

The Characteristics and Outcomes of Endoscopic Treatment of Cholangiocarcinoma at NKC Institute: A Retrospective Analysis

Jiraprayuklert S¹
Attasaranya S²
Ovartlanporn B²

ABSTRACT

Background & Aims: Cholangiocarcinoma (CCA) is the common cause of biliary tract obstruction in Thailand. The objective of this study is to analyze the characteristics and outcomes of endoscopic drainage for CCA in the Southern part of Thailand.

Methods: A retrospective analysis of a prospectively recorded ERCP database of patients with unresectable CCA underwent plastic stent insertion the NKC institute, Songklanakarind Hospital from 2008-2011. CCA was diagnosed by clinical data or histology. The demographic data, endoscopic success rate, clinical response rate, complications and survival were collected and analyzed.

Results: Seventy two patients (34 males, and 38 females) with a mean age \pm SD of 63.6 \pm 13.3 years were recruited. Endoscopic success was obtained in 69 of 72 patients (95.8%), clinical success drainage was achieved in 39 of 51 evaluable cases (76.4%) with 34 required one ERCP session and 5 required 2 ERCP sessions. The clinical success rate in hilar CCA (HCCA) and distal CCA (DCCA) was similar. The complication rate was comparable to other reports. The overall median survival time was 112 days (95% CI = 74-169), with the cumulative 3 month, 6 month 1 year survival rates of 55.2%, 34.3% and, 12.7% respectively. The median survival time in HCCA was 93 days (95% CI 61-169) and in DCCA was 164 days (95% CI 46-NA) ($p > 0.05$). The median survival time of successful drainage cases was 165 days (95% CI 115-272) compared with unsuccessful drainage cases was 14 days (95% CI 4-NA) ($p < 0.05$).

Conclusion: The demographic data in this study are showed equal frequency in both genders whereas another reports showed male predominant. The endoscopic drainage and clinical success rates in this study are higher and the median survival time is longer compared with another study in the similar endoscopic drainage.

Key words : Cholangiocarcinoma, ERCP, endoprosthesis

[Thai J Gastroenterol 2013; 14(3):149-153.]

¹Division of Gastroenterology/Hepatology, Department of Medicine, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkla, Thailand.

²NKC Institute of Gastroenterology and Hepatology, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkla, Thailand.

Address for Correspondence: Bancha Ovartlanporn, M.D., NKC Institute of Gastroenterology and Hepatology, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkla, Thailand.

INTRODUCTION

Cholangiocarcinoma (CCA) is a common biliary malignant tumor in Thailand⁽¹⁾. CCA is associated with liver flukes infection in the Northeastern region of Thailand⁽¹³⁻¹⁵⁾. The characteristics of CCA in the Northern region (endemic area) of Thailand have been reported previously⁽¹⁰⁾. There are some reports available from non-endemic area, the Central of Thailand, which report only hilar CCA (HCCA) by Reknimitr et al⁽¹⁸⁾ and Akaraviputh et al⁽¹³⁾. Most of patients in all reports were unresectable at presentation. Of our knowledge, there is no report from the Southern region of Thailand.

Palliative endoscopic drainage is the preferred method in most centers for unresectable CCA with jaundice^(2,4). One report of endoscopic treatment comparing using metallic and plastic stent in CCA from endemic area showed the better survival from metallic than plastic stent⁽¹⁰⁾. The median survival of the plastic stent group was 49 days in that study. There were limited reports regarding the outcome of endoscopic drainage for CCA in non-endemic area available^(13,18) and there is no report from the southern part of Thailand where CCA is not associated with liver fluke infection. The aim of this study is to analyze the characteristics of CCA in Southern part of Thailand and the outcome of endoscopic biliary drainage, complication and survival of patients with unresectable CCA.

MATERIALS AND METHODS

This is a retrospective study of a prospectively recorded ERCP database (Endosmart software) at NKC institute from January 2008 to December 2011. All patients with CCA or biliary stricture were retrieved. All the medical records and ERCP reports of the relevant patients were retrieved and reviewed. The diagnosis of CCA was made either by imaging studies with CT scan and/or MRI/ MRCP or ERCP, clinical course, or by cytology and/or histopathology. All patients with unresectable CCA by imaging study or unfit for surgery were included in the analysis.

A prophylactic antibiotic with ciprofloxacin was given before the ERCP procedures. The measures to minimize the contamination of undrained bile ducts were done by using a guide wire probing and injection of air or contrast to the bile duct after the guidewire was successfully accessed the stricture. The suitable

bile ducts for drainage were selected by imaging study. The number of stent and type of stent were selected at the discretion of the endoscopists performing the procedures. The lesions were biopsies by forceps and brushing for cytology before stent insertion. All the stents in this study were 7 or 10 Fr. plastic stents.

The endoscopic success was defined as a successful stent insertion and the clinical response was defined as falling of bilirubin level greater than 50% from base line. Ascending cholangitis defined as body temperature more than 38.5°C without other source, pancreatitis was defined as abdominal pain lasting more than 24 hours with elevated amylase more than 3 times of upper normal limit, perforation, bleeding and mortality within 30 days after the procedure were defined as procedure related complications^(12,19).

The demographic data, endoscopic success, clinical response and complications were analyzed using descriptive statistics, comparison between continuous variables was performed by student-t test, comparison between discrete variables was performed by Chi-square test/Fisher exact and survival was analyzed by Kaplan Mayer curve/compare different by Cox proportion hazard. This study was approved by the Songklanakarind University Ethics Committee for Human Research.

RESULTS

There were 73 patients retrieved from the data base. One patient was excluded due to a very long survival of more than 3 years. Seventy two patients were included with 34 men (47.2 %) and 38 women (52.8%) and the mean age \pm SD of the group was 63.6 \pm 13.3 years. Sixty eight patients (94.4%) were native southern people and four patients (5.6%) were not native people (2 from Northeast part of Thailand).

The clinical presentations were jaundice in 68 patients (95.8%), abdominal pain in 40 patients (56.3%), weight loss in 48 patients (67.6%) and cholangitis in 16 patients (22.5%). CCAs were diagnosed by clinical course and imaging in 50 patients (69.4%) and by histology in 22 patients (30.6%) (Table 1). Fifty nine patients were HCCA and 13 patients were DCCA. Patients in the HCCA were able to be classified as Bismuth I, II, III and IV in 50 (Table 2).

The endoscopic success rate was 95.8 % (69/72). The data for analysis of clinical response were available in 51 patients (44 HCCA and 7 DCCA). The clini-

cal response after the first ERCP was achieved in 34 from 51 patients (66.7%). In 17 patients who did not respond by the first ERCP, 5 patients responded by the second ERCP, 1 patient responded by both ERCP and PTBD, 6 patients responded by PTBD, and 5 patients had no further intervention. The overall clinical response by ERCP was 39 from 51 patients (76.47%). In HCCA and DCCA the response rate were 72.3%

Table 1. Baseline characteristics of the patients.

Baseline characteristics	N=72	Percentage (%)
Gender (M/F)	34/38	47.2/52.8
Mean age range	63.6±13.3	
Symptom		
Jaundice	68/72	95.8
Abdominal pain	40/72	56.3
Weight loss	48/72	67.6
Cholangitis	16/72	22.5
Total bilirubin before stent	22.97±11.7	$p < 0.001$
Total bilirubin after stent	11.0±9.7	

Table 2. Type of hilar CCA according to Bismuth's classification.

Type hilar CCA	Patients (N)
I	6
II	14
III	16
IV	14
Undetermined	9

(34/44) and 85.7% (6/7), respectively. (Fisher's exact test $p=1$). The overall clinical response for ERCP and PTBD combination was 46/51 (90.19%).

The complications related to ERCP procedures are showed in Table 3. Four had pancreatitis, 8 had cholangitis, and one had bleeding. The complication rate between HCCA and DCCA was not statistically different although the cholangitis exclusively occurred in HCCA group.

The overall median survival time for all CCA was 110 days (95% CI; 65-169), with the cumulative 3 months, 6 months and 1 year survival rates of 54.5%, 33.3%, and 12.7%, respectively (Figure 1A). The median survival time of HCCA was 93 days (95% CI; 61-169) and of DCCA was 164 days (95% CI; 46-NA) but the difference between the two groups was not statistically significant ($p > 0.05$) (Figure 1B). The median survival time in successful drainage group was 165 days (95% CI; 115-272) compared with 14 days (95% CI 4-NA) in unsuccessful drainage group and the difference was statistically significant ($p < 0.05$) (Figure 2).

DISCUSSION

The demographic data of the patients in this study were generally similar to the previous report by Sangchan A, et al.⁽¹⁰⁾ The main difference was the distribution of gender, our data showed similar distribution of CCA by gender whereas the study of Sangchan A⁽¹⁰⁾ showed predominantly male gender. Most of the patients in this study had HCCA and this was similar to other reports^(10,13,14,15). The majority of Bismuth type in our study were Bismuth III and IV that was similar to Rerknimitr study⁽¹⁸⁾ (53.6 % vs. 41.6 %), whereas Sangchan A⁽¹⁰⁾ et al reported that Bismuth III and IV

Table 3. Complications of ERCP with stent according to location of CCA.

		Distal CCA (N=7)	Hilar CCA (N=44)	p-value
Pancreatitis	No	6 (85.7)	41 (93.2)	0.457
	Yes	1 (14.3)	3 (6.8)	
Cholangitis	No	7 (100)	36 (81.8)	0.579
	Yes	0 (0)	8 (18.2)	
Bleeding	No	7 (100)	43 (97.7)	1.000
	Yes	0 (0)	1 (2.3)	

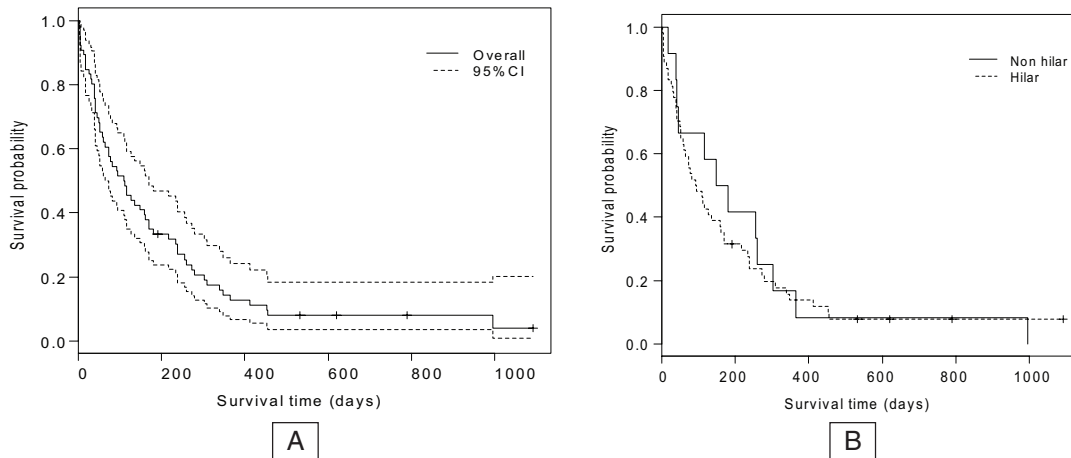


Figure 1. A. Kaplan-Meier analysis of overall survival.
B. Kaplan-Meier analysis of survival according to HCCA or DCCA.

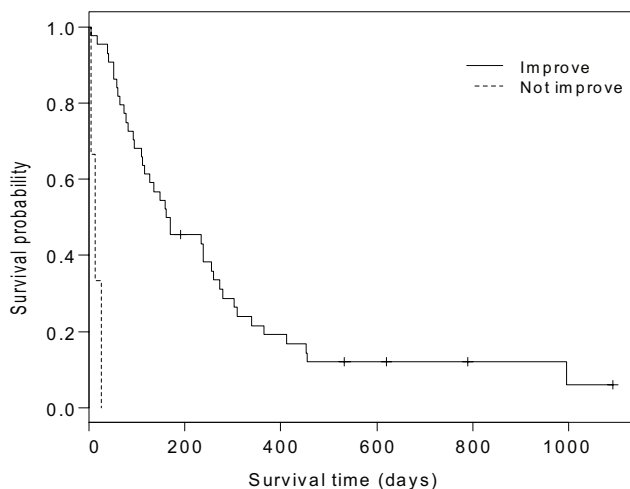


Figure 2. Kaplan-Meier analysis of survival of patients with successful drainage and unsuccessful drainage.

as high as 84.1%. The difference was due to Sangchan et al excluded Bismuth I from the study.

The endoscopic success rate in the present study was 95.8% and was in range of reported from other centers. There were three centers reported the success rate of endoscopic insertion, which were 85.2%, 91.1% and 96.8% by Sangchan et al⁽¹⁰⁾, Akaraviputh et al⁽¹³⁾ and Rerknimitr et al⁽¹⁸⁾, respectively. The clinical response in the first ERCP attempts was 66.7% which is rather low but with second ERCP in the non-responders, the overall success drainage was increased to 76.47% and this is comparable to the 81% result from a landmark study by De Palma et al which compared

endoscopic biliary drainage by plastic stent in malignant hilar obstruction⁽²⁰⁾. The clinical response in the first ERCP attempts was 66.7% in this study whereas in Sangchan et al⁽¹⁴⁾ Akaraviputh et al⁽¹³⁾ were 46.3% and 48%, respectively. The HCCA patients had successful drainage of 85%, all of these using plastic stent. This is similar to the metallic stent group reported by Sangchan et al and it is much better than the figure in the plastic stent group in that study (46.3% vs. 76.5%)⁽¹⁰⁾. The difference between our data and that of previous study may be due to different population recruited and different endoscopic drainage technique. A prospective comparative study between this region and the other region in the previous studies is needed to confirm this hypothesis. The complication rate in our study was comparable to the rate reported in the literature^(10,20). Early complication from Sangchan et al⁽¹⁰⁾, Akaraviputh et al⁽¹³⁾, and Rerknimitr et al⁽¹⁸⁾ were 47%, 18% and 27.8% respectively. The cholangitis was found exclusively in HCCA, we expected from some undrained bile duct were encountered during the procedures.

Survival analysis was only performed by Sangchan et al. The survival of the DCCA is longer than that of HCCA even though the difference was not significant. The survival of HCCA in our study was approximately twice (93 vs. 49 days) of the survival reported in HCCA treated by plastic stent by Sangchan et al.⁽¹⁰⁾ This may be due to the different population recruited. Most of the cases in the study from Khonkaen and Ubonrachathani⁽¹⁰⁾ were in the endemic area of liver fluke and the economic status was lower com-

pared with population in the South. The nutritional status may be poorer and the time of seeking medical treatment may be longer in the Northeast compared with those in the South. For patients with successful drainage, the median survival of 165 days was significantly longer compared with those with unsuccessful drainage (14 days) and this underscored the importance of successful drainage to improve survival and probably quality of life. However, the number of patients with unsuccessful drainage was small and the difference may be over exaggerated. There are some limitations of this study. Firstly, CCA was histologically confirmed in 1/3 of cases. Secondly, this study is retrospective study and some missing data were inevitable.

REFERENCES

1. International Agency for Research on Cancer. Infection with liver fluke (*Opisthorchis viverrini*, *Opisthorchis felineus* and *Clonorchis sinensis*). IARC monograph on the evaluation of carcinogenic risk to humans. 1994;61:121-75.
2. Ogura Y, Mizumoto R, Tabata M, *et al.* Surgical treatment of carcinoma of hepatic duct confluence: analysis of 55 resected carcinomas. *World J Surg* 1993;17:85-92.
3. Parc Y, Frileux P, Balladur P, *et al.* Surgical strategy for the management of hilar bile duct cancer. *Br J Surg* 1997;84:1675-9.
4. Moss AC, Morris E, Leyden J, MacMathuna P. Malignant distal biliary obstruction: a systematic review and meta-analysis of endoscopic and surgical bypass results. *Cancer Treat Rev* 2007;33:213-21.
5. Madoff DC, Wallace MJ. Palliative treatment of unresectable bile duct cancer: which stent? Which approach? *Surg Oncol Clin N Am* 2002;11:923-39.
6. Dowsett JF, Russel RCG, Hatfield ARW, *et al.* Malignant obstructive jaundice: what is the best management? A prospective randomized controlled trial of surgery and endoscopic stenting. *Gut* 1988;29:A1493.
7. Burcharth F, Jensen LI, Olesen K. Endoprosthesis for internal drainage of the biliary tract. *Gastroenterology* 1979;77:133-7.
8. McPherson GA, Benjamin IS, Hodgson HJ, *et al.* Preoperative percutaneous transhepatic drainage: the result of a controlled trial. *Br J Surg* 1984;71:371-5.
9. AB Ballinger, M McHugh, SM Catnach, *et al.* Symptom relief and quality of life after stenting for malignant bile duct obstruction. *Gut* 1994;34:467-70.
10. Sangchan A, Kongkasame W, Pugkhem A, *et al.* Efficacy of metal and plastic stents in unresectable complex hilar cholangiocarcinoma: a randomized controlled trial. *Gastrointest Endosc* 2012;76:93-9.
11. Weber A, Gaa J, Rosca B, *et al.* Complications of percutaneous transhepatic biliary drainage in patients with dilated and nondilated intrahepatic bile ducts. *Eur J Radiol* 2009;72:412-7.
12. Cotton PB, Lehman G, Vennes J, *et al.* Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991;37(3):383-93.
13. Akaraviputh T. Endoscopic endoprosthesis insertion in unresectable hilar cholangiocarcinoma patient. *Siriraj Med J* 2006;58:640-3.
14. Wongsanook A, Sukepaisarnjaroen W, Mairiang P, *et al.* Survival analysis of hilar cholangiocarcinoma treated by endoscopic biliary drainage at Srinagarind hospital, Khon Kaen. *Thai J Gastroenterol* 2006;7:132-6.
15. Tipsunthonsak N, Piriyaupong T, Piriyaanon. Efficacy of biliary stent drainage and factors associated with complications in endoscopic palliative treatment of patients with hilar cholangiocarcinoma. *Thai J Surg* 2011;32:26-34.
16. Peters RA, Williams SG, Lombard M, *et al.* The management of high-grade hilar strictures by endoscopic insertion of self-expanding metal endoprostheses. *Endoscopy* 1996;28:10-6.
17. Weber A, Gaa J, Rosca B, *et al.* Complications of percutaneous transhepatic biliary drainage in patients with dilated and nondilated intrahepatic bile ducts. *Eur J Radiol* 2009; 72:412-7.
18. Rerknimitr R, Kladcharoen N, Mahachai V, *et al.* Result of endoscopic biliary drainage in hilar cholangiocarcinoma. *J Clin Gastroenterol* 2004; 38:518-23.
19. Freeman ML, Nelson DB, Sherman S, *et al.* Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996; 335:909-18.
20. De Palma GD, Galloro G, Siciliano S, *et al.* Unilateral versus bilateral endoscopic hepatic duct drainage in patients with malignant hilar biliary obstruction: results of a prospective, randomized, and controlled study. *Gastrointest Endosc* 2001;53:547-53.