

# Palliative Surgical Bypass versus Percutaneous Transhepatic Biliary Drainage on Unresectable Hilar Cholangiocarcinoma

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**Objective:** To compare the survival probability of unresectable hilar cholangiocarcinoma patients who have been managed by palliative surgical bypass versus percutaneous transhepatic biliary drainage (PTBD).

**Material and Method:** A historical (retrospective) cohort study was performed by retrospective and prospective data collection. From January 1, 2000 to December 31, 2002, all unresectable hilar cholangiocarcinoma patients who received only one type of palliative surgical bypass or PTBD in Srinagarind Hospital, Khon Kaen University were included in the present study. The patients were followed until December 31, 2004. Survival analysis was completed for all of the patients.

**Statistic analysis:** Survival analysis was analyzed with the Kaplan-Meier method, Cox regression analysis, and Log-rank test. A *p*-value of less than 0.05 was considered significant.

**Results:** During the study period, 83 patients were included. Palliative surgical bypass was performed in 42 patients and PTBD was performed in 41 patients. Demographic data, peri-operative complication rate, and late complication rate were comparable. The median survival time of the palliative surgical bypass group was 160 days (95%CI: 85.33, 234.67) and 82 days (95%CI: 29.76, 134.24) for PTBD group. Comparing survival experience by Log-rank test gave statistical significant difference (*p* = 0.0276). Hazard ratio was 0.599 (*p* = 0.03)

**Conclusion:** Survival rate of the palliative surgical bypass group was higher than the PTBD group. The survival rate of both groups was comparable to previous reports.

**Keywords:** Cholangiocarcinoma, Hilar, Klatskin's tumor, Unresectable, Palliative surgical bypass, PTBD, Survival rate

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The term 'cholangiocarcinoma' is defined as adenocarcinoma originating anywhere in the biliary tree. Although the entire biliary tree is potentially at risk, tumors involving the biliary confluence or the right or the left hepatic ducts (hilar cholangiocarcinoma or Klatskin's tumor) are most common and account for 40%-60% of all cases<sup>(1)</sup>. Most cases of hilar cholangiocarcinoma develop obstructive jaundice and die from liver failure and sepsis rather than from distant

metastasis<sup>(2)</sup>. Reports from experienced groups indicated that only 25%-35% of patients are resectable for cure at the time of diagnosis, and a 5-year survival after resection for cure is achieved in only 10%-20% of cases<sup>(3-5)</sup>. Palliations for relief of symptoms are the alternatives for the patients with unresectable hilar cholangiocarcinoma such as palliative surgical bypass, percutaneous transhepatic biliary drainage (PTBD), endoprostheses, etc.

The population of Northeast Thailand has one of the highest known rates of cholangiocarcinoma<sup>(6,7)</sup>. The Srinagarind Hospital, Khon Kaen University (KKU) is the main treatment center for cholangiocarcinoma in

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this area. In recent years, management of patients with unresectable hilar cholangiocarcinoma at our institute has been directed achieving palliative surgical bypass. Patients judged unsuitable for surgery based on clinical assessment or patients who refused surgery have been managed by PTBD. The main objective of the present study was to compare survival probability of unresectable hilar cholangiocarcinoma patients who were managed by palliative surgical bypass versus PTBD.

### Material and Method

The present study was designed as the historical (retrospective) cohort and was conducted after approval of the Khon Kaen University Ethics Committee for Human Research. The medical records of patients with unresectable hilar cholangiocarcinoma admitted to the Srinagarind Hospital, KKU from January 1, 2000 to December 31, 2002, were reviewed. The patients who were managed by only one type of palliative surgical bypass or PTBD were included in the present study. Demographic data, presenting symptoms, laboratory results, treatments, complications were recorded in retrospective data collection pattern. The patients or their relatives were contacted by mail or telephone to review the status of life until December 31, 2004. The survival data were recorded in a prospective data collection pattern.

### Statistic analysis

The Kaplan-Meier method was used to calculate survival probability and Cox regression analysis was used to calculate Hazard ratio (HR). The survival experience of the two groups was compared using Log-rank test. Continuous variables were compared using t-test and categorical variables were compared using Z-test. All data analysis was performed with statistical significant difference at the  $p$ -value  $< 0.05$ .

### Results

Eighty-three patients were included in the present study, 42 patients were assigned to the palliative bypass group and the other 41 patients to the PTBD group. Demographic data, presenting symptoms, and laboratory results were comparable (Table 1).

Statistically significant difference was observed in the mean hospital stay. Mean hospital stay was 25.88 (SD = 10.3) days in the palliative surgical bypass group and 13.39 (SD = 10.23) days in the PTBD group ( $p < 0.0005$ , 95% CI: 8.88, 16.20). The difference in number of co-intervention especially chemotherapy

in both groups (11 in the palliative surgical bypass group versus 1 in the PTBD group) showed statistically significant difference ( $p = 0.000105$ , 95% CI: 0.086, 0.389).

Overall peri-operative complication rate was comparable. The common complication was cholangitis that was found in both groups with no statistically significant difference. 'Bile leakage' was a specific complication that showed statistically significant difference, 4.76% in the palliative surgical bypass group compared 9.76% in the PTBD group (RR = 2.05, 95% CI: 1.11, 3.78). Peri-operative death was observed, 11.90% in the palliative surgical bypass group and 24.39% in the PTBD group, and showed statistically significant difference (RR = 2.05, 95% CI: 1.32, 3.19). There was no statistically significant difference in the late complication rate. The main complication was cholangitis.

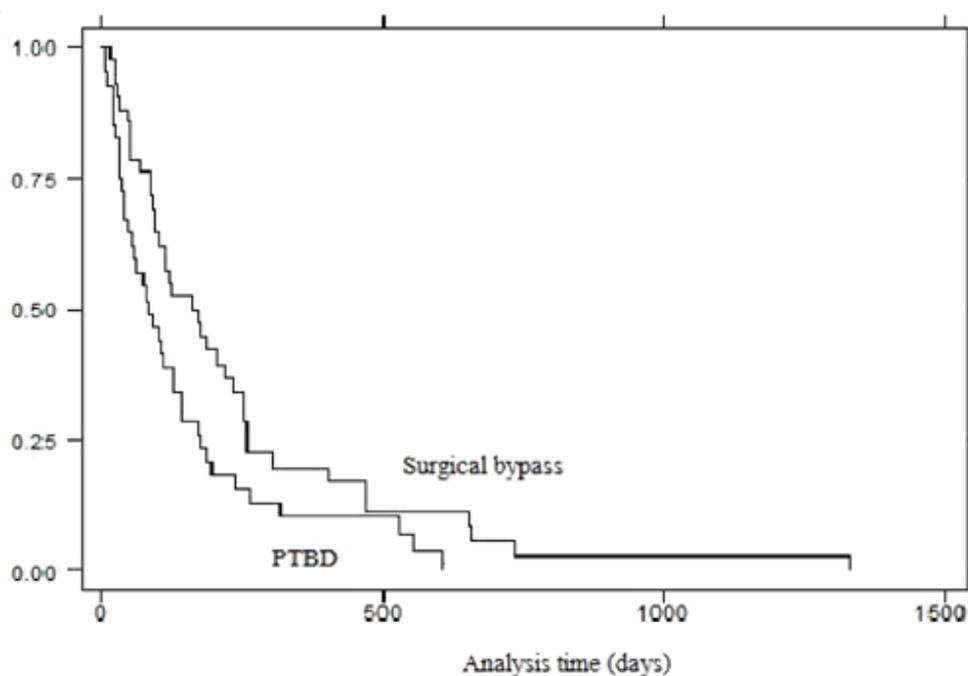
The PTBD group had catheter problems such as catheter obstruction and catheter dislodge. 'Catheter obstruction' was found 9.76% and 18.07% in the peri-operative and late periods, respectively. 'Catheter dislodge' occurred in 21.95% and 26.83% in the peri-operative and late periods, respectively. Catheter problems were the causes of catheter reinsertion or changing.

Survival analysis gave 39 cases of completed observation and 3 cases of censored observation in the palliative surgical bypass group and gave 38 cases of completed observation and 3 cases of censored observation in the PTBD group. Comparing survival experience by Log-rank test gave a statistically significant difference ( $p = 0.0276$ ). The median survival time of the palliative surgical bypass group was 160 days (95% CI: 85.33, 234.67) and 82 days (95% CI: 29.76, 134.24) for the PTBD group (Fig. 1). The 1-year and 1.5-year survival rates were 19.7% (95% CI: 8.9, 33.7) and 11.3% (95% CI: 3.6, 23.8) for the palliative surgical bypass group and 10.3% (95% CI: 3.3, 22.1) and 6.9% (95% CI: 1.5, 18.4) for the PTBD group, respectively. Probability of death of the palliative surgical bypass group was 0.599 times compared to the PTBD group (HR = 0.599,  $p = 0.03$ , 95% CI: 0.378, 0.952).

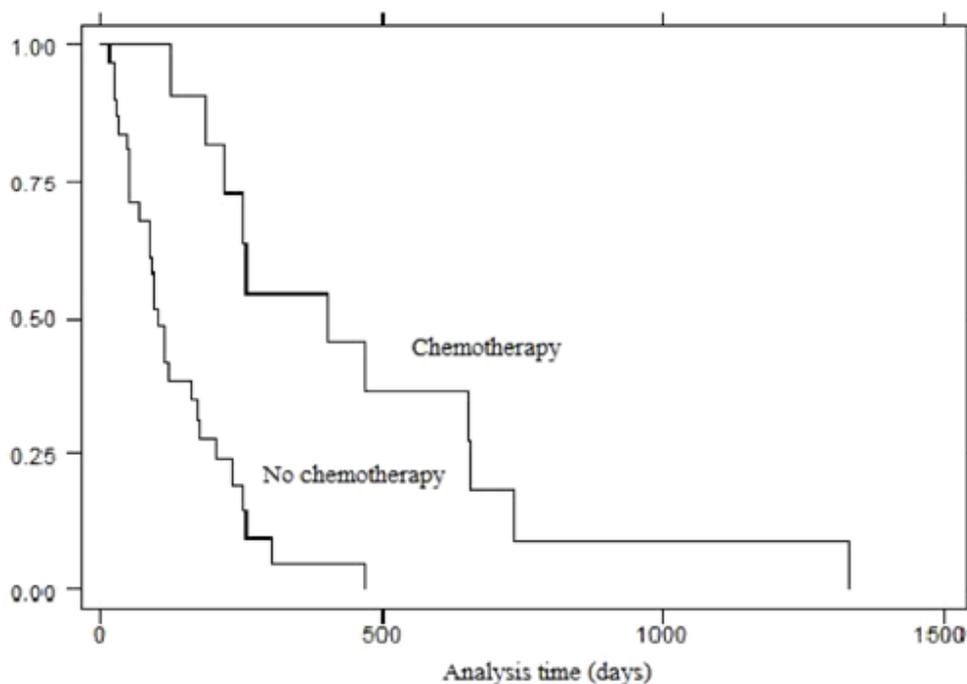
The authors were concerned about the effect of co-intervention on survival outcome. 'Chemotherapy' or 'No chemotherapy' had a significant impact on survival of the palliative surgical bypass group. Comparing survival experience by Log-rank test gave a statistically significant difference ( $p = 0.0003$ ). The median survival time of the chemotherapy group was 403 days (95% CI: 174.27, 631.73) and 99 days (95% CI: 72.82, 125.18) for the no chemotherapy

**Table 1.** Patient characteristics, presenting symptoms and laboratory results

	Palliative surgical bypass (n = 42)	PTBD (n = 41)
Male	30 (71.43%)	32 (78.05%)
Female	12 (28.57%)	9 (21.95%)
Age (year) (mean (SD))	58.26 (9.11)	60.07 (9.49)
Presenting symptoms (n (%))		
Abdominal pain	25 (59.52%)	23 (56.09%)
Jaundice	42 (100.00%)	41 (100.00%)
Dark urine	42 (100.00%)	41 (100.00%)
Pale stool	41 (97.62%)	41 (100.00%)
Pruritus	41 (97.62%)	41 (100.00%)
Weight loss	31 (73.81%)	34 (82.93%)
Fever	15 (35.71%)	20 (48.78%)
Laboratory results (n (%))		
Anemia	25 (59.52%)	31 (75.61%)
Leucocytosis	24 (57.14%)	22 (53.66%)
Azotemia	12 (28.57%)	10 (24.39%)
Hypoalbuminemia	21 (50.00%)	24 (58.54%)
Coagulopathy	21 (50.00%)	22 (53.66%)
Total bilirubin (mean (SD))	26.42 (8.79)	25.66 (10.55)
Direct bilirubin (mean (SD))	15.57 (5.43)	14.62 (5.23)
Alkaline phosphatase (mean (SD))	536.61 (326.25)	594.38 (334.51)



**Fig. 1** Kaplan-Meier survival curves of the palliative surgical bypass group and the PTBD group



**Fig. 2** Kaplan-Meier survival curves of the chemotherapy group and no chemotherapy group (subgroup of the palliative surgical bypass group)

group (Fig. 2). Probability of death of the chemotherapy group was 0.220 times compared to the no chemotherapy group (HR = 0.220,  $p = 0.001$ , 95% CI: 0.091, 0.531).

### Discussion

Cholangiocarcinoma is one of the major cancers in the Northeastern region of Thailand. Most patients presented with advanced hilar lesion that precluded curative treatment. Palliations for relief of symptoms seem to be the best care for these patients. Palliative surgical bypass is an aggressive treatment when compared to other treatments. Nowadays, PTBD is a desired option for these patients especially those who do not tolerate the aggressive treatment.

The present study shows that the survival outcome of the palliative surgical bypass group was better than the PTBD group, but, the palliative surgical bypass group had more co-intervention especially chemotherapy that affected survival outcome. Peri-operative complications of both groups were similar except the PTBD group, which had more bile leakage than the palliative surgical bypass group. The palliative surgical bypass group had less peri-operative death than the PTBD group. Late complications of

both groups were similar. The common complication of both periods was cholangitis.

The mean hospital stay of the palliative surgical bypass group was longer than the PTBD group. This may explain why patients in the palliative surgical bypass group received more aggressive procedure, so they needed more time for preparing the patients before the operation and for recovery after the operation.

When comparing the results of each group to previous studies, we can see the following for the palliative surgical bypass group. The median survival time is similar to the Nordback's study<sup>(8)</sup>, but shorter than Jarnagin's study<sup>(9)</sup>. The peri-operative complication rate is similar to Nordback's study and Jarnagin's study. The common complication is cholangitis that is similar to Nordback's study, but in contrast to Jarnagin's study that the common complication was anastomosis leakage.

For the PTBD group, the median survival time is similar to Joseph's study<sup>(10)</sup>, but shorter than Milella's study<sup>(11)</sup>. Catheter problem and peri-operative death are lower than Joseph's study. Catheter problem is a leading cause of re-do intervention and readmis-

sion, so it increases the risk of catheter related infection. This may increase the cost and time of PTBD.

In conclusion, nowadays, the survival outcome of the patients with unresectable hilar cholangiocarcinoma has not improved and peri-operative complications were unchanged. The present study shows that palliative surgical bypass was not truly better than PTBD because there may be an effect from co-intervention especially chemotherapy. Future study should be carried out on other interventions that may affect the survival outcome.

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**ผลการรักษาผู้ป่วยมะเร็งท่อน้ำดีบริเวณขั้วตับชนิดที่ไม่สามารถผ่าตัดเอาเนื้อมะเร็งออกได้หมด:  
การผ่าตัด ทำทางลัดท่อน้ำดี เปรียบเทียบกับการใส่ท่อระบายน้ำดีออกภายนอกร่างกาย**

ณรงค์ชัย ว่องกลกิจศิลป์, เอก ปักเข็ม, เกรียงศักดิ์ เจนวิถีสุข, โกวติอ แซ่เขียว, วัชรพงศ์ พุทธิสวัสดิ์

**วัตถุประสงค์:** เพื่อศึกษาผลการรอดชีพของผู้ป่วยมะเร็งท่อน้ำดีบริเวณขั้วตับ ชนิดที่ไม่สามารถผ่าตัดเอาเนื้อมะเร็งออกได้หมดโดยการผ่าตัดทำทางลัดท่อน้ำดี เปรียบเทียบกับการใส่ท่อระบายน้ำดีออกภายนอกร่างกายในโรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น

**วัสดุและวิธีการ:** ทำการศึกษาเชิงวิเคราะห์แบบเก็บข้อมูลย้อนหลังและไปข้างหน้าในผู้ป่วยมะเร็งท่อน้ำดีบริเวณขั้วตับชนิดที่ไม่สามารถผ่าตัดเอาเนื้อมะเร็งออกได้หมดโดยการผ่าตัดทำทางลัดท่อน้ำดี และการใส่ท่อระบายน้ำดีออกภายนอกร่างกาย ในโรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น ตั้งแต่ 1 มกราคม พ.ศ. 2543 ถึง 31 ธันวาคม พ.ศ. 2545 และเฝ้าติดตามผู้ป่วยจนถึง 31 ธันวาคม พ.ศ. 2547

**สถิติ:** ใช้การวิเคราะห์ระยะปลอดเหตุการณ์โดยใช้ Kaplan-Meier method, Cox regression analysis และ Log-rank test

**ผลการศึกษา:** ผู้ป่วยทั้งหมด 83 คน ผู้ป่วย 42 คน ได้รับการผ่าตัดทำทางลัดท่อน้ำดี ผู้ป่วย 41 คน ได้รับการใส่ท่อระบายน้ำดีออกภายนอกร่างกาย ข้อมูลพื้นฐาน อัตราการเกิดภาวะแทรกซ้อนในระยะสั้นและระยะยาวของ ทั้ง 2 กลุ่มใกล้เคียงกัน ระยะรอดชีพเฉลี่ยของกลุ่มที่ได้รับการผ่าตัดทำทางลัดท่อน้ำดีเท่ากับ 160 วัน (95%CI: 85.33, 234.67) ระยะรอดชีพเฉลี่ยของกลุ่มที่ได้รับการใส่ท่อระบายน้ำดีออกภายนอกร่างกายเท่ากับ 82 วัน (95%CI: 29.76, 134.24) การรอดชีพของทั้ง 2 กลุ่มมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ( $p = 0.0276$ ) และ Hazard ratio เท่ากับ 0.599 ( $p = 0.03$ )

**สรุป:** ผลการรอดชีพของผู้ป่วยมะเร็งท่อน้ำดีบริเวณขั้วตับชนิดที่ไม่สามารถผ่าตัดเอาเนื้อมะเร็งออกได้หมดโดยการผ่าตัดทำทางลัดท่อน้ำดี ดีกว่าการใส่ท่อระบายน้ำดีออกภายนอกร่างกาย ผลการรอดชีพของทั้ง 2 กลุ่มใกล้เคียงกับการศึกษาก่อนหน้านี้

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