

Malignant Biliary Obstruction: Clinical Outcome of Endoscopic Intervention - An Experience of Tertiary Centers

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Summary:

Most patients with malignant obstructive jaundice present at a stage when they are beyond the scope of curative surgery. Endoscopic stenting is the approach of choice worldwide to improve quality of life and survival of such patients. The aim of this study was to find out overall clinical outcome of endoscopic intervention in malignant obstructive jaundice. This prospective study done in two tertiary gastroenterology centers in Dhaka included consecutively admitted 79 adult patients with malignant biliary obstruction for endoscopic stenting, followed by a follow-up period of six months. Outcome evaluation included success rate of stenting and drainage, complications, and mortality rate at one-month, and survival up to six-months. ERCP revealed carcinoma of pancreas, periampullary carcinoma, cholangiocarcinoma,

carcinoma of gallbladder, and metastasis in the biliary trees in 22 (27.8%), 22 (27.8%), 20 (25.3%), 11 (13.9%), and 04 (5.1%) cases respectively. Successful stenting and drainage could be achieved in 62 (78.5%) and 58 (73.4%) cases. Stent blockage (23.9%) and cholangitis (19.4%) were the main complications. Total death at one-month was nine of 55 (16.4%), and 21 (38.2%) patients survived up to six-months, with no difference in one-month mortality rate among the malignancies ($P>0.05$). Stenting prolonged six-month (88.2%) and mean survival (121.2±67.7 days) only in patients with periampullary carcinoma ($P<0.001$).

Endoscopic stenting can safely be done in malignant biliary obstruction to offer palliation with an outcome, which is not unsatisfactory.

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Introduction:

Surgery is the standard treatment of malignant biliary obstruction, the second most common cause of obstructive jaundice. Unfortunately in only 20% patients these malignant lesions are resectable, except ampullary tumours¹⁻⁷. With inoperable biliary tumours the prognosis is poor in terms of survival and quality of life^{8, 9}. Endoscopic biliary drainage is an established procedure of palliation in such situation to relieve jaundice, and to help maintain a good quality survival¹⁰⁻¹⁹. Lower procedure-related complications and the relative non-invasive nature of endoscopic treatment have relegated surgical management to a subsidiary role²⁰⁻²⁸.

Endoscopic retrograde cholangiopancreatography (ERCP) is done in several centers in Bangladesh for more than one and half decade. With malignant obstructive jaundice patients are admitted at the 'Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine & Metabolic Disorders' (BIRDEM) Hospital, and other institutions, and during ERCP many of them receive endoscopic stenting, if found unfit for surgery. Hasan et al²⁹ reported their experience of diagnostic ERCP in a study done in Dhaka. However, till now there is no published report on the outcome of endoscopic

intervention in patients with malignant obstructive jaundice. A study was therefore conducted on 79 patients, and we report the experiences on success rate of endoscopic stenting, successful drainage achieved, about early and late complications, and the impact of endoprosthesis implantation on quality of life and survival.

The purpose of this study was to obtain the results of endoscopic palliation in patients with malignant biliary obstruction.

Materials and method:

Irrespective of sex, consecutively admitted 79 adult patients with features of malignant obstructive jaundice were included in this prospective study during April to December 2000. This study was done in the Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine & Metabolic Disorders (BIRDEM) Hospital, and in Gastro liver Hospital & Research Institute, Dhaka, the tertiary gastroenterology centres of this country. The purpose of this study was explained to every patient, and they were included after they gave their verbal consent. Common bile duct diameter of more than 8 mm in ultrasonogram was considered as an evidence of biliary obstruction³⁰. Besides ultrasonography and before ERCP liver function and relevant biochemical tests, CT scan of abdomen was done in all the patients. Duodenoscope (Fujinon, 400 series) with a working channel of 4.2 and 3.8 mm. were used for ERCP. Biopsy was obtained only in case of suspected periampullary carcinoma, or carcinoma of head of the pancreas infiltrating the duodenum. In all other cases diagnosis was done correlating cholangiographic findings with clinical and laboratory features. Neither collection of juice from common bile duct (CBD), nor any brush cytology was included for histological diagnosis. Irrespective of type or site of lesions endoprosthesis implantation was the objective. Plastic stents, 10Fr., or in some cases 7Fr. (Amsterdam type), with flaps on either end were used for this purpose. In case of hilar obstruction, the aim was to implant only unilateral stenting.

Successful endoscopic stenting and drainage were defined respectively as passage of endoprosthesis across the stricture with restoration of bile flow, and at least a 30% reduction of serum bilirubin within 10 days of intervention, with recovery from cholangitis, if any. Early complication and one-month mortality were defined as those events occurring within 30 days of the first attempt of endoscopic intervention.

After discharge from the hospital, follow up of all the patients were done at the interval of 15 to 30 days, for six months. Follow up included history taking, physical examination, and laboratory investigations, if needed. Monitoring was done over telephone in case any patient was unable to attend the outpatient department. No one was lost to follow up. After recurrence of biliary obstruction a review ERCP was done, followed by restenting, if needed.

Outcome evaluation included success rate of stenting and drainage, morbidity of the procedure, patient's mortality at one-month, and survival up to six month.

Exclusion criteria:

Patients with malignant biliary obstruction, but having marked narrowing of the duodenal channel or any other morbid diseases were not included in this study.

Statistical Analysis: Statistical analysis was done using SPSS software. The significance level in comparison between variables was set at 0.05.

Results:

Entry characteristics:

Of the 79 patients, 50 (63.3%) were male and 29 (36.7%) female with an age range of 23-85 years (mean 56.3±12.0yrs). Majority patients were in the age group of 51–70 years (59.5%) [Table-I]. Major clinical features were pruritus (74.7%), abdominal pain (65.8%), weight loss (49.4%), weakness (48.1%), anorexia (35.4%), fever (25.3%), and nausea (24.1%). Mean duration of jaundice was 67±26.7 days, with their serum bilirubin and alkaline phosphatase level of 12.5 ± 5.9 mg/dl and 1132 ± 802 IU/L respectively.

Table-I*Patients characteristics- at entry & after ERCP.*

Gender	At entry Age Range				Total					
	23-30	31-50	51-70	≥71						
Male	01 (1.3)	15 (19)	29 (36.7)	05 (6.3)	50					
Female	02 (2.5)	08 (10.1)	18 (22.8)	01 (1.3)	29					
Findings after ERCP										
Characters	Periam- carcinoma		Carcinoma- pancreas		Cholangio Carcinoma-		Carcinoma- gallbladder		Metastasis	
	M	F	M	F	M	F	M	F	M	F
≤50 (yrs) (25)	09	02	02	02	05	02		02		01
≥51 (yrs) (54) †	07	04	13	05	08	05	05	04	01	02
Mean age (years)	51.64±11.5		59.6±12.1		57.1±10.9		59.9±10.8		49.5±17.8	
Age range (years)	29-75		26-85		45-78		40-78		23-61	

† Male sex $P \leq 0.05$, [between two different age range ≤ 50 and ≥ 51]*Findings after ERCP:*

ERCP was done in all the 79 patients. Findings were suggestive of carcinoma of pancreas, periampullary carcinoma, cholangiocarcinoma, carcinoma of gallbladder and biliary tree in 22 (27.8%), 22 (27.8%), 20 (25.3%), 11 (13.9%) and 04 (5.1%) cases respectively. Higher distribution of these malignancies, except periampullary carcinoma, was seen after the age of 50 years, but, significantly, only in case of male (43%) ($P < 0.05$) (Table-I). Of the 20 cases of cholangiocarcinoma, twelve were seen in the perihilar region (type I-one, type II-three, type IIIb-two, and type IV-six), and rest eight were in the extra-hepatic bile duct. Biopsy obtained in 27 patients from obvious lesions in ampullary region revealed periampullary carcinoma in 22 cases, carcinoma of pancreas in four, and cholangiocarcinoma in one.

Endoscopic intervention and outcome:

In three patients with periampullary carcinoma papillotomy was done with no stenting, which restored adequate biliary drainage. Endoscopic palliation was not attempted in 12 patients due to

unsuitable cholangiographic picture, and in five patients attempt of stenting was unsuccessful. However, it was done successfully in rest 59 patients that included 18 cases with periampullary carcinoma, 18 with carcinoma of pancreas, 12 with cholangiocarcinoma, 10 with carcinoma of gall bladder and one with biliary metastasis [Table-II]. Within two days of stenting two patients expired, and there was no improvement in another two. With an intention to treat basis successful stenting, and drainage could be done in 62(78.5%), and 58(73.4%) cases respectively.

After unsuccessful attempt of stenting in five patients three of them were treated by PTBD (percutaneous transhepatic biliary drainage). Two of the 12 patients, not included for endoscopic intervention also received PTBD. Rest 12 patients left abandoned without any intervention died within one month. Within the same period there was death of one patient after PTBD. Following successful stenting Whipple's operation was done in four cases with periampullary carcinoma, and two with carcinoma of pancreas. However, two days after surgery, one patient died of

Table-II

Malignancies	Papillotomy and stenting		ERCP abandoned		ERCP Failed		P * value
	≤ 50	≥ 51	≤ 50	≥ 51	≤ 50	≥ 51	
	Periampullar-ca ‡	11	10		01		
Ca-pancreas	03	15	01	02		01	≥ 0.05
Cholangiocarcinoma	05	07	01	04	01	02	
Ca-gallbladder	02	08	01	00			
Metastasis	01	0	0	02		01	
Total	22	40	3	09	01	04	
	(27.8)	(50.6)	(3.8)	(11.4)	(1.3)	(5.1)	

‡ Papillotomy was done in three patients without stenting.

* Each procedure of two-age range [≤ 50, & ≥ 51]

adult respiratory distress syndrome (ARDS). But rest six survived for more than six months. After stenting, palliative surgery was done in a patient with cholangiocarcinoma, who had marked stricture in the common hepatic duct. (Table-IV). He also survived for six months.

Early complications and death after endoscopic intervention:

Different complications were seen in 11(16.4%) patients within 30 days of an attempt of intervention in 67 cases. During procedure significant bleeding started from papillotomy site in two (3.0%) patients, and perforation occurred in one (1.5%). Two days later, cholangitis, acute pancreatitis, and peritonitis were noticed in 03 (4.5%), 02 (3.0%) and 03 (4.5%) patients respectively; and all these complications were seen mostly with distal malignancies (Table-III). With conservative management they recovered well.

One month after endoscopic drainage total death was nine of 55 (16.4%), and there was no significant difference in patients' mortality rate with different malignancies (P>0.05) (Table-IV).

Late complications after endotherapy:

Forty-six patients were alive after one month of intervention. At variable intervals (median four months) 14 (30.4%) patients presented with jaundice

and of them 10 (21.7%) with cholangitis (Table-III). Review ERCP revealed stent blockage in 11 (23.9%) cases. Restenting was done once in eight patients, and on two occasions in other three relieved biliary obstruction. Jaundice in rest three patients was due to blockage of bile flow at the CBD outflow tract by extension of tumour mass of periampullary carcinoma. This time they received their first stenting. Two (4.3%) patients suffering from cholangiocarcinoma presented with liver abscess as a late complication, but recovered with conservative management.

Survival at six month (after stenting)

Finally 21(38.2%) patients were alive after a six-month follow up. With carcinoma of gallbladder (10), and biliary metastasis (01) none survived up to six months (Table-IV). Mean survival with the former was 88.7±47.1 days; and with the later, the survival was 35 days only. With cholangiocarcinoma and carcinoma of pancreas, 04 (36.4%) and 02 (12.5%) patients were alive after six months, and mean survival with these malignancies were 114.5±77.2 and 97.6±64.5 days respectively. However, with periampullary carcinoma, 15 (88.2%) patients were alive after six months, a difference with others, which was statistically significant (P<0.001) (Table-IV). Age, sex, or site of lesion did not influence the outcome of endoprosthesis.

Table-III

Type of Complications	No. of patients / period after intervention				
	Early (≤ 30 days)		Late (≥ 31 days)		
	Periampullar-Ca	Ca-pancreas	Periampullar- Ca	Ca-pancreas	Cholangiocarcinoma
Bleeding	02				
Perforation		01			
Cholangitis	02	01	06	03	01
Pancreatitis	02				
Peritonitis		03			
Liver abscess					02
Stent blockage			05	05	01
Total	06	05	11	08	04

Table-IV

Diseases / Characters	Survival of patients in days after different procedures / management					P * value <0.001	
	Papillotomy/stenting n=55		Abandoned / Failed ¶ n=12	Surgery n=07			PTBD φ n=5
	≤ 30 §	≥ 180	≤ 30	≤ 30	≥ 180		≤ 30
Periampullar-ca	01(5.9%)	15(88.2%)	01	01	03		
Ca-pancreas	04(25%)	02(12.5%)	03		02		
Cholangio-carcinoma	03(27.3%)	04(36.4%)	06		01	01	
Carcinoma gallbladder	01(10%)						<0.001
Metastasis			02			01	
Total	09(16.4%)	21(38.2%)	12(15.2%)	01	06	01	
Mean survival φ (days)	121.2±67.7		12.1±8.3	154.6± 67.3		76.8±63.1	

§ P \geq 0.05,

* Between malignancies (long-term survival)

φ PTBD (percutaneous transhepatic biliary drainage) done after attempt of stenting abandoned / attempt failed

¶ No sort of intervention was done

φ Mean of all the patients with individual management
Percentage done in each category of patients

Discussion:

This is the first study in this country to find out a data on the outcome of endobiliary prosthesis implantation which was conducted on 79 patients with jaundice of 67 ± 26.7 days duration. Carcinoma of the pancreas, gallbladder, or bile ducts is the cause of malignant obstruction of the biliary trees^{31, 32}. Some western studies have reported pancreatic malignancy as the most common cause^{33, 34}. In this study carcinoma of pancreas, periampullary carcinoma and cholangiocarcinoma were found as the common biliary malignancies, which together comprised 81% of all the cases, with a prevalence rate varying from 25-28% for each of them. Kapoor and McMichael³⁵ reported a higher prevalence of carcinoma of gallbladder in north and central India. However, in our study carcinoma of gall bladder could be detected in 11(13.9%) cases only. This variation is not unexpected as this study was done on different race and population, and it is unusual that all the patients with obstructive biliary malignancies would come to us for palliation.

With an intention to treat basis the success rate of stenting and drainage, that was achieved in 78.5% and 73.4% cases respectively is relatively lower to others. De Palma et al⁹ from Italy reported this outcome in 96.7% patients; and similar higher rate of success has even been reported by some other studies^{6, 24-27}. One of the possible reasons was biliary obstruction of advanced duration, for which stenting had to be abandoned in 12 cases. However, the drainage that was achieved in 73.4% patients was successful as there was gradual improvement of pruritus, fever and anorexia followed by that of jaundice and general well being. Luman et al²⁵ and few others^{15,24-25} reported a similar outcome on quality of life after endoscopic intervention. After stenting average hospital stay of these patients was three days on an average. Plastic stents were however in all these cases.

Apparently, no difference was found in morbidity pattern when compared it to others.⁶⁻⁹ Early complications were seen in 11 (16.4%) cases, with cholangitis in 4.5% of them. Polydorou et al⁸ in his study reported the same result in 19.1% and 7% cases respectively. Overall complications have even been

reported in 19–27% patients²⁷⁻²⁸. Probably use of prophylactic antibiotic in each and every patient had a role in reducing the morbidity. One month mortality rate was 16.4%, which was relatively higher in patients with cholangiocarcinoma and carcinoma of pancreas than others. None of these findings differ from other published reports^{8,36}. Similarly, if it is analyzed, 11(23.9%) patients presented with jaundice due to stent blockage, and 10 (21.7%) of them with cholangitis, a higher rate of late complications, as it appears. But some other studies have found the same morbidity in 30% and 16.3% cases respectively^{9, 22-25}.

Long-term survival did not reveal a favourable finding as only 21 (38.2%) patients survived up to six months, including none with carcinoma of gallbladder and biliary metastasis. The outcome was even poorer with carcinoma of pancreas (12.5%). However, the picture was totally different with periampullary carcinoma, as six-month survival was 88.2%. This was probably due to relatively benign course of the disease. Polydorou et al⁸ in his study reported shorter survival of patients with carcinoma of pancreas and biliary metastasis in comparison to others. In this study, in addition, the outcome was also worse with carcinoma of gallbladder. Weaver et al¹⁸ in his study reported a long-term survival rate of 20.4% only. However, they did their follow up for over one year. In this study, out of survived 21 cases. If 15 (88.2%) with periampullary carcinoma are taken in consideration, then only six (10.9%) patients survived up to six month, a rate which is much lower to Weaver et al¹⁸.

Overall clinical outcome achieved in this study is not comparable to those reported in western countries^{8,9,15,21-24,27-28}. Whether biliary obstruction of advanced duration, and or re-use of accessories, or use of plastic stents affected the results remains to be explored, as there was no control group of patients. There are some of the limitations of this study. Follow up period was shorter, and there was no option of brush cytology or no biopsy was there to do a histological diagnosis for all the patients. However, the main goal was to find out a data of endoscopic intervention in patients with malignant biliary obstruction, and that was obtained. In that sense, this study has served the primary purpose.

In conclusion, it may be said that carcinoma of pancreas, periampullary carcinoma and cholangiocarcinoma are the common obstructive biliary malignancies in the patients with malignant obstructive jaundice. Endoscopic palliation reduces one-month mortality, and improves quality of life. However, long-term survival is not significantly prolonged, except in periampullary carcinoma. It may also be said that in patients with malignant jaundice endoscopic intervention can safely be done with an outcome, which is not unacceptable. This study provides a rationale to do properly designed further studies on a larger number of such patients.

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