aim: To assess the early morbidity and mortality of patients with pancreatic cancer who underwent cholecystojejunal derivation, and to assess the success of this procedure in relieving jaundice. Method: This retrospective study examined the medical records of patients who underwent surgery. They were categorized into early death and non-early death groups according to case outcome. Results: 51.8% of the patients were male and 48.2% were female. The mean age was 62.3 years. Early mortality was 14.5%, and 10.9% of them experienced surgical complications. The cholecystojejunostomy procedure was effective in 97% of cases. There was a tendency of increased survival in women and patients with preoperative serum total bilirubin levels below 15 mg/dl. Conclusion: Cholecystojejunal derivation is a good therapeutic option for relieving jaundice in patients with advanced pancreatic cancer, with acceptable rates of morbidity and mortality.

INTRODUCTION

Pancreatic cancer is the fourth leading cause of death from malignant neoplasms in the United States⁴, and is three times more common in smokers. The disease is typically classified into two groups: exocrine, which originates in the ductal cells responsible for producing enzymes that aid in digestion, and exocrine, which forms in cells that specialize in producing hormones like insulin. Among exocrine tumors, adenocarcinoma accounts for about 95% of cases, with the majority located in the head of the pancreas. In Brazil, data from the National Cancer Institute (INCA) show that of all types of cancer diagnosed, the incidence of pancreatic cancer has increased to approximately 2% of all cancers and is responsible for more than 8000 cases each year⁵. However, fewer than 30% of patients are subjected to this procedure⁶,⁷,⁸,⁹,¹⁰,¹¹, because either the disease is initially encountered in a locally advanced state or is metastatic, or because the patient is in poor clinical condition, making large-scale surgical procedures not feasible. Consequently, knowledge of palliative treatment is fundamental; this includes endoscopic, surgical, or radiological procedures or clinical therapeutic measures to relieve pain and obstructive jaundice and to clear duodenal obstruction¹².

Palliative treatment of obstructive jaundice stands out because of the frequency of this condition¹³,¹⁴,¹⁵. Because of the morbidity related to obstructive jaundice, particularly the risk of development of cholangitis (inflammation of the biliary duct system, intrahepatic and extra-hepatic inflammation, or both) treatment is essential.
The choice of the best therapeutic modality should be based on cost, effectiveness, and ease of execution.

Although endoscopic or radiological treatments are less invasive, they are not free from complications such as hemorrhage, duodenal perforation, and cholangitis. In the long term, jaundice and cholangitis may return due to migration or occlusion of the stent. As a result, surgical treatment should not be overlooked.2,3,10,12,13,16,20

Surgical palliation of obstructive jaundice is obtained through biliodigestive derivations, which can be hepaticojejunostomy, cholecystojejunostomy, or choledochojejunostomy anastomoses. Cholecystojejunal derivation can contribute to palliative treatment in a greater number of patients because it is a simpler, faster technique that is reproducible in various centers.

The objective of this study was to assess the morbidity and mortality of patients with pancreatic cancer who underwent cholecystojejunal derivation, as well as the success of this procedure in relieving jaundice.

**METHOD**

This study was submitted to and approved by the Research Ethics Committee of Santa Casa de São Paulo.

Data obtained from medical records in the Medical File and Statistical Service (SAME) for patients diagnosed with pancreatic cancer who underwent cholecystojejunal anastomosis procedures at the Pancreas and Bile Duct Group at the Surgery Department of the Irmandade da Santa Casa de Misericórdia de São Paulo Hospital between January 2002 and December 2013 were retrospectively analyzed.

Inclusion criteria were patients with pancreatic cancer confirmed by biopsy as adenocarcinoma of pancreatic origin for whom resection was not possible (because of either advanced disease or poor clinical condition) and in cases where there was at least 2 cm of space in the main bile duct between the tumor and the implantation of the cystic duct.

Candidates who underwent cholecystojejunal derivation but did not have adenocarcinoma of the pancreas were excluded. Patients with incomplete medical records were also excluded from the analysis.

The data analyzed by this study were: gender, age, cholangitis (defined as inflammation of the bile duct), serum levels of albumin, creatinine, pre- and post-operative total bilirubin (TB) and direct bilirubin (DB), glutamic oxalacetic transaminase (SGOT), glutamic pyruvic transaminase (SGPT), prothrombin activity (PA), hemoglobin (Hb), comorbidities, previous surgeries, duration of surgery, need for intraoperative transfusion, length of hospital stay, morbidity as well as median overall survival (OS), cases of early mortality, and improvement rate for jaundice.

**Statistical analysis**

The Kaplan-Meier method was used for statistical analysis of OS, with a log rank test for comparison between groups. P values <0.05 were considered statistically significant. Variables for which univariate analysis reached values of p<0.10 were tested in multivariate analysis using the Cox regression method.

**RESULTS**

Were analyzed 55 patients who underwent cholecystojejunal biliodigestive derivation to treat adenocarcinoma of the pancreas. Of these, 51.8% were male and 48.2% were female. Median age was 61 years (variation: 37–93). The main laboratory data obtained are shown in Table 1.

Of the patients studied, 16.3% underwent surgery because of cholangitis, and 83.6% had associated comorbidities, most frequently high blood pressure (69%) (Figures 1 and 2). The median duration of surgery was 140 min, ranging from 60 to 300 min. Only two patients required intensive care treatment during the post-operative period. The median hospitalization time after the procedure was four days.

**FIGURE 1 - Patient comorbidities according to type and number**

**FIGURE 2 - Number of comorbidities per patient, comparing early death and non-early death**

The early mortality rate (death within 30 days after the procedure) was 14.5%. As for morbidity, 9.0% of patients had no surgical complications while 10.9% developed surgical complications (Figure 3). The cholecystojejunostomy was not successful in 2 cases, 3.3% of patients. In the first case, removal of the biliary obstruction worked until the third month, when the patient became jaundiced again. At this time, hepaticojejunal anastomosis was performed, and the jaundice was resolved for another five months. In the other case, the jaundice was not resolved from the beginning; this is probably because the patient had multiple liver metastases, voluminous ascites and carcinomatosis, and the jaundice was not relieved even after transparieto-hepatic drainage. This patient died within 45 days.

**TABLE 1 - Preoperative characteristics of the participating patients**

| Parameters                                | Male  | Preoperative | Age (years) | Preoperative albumin (mg/dl) | Preoperative creatinine (mg/dl) | Preoperative total bilirubin (mg/dl) | Preoperative direct bilirubin (mg/dl) | Preoperative sGOT (mg/dl) | Preoperative sGPT (mg/dl) | Preoperative pre-thrombin activity (%) | Preoperative hemoglobin (mg/dl) |
|-------------------------------------------|-------|-------------|-------------|------------------------------|--------------------------------|-------------------------------------|-------------------------------------|--------------------------|--------------------------|--------------------------------------|-----------------------------|
| Male                                      | 29/55 | Yes=9/55    | 62.3        | 3.15±0.73                    | 0.74±0.56                      | 19.65±8.91                         | 15.15±7.68                         | 169.98±132.6             | 200.92±155.63            | 77.8±14.14                         | 11.28±2.02                   |
| Preoperative cholangitis                  |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Age (years)                               |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative albumin (mg/dl)              |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative creatinine (mg/dl)           |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative total bilirubin (mg/dl)      |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative direct bilirubin (mg/dl)     |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative sGOT (mg/dl)                 |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative sGPT (mg/dl)                 |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative pre-thrombin activity (%)    |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |
| Preoperative hemoglobin (mg/dl)           |       |             |             |                              |                                |                                     |                                     |                          |                          |                                      |                             |

*Data obtained are shown in Table 1.*
follow-up or death. Among the four patients who exhibited new episodes of jaundice, this occurred more than six months after the procedure.

TABLE 2 - Comparison of the profiles of patients with and without early death

| Parameters                  | Early death group (n=8) | Non-early death group (n=47) | p     |
|-----------------------------|-------------------------|------------------------------|-------|
| Male                        | 6                       | 23                           | 0.2574|
| Age                         | 65.5±11.8               | 61.8±11.6                    | 0.4091|
| Cholangitis                 | 2                       | 7                            | 0.6044|
| Preoperative hemoglobin (mg/dl) | 12.22±3.167          | 11.12±2.049                  | 0.1577|
| Preoperative leukocytes (mg/dl) | 10.35±4.486          | 8.72±3.655                   | 0.2669|
| Total bilirubin (mg/dl)     | 28.61±14.509           | 18.4±4.722                   | 0.0126|
| Preoperative creatinine (mg/dl) | 1.05±1.258           | 0.68±0.328                   | 0.0996|
| Preoperative sGOT (mg/dl)   | 158±57.814             | 172±142.120                  | 0.7829|
| Preoperative sGPT (mg/dl)   | 176±37.360             | 205.5±167.074                | 0.6304|
| Preoperative pre-thrombin activity (%) | 84%±12%            | 76%±14%                      | 0.1342|
| Preoperative albumin (mg/dl) | 3±0.816               | 3.18±0.721                   | 0.5035|
| Surgery duration (min)      | 160±78.010             | 142±12.54±70                 | 0.4257|

DISCUSSION

Obstructive jaundice is one of the main presentations of pancreatic cancer, especially when this cancer is located in the head of the pancreas\(^1\). In this series of 185 patients, obstructive jaundice was present in 73% of the 114 patients with tumors located in the pancreatic head, compared with only 11% in cases with tumors located in the body of the pancreas and 0% when tumors were located in the pancreatic tail\(^1\). Malignant biliary obstruction can lead to harmful consequences such as risk of cholangitis, pruritus, or delayed start of surgical or chemotherapeutic treatment, and can also increase mortality.

Palliative biliary decompression can bring comfort to the patient by improving jaundice and reducing pruritis\(^1\). Obstructive jaundice can be treated endoscopically, radiologically, or surgically. Endoscopic therapy is a less-invasive technique and has lower mortality rates compared to surgical treatment, but has higher rates of jaundice recurrence\(^1\). Furthermore, the endoscopic procedure is not always available; many hospitals and even cities do not offer this service 24 h per day, and even places within the same hospital that can perform the endoscopic procedure often lack the specific materials that are needed to conduct this procedure or the endoscopist is not available.

In a recent meta-analysis of five randomized studies\(^1\) that compared surgical decompression with endoscopic stent placement, there was no statistical difference in success rates between the two techniques (relative risk [RR] 0.99, CI 95% 0.93–1.05, p=0.67). Complication and mortality rates also did not differ between the groups (RR 1.54; CI 95% 0.87–2.71, p=0.14). In this meta-analysis, surgical treatment exhibited a mortality rate of approximately 15%, while the mortality rate of the endoscopic treatment was 12% (p=0.40); in our series, the mortality rate was 14.5%. The length of hospital stays evaluated in the meta-analysis was relatively long for both decompression techniques (21.8 days in the surgical group versus 14.6 days in the endoscopic group), while our median hospitalization time was only four days for the cholecystojejunal derivation procedure. Additionally, the recurrence rate for jaundice was an average of nine times lower in patients who underwent surgical treatment compared with endoscopic treatment (RR 0.14; CI 95% 0.03–0.63; p<0.01). However, it should be stressed that of the five studies included in the analysis, four used plastic stents, and in comparison with metal stents plastic is known to have a lower success rate in relieving jaundice\(^1\).

Although surgical treatment is more invasive, it alleviates the jaundice for a longer period, so fewer re-admissions are
necessary. Furthermore, surgical treatment can be performed in several surgical centers, since complex materials and specialized equipment are not required. Moreover, with advanced diagnostic techniques, such as 3D imaging, the procedure can be performed with less morbidity in patients with advanced pancreatic cancer. However, considering the nature of the disease, the procedure should be prioritized, particularly in patients with advanced pancreatic cancer. In addition, the surgical technique must be tailored to the patient’s individual characteristics, such as age, comorbidities, and tumor location. In conclusion, the cholecystojejunal anastomosis technique can be performed in surgical centers with advanced pancreatic cancer as a therapeutic option to relieve jaundice in patients with advanced pancreatic cancer, which can be performed with less morbidity and mortality.