

# Malignant biliary strictures

## Diagnosis and management

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### ABSTRACT

**Objectives:** To identify the cause, methods of diagnosis and management of malignant biliary strictures in our institution and compare with studies from other communities.

**Methods:** From March 1998 through to August 2002, we reviewed 1000 files of patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) at the Gastroenterology unit, King Khalid University Hospital in Riyadh, Kingdom of Saudi Arabia for malignant biliary strictures (MBS). Clinical, laboratory data, method of diagnosis and management were recorded.

**Results:** Seventy-two patients (72/1000) with MBS were encountered. Forty one (57%) were males and 31 (43%) were females and the majority were Saudi nationals (82%). Jaundice and right upper quadrant pain were the most frequent symptoms in 84.7% and 52.8% of patients.

Cholangiocarcinoma was present in 31 (43%) and pancreatic adenocarcinoma in 23 (31.9%) patients. Other malignancies found included gallbladder carcinoma in 5 patients (6.9%), ampullary carcinoma in 5 (6.9%), metastatic liver carcinoma in 4 patients (5.6%), hepatocellular carcinoma in 2 (2.8%) and lymphoma in 2 (2.8%). The diagnosis was entertained mainly by ERCP (93%). Endoscopic palliation was carried out in 77.8% of patients, percutaneous transhepatic drainage in 13.9% and surgery in 6 (8.3%). The mean survival was higher for the endoscopic compared to the percutaneous transhepatic and surgery groups ( $6.9 \pm 4.13$ ,  $4.27 \pm 4.29$  and  $3.67 \pm 2.65$  months).

**Conclusion:** In non-resectable tumors, ERCP is the optimal method of diagnosis and palliation of MBS.

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Malignant biliary stricture may result from an intraluminal cholangiocarcinoma or from extraluminal tumors including pancreatic head cancer, gallbladder cancer, hepatocellular carcinoma, metastatic carcinoma and lymphoma. Pancreatic carcinoma and cholangiocarcinoma are uncommon in the Kingdom of Saudi Arabia. They represented 1.5% and 1.2% of all gastrointestinal tumors.<sup>1</sup> At the time of diagnosis, majority (80-90%) of malignant strictures are non-curable.<sup>2</sup> Common clinical presentations include obstructive jaundice, anorexia, weight loss and

pruritus. Raised alkaline phosphatase, bilirubin, serum transaminases and prothrombin time are the usual laboratory abnormalities.<sup>3,4</sup> Various imaging modalities including ultrasonography (US), computerized tomography (CT), endoscopic ultrasonography (EUS), magnetic resonance cholangio-pancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are helpful in the diagnosis of malignant biliary strictures. However, ERCP is considered as the gold standard in the diagnosis of biliary strictures and also has the

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advantage as a therapeutic modality.<sup>5-8</sup> The aim of this study was to find out causes of malignant biliary stricture in our institution, methods of diagnosis and management.

**Methods.** We retrospectively reviewed 1000 ERCP files of patients who were seen at the Gastroenterology unit, King Khalid University Hospital in Riyadh, KSA, from March 1998 through to August 2002. From these 1000 ERCP files, we analyzed each file for the presence of biliary strictures. Cases indicating malignant biliary stricture (MBS) were reviewed to identify the cause, site of stricture, demographic characteristics of patients, clinical presentations, laboratory profiles, available imaging results and the management protocol instituted. Ultrasound was carried out prior to ERCP. Endoscopic retrograde cholangiopancreatography was performed by 3 experienced consultant gastroenterologists. All patients with MBS received cefuroxime 1g

intravenously 30 minutes prior to ERCP or percutaneous transhepatic cholangiography (PTC). Patients were put under sedation with diazepam or midazolam and pethidine. Large channel (4.2 mm) video endoscope (Olympus or Pentax sideviewing duodenoscope was used, cholangiography performed and site of biliary stricture allocated. Biopsy or cytology material was obtained (not in all patients) with subsequent dilation with Sohendra dilators and a large caliber (10-12F) straight or piggy tail stent was inserted.

Data collected were systematically entered into the computer using Microsoft Excel. Statistical measures and correlations were carried out through the database in both Excel and Statpac gold analysis programs.

**Results.** The reviewed 1000 ERCP files constituted 72 MBS. There were 41 (57%) males with a mean age of  $64.9 \pm 11.7$  years and 31 (43%) were females with a mean age of  $59.2 \pm 11.9$  years. The age ranged from 30-100 years and the majority of these

**Table 1 -** Demographic characteristics of malignant biliary strictures.

	Males	Females	Both Sexes
n of cases	41 (56.9)	31 (43.1)	72
Mean Age (SD)	64.9 $\pm$ 11.7 years	59.2 $\pm$ 11.9 years	62.4 $\pm$ 11.7 years
<b>Nationalities</b>			
Saudi	34	25	59 (81.9)
Non-Saudi	7	6	13 (18.1)
<b>Symptomatology</b>			
Jaundice	36	25	61 (84.7)
RUQ pain	18	20	38 (52.8)
Weight loss	6	5	11 (15.3)
Fever	2	5	7 (9.7)
Anorexia	3	4	7 (9.7)
Vomiting	0	1	1 (1.3)
RUQ - right upper quadrant			

**Table 2 -** Site of malignant biliary stricture.

Site (Diagnosis)	Distal	Middle	Proximal	Total	(%)
Cholangiocarcinoma	11	9	11	31	43
Pancreatic head carcinoma	17	6	-	23	31.9
Ampullary carcinoma	5	-	-	5	6.9
Gallbladder carcinoma	-	2	3	5	6.9
Metastatic carcinoma	-	-	4	4	5.6
Hepatocellular carcinoma	-	-	2	2	2.8
Lymphoma	2	-	-	2	2.8
<b>Total (%)</b>	<b>35 (48.6)</b>	<b>17 (23.6)</b>	<b>20 (27.7)</b>	<b>72</b>	<b>100</b>

**Table 3** - Management procedure and outcome.

Management procedure	Males	Females	Total (%)	Mean survival months
Endoscopic	32	24	56 (77.8)	6.9 ± 4.13*
Percutaneous	6	4	10 (13.9)	4.27 ± 4.29
Surgical	3	3	6 (8.3)	3.67 ± 2.65
<b>Total</b>	<b>41</b>	<b>31</b>	<b>72 (100)</b>	<b>5.7 ± 4.08</b>
* survival analysis of 48 patients (8 patients failed to follow up)				

patients were Saudi nationals (82%). Jaundice was evident in 61 patients (84.7%), right upper quadrant pain in 38 patients (52.8%) and weight loss in 11 patients (15.3%). Seven patients (9.7%) presented with fever and anorexia each, while vomiting was encountered in only one patient. (Table 1) Cholangiocarcinoma was the most common underlying malignant cause of stricture in 31 patients (43%). Other malignancies included pancreatic adenocarcinoma in 23 patients (31.9%), gallbladder and ampullary carcinoma in 5 patients each (6.9%), metastatic carcinoma in 4 patients (5.6%), hepatocellular carcinoma in 2 patients (2.8%) and lymphoma in two patients (2.8%). The distal bile duct was the most frequently involved segment in 35 patients (48.6%). Pancreatic head carcinoma was responsible for 48.6% and 35.3% of distal and middle MBS, while cholangiocarcinoma accounted for 11 (31.4%) of the distal, 9 (52.9%) of the middle and 11 (55%) of the proximal MBS. Ampullary carcinoma in five patients accounted for 14.3% of distal MBS. Strictures of the proximal segment of the bile duct were mainly due to cholangiocarcinoma (55%). (Table 2) The mean total bilirubin level was  $184.61 \pm 120.8$  mmol/L and the mean direct bilirubin level was  $138.1 \pm 98.5$  mmol/L. Aspartate and alanine transaminases (AST and ALT) were elevated with mean values of  $107.8 \pm 45.7$  IU/L and  $66.94 \pm 35.6$  IU/L. The mean alkaline phosphatase (APh) and gamma glutamyl transferase (GGT) levels were also elevated at  $145.5 \pm 57.5$  mmol/L and  $436.5 \pm 325.1$  mmol/L. Ultrasound was performed prior to ERCP in 68 patients (94%) and 49 (72%) revealed abnormal findings suggestive of a malignant lesion. It has shown stricture in 32 patients (47%) and proximal dilatation in 43 (63%) patients. Endoscopic retrograde cholangiopancreatography was successful in establishing or confirming the diagnosis in majority of patients (93%), the other 5 patients (7%) the diagnosis based on other imaging techniques. While endoscopic management in the form of EPT with dilatation and stent insertion was successful in 56 patients (78%), percutaneous transhepatic drainage

(PTD) was performed in 10 patients (14%). Six patients (8.3%), 3 with cholangiocarcinoma, one each for pancreatic adenocarcinoma, gallbladder adenocarcinoma and metastatic carcinoma underwent surgery, which was palliative in all patients. Removal of clogged biliary stents and replacement of a new stent with good drainage was carried out in 26 patients (36%) in a mean period of  $2.31 \pm 1.86$  months. Seven of these restented patients (7/26) underwent replacement of clogged stents for the second time over a mean period of  $2.87 \pm 1.93$  months. Six (8.3%) ERCP patients needed to undergo surgery mostly due to severe strictures and dilatation by balloon was not possible. From the initiation of ERCP to analysis of results, the mean survival period for 64 (89%) patients was  $5.7 \pm 4.08$  months. The remaining 8 patients were excluded from survival analysis due to failure in follow up. Endoscopically managed patients had a mean survival time of  $6.9 \pm 4.13$  months. Percutaneously managed patients had a mean survival period of  $4.27 \pm 4.29$  months. While surgically managed patients had a shorter survival time of  $3.67 \pm 2.65$  (Table 3).

**Discussion.** In our center, a 7.2 prevalence rate of MBS was significant. There is a recent trend of increasing prevalence of different malignancies in the KSA. In KSA, the prevalence has been 1.2% and 1.5% of gastrointestinal tumors, for cholangiocarcinoma and pancreatic head carcinoma.<sup>1</sup> The mean age of our patients was higher than reported from India<sup>9</sup> but lower than in Canada.<sup>4</sup> Majority of our patients presented with jaundice and right upper quadrant pain. These symptoms although not specific, however, they should raise the suspicion index especially in the presence of raised bilirubin and alkaline phosphatase serum levels. We found a 10-fold increase in the mean total serum bilirubin level, of which 75% was direct bilirubin. A serum bilirubin level of  $\geq 75$  umol/L has been highly predictive of malignancy in patients with biliary strictures. In agreement with Bain et al,<sup>4</sup> we found also elevation of

alanine as well as aspartate transaminases, gamma glutamyl transpeptidase and alkaline phosphatase mean serum levels. Furthermore, prothrombin time prolongation has also been considered as a usual finding in patients with malignant biliary stricture.<sup>10</sup> Ultrasonography and CT of the biliary tree have been useful in the diagnosis of biliary strictures, nevertheless, their accuracy and reliability is far less than ERCP.<sup>11</sup> More recently multislice CT (MS-CT) has been more accurate and reliable in detection of tiny biliary tumors.<sup>12</sup> It allows a multiphasic imaging with a viable alternative cholangiography to MRCP.<sup>13</sup> It has become as the modality of choice for biliary and pancreatic tumor imaging.<sup>14</sup> Although we routinely perform US in all patients prior to ERCP, it didn't detect significant abnormalities in all patients with MBS. Therefore, we regarded ERCP as the gold standard in the diagnosis of biliary strictures. This has been also supported by Hatano et al,<sup>15</sup> who found ERCP more suitable than MRCP in evaluation of biliary strictures. In addition, ERCP can effectively localize, diagnose and relieve symptoms of biliary obstructive lesions. At the time the diagnosis of MBS has been established, it is often late for curable resection.<sup>16</sup> Histopathological and cytological confirmation through biopsy is warranted to confirm diagnosis by ERCP for further management protocols. ERCP, diagnostic or therapeutic has been considered as a useful initial procedure of MBS evaluation. In the majority of cases appropriate palliation may be achieved by stenting.<sup>5</sup> In this series, the diagnosis was achieved by ERCP in 93% of patients and successful palliation in 78%. Endoscopic stenting has been considered as the standard method for treating MBS.<sup>2,3,5</sup> The mean survival time of our patients varied according to the modality of treatment used. Patients who underwent endoscopic and percutaneous methods had longer mean survival time compared to those who underwent surgery.

In conclusion, ERCP is the standard method of diagnosis and palliation of surgically non-resectable MBS. It is associated with a longer survival than the percutaneous and surgical approaches.

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