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SURVIVAL OF PATIENTS WITH METASTATIC PANCREATIC CANCER UNDERGOING BILIARY DRAINAGE

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Abstract: Pancreatic cancer is one of the most lethal neoplasms in the world, with a high incidence, ranking fourth in the total number of cancer-related deaths, and in Brazil, it is responsible for 2% of all types of cancer and 4% of the total deaths from this disease. It affects patients of both genders. The association of new less invasive techniques such as biliary drainage in patients with pancreatic cancer helps in the treatment of the disease, thus increasing their quality of life and survival, with very low complication rates. This study sought to identify in the literature the survival of patients with metastatic pancreatic cancer undergoing biliary drainage. It was carried out through a bibliographic review, in the Scielo and Lilacs databases, in the period between 2009 and 2017. The average survival of patients with advanced stage pancreatic cancer is around six to eleven months, and in Literature has shown that, in relation to endoscopic biliary drainage, there is a decrease in bilirubin levels, improving the social and psychological function of the patient. In the literature review, it was evident that the statistically significant factor related to greater survival is related to the greater number of chemotherapy lines received.
Keywords: Pancreatic cancer. Biliary drainage. Pancreatic neoplasm. adenocarcinoma.

INTRODUCTION

Pancreatic cancer is one of the deadliest neoplasms worldwide, and ranks fourth in the total number of cancer-related deaths in patients of both genders. [1]

The pancreas can be divided anatomically, in a simple way, into head, body and tail. Tumors can be located anywhere on the gland. However, when they appear on the body and tail, due to the absence of symptoms, they progress to invade noble structures or present distant metastases, becoming unresectable. Those that develop in the head of the organ often invade the common bile duct, causing obstructive jaundice, which provides the diagnosis in most cases. Its blood supply derives from the main branches of the celiac trunk and the superior mesenteric artery, and knowledge of this complex anatomy and its variations is mandatory for surgeons who are willing to operate in this region.[2]

In 2013, the United States recorded about 45,000 new cases of pancreatic cancer, where the number of expected deaths was very close to the number of new cases. Survival over 5 years was around 2 to 6%.

Pancreatic adenocarcinoma is the most common type of pancreatic tumor and, with all its subtypes, represents 85% of cases.[1]

The chance of long-term survival is curative surgical resection of this tumor. The predominant location of the tumors is in the pancreatic head, which, due to its anatomical characteristics and to preserve the oncological principles, must be resected together with the duodenum. This resection is called a pancreatoduodenectomy. Although appropriate, this procedure is only applicable to a minority of patients, as the majority present with advanced disease. [2, 3]

Only 5% to 20% of carcinomas of the head of the pancreas are resectable at the time of diagnosis. The surgeon is always faced with a dilemma in ineradicable cases, which usually present with obstructive signs of the biliary or duodenal pathways. [4]

Most diagnoses of malignant tumors are made in the advanced stage of the disease, so about 85% of patients with such diseases are not candidates for curative surgical treatment. Due to late diagnosis, jaundice is a very frequent clinical sign in these patients, which means that methods for draining the obstructed bile duct must be used, as untreated biliary stasis can cause intense pruritus, anorexia, liver dysfunction, cholangitis. and even early death. [5]

In many cases, surgery offers definitive treatment with palliative or therapeutic intent, but it is not without complications. Stenoses and fistulas are more frequent in the postoperative context, in young patients and in the active population. [6]

The development of endoscopic technology and interventional radiology has offered a safe option for the treatment of these complications, such as: Endoscopic Retrograde Cholangiopancreatography (ERCP) and Percutaneous Transhepatic Drainage (DPTH).

Endoscopic Retrograde Cholangiopancreatography (ERCP) with passage of a biliary prosthesis is the method of choice in the palliative treatment of obstructive jaundice and for the drainage of the obstructed bile duct. However, there is a failure rate of around 10%. In these cases, alternative techniques will be applied, such as percutaneous transhepatic drainage (DPTH) and surgical drainages. [5, 7]

Endoscopic bile duct drainage in inoperable cases of malignant obstruction is currently the conduct of choice. cases. [5,8]

In endoscopic drainage of the bile duct, self-expanding metallic prostheses are used, which present better results compared to plastic prostheses, due to the lower rates of obstruction. [8]

In order to overcome the shortcomings of ERCP, the morbidities of palliative surgery and DPTH, therapeutic echoendoscopy has been used as an alternative method for biliary clearance. This technique uses an echo-guided access to the bile duct through the lumen of the gastrointestinal tract. There are two types of access: intrahepatic and extrahepatic; There are three access routes: transmural, anterograde transpapillary and retrograde transpapillary. [5]

Thus, we can say that the association of new less invasive techniques such as biliary drainage in patients with pancreatic cancer has been collaborating in the treatment of the disease, thus increasing their quality of life and survival, with very low complication rates, with a favorable outcome to the procedure, taking into account the severity of the disease.

The present study came to present the relevance of biliary drainage as a supporting treatment in patients with pancreatic cancer.

GOAL

To identify the survival of patients with metastatic pancreatic cancer undergoing biliary drainage.

MATERIAL AND METHOD

This study was a literature review, based on the need to build knowledge about the subject to be studied. The descriptive research makes a selection of the collected materials, and these were observed, registered, analyzed, classified and interpreted, reaching the final objective.

Thus, the research was carried out in the database: Latin American and Caribbean Literature in Health Sciences (LILACS), *Scientifc Electronic Library Online* (SCIELO), Regional Library of Medicine (BIREME), Nursing Database (BDENF), Coordination for the Improvement of Higher Education Personnel (CAPES).

The time frame was from 2009 to 2017, considering more recently published studies in the field.

As inclusion criteria, descriptors related to health areas were searched that addressed the keywords "pancreatic cancer", "bile drainage", "pancreatic neoplasia", "adenocarcinoma". Articles published in Brazil in Portuguese were used, covering the period between 2009 and 2017.

The exclusion criteria used were: articles without online access, articles that did not have access to the full text, that did not respond to the theme of our objective and that were

outside the period between 2009 and 2017, and articles that were not in the portuguese language.

After the bibliographic survey, the articles and books were read, and the respective records. Then, the articles were grouped by similarity and relevance, and then the discussions were presented.

RESULTS

Based on the importance of identifying the survival of patients with metastatic pancreatic cancer undergoing biliary drainage, a total of 28 articles were found in which 15 articles were used because they are relevant to the topic.

DISCUSSION

Pancreatic cancer is the fourth leading cause of cancer death in the US, with the prospect of becoming the second most frequent in 2030. In Brazil, it is responsible for 2% of all types of cancer and 4% of all deaths from cancer. this disease. The most important risk factors include gender (slightly more common in men), age, smoking, and body mass index.[9].

It is a neoplasm, in most cases, it is very difficult to control, however, it is treatable through surgery, when detected early, but, due to the absence of symptoms in its initial phase, pancreas cancer usually spreads before of diagnosed[10].

Most diagnoses occur after 50 years of age, with a peak incidence around 70 to 75 years of age. It is more common in men. Other risk factors related to pancreatic cancer are: smoking, chronic pancreatitis, cirrhosis, obesity, sedentary lifestyle, diet high in fat and cholesterol, diabetes mellitus, occupational exposure to carcinogens, Jewish (Ashkenazi) ancestry, and low socioeconomic status.[11].

It is a disease with high mortality, and its survival is around 5% in five years. Mortality has not changed much despite advances in surgical techniques in the last 80 years, after the introduction of pancreatoduodenectomy. Surgical resection is the only potential cure for ADP, but in 80% of patients with symptoms, the tumor is already unresectable at the time of diagnosis. For patients who are candidates for surgical resection, survival is, on average, 12 months and, for those who are not candidates for surgical treatment, 3.5 months[9].

Endoscopic treatment for pancreatic fluid drainage is accepted as a less invasive option than surgical or percutaneous drainage. The endoscopic procedure consists of wide biliary papillotomy aiming at easy biliary drainage and passage of a plastic prosthesis in order to, by capillarity, direct the flow in a distal direction, reducing the fistular output. The prosthesis also acts as a factor of transpapillary patency, preventing the inflammatory process by the electrothermal action after papillary section.[12].

In the Unified Health System, adequate treatment of pancreatic adenocarcinoma becomes a challenge, not only for health providers, but also for surgeons and patients. [13].

Indications for endoscopic drainage are usually based on the patient's symptoms. The main symptoms that indicate the procedure are abdominal pain, delayed gastric emptying, early satiety, weight loss and jaundice, but other indications are cystic infection or increase in its size. In patients with unfavorable clinical conditions, endoscopic treatment must be preferred, given its lower morbidity.[13].

Palliative biliary decompression can bring comfort to the patient by improving jaundice and reducing pruritus. The treatment of obstructive jaundice can be performed endoscopically, radiologically or surgically. Endoscopic therapy is a less invasive technique with lower mortality rates when compared to surgical treatment, but with higher rates of recurrence of jaundice[14].

Number of Articles Found	Number of Excluded Articles	Number of Articles used
28	13	15

Table 1 – Result of Research Conducted in Databases. Sao Paulo, 2018.

Article Authors	Year	Title	Abstract
Gobbi PG, Bergonzi M, Comelli M, Villano L, Pozzoli D, Vanoli A, Dionigi P.	2013	Symptoms and patient factors associated with diagnostic ranges for pancreatic cancer. a prospective cohort study.	The poor prognosis of pancreatic carcinoma seems to depend, in part, on the delay in diagnosis and this, in turn, is influenced by the type of symptoms presented.
Toneto MG, Lopes MHI.	2014	Historical evolution of the surgical treatment of pancreatic cancer.	Despite the safety with which pancreatoduodenectomy is currently performed, postoperative survival in pancreatic cancer is still insufficient, suggesting that technical operative issues represent only one of the necessary steps for progressing results
Torres OJM, Moraes Junior JMA, Fernandes ESM.	2013	Distal pancreatectomy with en bloc resection of the celiac trunk for locally advanced pancreatic body adenocarcinoma (Appleby operation): case report	The results indicate that the overall five-year survival rate remains below 5% with a low possibility of resection.
Ilias EJ.	2009	What is the best palliative management for ineradicable cancer of the head of the pancreas?	Postoperative chemotherapy and/or radiotherapy did not bring a significant increase in survival.
Loureiro JFM, Artifon ELA, Ilias EJ.	2010	What is the role of echoendoscopy in palliative drainage of the bile duct due to malignant obstruction?	Echo-guided biliary drainage is effective and safe, with acceptable complication rates and does not alter the favorable outcome of the procedure.
Ruiz RF, Bicalho LGMF, Ferreira BA, Sakai P, Ishioka S, Martins BC, Rios JT.	2014	Placement of a self-expanding metallic prosthesis, partially covered in the distal bile duct, and a plastic prosthesis in the cystic duct in a patient with pancreatic head neoplasia.	The use of self-expanding metallic prostheses presents better results compared to plastic prostheses due to the lower rates of obstruction.
Soldan, M.	2017	Pancreatic cancer screening	Ductal adenocarcinoma of the pancreas (ADP) originates in the exocrine pancreas and is responsible for 95% of pancreatic cancers.
Artifon, M. BuCh , L. Bonini, DPS,. Aparicio GED.	2013	Critical pancreas injuries	Cystic lesions of the pancreas must be evaluated by a multidisciplinary approach, thus achieving the best possible treatment for the patient.
Artifon ELA, Couto Júnior DS, Sakai P.	2010	Endoscopic treatment of bile duct injuries.	Malignant strictures are related to cholangitis, jaundice and pain and to systemic changes related to biliary sepsis.
Oliveira MB, Santos BN, Moricz, E, Pacheco-Junior AM.	2017	Cholecystojejunal bypass for palliative treatment of advanced pancreatic cancer	Cholecystojejunal bypass is a good therapeutic option to relieve jaundice in patients with advanced pancreatic cancer.
Usón Junior PL, França MS, Rodrigues HV, Macedo AL, Goldenberg A, Smaletz O, Armentano DP, Simon SD, Gansl RC	2015	Improved overall survival in patients with metastatic pancreatic cancer	The number of chemotherapy lines was significantly associated with survival, with an estimated median survival of 10.2 months for patients who received up to two lines of treatment and 23.5 months for those who received more than two lines.

Table 2: Articles sorted by: Author name, year of publication, article title, abstract. Sao Paulo, 2018.

Biliary obstruction occurs in around 37% of patients with pancreatic tumors. Treatment of biliary obstruction involves the bypass procedure, endoscopic retrograde cholangiopancreatography, or percutaneous transhepatic drainage.

Technological advances in therapeutic endoscopy have promoted the alternative possibility of effective treatment of these benign obstructions. Considerations regarding the time of rehospitalization and procedures must be investigated in detail and considered in relation to the surgery. Malignant strictures are related to cholangitis, jaundice and pain and, consequently, to the systemic changes related to biliary sepsis. The endoscopic approach creates a shunt of bile juice to the duodenum, being a true endoscopic biliodigestive shunt and using plastic or metallic prostheses.[12].

The median survival of patients with locally advanced pancreatic cancer is approximately 6 to 11 months. In cases of metastatic disease, chemotherapy increases overall survival and improves symptoms. The greatest median overall survival gain reported in the metastatic setting was 11.1 months, which was achieved with the combination of fluorouracil, leucovorin, irinotecan, and oxaliplatin.[15].

Regarding quality of life, there are studies demonstrating that after the first month of endoscopic biliary drainage with decreased bilirubin levels, there is a significant improvement in social and psychological function[13].

In a retrospective study comparing palliative tumor resection and biliary and gastric bypass, it was observed that the median survival time for the first procedure was 7.5 months and for the second 6 months. However, there was no statistically significant difference between the procedures in terms of survival and morbidity, but there was a better quality of life in those undergoing double bypass.[14].

In another study, it was shown that drainage of the bile duct by transhepatic puncture is indicated in cases of proximal obstructive tumors and in cases where endoscopic therapy fails. Patients undergoing this procedure have a mean hospital stay of 20 days, with 19% showing no significant reduction in bilirubin. Complications found were cholangitis and pancreatitis. Deaths occurred due to cholangitis and pneumonia, with a mean time between the drop in bilirubin and the patient's death of 25 days. Percutaneous biliary drainage proved to be effective in relieving pruritus in patients with malignant periampullary neoplasia, but it did not bring a statistically significant improvement in the patients' quality of life. Patients had a median survival of 4.74 months after drainage[14].

In research carried out to determine the overall survival of patients with advanced pancreatic cancer and to assess factors with prognostic impact. However, the number of chemotherapy lines was significantly associated with survival (log-rank p=0.013), with an estimated median survival of 10.2 months for patients who received up to two lines of treatment and 23.5 months. for those who received more than two lines. The only statistically significant factor related to greater survival was a greater number of chemotherapy lines received[15].

CONCLUSION

This study sought to identify in the literature the survival of patients with metastatic pancreatic cancer undergoing biliary drainage.

The average survival of patients with advanced stage pancreatic cancer is around six to eleven months, and the literature has shown that, in relation to endoscopic biliary drainage, there is a decrease in bilirubin levels, improving social function. and psychological

of the patient. In the literature review, it was evident that the statistically significant factor related to greater survival is related to the greater number of chemotherapy lines received.

The literature is scarce regarding the survival of patients with pancreatic neoplasia and biliary braking, as there are few published studies on this topic, leading to the conclusion that the objective of this study was partially achieved. It is suggested that further studies on this topic be carried out, especially with regard to nursing.

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