European Review for Medical and Pharmacological Sciences 2024; 28: 1554-1561

Factors affecting survival in patients undergoing percutaneous transhepatic biliary drainage for malignant biliary obstruction

Y. DUZKOPRU[1], T. EREN[1], A. KOCANOGLU[1], O. DOGAN[1], O.A. ISAK[1], O. ERGUN[2]

[1]Department of Medical Oncology, Ankara Etlik City Hospital, Ankara, Turkey
[2]Department of Radiology, Uskudar University, Istanbul, Turkey

Abstract. – OBJECTIVE: The general approach to malignant biliary obstruction (MBO) is to provide drainage in all patients with jaundice. However, the procedure is often palliative, and its contribution to survival is debated. This study aimed to investigate prognostic factors in patients undergoing percutaneous transhepatic biliary drainage (PTBD) for MBO.

PATIENTS AND METHODS: All laboratory values were divided into two groups based on median values: low and high. Chi-square analysis was performed for dichotomous data. The time from the PTBD procedure to the date of death or last follow-up was considered overall survival (OS). Univariate and multivariate analyses were calculated using the Cox regression model.

RESULTS: A total of 152 patients were included in the study, of whom 84 (55.3%) were male. The median OS was 71 ± 12.6 days (95% CI: 46.3-95.7). The 1, 3, 6, and 12-month OS rates were 74.3%, 45.2%, 29.2%, and 13%, respectively. In the multivariate analysis, comorbidity (p=0.029), Eastern cooperative oncology group performance status (ECOG PS) (p=0.007), pre-PTBD albumin (p=0.025), post-PTBD aspartate aminotransferase (p=0.025), chemo naive (p<0.001), and post-PTBD chemotherapy (CT) (p=0.01) were found to be independent prognostic factors.

CONCLUSIONS: In patients with poor prognosis MBO, the decision for PTBD should be made multidisciplinarily, taking into consideration ECOG PS, comorbidities, albumin levels, and prior CT status.

Key Words:
Cancer, Malign biliary obstruction, Obstructive jaundice, Percutaneous biliary drainage, Prognostic factors.

Introduction

Patients with advanced cancer can present with biliary obstruction during diagnosis or follow-up[1]. While biliary obstruction has various benign and malignant causes, in oncology practice, malignant biliary obstruction (MBO) due to primary liver malignancies, liver metastases, or malignancies causing external compression on the bile ducts is frequently encountered. These patients may occasionally be unable to receive chemotherapy (CT) due to hyperbilirubinemia or experience treatment delays. Additionally, symptoms like itching, which impairs quality of life, infections, and poor prognosis, are known to be associated with jaundice in malignant diseases[2-5].

When MBO develops, drainage is generally successfully achieved either endoscopically or percutaneously[1]. Due to being less invasive, endoscopic methods are preferred as the initial choice. Percutaneous interventions are attempted more in cases where surgery and endoscopic interventions are inadequate or not feasible[6]. However, the critical aspect is not in the method of the procedure, but rather in the selection of patients for the procedure. There are no well-defined parameters for this. Therefore, evaluation by a multidisciplinary team comprising oncology, gastroenterology, general surgery, interventional radiology, and other relevant disciplines is of paramount importance. Upon reviewing the literature, it can be observed that the majority of studies[3,7,8] conducted on the topic are retrospective, most have a heterogeneous patient population, and varying outcomes have been obtained.

The general approach to MBO is to provide drainage in all patients with jaundice. However, the procedure performed is often palliative, and its contribution to survival is debatable. Additionally, factors predicting which patient will benefit from biliary drainage are not well known. This study aims to investigate prognostic factors in patients undergoing percutaneous transhepatic biliary drainage (PTBD) for MBO.

Corresponding Author: Yakup Duzkopru, MD; e-mail: yakupduzkopru@gmail.com; yakup.duzkopru@sbu.edu.tr

Patients and Methods

For this study, a total of 158 patients aged 18 years and above who underwent PTBD due to MBO between 2010 and 2021 were screened at the Medical Oncology Clinic of Diskapi Yildirim Beyazit Training and Research Hospital. All patients had a histopathologically confirmed malignant diagnosis. Excluding 6 patients with incomplete data, a total of 152 patients were included in the study. The patients' primary diagnoses, Eastern Cooperative Oncology Group Performance Status (ECOG PS), age, gender, whether they received CT before and after PTBD, bilirubin concentration, alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) values were retrospectively collected from the hospital database and patient files. Laboratory values included pre-PTBD values one day before the PTBD procedure and the lowest values within 15 days after PTBD. Additionally, age and all laboratory parameters were divided into two groups, low and high, based on their median values. The time interval from the date of PTBD placement to the date of death (OS) was recorded.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistical Software (SPSS 22.0, IBM Corp., Armonk, NY, USA). The clinical and demographic characteristics of the patients were analyzed through descriptive analysis. Categorical and numerical variables were presented as numbers and percentages (n, %). Continuous data were presented as means ± standard deviation if the data followed a normal distribution; otherwise, they were presented as median and range. Chi-square analysis was used for dichotomous data, and Fisher's exact test was applied where appropriate. Pearson correlation analysis was performed to assess the relationship between OS and laboratory values. Progression-free survival (PFS) and OS were calculated using the Kaplan-Meier method. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using the Cox regression model. Differences between groups were assessed using the log-rank test. A p-value < 0.05 was considered statistically significant for all analyses.

The study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Institutional Ethics Committee on May 31, 2021, with protocol number 112/04.

Results

A total of 152 patients were included in the study, with 84 (55.3%) being male. The median age was 62 (27-86) years. Comorbid disease was present in 83 patients (54.6%). The ECOG PS was 1, 2, and 3 for 36 (23.7%), 51 (33.6%), and 65 (42.8%) patients, respectively. The most common primary tumor was pancreatic cancer (n=48, 31.6%). Among the patients, 112 (73.7%) were metastatic at the time of diagnosis. The cause of obstruction was metastasis in 82 patients (53.9%) and primary tumor compression in 70 patients (46.1%). It was observed that 44 (28.9%) patients underwent PTBD once, 55 (36.2%) underwent it twice, and 53 (34.9%) underwent three or more PTBD procedures. A total of 114 (75%) patients received at least one line of CT in the metastatic setting before PTBD. The number of patients who could receive at least one cycle of CT after PTBD was 83 (54.6%). The clinical and demographic characteristics of the patients are presented in Table I.

The median OS was 71 days (standard error: 12.6, 95% CI: 46.3-95.7). The 1-, 3-, 6-, and 12-month OS rates were 74.3%, 45.2%, 29.2%, and 13%, respectively (Figure 1). Univariate analysis identified several parameters as statistically significant factors affecting OS, including ECOG PS (p<0.001), comorbidity (p=0.014), age group (p=0.03), pre-PTBD albumin (p<0.001), post-PTBD aspartate aminotransferase (AST) (p=0.001), post-PTBD bilirubin (p<0.001), post-PTBD albumin (p=0.001), chemo-naive status (p<0.001), and post-PTBD CT (p<0.001). Multivariate analysis considering the significant parameters from univariate analysis found comorbidity (p=0.029), ECOG PS (p=0.007), pre-PTBD albumin (p=0.025), post-PTBD AST (p=0.025), chemo-naive status (p<0.001), and post-PTBD CT (p=0.01) as independent prognostic factors for OS. The results of univariate and multivariate analysis of prognostic factors are presented in Table II.

Discussion

MBO is a frequently encountered problem in oncology practice that requires a multidisciplinary approach. Many studies, mostly retrospective, focusing on percutaneous interventions can be found in the literature. However, despite all these studies, predictive and prognostic fac-

Table I. Clinical features of patients

Features	n (%)
Age, median (years)	62 (27-86)
Gender	
Female	68 (44.7)
Male	84 (55.3)
Comorbidity	
Yes	83 (54.6)
No	69 (45.4)
ECOG PS	
1-2	87 (57.2)
3	65 (42.8)
Stage at diagnosis	
Stage 1	3 (2.0)
Stage 2	8 (5.3)
Stage 3	29 (19.1)
Stage 4	112 (73.7)
Cause of obstruction	
Primary tumor	70 (46.1)
Metastasis	82 (53.9)
Oncological diagnosis	
Pancreas	48 (31.6)
Gastric	31 (20.4)
Colorectal	24 (15.8)
Cholanciocarcinoma	26 (17.1)
Gallbladder	14 (9.2)
Other	9 (5.9)
Number of PTBD	
1	44 (28.9)
2	55 (36.2)
≥ 3	53 (34.9)
Metastatic CT line	
Chemo naive	38 (25.0)
1	40 (26.3)
≥ 2	74 (48.7)
Post-PTBD CT	
Yes	83 (54.6)
No	69 (45.4)

CT: Chemotherapy, ECOG PS: Eastern Cooperative Oncology Group Performance status, PTBD: Percutan transhepatic biliary drainage.

tors for the PTBD procedure have not been fully elucidated. This study aimed to investigate the effects of clinical characteristics and both pre-PTBD and post-PTBD laboratory values on prognosis in patients undergoing PTBD.

In our study, the median OS was 71 (standard error: 12.6, 95% CI: 46.3-95.7) days. In previous retrospective analyses, the median OS was found to be 44, 46, 63, and 143 days, respectively. The median survival rates at 1, 3, 6, and 12 months were higher in our study compared to the rates reported in the mentioned initial three studies[3,7-9]. The results of previously published articles are summarized in Table III.

Among our patients, 114 (75%) had received at least one line of CT before PTBD, and this group had a statistically significantly shorter OS than the chemo-naive group (Figure 2). In Şahinli and Ozet[3] study, there was no significant relationship between CT before PTBD and OS, while in Tuqan et al[9] study, as in our study, receiving CT before PTBD was found to be an independent risk.

Among our patients, 83 (54.6%) had received CT after PTBD, and this group had a statistically significantly longer overall survival compared to those who did not receive CT. When considering patients who received post-PTBD CT and those who did not, the median OS was 273 days and 65 days in the study conducted by Kasuga et al[10], and 285 days and 150 days in the study conducted by Zhang et al[11], respectively. Similarly, as mentioned earlier, in both the Şahinli and Ozet[3] study and the Afshar et al[7] study, the median OS was significantly longer in the group that received CT after PTBD

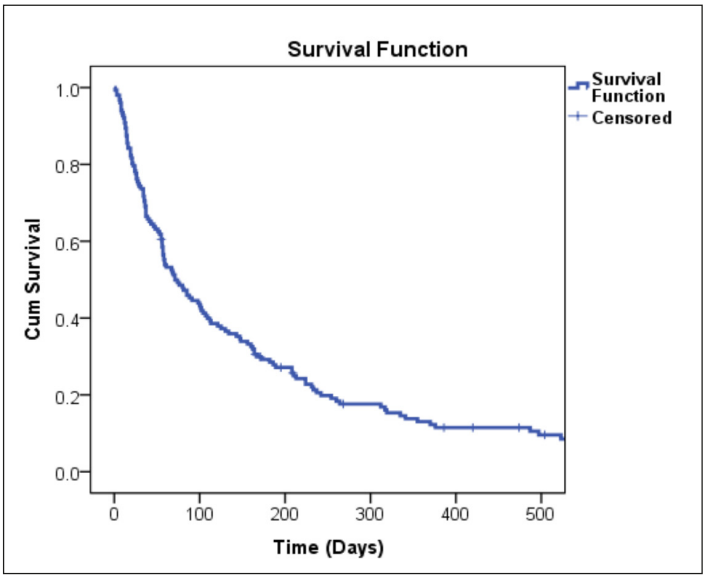

Figure 1. Survival rates at 1 month, 3 months, 6 months, and 12 months were 74.3%, 45.2%, 29.2%, and 13%, respectively. Median OS: 71 days (std error: 12.6, 95% CI: 46.3-95.7).

Table II. Prognostic factors on survival with univariate and multivariate analysis.

	Univariate analysis				Multivariate analysis	
	Median (days)	Std. Error	95% CI	*p*-value	HR (95% CI)	*p*-value
Gender						
Female	76	13.9	48.7-103.3	0.484		
Male	67	17.1	33.5-100.5			
Comorbidity						
Yes	61	10.4	40.6-81.4	**0.014**	0.59 (0.4-1.0)	**0.029**
No	109	30.1	50.0-168.0			
ECOG PS						
1-2	134	24	86.9-181.1	**< 0.001**	1.85 (1.2-2.9)	**0.007**
3	37	7.5	22.3-51.7			
Age						
< 62	80	32.7	15.9-144.1	**0.03**	1.35 (0.9-2.1)	0.194
≥ 62	67	13.2	41.0-93.0			
Pre-PTBD Albumin						
Low	48	7.8	32.8-63.2	**< 0.001**	0.60 (0.4-0.9)	**0.025**
High	182	16.9	148.9-215.1			
Pre-PTBD AST						
Low	71	12.6	46.3-95.7	0.801		
High	71	23	26.0-116.0			
Pre-PTBD ALT						
Low	71	13	45.5-96.5	0.475		
High	76	21.5	33.8-118.2			
Pre-PTBD Bilurubin						
Low	98	18.1	62.4-133.6	0.231		
High	57	14.2	29.2-84.8			
Pre-PTBD GGT						
Low	121	29.9	62.4-179.6	0.216		
High	56	11.3	33.8-78.2			
Post-PTBD AST						
Low	121	19.2	83.3-158.7	**0.001**	1.67 (1.1-2.6)	**0.025**
High	56	8.3	39.8-72.2			
Post-PTBD ALT						
Low	71	11.1	49.3-92.7	0.528		
High	85	22	41.8-128.2			
Post-PTBD Bilurubin						
Low	125	31.8	62.6-187.4	**< 0.001**	1.17 (0.7-1.9)	0.504
High	56	8.1	40.2-71.8			
Post-PTBD GGT						
Low	71	28.9	14.3-127.7	0.836		
High	76	20.2	36.5-115.5			
Post-PTBD Albumin						
Low	56	8.2	39.8-72.2	**0.001**	0.90 (0.6-1.4)	0.653
High	160	38.4	84.8-235.2			
Cause of obstruction						
Primary tumor	107	27.3	53.5-160.5	0.055		
Metastasis	57	9.1	39.3-74.7			
Chemo naive						
Yes	148	57.6	35.2-280.8	**< 0.001**	3.07 (1.7-5.5)	**< 0.001**
No	57	6.48	44.3-69.7			
Post-PTBD CT						
Yes	156	29.8	97.7-214.3	**< 0.001**	1.78 (1.2-2.8)	**0.01**
No	36	3	30.2-41.8			

compared to the non-CT group. In our study, the median overall survival was 156 days in the group that received post-PTBD CT and 36 days in the group that did not receive CT (Figure 3).

Patients with ECOG PS 1-2 had significantly longer survival compared to those with ECOG PS 3 and those without comorbidities. Similarly, previous studies[12,13] have shown that patients with

Table III. Clinical features of patients and outcomes of the published studys.

	Duzkopru et al (*)	Afshar et al[7]	Şahinli et al[3]	Tuqan et al[9]	Nikolic et al[8]
Number of patients (n)	152	194	90	72	89
Age, median (years)	62 (27-86)	69 (24-95)	64	56 (30-84)	Mean 62.8 (40-84)
Gender					
Female	68 (44.7)	NA	39 (43%)	34 (47.3%)	34 (38.2%)
Male	84 (55.3)	NA	51 (57%)	38 (52.7%)	55 (61.8%)
Cause of obstruction					
Primary tumor	70 (46.1)	144 (74%)	43.3%	67.2%	NA
Metastasis	82 (53.9)	50 (26%)	56.7%	32.8%	NA
Post-PTBD CT					
Yes	83 (54.6)	59 (30%)	22 (24.2%)	NA	9 (9.9%)
No	69 (45.4)	135 (70%)	68 (75.8%)	NA	80 (90.1%)
Median OS (days)	71	143	44	46	63
Survival rates					
1 month	74.3%	NA	58%	64%	72.3%
3 months	45.2%	NA	33%	27%	NA
6 months	29.2%	NA	8.9%	7%	NA
12 months	13%	NA	NA	1%	NA

CT: Chemotherapy, OS: Overall survival, PTBD: Percutan transhepatic biliary drainage. *Present study.

ECOG PS 3 or 4 have a worse prognosis. In our study, median survival was 134 days for patients with ECOG PS 1-2 and 37 days for those with ECOG PS 3. The better treatment feasibility, tolerance, and compliance of patients with good ECOG PS might explain the difference between these groups.

The significance of pre-PTBD albumin levels as a prognostic indicator has been shown in previous studies[3,9,14]. In our study, the median overall survival was 182 days for the high albumin group and 48 days for the low albumin group (Figure 4). Our study also found pre-PTBD albumin levels to be an independent prognostic factor. Several studies[15,16] evaluating the nutritional status of malignant patients suggest that the nutritional status is related to overall survival. Studies[17,18] evaluating albumin and albumin-associated prognostic nutritional index as indicators of nutrition have shown that higher albumin levels are associated with longer survival, while lower albumin levels are associated with shorter survival.

In a study by Abali et al[1], post-PTBD AST and ALT levels were found to be independent

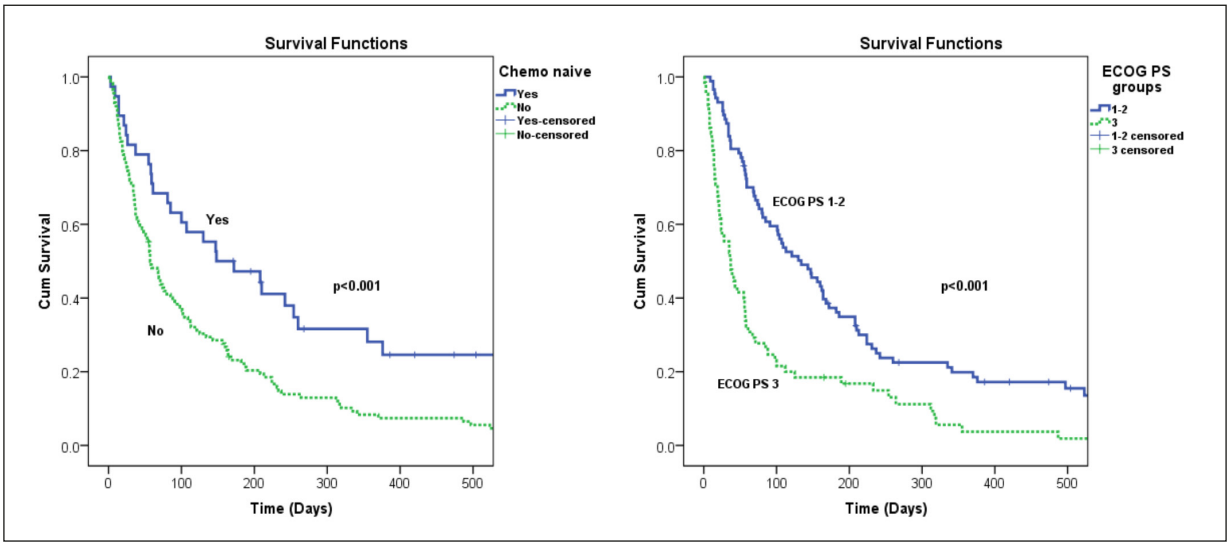

Figure 2. Survival (univariate analysis) of patients according to receiving CT before PTBD and ECOG PS. CT: Chemotherapy, ECOG PS: Eastern Cooperative Oncology Group Performance Status.

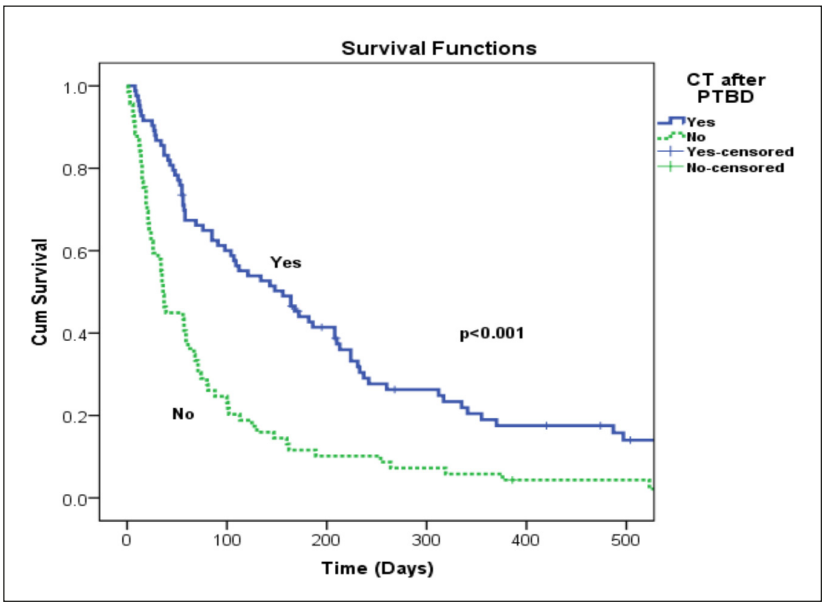

Figure 3. Survival (univariate analysis) of patients according to receiving CT Post-PTBD . CT: Chemotherapy, PTBD: percutaneous transhepatic biliary drainage.

risk factors, while in other studies[3,19], despite numerical differences, no statistically significant difference was found. In our study, the median overall survival was 121 days for the low post-PTBD AST group and 56 days for the high group. Abali et al[1] noted the difficulty in explaining this situation.

Overall, it can be observed that the studies available in the literature have been conducted in different geographical regions and on different races. Similarly, despite similarities in the patient characteristics included in the studies, patient groups seem to be distributed quite heterogeneously. Therefore, it is not possible to directly compare the results of the studies, and interpreting the differences between the results is challenging. However, in general, it can be said that patients with good ECOG PS and those who received CT after PTBD have longer survival.

Limitations

The primary limitation of our study is that it is a single-center retrospective study including heterogeneous patient groups. Given that each cancer

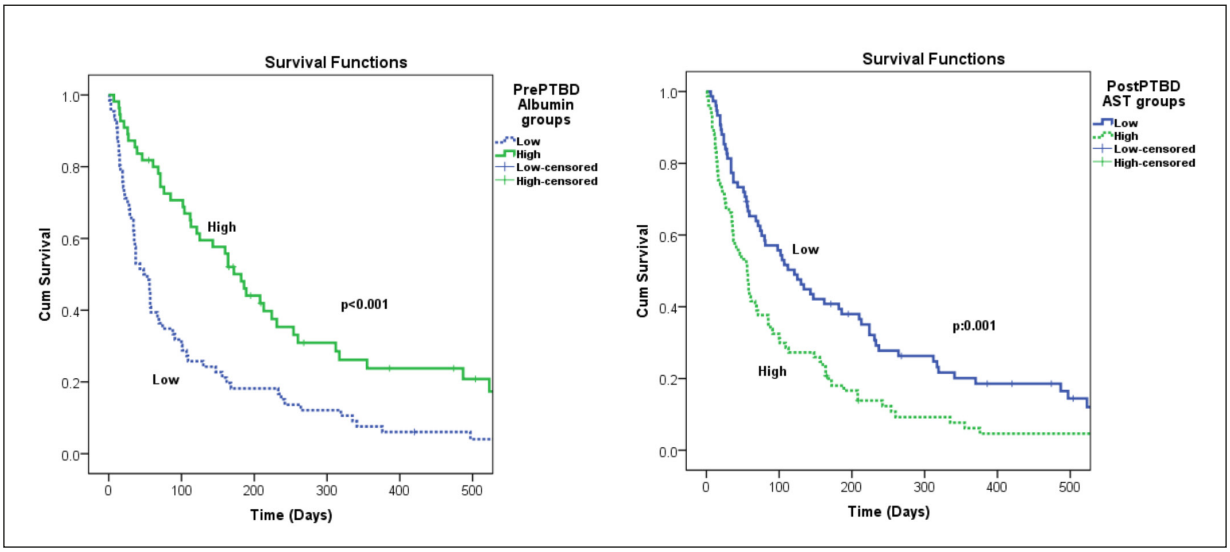

Figure 4. Survival (univariate analysis) of patients according to pre-PTBD albumin and Post-PTBD AST levels. AST: Aspartate aminotransferase, PTBD: percutaneous transhepatic biliary drainage.

type has different treatment strategies, there is a need for higher volume prospective studies with a more homogeneous distribution. However, many of the previous studies were also retrospective.

Conclusions

Patients with MBO have a poor prognosis. For these patients, PTBD should be applied to provide palliation and enable the administration of CT. However, considering that patients with poor ECOG PS, comorbidities, low albumin levels, and prior CT have shorter survival, the decision regarding PTBD should be made in a multidisciplinary manner.

Conflict of Interest
The authors declare that no conflict of interest.

Acknowledgements
We would like to express our sincere gratitude to Prof. Dr. O.B.Ç. Oksuzoglu, Prof. Dr. M. Altinbas, Prof. Dr. M. Baykara, and Prof. Dr. S. Kilickap for their invaluable contributions to our educational journey, their guidance throughout our work, and their editorial support.

Funding
None.

Availability of Data and Materials
Raw data were generated at Health Sciences University Diskapi Training and Research Hospital. Derived data supporting the findings of this study are available from the corresponding author, Y.D., on request.

Informed Consent
Not applicable due to the retrospective nature of the study.

Ethics Approval
The study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Health Sciences University Diskapi Yildirim Beyazit Training and Research Hospital Ethics Committee on May 31, 2021, with protocol number 112/04.

Authors' Contribution
Y. Duzkopru and A. Kocanoglu: study concept, study design, and statistical analysis; O. Dogan and T. Eren: data acquisition, data analysis, and interpretation; O.A. Isak and O. Ergun: manuscript editing. All authors contributed to the article and approved the submitted version.

ORCID ID
Y. Duzkopru: 0000-0003-2314-5870
T. Eren: 0000-0002-0088-1149
A. Kocanoglu: 0000-0002-5579-2135
O. Dogan: 0000-0003-1023-8410
O.A. Isak: 0000-0003-4082-4867
O. Ergun: 0000-0002-0495-0500

References

1) Abali H, Sezer A, Oguzkurt L, Gurel K, Ozkan U, Besen AA, Sumbul AT, Kose F, Disel U, Muallaoglu S, Ozyilkan O. Which patients with advanced cancer and biliary obstruction benefit from biliary stenting most? An analysis of prognostic factors. Support Care Cancer 2013; 21: 1131-1135.
2) Barkay O, Mosler P, Schmitt CM, Lehman GA, Frakes JT, Johanson JF, Qaseem T, Howell DA, Sherman S. Effect of endoscopic stenting of malignant bile duct obstruction on quality of life. J Clin Gastroenterol 2013; 47: 526-531.
3) Sahinli H, Ozet A. Prognostic and predictive factors in cancer patients with obstructive jaundice treated by percutaneous transhepatic biliary drainage: A single-center experience. J Cancer Res Ther 2020; 16: S99-S103.
4) Saluja SS, Gulati M, Garg PK, Pal H, Pal S, Sahni P, Chattopadhyay TK. Endoscopic or percutaneous biliary drainage for gallbladder cancer: a randomized trial and quality of life assessment. Clin Gastroenterol Hepatol 2008; 6: 944-950 e943.
5) Mahdavifar N, Mohammadian M, Salehiniya H. Gallbladder cancer in the world: epidemiology, incidence, mortality and risk factors. WCRJ 2018; 5: e1124.
6) Niemela J, Kallio R, Ohtonen P, Perala J, Saarnio J, Syrjala H. Is Palliative Percutaneous Drainage for Malignant Biliary Obstruction Useful? World J Surg 2018; 42: 2980-2986.
7) Afshar M, Ma YT, Punia P, Khanom K. Biliary stenting in advanced malignancy: an analysis of predictive factors for survival. Cancer Manag Res 2014; 6: 475-479.
8) Nikolić I, Radić J, Petreš A, Djurić A, Protić M, Litavski J, Popović M, Kolarov-Bjelobrk I, Dragin S, Popović L. The Clinical Benefit of Percutaneous Transhepatic Biliary Drainage for Malignant Biliary Tract Obstruction. Cancers 2022; 14: 4673.
9) Tuqan W, Innabi A, Alawneh A, Farsakh FA, Al-Khatib M. Prediction of Survival Following Per-

cutaneous Biliary Drainage for Malignant Biliary Obstruction. J Transl Int Med 2017; 5: 127-131.

10) Kasuga A, Ishii H, Ozaka M, Matsusaka S, Chin K, Mizunuma N, Yukisawa S, Matsueda K, Furuse J. Clinical outcome of biliary drainage for obstructive jaundice caused by colorectal and gastric cancers. Jpn J Clin Oncol 2012; 42: 1161-1167.
11) Zhang GY, Li WT, Peng WJ, Li GD, He XH, Xu LC. Clinical outcomes and prediction of survival following percutaneous biliary drainage for malignant obstructive jaundice. Oncol Lett 2014; 7: 1185-1190.
12) Lamarca A, Rigby C, McNamara MG, Hubner RA, Valle JW. Impact of biliary stent-related events in patients diagnosed with advanced pancreatobiliary tumours receiving palliative chemotherapy. World J Gastroenterol 2016; 22: 6065-6075.
13) Prigerson HG, Bao Y, Shah MA, Paulk ME, LeBlanc TW, Schneider BJ, Garrido MM, Reid MC, Berlin DA, Adelson KB, Neugut AI, Maciejewski PK. Chemotherapy Use, Performance Status, and Quality of Life at the End of Life. JAMA Oncol 2015; 1: 778-784.
14) Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J 2010; 9: 69.
15) Shi Y, Zhang Y, Niu Y, Chen Y, Kou C. Prognostic role of the prognostic nutritional index (PNI) in patients with head and neck neoplasms undergoing radiotherapy: A meta-analysis. PLoS One 2021; 16: e0257425.
16) Guller M, Herberg M, Amin N, Alkhatib H, Maroun C, Wu E, Allen H, Zheng Y, Gourin C, Vosler P, Tan M, Koch W, Eisele D, Seiwert T, Fakhry C, Pardoll D, Zhu G, Mandal R. Nutritional Status as a Predictive Biomarker for Immunotherapy Outcomes in Advanced Head and Neck Cancer. Cancers (Basel) 2021; 13: 5772.
17) Demirelli B, Babacan NA, Ercelep O, Ozturk MA, Kaya S, Tanrikulu E, Khalil S, Hasanov R, Alan O, Telli TA, Koca S, Aribal ME, Kuzan B, Dane F, Yumuk PF. Modified Glasgow Prognostic Score, Prognostic Nutritional Index and ECOG Performance Score Predicts Survival Better than Sarcopenia, Cachexia and Some Inflammatory Indices in Metastatic Gastric Cancer. Nutr Cancer 2021; 73: 230-238.
18) Sohda M, Sakai M, Yamaguchi A, Watanabe T, Nakazawa N, Ubukata Y, Kuriyam K, Sano A, Yokobori T, Ogawa H, Shirabe K, Saeki H. Pre-treatment CRP and Albumin Determines Prognosis for Unresectable Advanced Oesophageal Cancer. In Vivo 2022; 36: 1930-1936.
19) Aktas G, Kus T, Balkan A, Metin T, Gulsen MT, Abali H. Prognostic factors in patients with advanced extrahepatic cholangiocarcinoma: A single center experience. Medicine (Baltimore) 2019; 98: e14556.