Original Article

Comparison of Quality of Life in Patients with Hilar Cholangiocarcinoma Pre- and Post-Treatment

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ABSTRACT

Background: Hilar cholangiocarcinoma is the most common cause of malignant biliary obstruction in Northeastern Thailand.

Aim: To assess the quality of life (QOL) in patients with hilar cholangiocarcinoma pre- and post-treatment using the EQ-5D Thai version.

Patients and methods: A total of 261 patients with hilar cholangiocarcinoma prospectively underwent any one of four treatment modalities (surgery, endoscopic retrograde cholangiopancreatography (ERCP) with biliary stent placement, percutaneous transbiliary drainage (PTBD), and palliative care). The EQ-5D Thai version was used for evaluation before and 2-4 weeks after treatment. Pre-treatment and post-treatment utility scores were analyzed.

Results: The EQ-5D scores in the ERCP with stent group significantly improved after treatment (p=0.049), especially in the subgroup with adequate biliary drainage (p=0.02). In the surgery and the PTBD groups, the EQ-5D scores also improved but without statistical significance.

Conclusion: ERCP with adequate biliary drainage improved QOL in patients with hilar cholangiocarcinoma.

Key words : Hilar cholangiocarcinoma, quality of life, EQ-5D Thai version

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INTRODUCTION

The prevalence of cholangiocarcinoma is highest among the Northeastern population of Thailand, with the incidence rate of 135.4 per 100,000 in males and 43.0 per 100,000 in females[1]. The observed geographical clusters of this liver cancer appear to be associated with the prevalence and the intensity of Opisthorchis viverrini infection[2]. Most cholangiocarcinomas are located in the hilar area (60-70%)[3]. Management of this biliary cancer with a relatively poor prognosis is a challenging clinical problem. Surgery continues to be the mainstay of therapy. Complete resection of the tu-

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mor with negative histologic margins offers the best possibility for long-term survival. Percutaneous transbiliary drainage (PTBD) and endoscopic retrograde cholangiopancreatography (ERCP) with stent drainage have offered additional non-surgical treatment options for patients in advanced stages of the disease as well as those with high operative risks[4]. The aims of drainage are to relieve symptoms, especially pruritus and jaundice, and to improve the quality of life (QOL).The aim of this study was to assess QOL in patients with hilar cholangiocarcinoma pre-and post-treatment.

MATERIAL AND METHODS

Patients

This study was approved by the Khon Kaen University Ethics Committee for Human Research. Patients were recruited from Srinigarind Hospital between 1 February 2013 and 1 February 2014. All patients gave an informed consent before entering the study. The diagnosis was made from a typical history, physical examination, biochemical tests, tumor markers, and evidence of biliary ductal dilatation with or without a mass at the hepatic bifurcation on computed tomography (CT) or on magnetic resonance cholangiopancreatography (MRCP). Histologic diagnosis was not made in every patient, but tissue was obtained from those patients who underwent surgery.

The stricture location was classified by Bismuth-Corlette Classification to 4 types (type I; tumor located within the common hepatic duct: type II tumor involved the confluence of the left and the right hepatic duct: type III similar to type II but with tumor invading into either the left or the right secondary hepatic ducts, and type IV tumor involved bilateral subsegmental ducts. Unresectable tumors were defined as follow: medical comorbidities resection necessary for curative surgery based on preoperative imaging, bilateral tumor extension to secondary biliary radicals, encasement or occlusion of the main portal vein, lobar atrophy with contralateral portal vein involvement, lobar atrophy with contralateral tumor extension to secondary biliary radicals, evidence of metastases to N2 level lymph nodes (peripancreatic, paraduodenal, periportal, celiac, superior mesenteric and/or posterior pancreaticoduodenal lymph nodes), presence of distant metastases, and patients refusal for treatment.

Patients were divided into 4 groups according to clinical diagnosis and treatment option (ERCP with stent, PTBD, surgery, palliative care).

Materials

The QOL was assessed by using the EQ-5D Thai version. EQ-5D is a non-disease-specific instrument for describing and scoring health-related quality of life. EQ-5D is primarily designed for self-completion by respondents and is ideally suited for use in postal surveys, in clinics and face-to-face interviews. It is cognitively simple, taking only a few minutes to complete. The EQ-5D format essentially consists of 2 pages - the EQ-5D descriptive system and the EQ visual analogue scale. The EQ-5D descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, extreme problems. EQ-5D has been validated in Thai patients (EQ-5D Thai version)[5].

The EQ-5D score was calculated by adding the scores of the five questions giving a range from 0 to 1. Scores were then transformed onto a scale of 0 (indicating worst possible status) to 100 (indicating best possible status). The EQ-5 Dalso included a global health state measurement on a visual analytic scale (VAS), ranging from 0 to 100.

Outcome measurement

Surgery was performed in patients diagnosed with resectable hilar cholangiocarcinoma. In unresectable hilar cholangiocarcinoma, each patient was asked to choose the treatment option by him/her self.

Patients were prospectively followed, and QOL was assessed at baseline (prior to treatment) and at 2-4 weeks after treatment. All patients were followed up either to the end of the study or to the time of death. The EQ-5D was administered by a well-trained interviewer.

Successful biliary drainage was defined as a decrease in total bilirubin of more than 50% of the pretreatment value in 2 weeks, or 75% of the pretreatment value in 4 weeks.

Statistics

Descriptive statistics were used for assessment of demographic characteristics and biochemical parameters. QOL data were checked and recorded according to the scoring guideline of EQ-5D Thai version. Com-

parison of QOL scores before and after treatment was made using paired *t*-test. The functional well-being was using Wilcoxon signed ranks test, based on normality test of Kolmogorov-Smirnov. Statistical significance was set at p-value < 0.05.

RESULTS

1. ERCP metallic stent group

Thirty-seven patients were included all underwent ERCP with metallic stent placement. The mean age was 62.1± 9.84. The presenting symptoms were jaundice (97.29%), pruritus (72.97%) and abdominal pain (56.78%). Three patients were classified as Bismuth I (8.1%), 4 as Bismuth II (10.81%), 5 as Bismuth IIIa (13.51%), 5 as Bismuth IIIb (13.51%) and 25 as Bismuth IV (54.05%). There were 8.1% of patients with right portal vein involvement, 2.7% with left portal vein involvement, and 5.41% with main portal vein involvement. Nine patients had local lymph node metastases, while 18.91% had distant lymph node metastases, 5.41% had peritoneum metastases, and 5.41% had lung metastases. The baseline biochemical parameters are shown in Table 2. In this group, 19 patients received adequate drainage, while 18 patients did not achieve an adequate drainage. The EQ-5D score for the ERCP stent group improved by 0.122 point, which was not statistically significant (p=0.049). The EQD score for the ERCP stent with adequate drainage subgroup improved by 0.158 point, which was not statistically significant (p=0.02).

2. PTBD group

Forty-seven patients were included. The mean age was 62.09 ± 10.9. The presenting symptoms were jaundice (98.7%), pruritus (92.21%), fever (46.75%) and abdominal pain (36.36%). Two patients were classified as Bismuth II (2.6%), 7 as Bismuth IIIa (9.09%), 7 as Bismuth IIIb (9.09%), and 61 as Bismuth IV (79.22%). There were 19.48% of patients with right portal vein involvement, 18.18% with left portal vein involvement, and 3.39% with main portal vein involvement. Twenty-seven patients had local lymph node metastases, while 15.58% had distant lymph node metastases, 1.3% had peritoneum metastases, and 3.9% had both peritoneal and lung metastases. The baseline biochemical parameters are shown in Table 2. In this group, 19 patients received an adequate drainage, while 28 patients did not achieve adequate drainage. The EQ-5D score for the PTBD group improved by 0.018 point, which was not statistically significant (p=0.64). The EQD score for the PTBD with adequate drainage subgroup decreased by 0.046 point after treatment.

3. Surgery group

Forty-two patients were included. The mean age of the patients was 57.07 ± 9.83. The presenting symptoms were jaundice (80.95%), pruritus (78.57%), fever (40.78%) and abdominal pain (45.24%). One patient was classified as Bismuth I (2.38%), 7 as Bismuth II (16.67%), 12 as Bismuth IIIa (24.04%) 8 as Bismuth IIIb (19.05%), and 15 as Bismuth IIII (37.71%). There were 14.29% of patients with right portal vein involvement, and 9.56% with left portal vein involvement. Seven patients had local lymph node metastases, 4.76% of patients had distant lymph node metastases, and 4.76% of patients had peritoneum metastases. The baseline biochemical parameters are shown in Table 2. In this group, 14 patients had resectable lesions, while the lesions in 28 patients were unresectable. Thirty-one patients received drainage before surgery. The EQ-5D score for the surgery group improved by 0.086 point, which was not statistically significant (p=0.12). In the surgically resectable subgroup, the EQ-5D score improved by 0.152 point, which was not statistically significant (p=0.14).

4. Palliative care group

One-hundred-and-four patients were included. The mean age of the patients was 67.17± 9.53. The presenting symptoms were jaundice (84.62%), pruritus (63.46%), fever (39.42%) and abdominal pain (40.38%). One patient was classified as Bismuth I (2.6%), 8 patients as Bismuth II (7.69%), 25 patients as Bismuth IIIa (24.04%), 15 patients as Bismuth IIIb (14.42%) and 54 patients as Bismuth IV (51.92%). Eleven patients had right portal vein involvement, 17 had left portal vein involvement, 9 had main portal vein involvement, and 1 had both main and left branch involvement. There were 39 patients with local lymph node metastases, 16.35% with distant lymph node metastases, 7.69% with peritoneum metastases, 1.92% with both peritoneal and lungs metastases, 2.88 % with both lymph node and lung metastases, with lymph node and peritoneum metastases, and 1.92% with lymph node, peritoneum as well as lung metastases. The baseline biochemical parameters are shown in Table

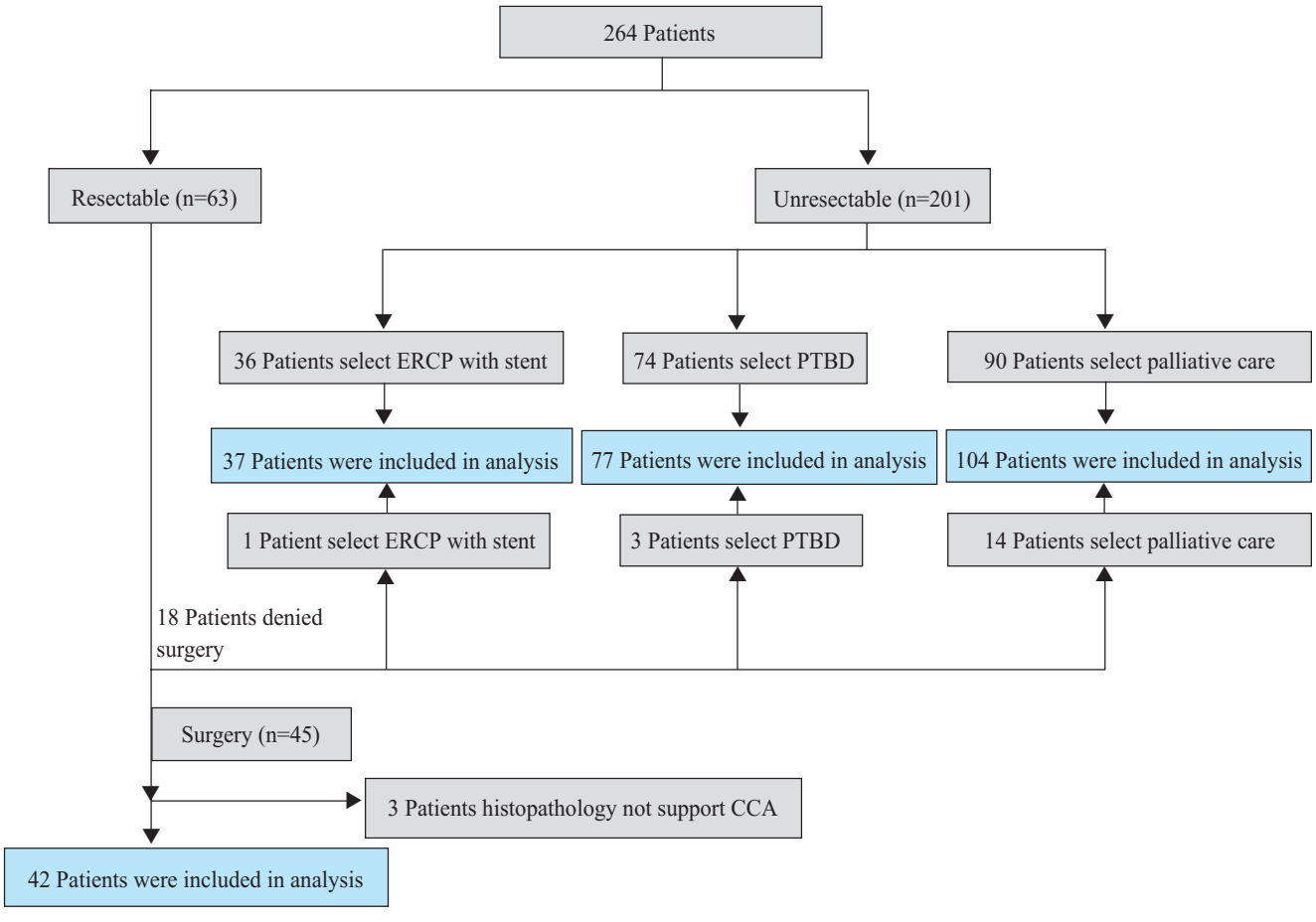

Figure 1. Screening and randomization of the study.

Table 1. Baseline characteristics of the patients.

Characteristics	ERCP (n = 37)	PTBD (n = 77)	Surgery (n = 42)	Palliative (n = 104)
Sex (M:F)	27: 10	53: 24	35: 7	77: 27
Age (yrs) ±SD	62.1 ± 9.84 (range 44-87)	62.09 ± 10.9 (range 37-82)	57.07 ± 9.83 (range 34-74)	67.17 ± 9.53 (range 34-87)
Underlying disease, n (%)				
DM	5 (13.51)	2 (2.6)	11 (26.19)	21 (20. 19)
HT	7 (18.92)	9 (11.69)	1 (2.38)	24 (23.08)
IHD	0	0	0	1 (0.96)
CKD	1 (2.7)	0	0	2 (1.92)
Asthma	1 (2.7)	0	0	1 (0.96)
COPD	0	0	0	1 (0.96)
Cirrhosis	0	0	0	1 (0.96)
Clinical presentation, n (%)				
Pruritus	27 (72.97)	71 (92.21)	33 (78.57)	66 (63.46)
Jaundice	36 (97.29)	76 (98.7)	34 (80.95)	88 (84.62)
Fever	15 (40.54)	36 (46.75)	17 (40.78)	41 (39.42)
Abdominal pain	21 (56.76)	28 (36.36)	19 (45.24)	42 (40.38)
Ascites	5 (13.51)	6 (7.79)	3 (7.14)	19 (18.26)

Table 2. Biochemical parameters of the patients.

Biochemical parameters	ERCP (n = 37)	PTBD (n = 77)	Surgery (n = 42)	Palliative (n = 104)
CA19-9 (U/mL)	105.92 ± 2934.31 (range 0.81-1,001)	530.41 ± 495.71 (range 0.05-2,383)	1,277.55 ± 5,711.53 (range 0.05-37,307)	580.39 ± 449.15 (range 0.05-1,001)
CEA (ng/mL)	49.96 ± 118.09 (range 1.86-635.9)	48.25 ± 150.75 (range 0.88-1,001)	922.99 ± 5,824.48 (range 0.59-37,308)	50.55 ± 136.25 (range 1.42-1,001)
TB (mg/dL)	18.43 ± 11.06 (range 1-44.3)	23.32 ± 11.43 (range 1.2-54.4)	17.52 ± 12.09 (range 0.3-40.3)	16.76 ± 12.73 (range 0.3-52.4)
Alb (mg/dL)	3.28 ± 0.59 (range 2.2-4.7)	3.24 ± 0.53 (range 1.8-4.3)	3.74 ± 0.56 (range 2.5-4.9)	3.29 ± 0.61 (range 2.2-4.6)
BUN (mg/dL)	14.11 ± 6.72 (range 7.6-37.9)	13.48 ± 7.83 (range 0.5-4.7)	12.93 ± 5.95 (range 0.4-36.1)	17.45 ± 15.9 (range 5.7-126.7)
Cr (mg/dL)	0.94 ± 0.33 (range 0.5-2.2)	1 ± 0.87 (range 0.4-7.2)	0.82 ± 021 (range 0.5-1.7)	1.38 ± 1.88 (range 0.6-13.1)
PT (Second)	21.69 ± 27.59 (range 1.56-141.16)	21.67 ± 22.03 (range 8.8-116.1)	18.06 ± 14.85 (range 5.92-87.24)	20.77 ± 21.93 (range 8.6-121)
INR	1.84 ± 2.08 (range 0.7-13.45)	2.05 ± 2.02 (range 0.87-10.56)	1.76 ± 1.44 (range 0.92-8.18)	1.99 ± 2.09 (range 0.8-11.19)

(Mean±SD)

Table 3. Baseline characteristics of the patients.

Characteristic	ERCP (n = 37)	PTBD (n = 77)	Surgery (n = 42)	Palliative (n = 104)
Bismuth classification, n (%)				
I	3 (8.1)	0	1 (2.38)	2 (1.92)
II	4 (10.81)	2 (2.6)	7 (16.67)	8 (7.69)
IIIa	5 (13.51)	7 (9.09)	12 (28.57)	25 (24.04)
IIIb	5 (13.51)	7 (9.09)	8 (19.05)	15 (14.42)
IV	20 (54.05)	61 (79.22)	15 (37.71)	54 (51.92)
Portal vein involvement, n (%)				
No	31 (83.78)	44 (57.14)	32 (76.19)	66 (63.46)
Rt branch	3 (8.1)	15 (19.48)	6 (14.29)	11 (10.58)
Lt branch	1 (2.7)	14 (18.18)	4 (9.52)	17 (16.35)
Main branch	2 (5.41)	4 (3.39)	0	9 (8.65)
Main+Lt branch	0	0	0	1 (0.96)
Local LN metastases, n (%)	9 (24.32)	27 (35.06)	7 (16.67)	39 (37.5)
Distance metastases, n (%)				
Distant LN	7 (18.91)	12 (15.58)	2 (4.76)	17 (16.35)
Peritoneum	2 (5.41)	1 (1.3)	2 (4.76)	8 (7.69)
Lung	2 (5.41)	0	0	9 (8.65)
Peritoneum+lung	1 (2.7)	0	0	2 (1.92)
LN+lung	0	3 (3.9)	0	3 (2.88)
LN+Peritoneum	0	0	0	1 (0.96)
LN+Peritoneum+lung	0	0	0	2 (1.92)

Table 4. EQ-5D Thai version score in each group.

Procedure	Pre-treatment	Post-treatment	Mean different of score	*p*-value
ERCP (n=37)	0.303 ± 0.209	0.425 ± 0.304	- 0.121	0.049*
Adequate drainage (n=19)	0.283 ± 0.206	0.468 ± 0.322	- 0.185	0.02*
Inadequate drainage (n=18)	0.325 ± 0.217	0.379 ± 0.285	- 0.054	0.41
PTBD (n=47)	0.316 ± 0.193	0.334 ± 0.314	- 0.018	0.64
Adequate drainage (n=19)	0.302 ± 0.217	0.256 ± 0.389	0.046	0.63
Inadequate drainage (n=28)	0.321 ± 0.187	0.359 ± 0.284	- 0.039	0.34
Surgery (n=42)	0.391 ± 0.225	0.477 ± 0.274	-0.085	0.12
Resected (n=14)	0.378 ± 0.242	0.53 ± 0.285	-0.152	0.14
Unresected (n=28)	0.398 ± 0.219	0.449 ± 0.269	-0.051	0.44
Prior drainage (n=31)	0.419 ± 0.181	0.474 ± 0.254	-0.054	0.34
Non-prior drainage (n=11)	0.313 ± 0.315	0.485 ± 0.338	- 0.173	0.23

2. In the palliative care group, the medical records and data were incomplete and data analysis for EQ-5D score was not made.

DISCUSSION

Two-hundred-sixty-one hilar cholangiocarcinoma patients were enrolled and divided into 4 groups according to the mode of treatment (surgery, ERCP with stent, PTBD and palliative care). In the palliative care group, data analysis for EQD score was not possible. Results of this study showed that patients in the ERCP with metallic stent group had a significantly improved utility score, from 0.303 to 0.425 (p=0.049), especially in the adequate drainage subgroup (p=0.02). In the PTBD group, on the other hand, the utility score not significantly improved, both in the adequate drainage and in the inadequate drainage group. In the surgery group, the utility score was not significantly improved, possible related to a high starting utility score and occurrence of post-operative pain. The utility score from this study can be used to calculate the Quality Adjusted Life Years (QALYs), which in turn can be used for cost effective analysis (CEA) and cost utility analysis (CUA) to work out an appropriate treatment policy in patients with hilar cholangiocarcinoma.

CONCLUSION

Significant improvement of EQ-5D score was noted in patients with hilar cholangiocarcinoma who receiving ERCP and metallic stent placement with adequate drainage.

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