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Prognostic factors in patients with advanced extrahepatic cholangiocarcinoma

A single center experience

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Abstract

Extrahepatic cholangiocarcinoma (ECC) is an aggressive malignancy causing a lot of fatalities and comorbidities. Endoscopic biliary stenting (EBS) is mostly needed for ECC. In this study, we aimed to investigate the prognostic factors for the overall survival (OS) and the factors predicting the patients eligible for chemotherapy after EBS in ECC.

We retrospectively screened 153 advanced ECC patients who underwent EBS for jaundice to make the patients eligible for chemotherapy. Patient's clinical and laboratory parameters were recorded. OS was estimated by the Kaplan–Meier method. All parameters were assessed by binary logistic regression analysis to predict which patients are eligible for chemotherapy.

The median OS of all patients was 12.0 months (10.1–13.8). The median OS of the patients treated with chemotherapy was 13.0 months (12.0–14.0), while it was 4.0 months (2.3–5.7) for patients unable for chemotherapy after EBS. Albumin, aspartate aminotransferase (ALT) and carbohydrate antigen 19-9 (CA 19-9) values were independent prognostic factors for OS. Higher albumin and lower prothrombin time (PT) levels were independent parameters to predict the patients eligible for chemotherapy after EBS.

Being suitable for chemotherapy was the main determinant for prolonged survival and albumin and PT levels were independent predictors for chemotherapy eligibility after EBS. Albumin, ALT, and CA 19-9 values were independent prognostic factors for OS in ECC.

Abbreviations: ALP = alkaline phosphatase, ALT = aspartate aminotransferase, AST = alanine aminotransferase, AUC = area under the curve, BTC = advanced biliary tract cancer, CA19-9 = carbohydrate antigen 19-9, CG = cisplatin with gemcitabine, CI = confidence Interval, EBS = endoscopic biliary stenting, ECC = extrahepatic cholangiocarcinoma, ECOG = Eastern Cooperative Oncology Group, HR = hazard ratio, LFT = liver function tests, NLR = neutrophil/lymphocyte ratio, OS = overall survival, PT = prothrombin time, ROC = receiver operating characteristic.

Keywords: effectiveness, endoscopic biliary stenting, extrahepatic cholangiocarcinoma, overall survival, predictive factors, prognostic factors

1. Introduction

Advanced biliary tract cancer (BTC) has an aggressive clinical course with low overall survival (OS) rates of 10.4 to 11.7 months and has limited sequential chemotherapy options with low response rates.[1–4] BTC includes a heterogeneous group of cancers which have distinct clinical courses and treatment options: gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma (ECC) divided as perihilar and distal cholangiocarcinoma.[5,6] Since the subtypes of BTC have different treatment options and response rates to chemotherapy, they should be evaluated separately in terms of prognostic factors in our opinion.[2,7] In this regard, we evaluated the prognostic clinical and laboratory parameters on patients with ECC to generate useful information for patients with this dismal group of diseases.

Patients with ECC mostly present with jaundice requiring endoscopic biliary stenting (EBS) which could be placed as plastic or metal. Initial insertion of a plastic stent is mostly cost-effective if the patient's life expectancy is shorter than 4 months according to the European Society of Gastrointestinal Endoscopy clinical guideline.[8] On the other hand, metal stenting has fewer dysfunction and longer survival, but it is suggested only for the patients predicted to have longer survival. Biliary obstruction causes elevated liver function tests (LFT) and attacks of cholangitis, putting an obstacle to effective systemic therapy and decreasing quality of life. Thus EBS is mostly required to restore forward biliary drainage. However, we encounter patients who are unable for chemotherapy even after EBS due to rapid disease progression and worsening Eastern Cooperative Oncology Group (ECOG) performance status (PS) or worse LFT. Although EBS is a rather simple 1-day procedure for the experienced gastroenterologist, it is not without side effects. Apart from endoscopy itself, a stent may have complications like misplacement, displacement, obstruction, perforation, bleeding, stent fracture or collapse, and infection. Since palliation is the main goal for terminal patients, those with a worse low ECOG PS and

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those ineligible for chemotherapy, plastic stents should be the treatment of choice. Therefore, it is crucial to select patients into 1 of these 2 categories (those with short survival and only require palliation and plastic stend placement or longer survival eligible for anticancer chemotherapy or metal stend placement) if possible right from the start. Furthermore, post-EBS chemotherapy was found to be an independent prognostic factor to predict a better survival after stenting in a previous study.[9] To our best of knowledge, the evidence is lacking. To answer this critical question, we aimed to investigate the prognostic factors for the OS and the factors predicting the patients eligible for chemotherapy after EBS in ECC.

2. Materials and methods

2.1. Study design

This was a single center retrospective study at Gaziantep University Hospital in Turkey. It was approved by the Institutional Ethics Committee and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

Its primary aim was to identify the prognostic parameters on the OS in ECC and second to assess the factors predicting the patients eligible for chemotherapy after EBS in patients with ECC.

2.2. Patients

We retrospectively screened patients diagnosed with ECC between November 2012 and December 2016 and who were not eligible for curative, or locoregional treatment options and also who underwent EBS due to the elevation of cholestasis enzymes. All patients enrolled had histopathological evidence for the diagnosis of ECC. After EBS, patients with ECOG PS of $\leq$2 and alanine aminotransferase (AST) and aspartate aminotransferase (ALT) of lower than 4 times of upper limit, total bilirubin levels of lower than 5 mg/dL and sufficient haematologic parameters were evaluated as suitable for chemotherapy. Platinum with gemcitabine therapy administered as first-line treatment and fluoropyrimidine-based chemotherapies for as second and further-lines. At least 2 cycles of chemotherapy were provided for considering to be received chemotherapy. Even metronomic treatment was evaluated as a chemotherapy line. Patients who were not eligible for chemotherapy due to reasons other than high LFT were excluded and these patients received palliative treatment.

Patient's age, gender, location of tumor (hilar or distant tumor), liver-limited disease or nonhepatic metastasis status, prestenting AST (IU/L) and ALT (IU/L), direct bilirubin (mg/dL), albumin levels (gr/dL), carbohydrate antigen 19-9 (CA19-9), alkaline phosphatase (ALP [U/L]), thrombocyte level, neutrophil/lymphocyte ratio (NLR), prothrombin time (PT) before EBS and whether the patient is eligible for chemotherapy or not, number of chemotherapy line after EBS were recorded. LFT after EBS was recorded. Serum biomarkers were measured with a spectrophotometric method using an autoanalyzer. Kinetic photometric assay for AST and ALT and endpoint photometric assay for total bilirubin and albumin were used. Values of an upper limit of normal were 35 IU/L, 35 IU/L, 0.2 mg/dL, 5.2 g/dL, 40 U/Ml, and 120 IU/L for AST, ALT, direct bilirubin, albumin, CA19-9, and ALP, respectively. Cut-off values based on the median value of the samples were used for all parameters.

2.3. Statistics

Laboratory variables were initially recorded as continuous variables and later dichotomized according to the median value of each variable including NLR, thrombocyte count, PT, direct bilirubin, ALP, AST, and ALT levels. Only CA 19-9 was evaluated as the continuous variable.

Clinical, demographic data, and laboratory values that could predict the patients who are suitable for chemotherapy after EBS and have an effect on OS were determined.

OS was estimated by the Kaplan–Meier method. We first performed a univariate assessment of the prognostic effect of each factor, comparing survival curves by the log-rank test. All potential prognostic factors with a probability value of <0.10 on univariate analyses were included in the multivariate Cox proportional hazard regression models. *P*-values of less than or equal to .05 were considered statistically significant and statistical analyses were carried out using the statistical software package SPSS 22.0.

Receiver operating characteristic (ROC) curves analysis was used to assess sensitivity and specificity of parameters (albumin and PT) for chemotherapy eligibility. Area under the curve (AUC) was evaluated as significant if it was more than 0.6.

All parameters were assessed by binary logistic regression analysis to predict the patients who are eligible for chemotherapy after EBS. Then, multivariate binary logistic regression analysis was performed.

3. Results

3.1. Clinicopathological features

In total, 153 patients who underwent EBS with cholestasis at diagnosis were included in this retrospective study. Among them, 53 (37.3%) were female, the remaining 96 (62.7%) were male and their mean age was 59.7 ($\pm$9.1) years. One hundred fifteen patients (75.2%) had a liver-limited disease, the remaining had extrahepatic metastasis including lymph nodes, lung, adrenals, peritoneal, and bone. Seventy-two patients (47.1%) had a perihilar tumor, the remaining had distal ECC. Twenty (13.1%) of the patients had metal stents and the others had plastic stents. Demographical and clinical data were shown in Table 1.

We evaluated the LFT of all patients after EBS. Seventy-seven point eight percent of patients (n = 119) received chemotherapy after EBS. However, LFT did not improved in 11.1 of patients (n = 17) after EBS and this group was not eligible for chemotherapy. On the other hand, 11.1% of the patients (n = 17) showed improvement in LFT after EBS, but this group was also not eligible for chemotherapy due to rapid disease or clinic progression. Comparison of the baseline clinical variables between patients eligible for chemotherapy after EBS and the others were given in Table 2.

3.2. Prognostic parameters

The median OS of all patients was 12.0 months (95% confidence interval [CI]: 10.1–13.8). For chemotherapy, 119 patients (77.8%) were eligible. The median survival time of the patients treated with chemotherapy was 13.0 months (95% CI: 12.0–14.0), while, it was 4.0 months (95% CI: 2.3–5.7) for the patients who were not eligible for chemotherapy ($P < .001$).

Median OS of the patients with low level of AST was 14.0 months (95% CI: 12.6–15.3), whereas it was 8.0 months (95% CI: 6.9–9.1) for the patients with higher level of AST ($P < .001$). The median OS of the patients with low value versus high values of ALT, direct bilirubin, ALP and PT were 14.0 (12.8–15.2) versus 8.0 (6.2–9.8) months ($P < .001$), 14 (12.7–15.2) versus 8.0 (6.4–9.5) months ($P < .001$), 13.0 (11.9–14.1) versus 6.0 (4.9–7.1)

Table 1

Demographical and clinical data of patients with extrahepatic cholangiocarcinoma.

		N (%)
Gender	Female	57 (37.3)
	Male	96 (62.7)
Median age, yr		60
Stage	Liver-limited	115 (75.2)
	Metastatic	32 (20.9)
Stent	Metal	20 (13.1)
	Plastic	133 (86.9)
Location	Perihilar	72 (47.1)
	Distal	81 (52.9)
Number of EBS	1	48 (31.4)
	2	90 (58.8)
	3	15 (9.8)
Chemotherapy	Suitable	119 (77.8)
	Not suitable	34 (22.2)
Chemotherapy Lines	1	20 (13.1)
	2	51 (33.3)
	3	48 (31.4)

EBS = endoscopic biliary stenting, ECC = extrahepatic cholangiocarcinoma.

Table 2

Comparison of the baseline clinical variables between patients eligible for chemotherapy after EBS and the others.

	Chemotherapy eligible Patients (n = 119) (median[min-max])	Others (n = 34) (median [min–max])	*P*-value
Age, yr	59 (37–79)	63 (43–82)	.492
AST, IU/L	87 (41–229)	108 (61–311)	.080
ALT, IU/L	86 (47–256)	108.5 (60–330)	.017
Direct bilirubin, mg/dL	6.4 (4–18.6)	9.3 (3.7–20.1)	<.001
ALP, IU/L),	203 (130–525)	263 (147–516)	<.001
Albumin, g/dL	3.4 (2.4–4.5)	3 (2.4–3.6)	<.001
CA19-9, U/mL	240 (76–962)	268 (96–880)	.130
PT, s	14 (11–18.9)	16 (11–21)	<.001

ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate amino transferase, CA19-9 = carbohydrate antigen 19.9, D Bil = direct bilirubin, PT = prothrombin time.

months ($P < .001$), and 13.0 (12.0–14.0) versus 7.0 (5.0–8.9) months ($P = .059$), respectively. Median OS of the patients with high level of albumin was 14.0 (12.7–15.3) months, while it was 8 (6.6–9.5) months for the patients with low level of albumin ($P < .001$) (Figs. 1–3). Median OS was 12.0 (10.8–13.2) months for the patients with limited disease, and it was 7.0 (5.4–8.6) months for the patients with metastatic disease.

To determine the prognostic power of LFT and clinical parameters on OS, first univariate analyses were performed. Lower levels of AST (<88 IU L), ALT (<87 IU/L), direct bilirubin (<6.8 mg/dL), ALP (<238 mg/dL), and CA 19-9, higher levels of albumin (>3.3 g/dL) and liver-limited disease were strongly positive prognostic factors for prolonged OS in patients with ECC (Table 3). We did not add chemotherapy eligibility to multivariate analysis for OS due to a strong statistical association between LFT, CA 19-9, and chemotherapy suitability. Afterwards, we found that albumin (hazard ratio [HR], 2.09; 95% CI, 1.4–3.2; $P = .001$), ALT (HR, 1.70; 95% CI, 1.0–2.9; $P = .045$) and CA 19-9 (HR, 1.001; 95% CI, 1.000–1.002; $P = .017$) values were independent prognostic factors in multivariate analysis (Table 2). Chemotherapy eligibility rate was not added to the multivariate analysis due to strong correlation with LFTs.

3.3. The factors predicting the patients suitable for chemotherapy after EBS

EBS may enable patients to receive chemotherapy by correcting the liver functions to acceptable levels, representing a kind of measure of effectiveness. The factors predicting the patients who are eligible for chemotherapy after EBS with regard to both suitable ECOG PS and LFT were as follows: lower levels of AST, direct bilirubin, ALP, PT, CA 19-9, and higher albumin levels (Table 3). Higher albumin (odds ratio [OR]: 17.85, 95% CI: 2.136–142.8, $P = .008$) and lower PT levels (OR: 2.840, 95% CI: 1.097–7.352, $P = .031$) were determined as independent predictors in multivariate analyses (Table 4).

According to ROC curve analysis;

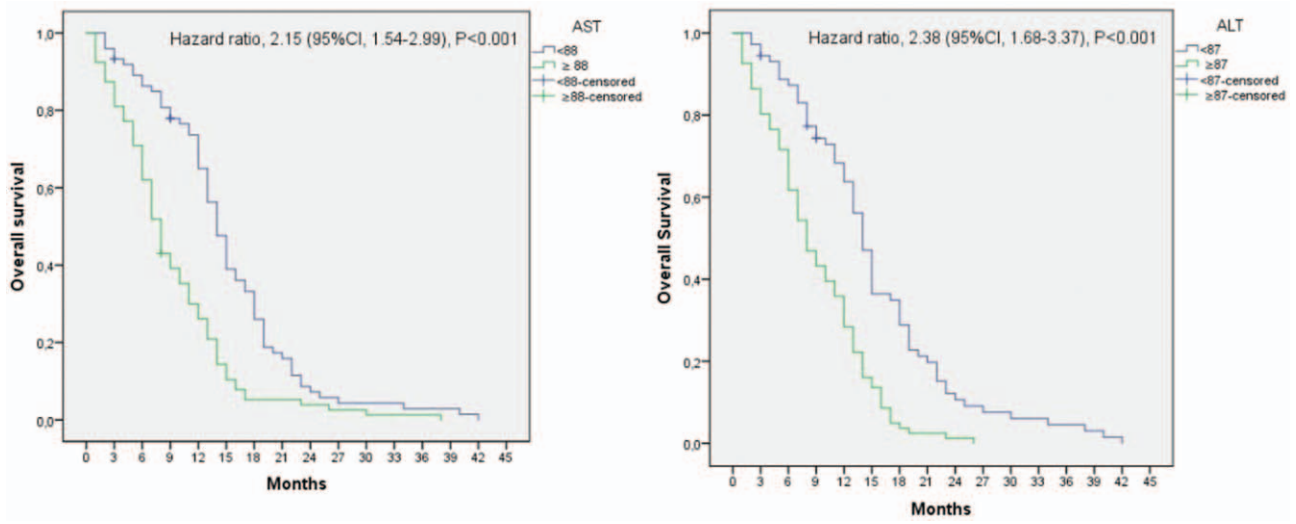

Figure 1. Association of AST and ALT with overall survival in patients with ECC in univariate analysis. ALT = alanine aminotransferase, AST = aspartate amino transferase, ECC = extrahepatic cholangiocarcinoma.

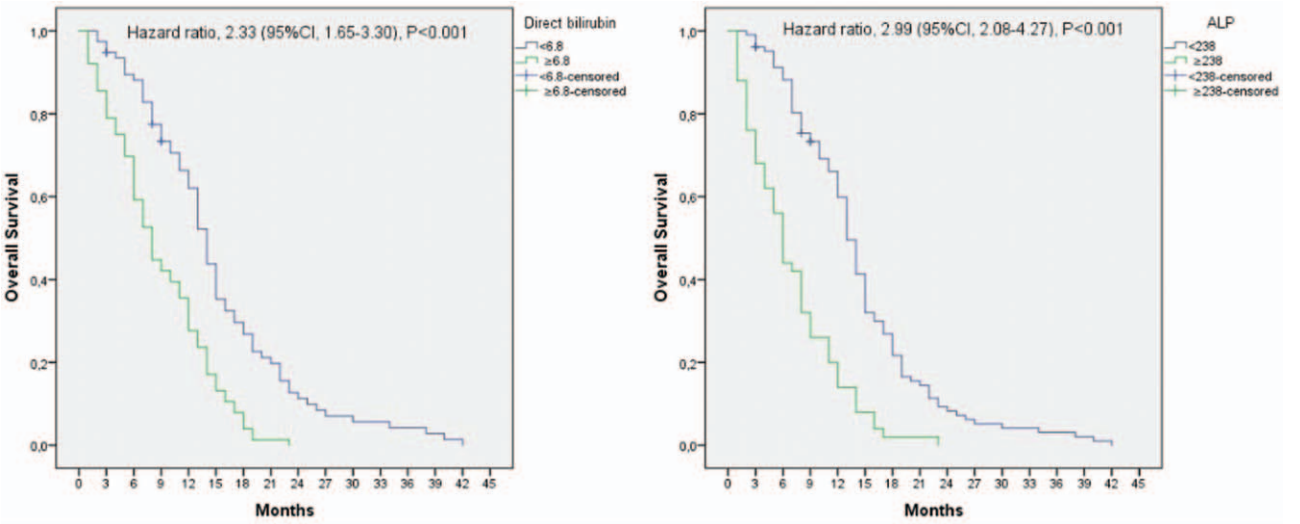

Figure 2. Association of ALP and direct bilirubin with overall survival in patients with ECC in univariate analysis. ALP = alkaline phosphatase, ECC = extrahepatic cholangiocarcinoma.

- When the cut-off value of PT was chosen as 14 seconds; AUC: 0.766 (95% CI 0.670–0.863), $P < .001$, sensitivity was %74, specificity was 64% for chemotherapy eligibility.
- When the cut-off value of albumin was chosen as 3.3 g/dL; AUC 0.756 (95% CI 0.678–0.834), $P > .001$, sensitivity was 66%, specificity was 83% for chemotherapy eligibility.

4. Discussion

Liver functions tests have prognostic significance in some types of cancer, such as gallbladder, colorectal cancers, and hepatocellular carcinoma.[10–12] Previously, it was shown that lower albumin and elevated levels of ALP, total bilirubin, direct bilirubin, and GGT were significantly correlated with shorter OS in patients with ICC,[13] however, they have not been studied comprehensively only in ECC patients until now. Owing not only its biologic pace but also to its strategic location, advanced ECC is a rapidly progressive disease deteriorates patient's general condition by worsening of LFTs due to the biliary obstruction which requires EBS. Therefore, an accurate evaluation of pretreatment clinical and laboratory parameters at diagnosis which has prognostic significance is essential during decision-making for the treatment plan to avoid unnecessary interventions. While EBS may be a simple procedure for an experienced gastroenterologist, it is not without side effects and risks. We evaluated the clinical and laboratory parameters including LFT to predict the OS in patients with ECC who had undergone biliary stenting procedure. Additionally, we separately assessed the parameters predicting the patients who would be suitable for chemotherapy after stenting. Accordingly, we showed that albumin, ALT and CA 19-9 values were determined as independent prognostic parameters for OS in ECC.

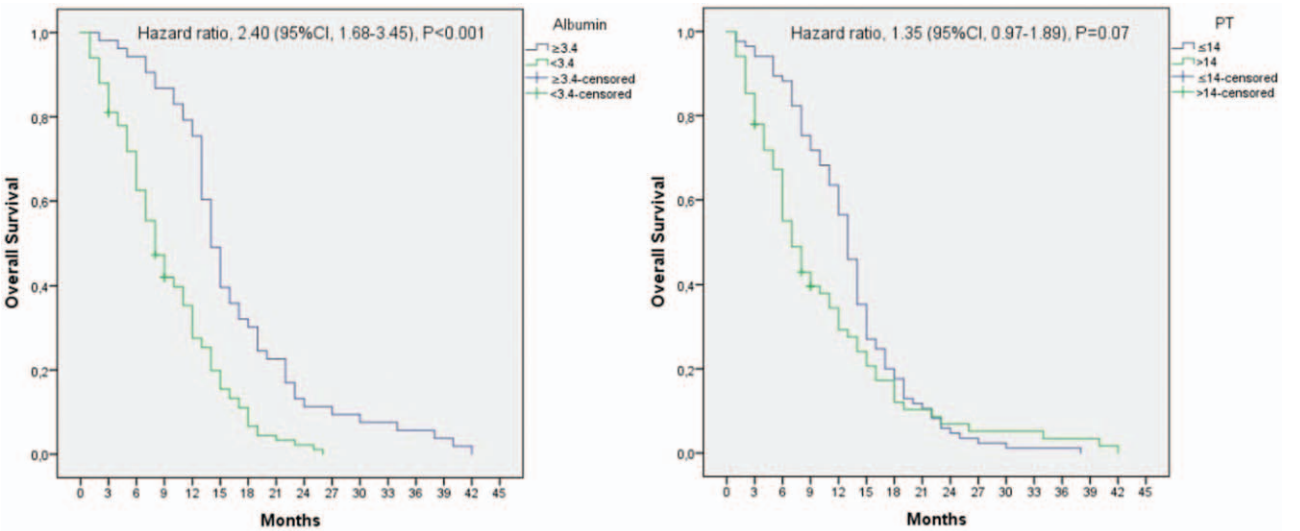

Figure 3. Association of albumin and prothrombin time with overall survival in patients with ECC in univariate analysis. ECC = extrahepatic cholangiocarcinoma.

Table 3

Prognostic factors on overall survival with univariate and multivariate analysis.

	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P*-value	HR (95%CI), *P*	*P*-value
Age: <65 versus >65	1.28 (0.6–1.2)	.25		
Gender: female versus male	0.55 (0.8–1.5)	.54		
Tumor location: hilar versus distal	0.42 (0.8–1.6)	1.14		
Stage: Liver limited versus metastatic	*1.61 (1.1–2.4)*	*.019*	1.11 (0.7–1.7)	.65
AST 88< versus ≥88 IU/L	*2.15 (1.5–3.0)*	*<.001*	1.36 (0.8–2.3)	.26
ALT 87< versus ≥87 IU/L	*2.38 (1.7–3.4)*	*<.001*	*1.70 (1.0–2.9)*	*.045*
Direct bilirubin <6.8 versus ≥6.8 mg/dL	*2.33 (1.7–3.3)*	*<.001*	1.36 (0.8–2.4)	.28
ALP 238< versus ≥238 mg/dL	*2.99 (2.1–4.3)*	*<.001*	1.77 (1.2–2.5)	.18
Albumin ≥3.4 versus <3.4 g/dL	*2.40 (1.7–3.5)*	*<.001*	*2.09 (1.4–3.2)*	*.001*
CA19-9U/L	*1.001 (1.000–1.002)*	*.003*	*1.001 (1.000–1.002)*	*.017*
NLR 2.4< versus ≥2.4	1.18 (0.8–1.7)	.33		
PT 14≤ versus >14 s	1.36 (1.0–1.9)	.073	1.38 (0.9–2.1)	.11
Thrombocyte 239 × 10^9/L< versus ≥	1.20 (0.9–1.7)	.27		

ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate amino transferase, CA19-9 = carbohydrate antigen 19.9, D Bil = direct bilirubin, HR (95%CI) = hazard ratio (95% confidence interval), NLR = neutrophil/lymphocyte ratio, OS = overall survival, PT = prothrombin time.

Based on ABC-02 and Japanese phase II trial, cisplatin with gemcitabine (CG) was approved standard first-line treatment of BTC, however, prognostic factors were not comprehensively evaluated.[1,3] Post-hoc analysis of the ABC-02 trial showed that stage, hemoglobin, bilirubin, and neutrophile levels as continuous variables were associated with OS in patients with ECOG PS 0 or 1.[14] On the other hand, hemoglobin level and neutrophil count were not found to be related to OS in British study when the cut-off values were chosen as the upper limit of normal.[15] The most comprehensive data included 740 patients with advanced BTC who were treated with first-line CG to determine the prognostic factors of BTC.[2] Accordingly, metastatic disease, poor ECOG PS, measurable disease, and elevated baseline CA 19-9 level were found as independent poor prognostic factors for OS. Although Kim et al found that elevated baseline CA 19-9 level was associated with negative survival, the Korean (Ca 19-9 compared as normal levels vs over)[7] and British studies (CA 19-9 compared as <1000 vs >1000)[15] did not found such an association. There were different results about the prognostic significance of CA 19-9 and other laboratory parameters, probably because of the different cut-off values and statistical methods. When we assessed the prognostic value of CA 19-9 levels only for patients with ECC, we showed that it was an independent prognostic parameter when chosen as continuously.

Albumin levels, that predict the survival of several cancer types, might be suppressed by malnutrition and cancer-related systematic inflammation and it can cause defective human immune defense mechanisms.[16–19] In the present study, levels of albumin were determined as independent prognostic parameters for OS in patients with ECC. Higher levels of albumin were also found as an independent predictor for patients who are eligible for chemotherapy after EBS. Correlation of albumin with poor ECOG PS, deteriorated liver function and higher tumor burden can explain this finding. Additionally, we first time evaluated the NLR, another inflammatory marker, in patients with ECC. Although NLR was observed to be associated with worse OS for several cancers types in literature, it was not found to be related with survival in our study.[20,21] Because a lot of other parameters may affect on OS of patients with ECC, this parameter can be found as insignificant.

Coagulation tests were not evaluated enough for the patients with BTC. Abali et al evaluated the effect of coagulation tests with ALT, AST, GTT, total bilirubin, direct bilirubin on OS in short survival and long survival groups who had pancreaticobiliary

Table 4

The factors predicting the patients suitable for chemotherapy after EBS.

	Univariate analysis		Multivariate analysis	
	OR (95%CI),	*P*-value	OR (95%CI)	*P*-value
Age: <65 versus >65	1.83 (0.8–4.1)	.14		
female versus male	0.69 (0.3–1.5)	.35		
Tumor location: hilar versus distal	1.36 (0.6–2.9)	.44		
Stage: Liver limited versus metastatic	2.04 (0.8–4.9)	.12		
AST 88< versus ≥88 IU/L	*2.79 (1.2–6.4)*	*.014*	*1.29 (0.3–4.9)*	*.77*
ALT 87< versus ≥87 IU/L	2.20 (1.0–4.9)	.055	1.11 (0.3–4.7)	.90
Direct bilirubin <6.8 versus ≥6.8 mg/dL	*2.60 (1.2–5.8)*	*.020*	2.05 (0.6–7.6)	.28
ALP 238< versus ≥238 mg/dL	*4.24 (1.9–9.4)*	*<.001*	1.74 (0.5–5.9)	.57
Albumin ≥3.4 versus <3.4 g/dL	*25.61 (3.4–193.4)*	*<.002*	*17.85 (2.1–142.8)*	*.008*
CA19-9U/L	*1.18 (1.1–1.3)*	*<.001*	1.001 (0.998–1.003)	.598
NLR 2.4< versus ≥2.4	1.17 (0.54–2.51)	.69		
PT 14≤ versus >14 s	*4.91 (2.1–11.5)*	*<.001*	*2.84 (1.1–7.4)*	*.031*

Multivariate binary logistic regression analysis was performed for liver function tests and CA 19-9.

ALP = alkaline phosphatase, CA19-9 = carbohydrate antigen 19-9, D Bil = direct bilirubin, NLR = neutrophil/lymphocyte ratio, OR (95%CI) = odds ratio (95% confidence interval), PT = prothrombin time.

cancer requiring biliary stenting and any association with OS were not found consistent with our study.[22] Patients with advanced cancer present with different degrees of abnormalities in coagulation tests.[23] For the first time, we evaluated the predictive value of PT on OS in such population. PT was found as a slightly prognostic parameter for OS and lower level of PT predicted the patients eligible for chemotherapy after stenting in our study. It also can be explained that higher PT reflects deteriorated liver function and higher tumor burden which are related with poor PS and low survival.

Higher levels of ALP was the other prognostic parameter for prolonged OS in the present study. This can be explained by the fact that ALP is an enzyme associated with cholestasis as well as an antigen associated with the tumor and higher activity in the nucleolus leads to tumor proliferation and progression.[24] On the other hand, ALT, the cellular markers of liver, indicating direct liver damage was found to be an independent prognostic marker for prolonged OS in ECC.

When we evaluate the clinical parameters such as age, gender, and tumor localization, none of them were related with OS, while the liver limited disease was a prognostic factor for longer OS in univariate analysis. In this regard, we can consider that patients with lower tumor volume are more advantageous for prolonged OS in ECC.

Furthermore, post-EBS chemotherapy was found to be an independent prognostic factor to predict a better survival after stenting in a previous study.[9] Since the patients who were able to receive chemotherapy after stenting may live longer than those who did not, we evaluated the chemotherapy suitability to select the patients who benefit more from EBS at diagnosis. Keeping in mind the aggressive biology of BTC, it is highly probable that a significant portion of biliary stentings is unnecessary in these patients. Thus, we should be wise to avoid ineffective but potentially harmful interventions like EBS or chemotherapy administration for patients who have possible low survival rates and not eligible for chemotherapy due to poor PS, with comorbidities, or absence of improvement in LFT after EBS. We found that higher albumin and lower PT values predicted the patients eligible for chemotherapy after EBS. A more cost-effective approach can be applied to these findings. Plastic stent placement can be selected for patients predicted to be unable for chemotherapy after EBS and metallic ones can be selected for patients predicted to be eligible for chemotherapy according to our findings.

The most important limitation of this study was that it was designed retrospectively. In addition, although all patients were under ECOG PS2 and below, the analysis was not performed according to the performance score.

This is the first study evaluating the prognostic parameters in ECC patients and achieving a homogeneous group of patients with a remarkable number of patients as 153. We also for the first time evaluated the parameters predicting the patients eligible for chemotherapy after biliary stenting in patients with ECC comprehensively. We showed that albumin, ALT, and CA 19-9 values were independent prognostic factors for OS in patients with ECC. Being suitable for chemotherapy was the main determinant for prolonged survival and albumin and PT levels were determined as independent predictors for chemotherapy suitability after biliary stenting. Since albumin and PT values are associated with the production function of the liver, and in this context are associated with tumor burden and liver involvement, this may prevent the patient from taking chemotherapy by worsening ECOG performance score. We believe that the prognostic parameters we identified will guide the clinicians in predicting patients who are more likely to benefit from chemotherapy administration, or who are only candidates for palliative treatment and plastic stent placement.

5. Conclusions

Being suitable for chemotherapy was the main determinant for prolonged survival and albumin and PT levels were determined as independent predictors for chemotherapy suitability after biliary stenting. Albumin, ALT, and CA 19-9 values were independent prognostic factors for OS in patients with ECC.

Author contributions

Conceptualization: Gokmen Aktas, Tulay Kus.
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