



## Endoscopic Stenting of Malignant Biliary Obstruction and Its Impact on Quality of Life

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### Abstract

**Background:** Endoscopic stent insertion is considered one of methods for palliation of malignant bile duct obstruction (MBDO). The aims of this study were to determine clinical characteristics that have the greatest adverse impact on quality of life in patients with malignant biliary obstruction, and to quantify changes in the quality of life of patients with malignant biliary obstruction after successful decompression with a plastic stent.

**Patients and Methods:** Patients undergoing endoscopic retrograde cholangiopancreatography for MBDO completed the Functional Assessment of Cancer Therapy-General questionnaire at baseline, at 1 month after stent insertion and was used to quantify quality of life.

### Introduction

Most malignant tumors causing bile duct obstruction, such as pancreatic adenocarcinoma, gallbladder carcinoma, or cholangiocarcinoma, have an extremely poor prognosis.<sup>1,2</sup> At the time of diagnosis the majority of these tumors will be unresectable, with a median survival of 4 to 6 months.<sup>3</sup> Biliary obstruction develops in 70-90% of cases, causing severe pruritis and shortens survival by leading to nutritional disturbances, progressive liver failure, cholangitis and coagulopathy. Thus in most patients the primary goal remains to relieve biliary obstruction by surgical, radiological and endoscopic means, and maintaining quality of life in the few months between diagnosis and death. Further technical improvements are required to solve the most important clinical problem of late stent occlusion. New developments such as expandable metallic stents and refinements in existing equipments and techniques have already

resulted in measurable gains and hold great promise for future expansion of their use in malignant gastric outlet obstruction secondary to tumor infiltration of the duodenum. Corresponding advances are being made in the field of percutaneous transhepatic intervention and Hepatobiliary surgery such that further prospective randomized trials are necessary to define optimal therapy<sup>[4][5][6][7]</sup>. Endoscopic stent insertion safely and effectively re-establishes bile flow, alleviates jaundice and pruritis and may improve quality of life and thus favoured for palliation of malignant biliary obstruction. Endoscopic insertion of a plastic or metal stent is technically successful in 90-95% of patients with malignant extrahepatic biliary obstruction. Plastic stents are used because of their efficacy and low cost. These stents are exchanged easily as long as there is no duodenal obstruction. A few available studies have demonstrated improved QOL in stented patients.<sup>8-11</sup>

This prospective analysis was undertaken to study possible relationships between presenting symptoms and baseline QOL. Also examined were the possible predictive abilities of these baseline variables on the subsequent outcome of QOL after successful biliary decompression with a plastic stent

### Materials and Methods

Patients with malignant biliary obstruction without liver metastasis and considered non-surgical candidate admitted to the department of Gastroenterology, Madras medical college for endoscopic palliation were recruited. This was a prospective study from February 2019 to April 2020. Diagnosis was initially made on the basis of typical history, clinical examination, abdominal USG and CT, which was substantiated by MRCP, if deemed necessary, and ERCP at the time of stenting. All the patients were offered stenting, patients who refused stenting were not included. The diagnosis of malignancy was established by:

- 1) Cytology/histology of the tumor at ERCP or operative biopsy.
- 2) FNAC of accessible sites like lymph nodes, ascites etc.
- 3) Imaging (USG, CT, MRI/MRCP or ERCP later) suggestive of malignancy.

### Inclusion Criteria

- 1) Clinical data and history suggestive of malignant bile duct obstruction, found to be unresectable after investigations.
- 2) Bilirubin level >9mg/dL.
- 3) Investigations: USG and CT or MRI performed before inclusion.

### Exclusion Criteria

- 1) Informed consent not obtained.
- 2) Unable or unwilling to follow-up.
- 3) Proper investigations not performed.
- 4) Candidate for surgical resection or suspected non-malignant obstruction.
- 5) Bilroth type II gastric resection, pyloric or duodenal obstructions.
- 6) Uncorrectable coagulopathy excluding sphincterotomy.
- 7) Previous biliary stenting.

- 8) Surgery within 4 weeks of induction into study.

### Endoscopic Intervention

All ERCPs were performed with a therapeutic duodenoscope. The bile duct was cannulated and stricture location and length were determined. A guide wire was advanced proximal to the stricture, a biliary sphincterotomy was performed at the discretion of the endoscopist, and the patient was then randomized to placement of a 10 or an 11.5-Fr biliary plastic stent. Technical success was defined as the passage of the stent across the stricture and the flow of contrast and/or bile through the stent. Clinical success was defined as a drop in bilirubin level to <75% of baseline within 2 weeks after stent insertion. Routine stent exchanges were not scheduled; however, if the patient developed signs and symptoms suggestive of stent occlusion (eg, cholangitis, jaundice) the stent was changed on an urgent basis.

### QOL outcome

The primary outcome was a documented change in QOL assessment over the first month after successful biliary drainage compared with that before decompression. Administration of the SF-36 Quality of Life scale at baseline and 1 month after stent insertion was used to assess this outcome. The SF-36 Health Survey (Medical Outcomes Trust, Inc., Boston, Mass.) is a multi-item scale measuring 8 health domains: physical functioning (PF), role limitations because of physical health problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations because of emotional problems (RE), and overall mental health (MH). This QOL measurement tool was selected as it has been extensively validated in populations with other cancers including breast, prostate, and tumors of the head and neck. Standardized scores for each of the 8 health domains are interpreted in relation to means and standard deviations in the general adult population of the United States.<sup>12</sup> Variables evaluated in relation to the observed QOL changes included

clinical characteristics such as the presence or absence of weight loss, jaundice, pruritus, abdominal pain, and anorexia (quantified by the percentage of skipped meals); body mass index (BMI) (in kg/m<sup>2</sup>); duration of symptoms; the site of biliary obstruction, and length of polyethylene (plastic) stent inserted. Collected data also included the following standard biochemical parameters: total bilirubin (TB), alkaline phosphatase (AP),  $\gamma$ -glutamyltranspeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin, white blood cell, and platelet counts. These data were obtained at initial presentation and at visits 7 days and 1 month after biliary decompression.

### Statistical analysis

Descriptive analysis was conducted by comparing the means and standard deviation of baseline values of QOL in each domain with its corresponding value 1 month after stent insertion. As well, the Kruskal-Wallis one-way analysis of variance (ANOVA) was performed to compare the individual domains of the SF-36 to the grouped clinical and biochemical variables of interest (e.g., by gender, location of obstruction). The chi-square test was used to compare proportions among the clinical characteristics. The Pearson correlation was used to quantify the improvement in the individual domains of the SF-36 with the improvement in total bilirubin in which baseline bilirubin was dichotomized at its median value to divide the cohort into those with a "high baseline bilirubin" versus "low baseline bilirubin." With this clinical cut-off, analysis was conducted to ascertain the association between improvement in baseline bilirubin and its effect on each domain of the SF-36 1 month after stent insertion. This analysis was conducted for both those patients who achieved successful biliary drainage (as defined above) and in the entire cohort. Once significant variables were identified by univariate analysis, clinically significant variables were considered in the creation of predictive models. Multivariate analysis was then performed to identify models predicting improved quality of life.

## Results

### Study Population

Sixty four patients (25 men, 39 women) were prospectively enrolled in the study. Mean age at enrollment was 68.4 years (SD 9.4 years). The mean weight of the cohort was 58.4 kg (SD 11.8 kg) and the mean BMI was 22.5 kg/m<sup>2</sup> (SD 4.7 kg/m<sup>2</sup>).

At baseline, 54% of patients complained of pruritus and 98% were jaundiced. Anorexia was reported by 32% and 82% had an ASA score of 3 or an ECOG score of 4. All had hyperbilirubinemia (mean bilirubin 16 mg/dL [8.1 mg/dL]). The mean duration of symptoms was 26 days. Subjective weight loss was noted by 80% of patients (Table 1). The baseline scores for each of the 8 domains of the SF-36 scores closer to 100 suggest few problems in a domain, or the absence of a negative state (limitation, disability, or pain). All baseline domain scores for the study population were significantly lower (table 2)

Among the 64 malignancies diagnosed there were 26 pancreatic cancers, 22 distal cholangio carcinoma, 5 tumors of the GB, 5 extra hepatic bile duct obstruction because of malignant nodal compression at or distal to the hepatic hilum, 7 hilar cholangio carcinoma. In no case was there overt liver metastases at enrollment. Endoscopic sphincterotomy was performed in 22% of patients to facilitate stent placement. There were no complications after the procedure related to biliary stent placement among the 64 patients.

By using ANOVA, baseline characteristics were identified that were strongly associated with poor QOL (as defined by significantly lower scores compared with 1 month post stenting). All 8 domains of the SF-36 were adversely associated with the presence of weight loss ( $p < 0.05$ ) and abdominal pain ( $p < 0.05$ ). In comparison, an elevated bilirubin level correlated with poor scores in the domains of physical role ( $p = 0.011$ ), vitality ( $p = 0.042$ ), and social function ( $p = 0.005$ ). No other clinical or biochemical characteristics were statistically significant.

Logistic regression modeling techniques were used to identify which of the 3 characteristics were

independently predictive of a poor QOL before stent insertion. The presence of weight loss at baseline resulted in a statistically significant deterioration of QOL scores in the domains of general health ( $p = 0.001$ ) and physical role ( $p = 0.001$ ). Multivariate analysis using the BIC criterion<sup>13</sup> revealed that the variable of weight loss was featured in 100% of the best models of general health and physical role, and in 79.8% of the best models of emotional role.

The presence of baseline hyperbilirubinemia also resulted in a significant deterioration in QOL scores in the domains of social function ( $p = 0.005$ ) and physical role ( $p = 0.006$ ) as shown by regression modeling. By using the BIC, multivariate analysis revealed that hyperbilirubinemia dominated in 96.2% of the best models of social function and in 91.3% of the best models of physical role.

The presence of baseline abdominal pain did not show a significant association with baseline QOL when subjected to multivariate analysis with either linear regression or BIC methodology.

**One month after stent insertion**

Complete data were available for 52 of the 64 patients at the 1-month assessment. Of the 12 patients for whom no 1-month data are available: 6 died before the 1-month visit, 6 were withdrawn because of stent blockage. Of the patients who failed to complete the 1-month evaluation, 40% were men. Others who completed 1-month assessment, 62% were men (mean age 72 years)

Among the remaining patients, 2 subgroups were identified that benefited best in terms of QOL improvements after biliary stent insertion (Table 3). The first group, patients with a “low baseline” bilirubin (<13 mg/dL), had a mean improvement of 20 points (26.4 points) in Social Function scores after stent insertion. By comparison, patients with a “high baseline bilirubin” (>13 mg/dL) had a mean deterioration of 5 points in the Social Function scores after stent placement ( $p = 0.03$ ). The second subgroup, the 78% of patients in whom drainage was successful, had improvement in QOL in the domains of Social Function ( $p = 0.03$ ) and Mental

Health ( $p = 0.03$ ). For the remaining 6 domains, there was no significant associated improvement.

**Table 1** Baseline characteristics of study population

Characteristic	Total	n=64
Mean age (SD)		68.4years
Female gender (%)		60%
Mean weight (kg) (SD)		58.4kg
Mean BMI (kg/m <sup>2</sup> ) (SD)		22.5kg/m <sup>2</sup>
Mean duration of symptoms (d) (SD)		26 days
Pruritus (%)		54%
Jaundice (%)		98%
Weight loss (%)		80%
Abdominal pain (%)		24%

**Table 2** Comparison of QOL scores before and after biliary decompression

Domain	Baseline mean(SD)	1 month after stent mean(SD)
Body pain	54.5(30.2)	64.4(24.8)
General health	55.2(24.6)	48.5(22.3)
Mental health	59.5(23.2)	68.4(21.6)
Physical function	48.2(29.7)	75.6(24.7)
Role physical	28.4(32.2)	24.3(22.2)
Role emotional	40.6(42.4)	61.7(29.5)
Social function	48.6(37.6)	58.6(31.1)
Vitality	44.3(21.5)	48.2(26.8)

**Table 3** Multivariate analysis of risk factors on baseline QOL

Variable	QOL Domain	Relative risk [95% CI]	p Value
Weight loss No* Yes	General health	1.0[0.0] 27.4(11.4, 74.0)	0.001
Weight loss No* Yes	Physical role	1.0[0.0] 39.3(11.2, 66.4)	0.001
Weight loss No* Yes	Emotional role	1.0[0.0] 37.4(16.1, 65.3)	0.018
Hyperbilirubinemia No* Yes	Physical role	1.0[0.0] 12.6(5.4, 37.2)	0.006
Hyperbilirubinemia No* Yes	Social function	1.0[0.0] 10.3(6.5, 33.4)	0.005

\*Reference category



## Discussion

Hyperbilirubinemia is one of the most important clinical consequences of MBDO. It is associated with a number of physiological ramifications<sup>14</sup> including renal impairment,<sup>15</sup> immune dysfunction,<sup>16</sup> jaundice, pruritus, anorexia, and weight loss,<sup>17</sup> all of which may adversely impact QOL. Endoscopic biliary stenting has become a standard treatment for MBDO, producing fewer complications than surgical bypass.<sup>18</sup> Despite the improved patency of metal stents, plastic stents are still widely used as an initial treatment, being especially cost effective in patients with an estimated survival of <4 months, and in countries with low-cost ERCP.<sup>19</sup> The quantification of the benefits in QOL achievable by biliary stent placement is important, as the main focus of this therapy is maximizing the patients' sense of well-being, rather than prolongation of the patients' life.

Previous studies have suggested improvement in different aspects of QOL after endoscopic stenting. Ballinger et al<sup>13</sup> used a 3-part questionnaire including the Rotterdam Symptom Checklist and Hospital Anxiety and Depression Scale, in 19 patients with pancreatic cancer. They showed that biliary stenting improved symptoms such as anorexia, indigestion, and weight loss and improved QOL. Luman et al<sup>15</sup> administered the European Organization for Research and Treatment of Cancer QOL questionnaire to 38 patients with MBDO before and 1 month after endoscopic tenting. In addition to the expected improvement in pruritus and jaundice, the patients also reported significant improvement of anorexia, diarrhea, and sleep pattern. Emotional, cognitive, and global health scores were significantly improved as well. The impact of endoscopic stenting on the QOL in MBDO by Abraham et al<sup>22</sup> used the 36-Item Short-Form Health Survey (SF-36) at baseline and 1 month after stent insertion and it demonstrated significant improvements in social function and mental health as in our study.

With use of the SF-36, the presence of weight loss and hyperbilirubinemia at baseline were identified as having the greatest negative impact on QOL. In

the present study, all patients with radiographic evidence of metastatic disease to the liver were excluded because jaundice in these patients would not be expected to respond to biliary decompression<sup>23</sup>. The present study quantified the impact of successful decompression on the different physical, psychologic, and social components of QOL. No threshold was identified with regard to an effect on the mental health domain.

As in other studies of patients with cancer, there may be a psychologic benefit associated with participation in a clinical trial that may impact subsequent mental health assessment (SF) after decompression.<sup>27</sup> Any psychologic benefit, however, should not invalidate the observation in this trial concerning the differential outcome among patients with high- versus low-baseline bilirubin.

In conclusion, weight loss and hyperbilirubinemia are baseline clinical characteristics that negatively impact baseline QOL. The present study also quantifies expected improvements in QOL domains (social function and mental health) after biliary decompression. This information may improve patient counseling and selection of patients for possible palliative therapies. These findings may result in a more adapted selection of patients for endoscopic biliary decompression

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