

Research Article
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Biliary Tract Cancer Retrospective Analysis of Last 10 Years

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ABSTRACT

Surgical resection could offer the only chance of a long-term survival for biliary tract cancer.

In fact, only a small number of these patients can undergo surgery with curative intent. The majority receive palliative chemotherapy or other systemic treatments. In patients with localized disease the only treatment is a complete resection.

We present herein our experience with 33 patients the last 10 years and summarize the surgical strategies and prognostic factors focusing on the role of surgical resection.

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 BTCs are known to have poor prognosis with an estimated 5-year overall survival rate $\leq 20\%$ when all cases and stages are analyzed together, and this result is attributable to the high rate of diagnosis in the advanced stages [2].

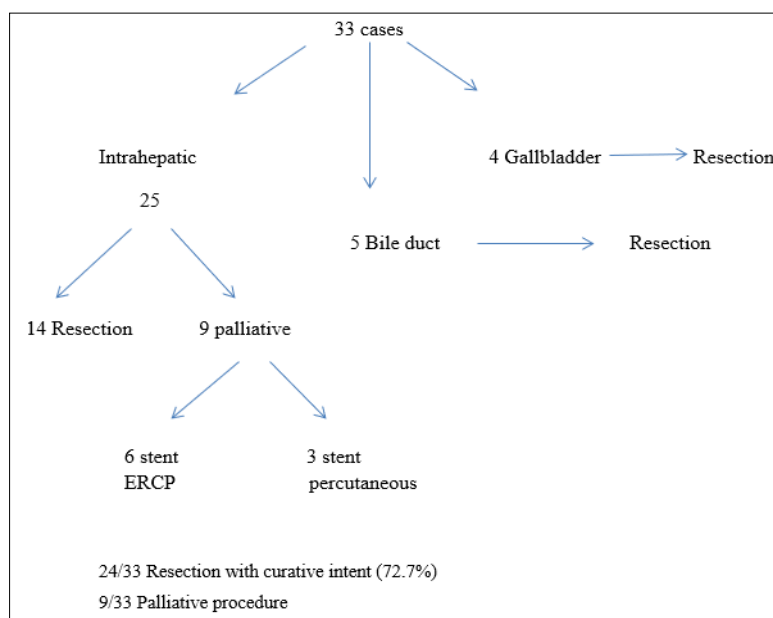
Introduction

 Biliary tract cancers (BTCs) are rare cancers with estimated incidence of < 6 cases per 100.000 habitants [1].

 In addition, for those patients diagnosed in early stages relapse rates remains high at $> 50\%$.

However, incidence is increasing mainly due to an increasing incidence of intrahepatic tumors (iCCA).

We present a retrospective analysis of our cases with biliary tract cancer in the last 10 years.


Figure 1: Biliary Tract Cancers

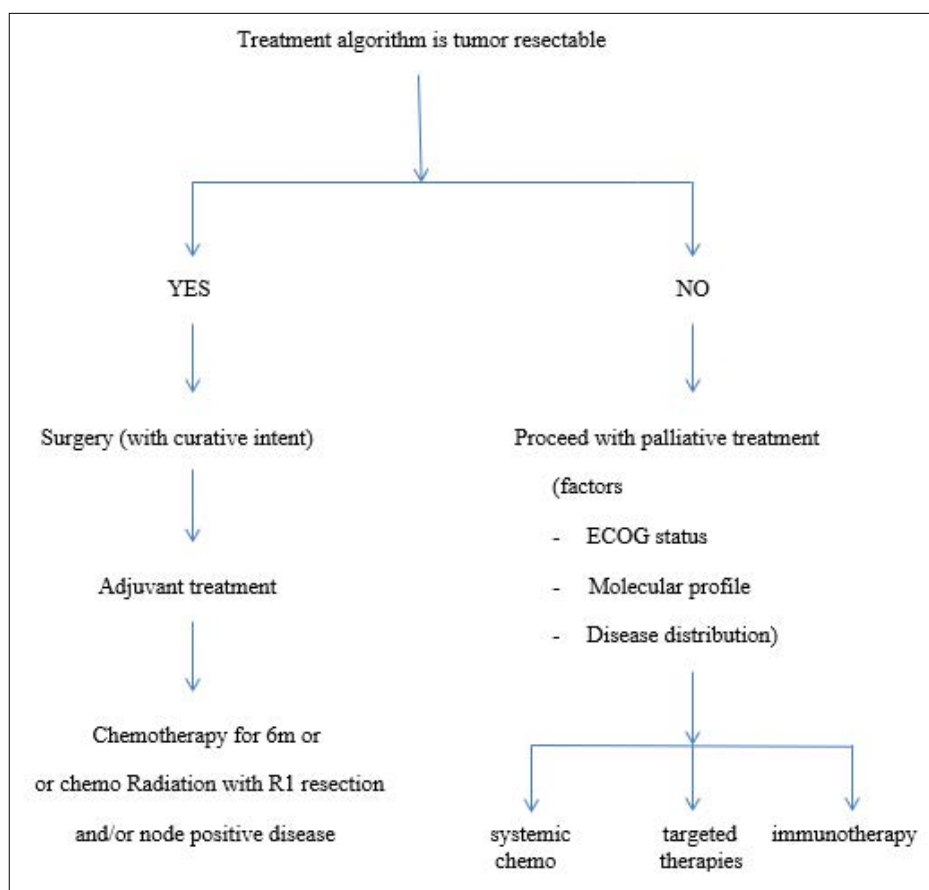


Figure 2: Treatment Algorithm

Material and Methods

From May 2013 until May 2023, thirty three patients biliary tract carcinoma are treated by the same team. The cancer distribution and treatment are presented in Figure 1.

Of the 33 patients, 12 are females and 21 mails.

The treatment algorithm of our team is presented in Figure 2. All patients are discussed in multidisciplinary tumor conference meeting and we observed the role of sex, age, tumor location and surgical treatment in Overall Survival (O.S.) and Disease Free Survival (DFS) as end-points of our study.

The complication raters are also evaluated.

Time-to-event outcomes were estimated using Kaplan-Meier curves. The log-rank test was used to assess the effect of the predictors, respectively, on Overall Survival (OS) and Disease-Free Survival (DFS). OS defined as the time from the surgery time to death (for any reason). DFS defined as the time from the surgery time to the recurrence of the disease or death (for any reason).

Continuous data are reported as median and categorical data are reported as number. All p values < 0.05 were considered to be statically significant. All data were analyzed using SPSS software version 26.0 (SPSS Inc., Chicago, IL) for Windows.

Results

Of the 33 patients included in the analysis, 12 females and 21 males, the 17 (51.5%) were <55 years old. 21 patients (63.6%) have died whereas 12 (36.4%) were the censored cases. The median overall survival time was 26 months (95% CI: 16.3 - 35.7). The median disease-free survival time was 18 months (95% CI: 7.4 - 28.6).

For age <55 years the median overall survival time was 28 months (95% CI: 4 - 52). For age ≥55 years the median overall survival time was 26 months (95% CI: 18.8 - 33.2).

A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of age. The survival distributions for the group of age <55 years wasn't statistically different from group of age ≥55 years, $\chi^2(1) = 1.318$ (p = 0.251).

For women the median overall survival time was 40 months (95% CI: 16.3 - 63.7). For men the median overall survival time was 16 months (95% CI: 5.5 - 26.5). A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of biological sex. The survival distributions for the women weren't statistically different from men, $\chi^2(1) = 2.618$ (p = 0.106).

For Common Bile duct the median overall survival time was 16 months (95% CI: 8.3 – 23.7). For Gallbladder the median overall survival time was 26 months (95% CI: not enough people with overall survival situation yet to estimate the lower and upper confidence). For Intrahepatic the median overall survival time was 26 months (95% CI: 16.2 – 35.8). For Left Lobe the median overall survival time was 48 months (95% CI: not enough people with overall survival situation yet to estimate the lower and upper confidence). For Right Lobe the median overall survival time was 14 months (95% CI: 6.3 – 21.7).

A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of location. The survival distributions for the location group were not statistically significantly different, $\chi^2(4) = 2.357$ ($p = 0.670$).

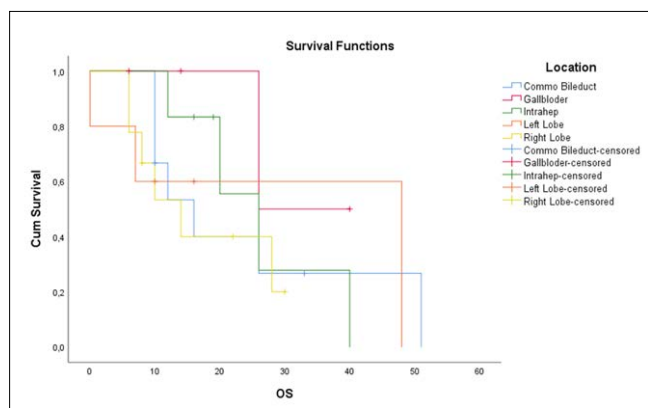


Figure 3: Survival Functions

For Hepatectomy the median overall survival time was 28 months (95% CI: 19.7 – 36.3). For Resection the median overall survival time was 26 months (95% CI: 2 – 50). For Stent the median overall survival time was 10 months (95% CI: 7.7 – 12.3).

A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of type of surgery. The survival distributions for the type of surgery group were statistically significantly different, $\chi^2(2) = 18.948$ ($p < 0.001$). Pairwise analysis showed that:

- Survival distribution of Stent was statistically different from Resection distribution, $\chi^2(1) = 4.994$ ($p = 0.025$).
- Survival distribution of Stent was statistically different from Hepatectomy distribution, $\chi^2(1) = 17.660$ ($p < 0.001$).

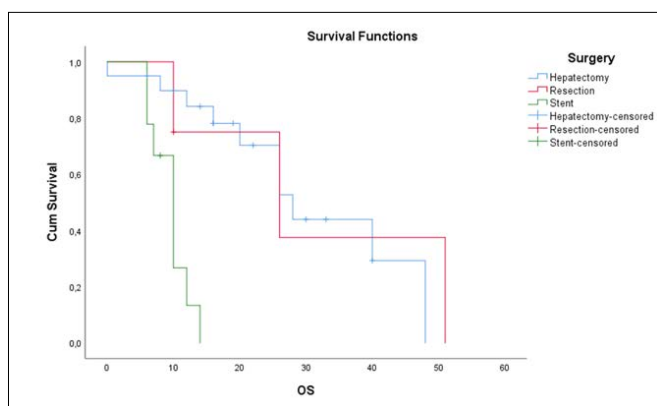


Figure 4: Survival Functions

For Common Bile duct the median disease-free survival time was 12 months (95% CI: 0 – 31.5). For Gallbladder the median disease-free survival time was 20 months (95% CI: not enough people with disease-free survival situation yet to estimate the lower and upper confidence). For Intrahepatic the median disease-free survival time was 18 months (95% CI: 7.5 – 28.5). For Left Lobe the median disease-free survival time was 40 months (95% CI: not enough people with disease-free survival situation yet to estimate the lower and upper confidence). For Right Lobe the median disease-free survival time was 4 months (95% CI: 0 – 13.8).

A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of location. The survival distributions for the location group were not statistically significantly different, $\chi^2(4) = 2.956$ ($p = 0.565$).

For Hepatectomy the median disease-free survival time was 20 months (95% CI: 8 – 32). For Resection the median disease-free survival time was 18 months (95% CI: 0 – 39). For Stent the median disease-free survival time was 0 months (95% CI: not enough people with disease-free survival situation yet to estimate the lower and upper confidence).

A log rank test was conducted to determine if there were differences in the survival distribution for the different groups of type of surgery. The survival distributions for the type of surgery group were statistically significantly different, $\chi^2(2) = 23.002$ ($p < 0.001$). Pairwise analysis showed that:

- Survival distribution of Stent was statistically different from Resection distribution, $\chi^2(1) = 8.533$ ($p = 0.003$).
- Survival distribution of Stent was statistically different from Hepatectomy distribution, $\chi^2(1) = 19.705$ ($p < 0.001$).

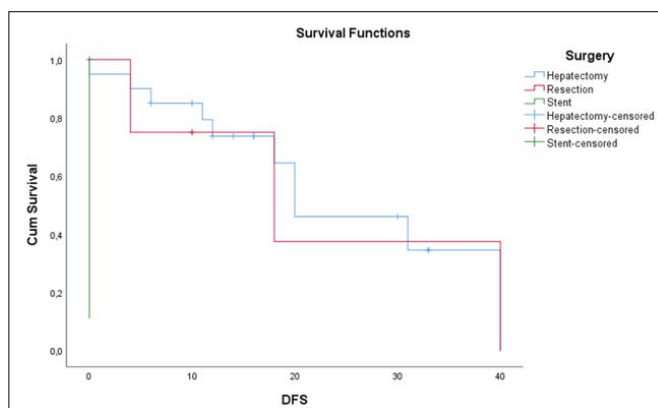


Figure 5: Survival Functions

Morbidity and Mortality Rates

There is one postoperative death (3.03%) due to massive pulmonary embolism in a 47 years old man with left liver hepatectomy for an intrahepatic cholangiocarcinoma.

There are three reoperations due to intra-abdominal bleeding and two cases of bile leakage which treated with total parenteral nutrition and intravenous antibiotics.

The mean hospital stay was 9.3 days (6-34) and the mean ICU stay was 1.8 days (1-14).

All these results presented in table 1.

Table 1: Post-Operative Events

Mortality	1:33	3.03%
Morbidity		
Intra-abdominal bleeding re-operation	3:33	9.1%
Bile leakage	2:33	6%
Wound infection	4:33	12.1%
Other	4:33	12.1%

Table 2: Cholangiocarcinoma

Nº	Age	Sex	Location	Surgery	DFS	OS	Follow-up
1	60	♂	Intrahep L	Cent Hep.	12	19	Alive
2	71	♂	Intrahep R	Cent Hep.	18	26	Death
3	48	♀	Intrahep R	Cent Hep.	6	12	Death
4	59	♀	Intrahep R	Right Hep.	31	40	Death
5	67	♀	Intrahep R	NAR	11	20	Death
6	44	♂	Intrahep R	Right Hep.	16	16	Alive
7	53	♂	Right Lob	Right Hep.	20	28	Death
8	48	♂	Right Lob	Right Hep.	16	22	Alive
9	37	♀	Right Lob	NAR	30	30	Alive
10	68	♂	Right Lob	NAR	4	8	Death
11	62	♂	Left Lob	Left Hep.	16	16	Alive
12	74	♀	Left Lob	Left Hep.	40	48	Death
13	61	♂	Left Lob	NAR	10	10	Alive
14	47	♂	Left Lob	Left Hep.	Death PostOPC		
15	46	♂	Common B D	Left Hep.	33	33	Alive
16	41	♀	Common B D	Resection	10	10	Alive
17	36	♀	Common B D	Resection	40	51	Death
18	35	♂	Common B D	Resection	4	10	Death
19	44	♂	Common B D	Right Hep.	12	16	Death
20	58	♂	Common B D	Resection	18	26	Death
21	73	♀	Gallbladder	NAR	20	26	Death
22	38	♀	Gallbladder	Right Hep.	14	14	Alive
23	44	♀	Gallbladder	Right Hep.	6	6	Alive
24	42	♂	Gallbladder	NAR	33	40	Alive
25	57	♂	Right Lob	Stent	0	10	Death
26	59	♂	Right Lob	Stent	0	6	Death
27	60	♂	Left Lob	Stent	0	7	Death
28	67	♂	Common B D	Stent	0	10	Death
29	47	♂	Common B	Stent	0	12	Death
30	58	♂	Right Lob	Stent	0	14	Death
31	62	♀	Right Lob	Percutaneous	0	8	Alive
32	35	♂	Right Lob	Percutaneous	0	6	Death
33	48	♀	Common B D	Percutaneous	0	10	Death

Discussion

Biliary tract carcinoma refers to a group of malignancies of the biliary epithelium. Based on anatomical origin is classified into the following categories:

- Intrahepatic Cholangiocarcinoma,
- Perihilar Cholangiocarcinoma,
- Distal Cholangiocarcinoma and
- Gallbladder Carcinoma [1, 2].

Surgical R0 resection with end porta hepatitis lymphadenectomy is the standard of care and offers the chance of long term survival [3].

However only a few patients are candidates for curative surgery due to distant metastasis or direct invasion of the major vessels [4].

Moreover even patients with R0 resection have poor outcome due to high rate of tumor recurrence.

The most important question which arises in the management of biliary cancer is what unresectable factors are there [5].

In these factors included the liver-metastasis the metastases to long, peritoneum and distal lymph nodes. Many discussion concerning the lymph nodes involved, define as N1 as metastases to lymph node in the hepatoduodenal ligament as resectable cases and N2 cases, metastasis to peripancreatic lymph node as unresectable cases. However in Japan, aggressive surgical resection is also being performed for cases N2 hilar cholangiocarcinoma and gallbladder cancer [6, 7].

In our group of patients, resection with curative intent was performed in 72.7% of the cases.

The intrahepatic involved with curative intent (resection plus hepatectomy) offers a median overall survival of 28 months (95% CI:19.7-36.3) versus 10 months (CI:7.7-12.3) for palliative stent placement (p<0.001).

The second main question is what are the prognostic factors after resection of bile duct cancer included in these factors are positive surgical margins, especially in the duct stump, lymph node metastasis, perineural invasion and combined surgical resection due to portal vein and/or hepatic artery invasion [8, 9]. The curative resectability of middle or lower bile duct cancer and also in the hilar cholangiocarcinoma is the absence of cancer remnant in the resection stump, but the lymph node metastasis is an important factor as well [10, 11].

There is also survival deference in right or left intrahepatic cholangiocarcinoma.

In our study the left intrahepatic cancer the median overall survival was 48 months and on the other hand the right intrahepatic cancer the median overall survival rate was 14 months (p<0.001).

Management of BT cancer requires significant expertise in patients' selection, interpretation of imaging and surgical experience.

As the incidence of these tumors increase and continue to present a challenge for clinicians [12]. Due the late diagnosis with occult clinical symptoms leads to the majority of patients presenting with locally unresectable or metastatic disease, and in resectable non metastatic disease R0 resection remains the only curative treatment. Therefore, the development of non-surgical treatment options is a pressing issue for these patients chemotherapy, targeted therapy, tumor agnostic treatment and immunotherapy are some treatments options for the majority of non-resectable patients but also as adjuvant systemic treatment in curative resected cases [13-15]. Data from these trials should lead to more effective treatment options for this "cold" malignancy.

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