

Endoscopic Biliary Drainage of Malignant Biliary Strictures: About A Moroccan Series and Review of the Literature

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1. Abstract

The development of interventional endoscopy has produced a profound upheaval in the treatment of malignant biliary obstruction as a palliative or bridge to surgery. The aim of our work is to report the experience of our department in the endoscopic treatment of Biliary tract cancers. We conducted a retrospective study of 127 patients with a malignant biliary obstruction, between January 2016 and June 2018. They benefited from endoscopic retrograde cholangiopancreatography (ERCP) which represents 24.9% of the all ERCPS during this period. The pancreatic head cancer was in 40.15% of the cases, in 38.5% a cholangiocarcinoma, 12.6% of the Vaterian ampulloma. The average age of patients was 60 years, without predominance of a sex, the Symptomatology was dominated by icteric syndrome, half of patients presented a cholangitis at the admission. Drainage was performed in 81% of patients (n = 103) by plastic prosthesis and 19% (n = 24) by uncovered metallic prosthesis. The overall success rate was estimated at 92%. The average survival was 16 months with 54% of survival after one year. Endoscopic biliary drainage takes a large place among the various therapeutic weapons in malignant biliary obstruction. It improves the quality of life of patients.

2. Introduction

Malignant biliary obstruction is a frequent pathology, requiring an urgent decision and prompt management. The main etiologies involved are intra- and extrahepatic cholangiocarcinomas including gallblad-

der cholangiocarcinomas, ampulloma, pancreatic head cancers, and metastatic lymphadenopathy [1].

The poor prognosis is due in part to the late diagnosis at an unresectable stage of these tumors [2, 3]. Most are therefore oriented towards palliative care; only 10 to 20% of cases will be candidates for curative resection [4-6].

The role of endoscopy can be crucial in diagnosis, therapeutic and palliative management, depending on the type and stage of the malignancy [7]. For this, several endoscopic techniques have been developed with promising results, such as cholangioscopy, interventional echoendoscopy, or confocal endomicroscopy (CME) [3].

3. Materials and Methods

This is a retrospective study including 127 patients with malignant stenosis of the bile ducts treated in the department of endoscopic explorations at the hospital HASSAN II in Fez, between January 2016 and April 2018. The diagnosis of malignant stenosis was based on endoscopic and / or histological results. We analyzed the nature of the tumor obstacle, the biological data, the type of prosthesis, the technical results and survival data.

4. Results

In our series, 127 patients referred for management of a malignant strictures of the bile ducts, underwent endoscopic biliary catheterization (ERCP) (Table 1) resume the main characteristics of our population.

Table 1: Characteristics of the study population

Age		60 years (27-87)
Sex ratio m / f		1
Average consultation time		2 months
Circumstances of discovery	Jaundice	100%
	Cholangitis	50%
	Pruritus	14%
	Digestive stenosis	0.70%
	Gastrointestinal bleeding	0.70%
Biological data	Bilirubin mean	220mg/l (48 – 601mg/l),
	thrombocytopenia	14.90%
	Renal failure	18.90%
Nature of the stricture	Head of the pancreas	40% (n=51)
	cholangiocarcinoma	38.5% (n=49)
	Ampulloma	13% (n=16)
	Gall bladder	10% (n=13)
	Digestive stenosis	5% (n=6)
	Metastasis	4% (n=5)
	Proximal	56%
Site of biliary stricture	Middle tier	23%
	Distal	20%
	Local	23%(n=30)
Stage of the disease	Locoregional	50%(n=64)
	Métastatic	42%(n=33)
treatment	Surgery	5%
	Palliative chemotherapy	39%
	Abstention	56%

The indication for biliary drainage, validated in multidisciplinary team meeting was mainly for palliative purposes in 93.7% of patients (n = 119) against 6.3% only for bridge to surgery. The tumor obstacle was in 40.15% of cases a tumor of the head of the pancreas, in 38.5% an intra or extra hepatic cholangiocarcinoma including 10.23% of gall bladder cancer, 12.6% of ampullomas, 4.7% of duodenal tumors, one case of gastric tumor invading the bile ducts and 3.9% of metastases.

The mean age of our patients was 60.1 years (27-87 years) with a sex ratio M / F of 1.03. Jaundice was present in all patients, half of them presented a cholangitis on admission, 14.17% had invalid pruritus, a single case admitted for gastrointestinal bleeding and another case for digestive obstruction. On clinical examination, we noted the pres-

ence of scratching lesions in 39% of patients, the Courvoisier terrier sign was positive in 8.6% of cases, an abdominal mass was found in 6.3% and hepatomegaly in 5 cases.

The average level of total bilirubin was 220 mg / l (48 - 601 mg / l), thrombocytopenia was noted in 15%, and renal failure in 19% of patients. All our patients underwent an ultrasound and an abdominal CT scan, Bili-MRI was performed in 34.6% of patients and endoscopic ultrasound in 11.8%. The morphological assessment located the stricture in the distal biliary tract in 56.2% of cases, in the mid main bile duct in 22.8% and proximal in 20% (Figures 1, 2).

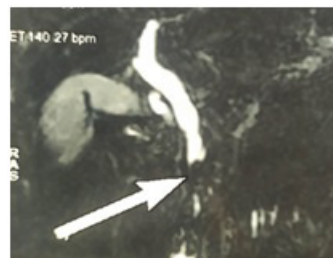


Figure 1: Frontal section of a biliary MRI showing irregular stenosis of the lower bile duct

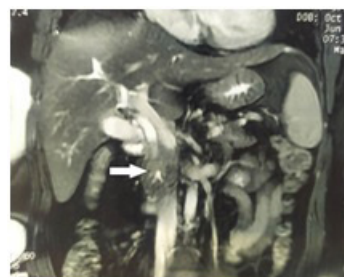
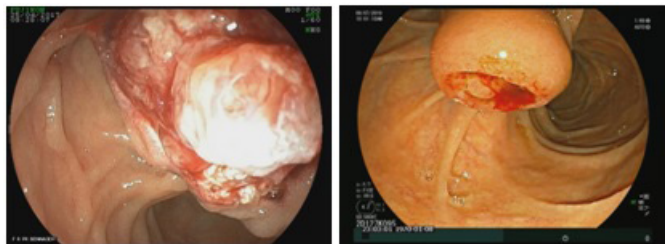


Figure 2: Frontal section of a Bili-MRI, showing a tumor process of the lower bile duct

The main bile duct access was performed by sphincterotomy in 78.7% of cases (n = 100) and by infundibulotomy in 21% of cases (n = 27). Cholangiography revealed a single stricture in 97% of these patients and multiple stenosis in 3%. The mean length of the stenosis was 20.45 mm. Drainage was performed in 81% of patients (n = 103) by plastic prosthesis and 19% (n = 24) by uncovered metal prosthesis. The overall success rate was estimated at 92% (Figure 4-7).



Figure 3: Transverse section of an abdominal MRI, showing dilation of the bile ducts upstream of a hilar cholangiocarcinoma



Figures 4: endoscopic images of an ampullary tumor process



Figure 5: Retrograde cholangiography showing dilation of the main bile duct and intrahepatic bile ducts upstream of a distal biliary stenosis



Figure 6: Placement of a metal prosthesis ensuring good biliary drainage by ERCP



Figure 7: Placement of a plastic biliary prosthesis by ERCP

In the event of failure, the patients benefited from trans hepatic drainage, the main cause of failure was the non-crossing of the stenosis by a guide wire in 40% of the cases, the presence of a digestive stenosis in 30 % of cases.

Complications were dominated by controlled bleeding in a single case (Table 2). 39.3% of our patients received chemotherapy, 4.7% curative surgery.

The use of a second drainage was performed in 18% of patients (n = 23) with a mean interval of 3.5 months. The mean survival was 16 months with a 1-year survival of 54% (Figure 8).

Table 2: results of endoscopic biliary drainage

Sphincterotomy	78.7% (n=100)
Infundibulotomy	24.4% (n=31)
mean length of the stenosis	20.4 mm
Plastic prosthesis	81% (n=103)
uncovered metal prosthesis	19% (n=24)
failure in extrahepatic cholangiocarcinoma	5% (n=7)
failure in intrahepatic cholangiocarcinoma	2% (n=3)
Transhepatic drainage	8%

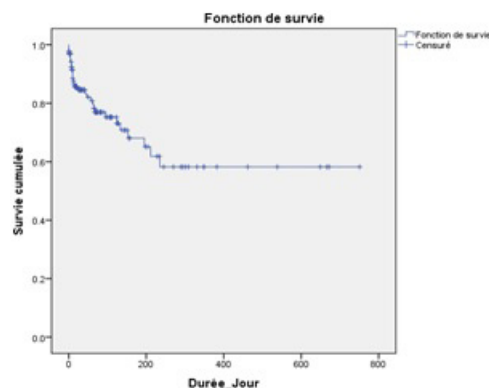


Figure 8: The survival time of our patients in days

5. Discussion

Malignant biliary stenosis is the result of intrinsic or extrinsic biliary tumor development, primary or secondary to metastases [8], which the two main etiologies are pancreatic adenocarcinoma and distal cholangiocarcinoma [3, 9, 10].

The annual incidence of biliary cancer in France is 1.4 and 0.7 cases per 100,000 inhabitants in men and women respectively, they represent 2-3% of digestive cancers, increasing in Western countries [11]. In Morocco, according to the cancer registry for the Casablanca region between 2005 and 2007, the incidence is 46 new cases per year [12], with a marked increase in recent years [13].

There is a male predominance (sex ratio: 2), with the exception of gallbladder cancer whose female / male sex ratio is close to 1.9 with a higher frequency in the sixth and seventh decades [11, 13-14].

The clinical symptomatology of biliary tract cancer is often vague and not very specific and the suggestive signs are later, of which jaundice is the main symptom [13]. A malignant pathology is suspected in front of an elevated total bilirubin [3, 15].

Significant progress has been made in the lesional diagnosis of tumor stenosis of the bile ducts based on non-invasive imaging methods; ultrasound, computed tomography, and bili-MRI or invasive such as endoscopic retrograde cholangiography, endoscopic ultrasound to reliably determine the level of the obstacle [16, 17]. Histological evidence was often difficult to obtain, using brush cytology or fine needle aspiration, but a definitive diagnosis is only made in approximately 50% of cases [6, 18]. These invasive examinations should only be performed for therapeutic purposes.

The most widely used tumor markers are carbohydrate (CA 19–9) and carcinoembryonic (ACE) antigens. A CA 19-9 > 37 U / mL has a high sensitivity of 74%, but very low specificity. [19, 20] Although they are useful as prognostic markers, their diagnostic value remains limited [3, 21].

The indications retained for biliary drainage for tumor biliary stenosis are; cholangitis [22] disabling pruritus, a high bilirubin level > 250 $\mu\text{mol} / \text{L}$ before curative surgery [23, 24], or a palliative chemotherapy and in patients who are not candidates for surgery since mortality drops from 10% to 50% in the absence of treatment [6, 25, 26]. The benefit of preoperative biliary drainage remains controversial [6, 27-29]. Current guidelines published by ESGE recommend preoperative biliary drainage [3, 30].

The indications for prosthesis in malignant stenosis of the extra-hepatic bile ducts are of 2 types: preoperative temporary drainage most often using removable plastic prostheses and final palliative drainage with metal prostheses ensuring lasting patency (9 months against 4 months) [6, 16, 31]. At present, there is no consensus on which prosthesis is covered or not, each of which has its advantages and disadvantages. The rate of migration is higher in covered prostheses, whereas tumor proliferation is greater in uncovered prostheses [3, 32, 33].

The major disadvantage of endoscopic drainage is the risk of infection. Other possible complications include pancreatitis, perforation, post-sphincterotomy hemorrhage [6, 34].

In 3 to 12% of cases, selective catheterization of the major papilla is unsuccessful. Surgical treatment or percutaneous biliary drainage should then be offered.

Palliative surgery for bile duct drainage has associated morbidity and mortality rates of around 35 to 50% and 10 to 15%, respectively. New biliary drainage techniques with good specificity and sensitivity (98%) [3, 35] can now be proposed as an alternative to percutaneous drainage and palliative surgery [36]; cholangioscopy by SPYGLASS, Endoscopic UltraSound (EUS) or Confocal end microscopy (CLE). These techniques are expensive, difficult to access and not used routinely [3], they are not possible in certain conditions, like massive ascites, aberrant ductal anatomy, multifocal biliary strictures or metastases, or in the event of a disturbance in the balance sheet hemostasis [37].

Interventional biliary endoscopic ultrasound requires a radial ultrasound probe inserted through the duodenoscopy on a guidewire during ERCP. There are several modalities, either the appointment technique (combined with an ERCP), or direct trans gastric drainage of the left intrahepatic ducts (HG hepatic-gastrostomy) or by the trans-duodenal approach of the common hepatic duct (choledocho-duodenostomy CD) [36, 37, 38, 39]. The biliary endoscopic ultrasound has also allowed tumor destruction by chemo ablation and radiofrequency techniques.

The location of the biliary obstruction (distal or proximal), endoscopic access to the major duodenal papilla will determine the procedure. The obstruction of distal bile ducts can be treated with the choledochoduodenostomy technique. Hepatic gastrostomy and the antegrade stent are primarily used for hilar cholangiocarcinoma [37].

Trans parietal treatment still has its place in advanced hilar cholangiocarcinoma classified as bismuth 3, 4 that is not accessible to ERCP, in the absence of other endoscopic therapeutic modalities [16]. The treatment endoscopic has been shown to be significantly superior to the percutaneous technique for drainage (81% vs. 61%) and 30-day survival (85% vs. 67%) [6, 16].

6. Conclusion

In our series, among 509 cases of catheterization performed in our department, 18.6% were indicated for malignant biliary stenosis. The main revealing symptom was isolated jaundice followed by cholangitis. The most common etiology was cancer of the head of the pancreas with a percentage of 40%, followed by cholangiocarcinoma. Biliary drainage finds its indication mainly in the palliative treatment of these tumors (39%), with a success of 92%. Endoscopic biliary drainage remains a technique that has many advantages for relieving the patient, starting systemic treatment, and operating on patients who are candidates for surgery.

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