

Biliary Stenting for Malignant Biliary Obstruction Secondary to Pancreatic Cancer

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ABSTRACT: Despite progresses made in oncology, pancreatic adenocarcinoma has a grim prognosis and commonly presents with rapidly advancing jaundice which requires endoscopic treatment. Aim: Our objective was to show the perspective of a high ERCP volume dedicated Center on endoscopic stenting for malignant biliary obstruction consecutive to pancreatic cancer. Methods: We conducted a retrospective study, between October 2017 and October 2020, and enrolled hospitalized patients within the Gastroenterology Department of the Clinical Emergency Hospital Bucharest, diagnosed with pancreatic cancer with secondary malignant biliary obstruction which underwent ERCP stenting. Results: We identified 269 patients which were admitted in our Clinic with a pancreatic lesion on computed tomography or magnetic resonance imaging and underwent EUS-FNA. 115 patients with proven pancreatic malignancy were selected and underwent ERCP stenting. 69 received plastic stents and 46 metal biliary stents, with the stent chosen based on patient's characteristics and availability at the time of the procedure. Per total 234 stents were used for relief of the cholestasis syndrome. The number of ERCP procedures was higher in the plastic stents group with a median of 1,8 whereas the SEMS had 1,5 range of procedures. Procedures were successful in 54 patients following plastic stents and 33 that underwent SEMS. At 30 days, overall mortality rate was of 5%. Conclusions: Malignant obstruction secondary to pancreatic cancer is amenable by ERCP. However, choosing the right stents still varies. SEMS seem to be more efficient on a long term with fewer complications rates and further studies should be performed.

KEYWORDS: Pancreatic cancer, endoscopic retrograde colangio pancreatography (ERCP), plastic stents, self-expandable metal stents (SEMS).

Introduction

Nowdays, pancreatic adenocarcinoma remains the most lethal cancer in both European Union and the United States, with 6th and 4th leading cause of cancer-related deaths, though being just the 11th most common cancer and accounting for just over 3% of all cancers in the United States [1-3].

Worldwide survival data for ductal adenocarcinoma of the pancreas are the lowest among the 60 most frequent types of organ cancers [4].

This unfavorable prognosis is associated with the advanced stage of disease at the time of diagnosis.

A Finnish nationwide study raised suspicion about pancreatic cancer curability, reviewing the records of 4922 patients, of whom only 10 out of 89 subjects who survived at 5 years were correctly diagnosed with pancreatic ductal adenocarcinoma, the rest being primarily

misdiagnosed: non-PDAC histology, or no second histology at all [5].

Patients with locally advanced pancreatic cancer can't benefit from radical surgery and often require palliation via biliary and duodenal endoscopic stenting, which were introduced in the early 1980s [5].

Before endoscopic biliary stenting, surgery was the primary treatment for cases of biliary obstruction, by means of hepatico-jejunal anastomosis [2].

Prolonged jaundice has deleterious effects if not treated promptly, as obstructive jaundice would lead to hepatocellular dysfunction, biliary cirrhosis and increases the incidence of cholangitis [2].

In this setting, it is commonplace for patients to do chemotherapy or other palliative endoscopic procedures such radiofrequency ablation [6,7].

In theory, this might reduce stent patency in patients with malignant biliary obstruction, as

immunosuppression can result in bacterial colonization of the stent.

Particularly, plastic stent might be susceptible to early stent dysfunction during chemotherapy, as biofilm and sludge formation are the main causes of plastic stent dysfunction, while fully-covered expandable metal stents (SEMS) are prone to migration or tissue in-growth in the case of uncovered expandable stents [8,9].

Our objective was to show the perspective of a high ERCP volume dedicated Center on endoscopic stenting for malignant biliary obstruction consecutive to pancreatic cancer.

Methods

We conducted a retrospective study during a three years period, between October 2017 and October 2020, which enrolled hospitalized patients within the Gastroenterology Department of the Clinical Emergency Hospital Bucharest, diagnosed with pancreatic cancer with secondary malignant biliary obstruction which underwent ERCP stenting.

All patients included underwent EUS-FNA for pancreatic cancer diagnosis and underwent biliary stenting due to malignant biliary obstruction.

We included only patients with expected survival of more than 4 months.

We separated them into inoperable and resectable and borderline-resectable, and compared both plastic and SEMS for efficacy, stent patency, ERCP number, complications.

The study variables were collected in a database designed exclusively for the study.

The data due to be obtained was: date of diagnosis, name, age, gender, CA 19-9, diabetes mellitus status, imaging method (computed tomography or magnetic resonance imaging), ERCP status prior to EUS, number of ERCPs per patient and type of stents used, pre-procedural biological values, surgical status and type of surgery done, information about the EUS procedure: type of needle used and number of passes, topographical details: location and diameter of the purported malignant nodule, common bile ducts status: dilated, not dilated, or with a stent in situ.

The study protocol was approved by the Ethics Committee of Clinical Emergency Hospital Bucharest, Romania.

For the description of the continuous variables, the mean and standard deviations were used, when the distribution was normal, and the median and the rank of percentiles

otherwise (the normality of a variable was verified by the Kolmogorov-Smirnov test).

The categorical variables were described by percentages.

The bivariate comparison of groups was carried out with the Student t-tests (normal continuous variables), U-Mann-Whitney (continuous non-normal variables) and χ^2 (categorical variables).

A $p < 0.05$ was considered statistically significant in all the tests.

For the analysis of the data, we used the statistical program GraphPad Prism 9.1 software (GraphPad Software, LLC, San Diego, CA, USA).

Results

We identified 269 patients which were admitted in our Clinic with a pancreatic lesion which raised malignancy suspicion on computed tomography or magnetic resonance imaging and underwent EUS-FNA.

After the procedure only 169 patients were diagnosed with pancreatic adenocarcinoma, whereas the others were neuroendocrine tumors (14), breast metastases (4), non-Hodkin's lymphoma (2), cystadenocarcinoma (10), acinary pancreatic tumor (1), solid-pseudopapillary neoplasm (1) and 68 patients were negative for malignancy after the first EUS-FNA.

We concluded 59 were benign lesions and other 9 were false negative results and required a second EUS-FNA.

Ultimately, patients amenable to radicality or complex surgical palliative procedures were sent to surgery, with a further 132 patients requiring biliary stenting due to cholangitis or jaundice, with 115 proven malignancies and 17 benign lesions consisting of pseudotumoral chronic pancreatitis.

Among the 115 subjects with proven pancreatic malignancy that underwent ERCP, 58 were men and 57 women, with an average of 63.9 years and a standard deviation of 11.6.

A large majority of these patients had a good ECOG performance status-grade 0 or 1 in the case of 68.7%-and just 3 patients had grade 3 (2.6%).

Diabetes mellitus was presented in 50 out of the total (43.5%).

No relationship among having diabetes mellitus and the type of stent was found (p -value=0.701).

Tumoral marker CA 19-9 was elevated in 63.6% of the tested patients, with a correlation with the final diagnostic of 68.2%.

There isn't a statistical significance or relationship among the tumoral marker CA 19-9 and the type of stent (p-value=0.5525).

As for the imaging, 89 subjects underwent computed tomography and just 26 magnetic resonance imaging with a correlation with the final diagnostic of 82%, respectively 88.5%.

Regarding EUS procedure, the average lesion was 36.1mm large, with a standard deviation of 14.9, the very big majority of them being placed

in the head of the pancreas (n=104), with very few of them in the body (n=11).

The distribution of the lesion size is the same across the two categories of patients (with plastic stents vs. metal biliary stents).

We used the 22G Expect needle from Boston Scientific for all procedures.

The number of passes per procedure was slightly higher in the first tertile, though generating a global average of 2 passes per patient, with a standard deviation of just 0.43 (Table I).

Table 1. Comparative characteristics of patients with plastic stent vs. metal biliary stent ^passed normality test; #didn't pass normality test

	Plastic stent (n=69)	Metal biliary stent (n=46)	p-value
Age [#] , years mean±SD median (interquartile)	64.19±12.19 67 (57-72.5)	63.37±10.95 63 (58.5-69.25)	0.3436
Gender, n, % Male	33, 47.83%	24, 52.17%	0.6478
Diabetes mellitus, n, %	29, 42.03%	21, 45.65%	0.701
Lesion size [#] , mm mean±SD median (interquartile)	36.17±16.69 33 (27.5-41.5)	36±11.95 34.5 (27.75-40)	0.8722
Location, n, % Head Body	60, 86.96% 9, 13.04%	44, 95.65% 2, 4.35%	0.1204
CA 19-9, n, % Elevated	17, 65.38%	14, 73.68%	0.5525
Correlation with the final diagnostic, n, % Yes	17, 65.38%	14, 73.68%	0.5525
Number of passes per procedure [#] mean±SD median (interquartile)	1.96±0.44 2 (2-2)	2.04±0.42 2 (2-2)	0.3392

Out of the 115 patients, 69 received plastic stents and 46 metal biliary stents, with the stent chosen based on patient's characteristics and availability at the time of the procedure.

Per total 234 stents were used for relief of the cholestasis syndrome.

The number of ERCP procedures was higher in the plastic stents group with a median of 1.8 whereas the SEMS had a 1.5 range of procedures.

Procedures were successful in 54 patients following plastic stents and 33 that underwent SEMS. At 30 days, overall mortality rate was of 5%. (Figure 1, 2)

Patients following plastic stents encountered complications in 21 cases and consisted of indwelling (68%), perforations (12%), bleeding (9%), secondary pancreatitis (6%) and other (5%).

Three patients had several complications related to two separate procedures.

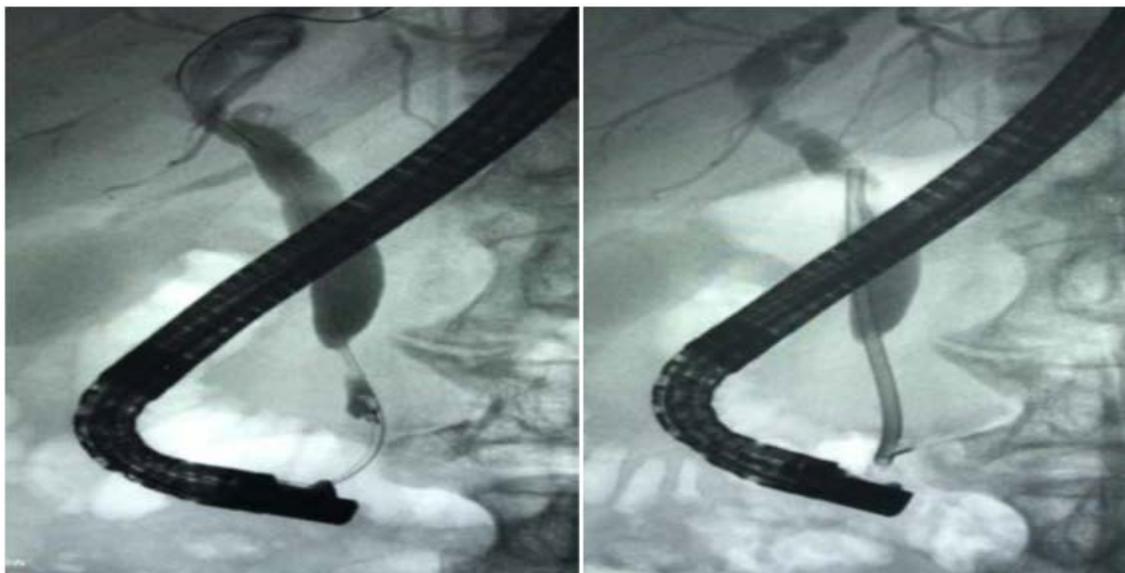


Figure 1. Main bile duct malignant stenosis due to pancreatic cancer with plastic stent insertion.

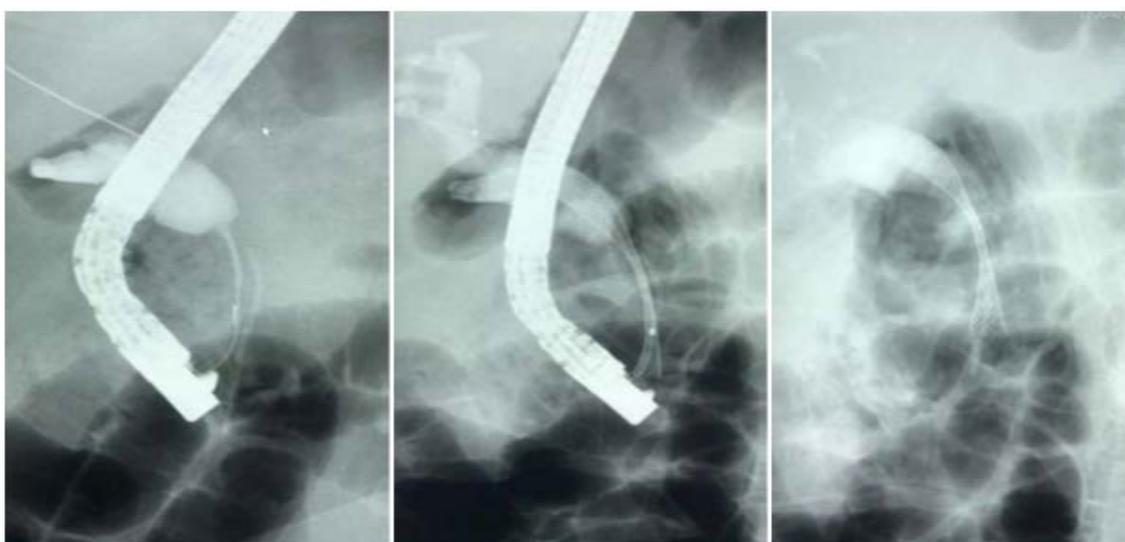


Figure 2. Main bile duct malignant stenosis due to pancreatic cancer with metallic stent insertion.

In the SEMS group, the most reported complication was clogging due to ingrowth tissue or decreased radial power, which was the case for 7 out of the 14 patients that required reintervention, uniformly distributed among the 3 SEMS types (4 for partially-covered SEMS, 2 for full-covered SEMS and one for uncovered SEMS).

Another complication which was encountered exclusively in the full-covered SEMS was the migration of the stent, which in 2 cases required restenting and in one case repositioning.

Other 4 patients had duodenal invasion, downstream of papilla, which lead to increased hydrostatic pressure in the biliary tract, thus requiring placement of a duodenal stent.

On a 6th month follow up, 34 patients with plastic stents and 22 patients with SEMS came for check-up, or for stent complication.

Patients with plastic stents required a change within 3 months, whereas patients with SEMS were changed after 6th months or if complications occurred.

Discussions

Patients with locally advanced pancreatic cancer can't benefit from radical surgery and often require palliation by means of biliary and duodenal endoscopic stenting, which were introduced in the early 1980s, or surgical hepatico-jejunal and gastro-jejunal bypasses to relieve jaundice or duodenal obstruction.

However, these palliative surgical alternatives carry risks similar to radicality, with up to 2% perioperative mortality and morbidity of about one third [10-12].

In this setting, whether locally advanced or metastatic, there are some treatment options such as chemoradiation and chemotherapy with various schemes, mostly with poor outcomes.

Plenty of drugs and combinations have been used to enhance potency of treatment, including gemcitabine monotherapy and gemcitabine combinations with erlotinib, oxaliplatin, cisplatin, capecitabine and nab-paclitaxel.

All these regimens are prone to lessening immune defence and augmenting bacterial colonisation of biliary tree so that adequate drainage is imperative [13-15].

We provided a retrospective study on patients diagnosed with pancreatic cancer complicated with malignant biliary obstruction that underwent biliary decompression.

ERCP in this situation is an established procedure, and plastic stents and SEMS are the main options.

While, our objective was not to compare plastic and expandable metal stents, SEMS seemed to be more reliable for stent patency and with fewer complications.

Moreover, differentiated their use from plastic stents by using them in patients with an expected survival of >4-6 months [16].

However, survival is difficult to estimate due pancreatic cancer aggressiveness, and stent type should be chosen according to the patient prognosis.

Controversy still prevails on the proper stent, drainage area and double stenting method [17].

Our success rate of biliary decompression was similar with other studies even though it was related to the endoscopist experience. SEMS use seem to be related to fewer complications and to a lower number of reinterventions.

Other studies also focused on the cost efficiency and proposed SEMS as a cheaper procedure due to longer patency and shorter hospital stay.

However, plastic stents are still a valid option for patients that are borderline-resectable and might be scheduled for surgery, or in advanced stage with a grim prognosis.

This study has several limitations.

Mainly it was a retrospective, non-randomized study, with no overall long overall survival follow-up.

We also did not assess cost-efficiency when using plastic and metal stents.

Conclusions

Malignant obstruction secondary to pancreatic cancer is amenable by ERCP.

However, choosing the right stents still varies.

SEMS seem to be more efficient on a long term with fewer complications rates and further studies should be performed.

Conflict of interests

None to declare.

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