

Impact of Palliative Biliary Drainage between Metal Stents and Plastic Stents on Survival Rate in Unresectable Distal Malignant Biliary Stricture in Songklanagarind Hospital

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Background: Palliative biliary drainage was used to improve obstructive jaundice, nutritional status and quality of life, along with the survival of unresectable distal malignant biliary stricture [DMBS] patients. Endoscopic retrograde cholangiopancreatography [ERCP] with biliary drainage is mainstay treatment for these patients. The benefits of biliary stent types, which are different in cost, on the survival rate and their efficacy of biliary drainage in DMBS patients, are still questionable in countries with limited health budget.

Objective: To assess the impact of endoscopic palliative biliary drainage stents on survival rates, nutritional status, cost and efficacy of biliary drainage for patients with DMBS.

Materials and Methods: All computerized medical records of DMBS patients, who underwent endoscopic biliary drainage during January 2012 to December 2015 in Songklanagarind hospital were retrospectively reviewed. ERCP with biliary drainage stents were undertaken at the discretion of the attending physicians. The overall survival time, nutritional status (body weight), cost and efficacy of biliary drainage (level of total bilirubin) after drainage procedure between the metal stent, plastic stent and plastic stent followed with metal stent group were compared.

Results: Sixty eight patients (45 males, mean age 63.7 years) were enrolled, 35 patients were classified into the plastic stent group, 18 patients were classified into the metal stent group and 15 patients were classified into the plastic stent followed with metal stent group. Demographic data, primary malignancy, tumor staging and ECOG score, initial total bilirubin and stricture length were similar between three groups. The median survival time was 5.4 months (95% confidence interval 3.2 to 8.5 months). Overall survival rate, weight reduction and the decline of bilirubin after biliary drainage, were not significantly different between biliary stent types. The plastic stent group had the lowest cost of total ERCP and biliary drainage procedure. The complication rates were not different between the biliary stent types.

Conclusion: Palliative biliary drainage by plastic stent in unresectable DMBS patient was similar in overall survival rate, nutritional status, efficacy of drainage and complications compared with metal stent or plastic stents followed with metal stent. However, the plastic stent group incurred the lowest cost of the completed procedure.

Keywords: Biliary drainage, Distal, Endoscopic retrograde cholangiopancreatography, Malignant biliary stricture, Stent

J Med Assoc Thai 2018; 101 [Suppl. 4]: S38-S43

Full text. e-Journal: <http://www.jmatonline.com>

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How to cite this article: Pattarapuntakul T, Netinatsuton N, Sottisuporn J, Witeerungrot T, Ovartlarnporn B. Impact of palliative biliary drainage between metal stents and plastic stents on survival rate in unresectable distal malignant biliary stricture in Songklanagarind Hospital. J Med Assoc Thai 2018;101;Suppl.4:S38-S43.

Distal malignant biliary stricture [DMBS] patients mostly present with obstructive jaundice, pruritus, weight loss and ascending cholangitis, which affect the overall survival and their quality of life. The most symptomatic patients are within the unresectable stage, and have a 5-year survival approximately 5% to 7%⁽¹⁾. An endoscopic retrograde cholangiopancreatography [ERCP] with biliary drainage is a standard and least invasive procedure for relief obstructive jaundice in unresectable DMBS^(2,3,11).

Biliary plastic stents have been used for the relief obstructive jaundice, but they are often occluded by sludge, bacterial biofilm and need to be changed every 3 to 4 months^(9,13). The self-expandable metal stents have longer patency than plastic stent, but they have an increased costing in Thailand by about 10 times^(4,7,8). In term of cost effectiveness, plastic stents are reported to be recommend in patients with a survival rate less than 4 months or evidence of distant metastasis⁽¹²⁾. If the survival rate is more than 6 months and the cost of ERCP is lower relative to a metal stent, then plastic stent based biliary drainage may be more cost-effectiveness^(5,10).

In Thailand, the cost of ERCP with biliary drainage in government hospital is approximately half price of a metal stent. Thus, the aim of the present study is to assess the impact of endoscopic palliative biliary drainage on the overall survival rate, efficacy of biliary drainage and total cost of biliary drainage procedure. This was dependent on the biliary stents type used for biliary drainage in the first 6 months for the relief of jaundice in unresectable DMBS patients in Songklanagarind hospital.

Materials and Methods

Study population

The present study was a retrospective analysis that was managed and followed-up at NKC institute, Songklanagarind Hospital, Faculty of Medicine, between January 2012 and December 2015. The study was approved by the ethic committee board of the Faculty of Medicine, Prince of Songkla University.

The diagnosis of distal malignant biliary stricture was confirmed by histopathology during ERCP or endoscopic ultrasound [EUS] with fine needle aspiration.

Patient inclusion criteria's were as follows; 1) Having DMBS confirmed by imaging and histopathology; 2) Having evidence of biliary obstruction by imaging studies or ultrasonography and having obstructive jaundice; 3) Having unresectable

disease (according to the disease stage or performance status of the patients). All patients were aged above 15 years, Eastern Cooperative Oncology Group [ECOG] status 0 to 3 with no major comorbid disease or previous history of abdominal surgery; 4) Having technically successful stent placement.

Biliary drainage procedure

ERCP was performed using a large channel duodenoscope (TJF-160R, TGF Q180V; Olympus Optical Co., Ltd., Tokyo, Japan). The biliary cannulation was undertaken by sphincterotome or cannula catheter and guidewire. All patients, who were success to biliary cannulation, were obtained biliary brushing cytology and intraductal biopsy to confirm diagnosis. The biliary stents were placed above stricture, confirmed by fluoroscopy. The ERCP with biliary drainage stents was performed at the discretion of the attending physicians.

The biliary plastic stents, which were used in the NKC institute, are straight stent varied in size (10 Fr and 12 Fr) by three different companies (Boston scientific, COOK and Olympus). The biliary, expandable metallic stent were uncovered and covered type of stent all of which can be expanded to a maximum of 10 mm, by 4 companies Teawong (Korea), Bona-SHIM (Korea), Hanaro(Korea) and Boston scientific (USA).

Histopathology

The brushing cytology was performed by wire guided cytology brush (Boston Scientific and COOK). A bile duct biopsy was performed by wire guided intraductal biopsy (COOK). The tissue was reviewed with a pathologist for definite diagnosis of malignancy.

Data collection

The demographic and clinical characteristics including age, gender, etiology of DMBS, stricture length, biliary stent type, complications, subsequent liver function test, body weight during treatment, and survival rate after biliary drainage were collected.

Statistical analysis

Patient baseline characteristics (demographical, clinical, and laboratory data) were compared between the 3 groups using non-normal distributed data, with the aid of Wilcoxon's test and student's t-test for normal distributed data. Categorical data were compared by Chi-squared test or Fisher's exact test. Overall survival rate of the whole cohort, was obtained by the Kaplan-Meier method. The significance of differences between curves, as classified by variable

category, was evaluated using the log-rank test for univariate analysis. Statistical significance was defined with p -value <0.05 . Analysis was performed using R program (Apical package R foundation for statistical Computing, 2008).

Results

During the study periods, there were a total of 68 patients with DMBS. All of them had confirmed diagnoses by histopathology, imaging and successful ERCP with biliary drainage procedure. Patient baseline characteristics for each group are shown in Table 1. Sixty-eight patients (45 males, mean age 63.7 ± 14.8 years) were enrolled; 35 patients were classified into the plastic stent group, 18 patients were classified into the metal stent group and 15 patients were classified into the plastic stent followed with metal stent group. The most common primary malignancy causing distal biliary stricture in the present study was pancreatic cancer (56%), ampullary cancer (23.5%) and cholangiocarcinoma (9%). Demographic data, primary malignancy, tumor staging and ECOG score, initial total bilirubin and stricture length were similar between the 3 groups with a slightly higher population in advanced stage and advanced age in the metal stent groups.

Bilirubin reduction after biliary drainage

There were no significant differences in the reduction of the total bilirubin level after biliary drainage procedure in DMBS patients between groups of biliary stent in 2 weeks, 1 month and 3 months ($p = 0.977$, $p = 0.669$ and $p = 0.644$, respectively) (Figure 1). The procedure complications and biliary stent complications were not different between groups.

Weight reduction after biliary drainage

The mean body weights were reduced in all groups of patients. There was no significant difference in mean body weight reduction after biliary drainage in 2 weeks, 1 month, 2 months and 3 months ($p = 0.217$, $p = 0.437$, $p = 0.377$, $p = 0.573$, respectively).

Cost of treatment

The cost of treatment was classified into the ERCP cost, biliary stent cost and total procedure cost. The ERCP cost is highest in the plastic followed with metal stent group, while there is no difference between plastic and metal stent groups ($38,424 \pm 10,268$ baht vs. $26,531 \pm 9,069$ baht vs. $22,113 \pm 7,732$ baht, respectively, $p < 0.01$). The biliary plastic stent group is the least expensive than that of the metal and plastic

followed with metal stent group; this was statistically significant ($2,480 \pm 1,495$ baht vs. $29,539 \pm 5,564$ baht vs. $29,965 \pm 6,382$ baht, respectively, $p < 0.001$). The total cost of the procedure was the highest in the plastic followed with metal stent group, the metal stent group and plastic stent group ($69,292 \pm 12,135$ baht vs. $55,471 \pm 14,398$ baht vs. $28,917 \pm 10,018$ baht, respectively, $p < 0.001$) (Figure 2).

Survival

The median survival time of all patients was 5.4 months. The overall survival rates of patients with unresectable DMBS who presented with obstructive jaundice and successful ERCP and biliary drainage with the plastic stent group, metal stent group and plastic

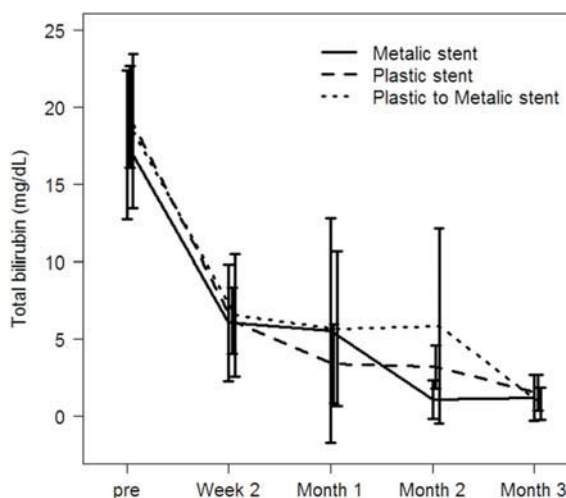


Figure 1. The efficacy of biliary drainage between each types of stent (level of total bilirubin).

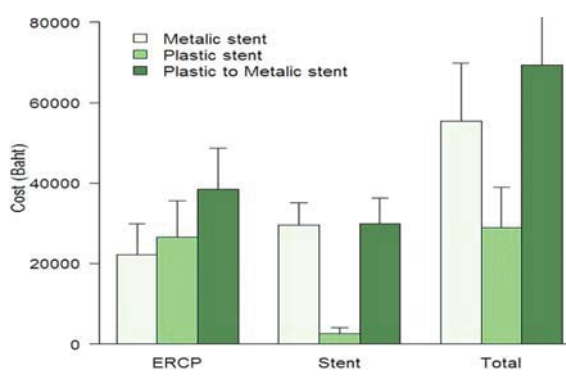


Figure 2. The mean cost of biliary drainage procedure between each type of the stent.

followed with metal stent group were 5.5 months, 3.2 months and 6.8 months, respectively ($p = 0.047$).

Discussion

In the present study, ERCP with biliary drainage showed no significant difference in the efficacy of biliary drainage or body weight change, even when including the complications in different types of biliary stent. Interestingly, the median survival time were slightly longer in the plastic stent followed with metal stent group. However, the study might have some bias in the selection of stent type as being demonstrated in Table 1 that patient underwent metal stent insertion had more advanced age and stage of disease, which may affect clinical outcomes. The overall survival time

in unresectable malignant biliary stricture could be affected by adequate biliary drainage, aggressive and disease stage^(15,16). However, previous studies showed no difference in overall survival between metal and plastic stent groups of unresectable malignant biliary stricture^(6,16) but the patency of plastic stents was less and it needed more re-intervention^(15,16).

The present study showed that the total cost of the procedure and biliary stents were different among nations. Expert opinions suggested that if the cost of ERCP is relatively lower than that of a metal stent, survival time less than 4 months and there is evidence of distant metastasis, the plastic stent-based endoscopic biliary drainage would be naturally more cost effective^(5,7,14). In our study, the mean cost of

Table 1. Demographic data of the 68 patients

Variables	Group 1 Plastic stent	Group 2 Metal stent	Group 3 Plastic-metal stent	<i>p</i> -value
Numbers	35	18	15	
Gender (male), n (%)	26 (74)	9 (50)	10 (66)	0.209
Age (year)*	61.2±15.1	71.3±12.6	60.7±14.6	0.040
Primary malignancy, n (%)				0.869
Pancreatic cancer	16 (46)	11 (61)	11 (73)	
Cholangiocarcinoma	4 (11.4)	1 (5.6)	1 (6.7)	
Ampullary cancer	10 (28.6)	4 (22.2)	2 (13.3)	
Neuroendocrine tumor	1 (2.9)	1 (5.6)	1 (6.7)	
Hematologic	2 (5.7)	0	0	
Metastasis	2 (5.7)	1 (5.6)	0	
Stage of disease, n (%)				0.076
I	6 (17.1)	5 (27.8)	3 (20)	
II	12 (34.3)	3 (16.7)	10 (66.7)	
III	6 (17.1)	2 (11.1)	0	
IV	11 (31.4)	8 (44.4)	2 (13.3)	
ECOG pre-treatment, n (%)				0.062
1	20 (57.1)	5 (27.8)	11 (73.3)	
2	12 (34.3)	9 (50)	4 (26.7)	
3	3 (8.6)	4 (22.2)	0	
Initial bilirubin (mg/dL)*	20.0±9.8	17.6±9.7	17.6±9.0	0.599
Body weight (kg)*	51.8±10.2	46.0±7.9	53.0±11.6	0.082
Stricture length (mm)*	27.4±16.0	22.7±12.9	25.2±18.6	0.596
Chemotherapy, n (%)	6 (17.1)	5 (27.8)	4 (26.7)	0.587
Complications, n (%)				1
ERCP	2 (5.7)	1 (5.5)	1 (6.7)	
Biliary stent	4 (11.4)	2 (11.1)	3 (20)	
Cost of ERCP (baht)*	26,531.0±9,069.0	22,113.0±7,732.0	38,424.0±10,268.0	<0.001
Cost biliary stents (baht)*	2,480.0±1,495.0	29,539.0±5,564.0	29,965.0±6,382.0	<0.001
Cost of total procedure (baht)*	28,917.0±10,018.0	55,471.0±14,398.0	69,262.0±12,135.0	<0.001

ERCP = endoscopic retrograde cholangiopancreatography

* Data are expressed as mean ± SD

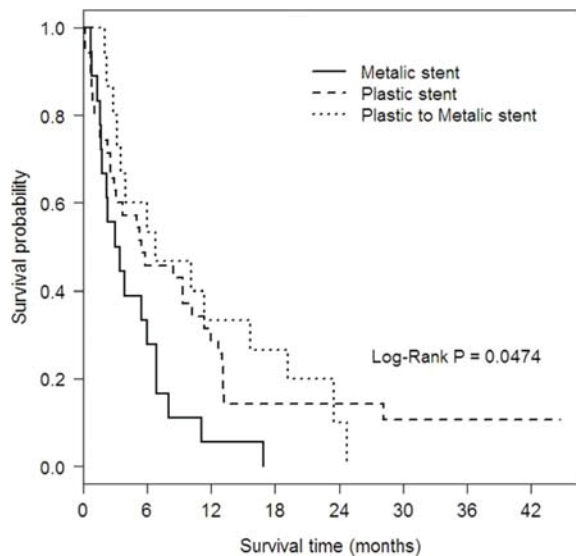


Figure 3. Kaplan-Meier survival curve of patients with distal malignant biliary stricture after endoscopic biliary drainage between each type of the stent.

palliative biliary drainage was higher in patients, who used the metal stent due to the sheer cost of such metal stents being higher than plastic stents by about 10 times. This finding made the cost of endoscopic biliary drainage with plastic stent lower than that of the metal stent, without significant difference in the median survival time or efficacy of biliary drainage. Hence this finding demonstrated an overall economic advantage.

The present study had some limitations. Firstly, it is a small sample sized, non-randomized retrospective study, and the distributions of baseline characteristics were unequal between groups. Secondly, the biliary stent types were chosen and the procedures were undertaken at the discretion of the attending physicians. Additionally, the present study had no predefined follow-up protocol; most of the stents were changed as per appointed schedules, symptoms/signs of stent dysfunction. Some patient's data were limited in a reason of re-interventions, stent clogging or migration and cause of patient death. Thus, this study could not strongly compare the efficacy and survival time of these 2 types of stent because of unequal stage of the disease in each group. However, to our knowledge, there has been no study that compares the cost and efficacy of metal stent based and plastic stent based endoscopic biliary drainage in these patients in Thailand, where the cost of ERCP was lower compared with the metal stent.

Conclusion

Palliative endoscopic biliary drainage with the use of plastic stent in unresectable DMBS was similar in the overall survival rate, nutritional status, efficacy of drainage and complications compared to that of metal stent or plastic followed with metal stent. However, the plastic stent incurred the lowest cost of the completed procedure.

What is already known on this topic?

Palliative biliary drainage with metal stent in unresectable DMBS is preferred to plastic stent unless the patient survival is short or there is distant metastasis.

What this study adds?

Palliative biliary drainage with plastic stents in unresectable DMBS has similar clinical outcomes and overall survival time compared with metal stents, but lower cost of total drainage procedure.

Acknowledgements

This study is funded by the Faculty of Medicine, Prince of Songkla University. The authors would like to thank Mr. Andrew Tait for correct the English grammar and review the present study.

Potential conflicts of interest

None.

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