Original Article
Middle East Journal of Cancer; October 2024; 15(4): 307-314

The Implication of Chuang's Prognostic Scale in Metastatic Gastric Cancer

Amrallah Mohammed*♦, MD, Adel Bakry*, MD, Shimaa A. Gharieb, MD, Amira H. Hanna**, MD, Ahmed A. Obaya**, MD**

**Medical Oncology Department, Faculty of Medicine, Zagazig University, Egypt*
***Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Zagazig University, Egypt*

Please cite this article as: Mohammed A, Bakry A, Gharieb SA, Hanna AH, Obaya AA. The implication of Chuang's prognostic scale in metastatic gastric cancer. Middle East J Cancer. 2024; 15(4):307-14. doi:10.30476/mejc.2024.100258.1980.

Received: September 26, 2023
Accepted: April 06, 2024

Abstract

Background: Patients with metastatic gastric cancer (mGC) endure a significant symptom burden following subsequent lines of therapy. Accurate survival estimation is crucial for healthcare professionals and patients to make informed decisions regarding therapy options. This study evaluates Chuang's Prognostic Scale (CPS) for predicting survival in mGC patients after receiving at least two lines of palliative systemic therapy (PST).

Method: This prospective study involved 202 patients with mGC. The CPS includes eight categories: cognitive impairment, performance status, weight loss, tiredness, edema, and ascites, with a scoring range from 0 to 8.5. A higher score indicates a poorer prognosis.

Results: After a median follow-up period of 3.35 months, the median CPS value was 4.2. 99 patients had a CPS < 4.2, with a median overall survival (mOS) of 5.86 months, while 103 patients with a CPS ≥ 4.2 had an mOS of 3.96 months ($P < 0.001$). According to the receiver-operating curve, the cut-off value for CPS was ≤ 4.7, with a disease prevalence of 76.7% and an area under the curve of 0.949 ($P < 0.0001$). The sensitivity was 82.6%, specificity was 97.87%, positive predictive value was 99.2%, and negative predictive value was 63%. Cox regression analysis revealed that CPS was statistically significantly associated with mOS ($P < 0.001$). Furthermore, CPS was statistically significantly correlated with metastases to the liver, lung, lymph nodes, and bone (P values were 0.03, 0.02, <0.001, and <0.001, respectively).

Conclusion: CPS is a valuable and accessible tool that can assist in selecting appropriate therapy for patients with mGC after two lines of PST.

Keywords: Stomach neoplasms, Chemotherapy, Survival, Chuang's Prognostic Score

♦Corresponding Author:
Amrallah Mohammed, MD
Medical Oncology Department, Faculty of Medicine, Zagazig University, Egypt
Email: amrallaabdelmoneem@yahoo.com

Introduction

Even with advancements in detection and therapy, gastric cancer remains a grave medical concern.[1] It was the fifth most common type of cancer worldwide and the third

Table 1. The Chuang's Prognostic Scale, items, scores, and severity levels

Category	Degree	Description	Score
ECOG PS	1	0-1	0
	2	2	1.5
	3	3	2
	4	4	3
Cognitive impairment	0	Never happened	0
	1	Lethargy	0.5
	2	Confusion	0.5
	3	Comatose	0.5
Tiredness	0	Never happened	0
	1	Mild	0
	2	Moderate	0
	3	Severe	1
Weight loss in last 3 months	0	None	0
	1	<5	0.2
	2	5-10	0.7
	3	>10	1
Edema	0	None	0
	1	Pitting edema<1/2 fingerbreadth	1
	2	Pitting edema1/2-1 fingerbreadth	1
	3	Pitting edema>1 finger breadth	1
Ascites	0	None	0
	1	Ultrasound detection	0
	2	Shifting dullness on clinical examination	1
	3	Umbilical protrusion	1
Liver metastasis	No	Absent	0
	Yes	Present	0.5
Lung metastasis	No	Absent	0
	Yes	Present	0.5

The total score ranged from 0 to 8.5; the lower score refers to a good prognosis. ECOG PS: Eastern Cooperative Oncology Group performance status

most common cause of cancer-related death.[2] Of the cases at the initial diagnosis, nearly one-third had metastatic gastric cancer (mGC).[3]

The overall condition among patients with mGC has gotten worse as the disease progresses following the initial treatment and beyond for a variety of reasons. Given that mGC is an incurable disease, palliative systemic therapy (PST) is the principal line of management.[4]

A significant number of patients with metastatic cancer typically receive anticancer treatment toward the end of their lives due to the discovery of numerous therapeutic drugs, either immune-stimulating or target-based.[5] An accurate estimation of survival may avoid overtreatment.

Chuang's Prognostic Scale (CPS) is a validated score used to predict the survival outcome of palliative cancer patients in the terminal stage.[6]

The objective of the following study is to evaluate CPS in the prognostication of survival in patients with mGC following two lines or more of PST.

Methods

In this prospective study, 202 patients diagnosed with mGC were enrolled. They received treatment at the Departments of Medical and Clinical Oncology, Faculty of Medicine, Zagazig University, Egypt.

Inclusion criteria

Participants were required to have a histopathological diagnosis, radiographic evidence of

metastasis, undergo at least three lines of systemic therapy, and be 18 years or older.

The primary responsible physician (MRP) evaluated the CPS during the patient's initial consultation. CPS encompasses performance status, weight loss, fatigue, cognitive impairment, ascites, edema, and metastases to the lungs or liver. These factors were graded on a scale ranging from 0 to 8.5, where a higher score indicated a poorer prognosis (Table 1). Follow-up was conducted via hospital admissions and telephonic communications after discharge, extending for a minimum of two months or until the patient's death.

Statistical analysis

Continuous variables were presented as mean ± SD and median (range), while categorical variables were shown as numbers (percentage). The Pearson chi-square test or Fisher's exact test was utilized for comparing percentages of categorical variables, as appropriate. Overall survival (OS) was defined as the time from CPS assessment to the last follow-up or death.

Survival estimates were made using the Kaplan-Meier curve, with the log-rank test applied to assess differences in survival. The receiver-operating curve, informed by the Youden index, determined the CPS cut-off value for predicting mortality. The Youden Index, defined as Sensitivity + Specificity - 1, evaluates both the actual favorable and accurate negative rates, where its maximum value is 1 (indicating a perfect test), and its minimum is 0 (indicating no diagnostic value).

Survival time was calculated from the date of CPS assessment to the date of death or last follow-up. Hazard ratios and their 95% confidence intervals (CI) were estimated using univariate Cox regression analysis. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant. Analyses were conducted using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for Windows (MedCalc Software bvba, Ostend, Belgium).

Ethical consideration

The study was approved by the Institutional Review Board (IRB) of Zagazig University (ZU-IRB #11215-25/10-20123). As the study posed no harm to patients, did not involve specific investigations or new therapies, and ensured data protection by securely storing data without patient identifiers linked to data collection forms via a serial code, informed consent was deemed unnecessary.

Table 2. Characteristics of the 202 patients with metastatic gastric cancer

Category	Number (%)
Age	
<60years	93(46.0)
≥60years	109 (54.0)
Sex	
Male	84 (41.6)
Female	118 (58.4)
Grade	
Grade I	27 (13.4)
Grade II	94 (46.5)
Grade II	81(40.1)
Liver metastasis	
Absent	95 (47.0)
Present	107 (53.0)
Lung metastasis	
Absent	200 (99.0)
Present	2 (1.0)
Bone metastasis	
Absent	139 (68.8)
Present	63 (31.2)
Lymph nodes metastasis	
Absent	163 (80.7)
Present	39 (19.3)
Type of chemotherapy	
Taxol	87(43.1)
Taxetere	30 (14.9)
Irinotecan	51 (25.2)
FOLFIRI	34 (16.8)
CPS	
Mean (SD)	3.9649 (1.77613)
Median	4.20
Median follow-up duration days (months)	100.5(3.35)
Outcome	
Alive	47 (23.3)
Died	155 (76.7)

CPS: The Chuang's Prognostic Scale; FOLFIRI: Leucovorin calcium (folinic acid), fluorouracil, and irinotecan hydrochloride

Results

Patient characteristics

Table 2 presents the demographic and clinical characteristics of the study participants. Paclitaxel emerged as the predominant chemotherapy agent used. The median follow-up duration was 3.35 months (range: 1.03–5.97), with a mean of 3.22

Table 3. Relationship between clinical pathological parameters and CPS in metastatic gastric cancer

	Continuous quantitative variable		*P*-value	Categorical variable		*P*-value
	Mean	Median		>4.7	≤4.7	
Age						
<60years	3.9742	4.2000	0.81	39.8%	60.2%	0.31
≥60years	3.9569	4.2000		33.0%	67.0%	
Sex						
Male	4.0119	4.2000	0.65	35.7%	64.3%	0.91
Female	3.9314	4.2000		36.4%	63.6%	
Grade						
I	3.8889	4.0000	0.15	22.2%	77.8%	0.12
II	3.7287	3.7000		34.0%	66.0%	
III	4.2642	4.2000		43.2%	56.8%	
Type of chemotherapy						
Taxol	3.8977	4.2000	0.16	32.2%	67.8%	0.48
Taxotere	4.4367	4.7000		46.7%	53.3%	
Irinotecan	4.1451	4.2000		39.2%	60.8%	
FOLFIRI	3.4500	3.5000		32.4%	67.6%	
Presence of metastasis						
Liver	4.0972	4.5000	0.11	43.0%	57.0%	0.03*
Lung	4.7000	4.7000	0.65	40.0%	60.0%	0.02*
Lymph nodes	5.6487	6.0000	<0.001	84.6%	15.4%	<0.001*
Bones	4.7127	6.0000	<0.001	61.9%	38.1%	<0.001*

CPS: The Chuang's Prognostic Scale; **P* value <0.05 is significant. FOLFIRI: Leucovorin calcium (folinic acid), fluorouracil, and irinotecan hydrochloride

± 1.00382 months. The median CPS score was 4.2, with 23.3% of patients surviving. 99 patients had CPS scores below the median (4.2), boasting a median OS of 5.86 months. Conversely, for the 103 patients with a CPS score of ≥ 4.2, the median OS was 3.96 months ($P = 0.001$) (Figure 1).

CPS analysis

According to the Youden index, the optimal cut-off value for CPS was ≤ 4.7. The sensitivity of this cut-off was 82.6% (95% CI: 75.7–88.2), and the specificity was 97.87% (95% CI: 88.7–99.9). The positive predictive value was calculated at 99.2% (95% CI: 94.8–99.9), and the negative predictive value stood at 63% (95% CI: 54.7–70.6) (Figure 2).

Correlation between CPS and metastasis

There was a statistically significant association between CPS scores and the presence of metastases to the liver, lungs, lymph nodes, and bones when analyzed as a categorical variable, with *P* values of 0.03, 0.02, <0.001, and <0.001, respectively. This significance persisted only for lymph nodes and bone metastases when analyzed as a continuous variable ($P = 0.001$) (Table 3).

Survival analysis

The survival analysis revealed a statistically significant correlation between CPS scores and metastasis to the liver, lung, lymph nodes, and bones, with *P* values of <0.001, 0.04, 0.05, and <0.001, respectively. Furthermore, univariate and multivariate Cox regression analyses demonstrated a statistically significant association between CPS scores and survival outcomes (Tables 4 and 5).

Discussion

The existing study revealed that the cut-off CPS was ≤4.7, and the area under the curve was 0.949 ($P<0.0001$), with a disease prevalence of 76.7%. The sensitivity was 82.6% (95% CI: 75.7–88.2), the specificity was 97.87% (95% CI: 88.7–99.9), the positive predictive value was 99.2% (95% CI: 94.8–99.9), and the negative predictive value was 63% (95% CI: 54.7–70.6). Moreover, the survival outcome was linked to CPS, as the univariate and multivariate Cox regression models demonstrated. Additionally, patients whose median CPS was less than 4.2 had a higher benefit in survival than patients

Table 4. Univariate Cox regression analysis of prognostic factors in 202 patients with metastatic gastric cancer

	HR	95.0% CI for HR		Survival	*P*-value
		Lower	Upper	Alive (%)	
Age					
<60 vs. ≥60 years	1.206	0.871	1.669	26.9 vs. 20.2	0.26
Sex					
Male and female	1.207	0.870	1.674	26.2 vs. 21.2	0.40
Grade					
I vs. II	0.978	0.609	1.569	14.8 vs. 21.3	0.92
I vs. III	1.667	1.021	2.722	14.8 vs. 28.4	0.04
Type of chemotherapy					
Taxotere	1.080	0.652	1.787	33.3	0.12
Irinotecan	1.223	0.827	1.809	21.6	0.77
FOLFIRI	0.692	0.428	1.119	26.5	0.40
Metastasis					
Liver (-ve vs. +ve)	1.004	0.731	1.379	16.8 vs. 29.0	0.04
Lung (-ve vs. +ve)	0.330	0.046	2.373	23.0 vs. 50	0.39
Lymph nodes (-ve vs. +ve)	1.432	0.666	3.080	9.2 vs. 82.1	<0.001*
Bone (-ve vs. +ve)	1.040	0.680	1.589	7.5 vs. 58.7	<0.001*
CPS	1.588	1.399	1.802	47	<0.001*

HR: Hazard ratio; CI: Confidence interval; CPS: The Chuang's Prognostic Scale; **P* value <0.05 is significant; FOLFIRI: Leucovorin calcium (folinic acid), fluorouracil, and irinotecan hydrochloride

whose CPS was more significant than 4.2 (OS of 5.86 vs. 3.96 months, respectively, $P < 0.001$).

The prediction of survival serves a crucial role in helping patients, and MRP makes decisions at every stage of the cancer journey.[7] Patients with mGC almost invariably deteriorate after two

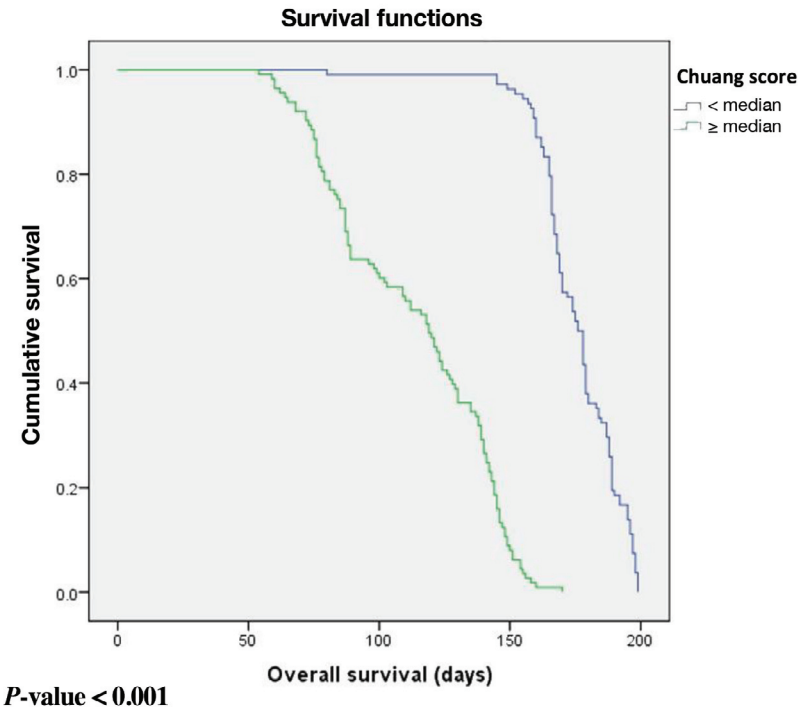

Figure 1. This figure shows the Kaplan-Meier survival curves for patients with metastatic gastric cancer, stratified by Chuang's Prognostic Scale Score.

Table 5. Multivariate Cox Regression Model of 202 patients with metastatic gastric cancer

	HR	95.0% CI for HR		*P*-value
		Lower	Upper	
Age				
<60 vs. ≥ 60years	1.120	0.791	1.585	0.76
Sex				
Male and female	1.147	0.806	1.631	0.10
Grade				
I vs. II	1.446	0.873	2.395	0.95
I vs. III	1.897	1.097	3.282	0.93
Type of chemotherapy				
Taxotere	1.273	0.739	2.191	0.37
Irinotecan	0.964	0.627	1.480	0.64
FOLFIRI	0.935	0.563	1.552	0.37
Metastasis				
Liver (-ve vs. +ve)	0.982	0.702	1.373	0.93
Lung (-ve vs. +ve)	0.158	0.020	1.263	0.28
Lymph nodes (-ve vs. +ve)	0.912	0.393	2.119	0.31
Bone (-ve vs. +ve)	1.279	1.279	2.065	0.02*
CPS	1.646	1.429	1.895	<0.001*

HR: Hazard ratio; CI: Confidence interval; CPS: The Chuang's Prognostic Scale; **P* value <0.05 is significant; FOLFIRI: Leucovorin calcium (folinic acid), fluorouracil, and irinotecan hydrochloride

treatment protocols, necessitating a re-evaluation of the rationale for subsequent therapy. This makes accurately estimating the patients' survival more critical.[8]

In phase three trials, just over one-third of patients receiving first-line therapy were given additional protocols. Variants such as increased disease spread, especially to the peritoneum, ascites development, cancer cachexia, and malnutrition increased by up to 69% are frequently linked to the progression of the disease. The general condition of the patients is mirrored in

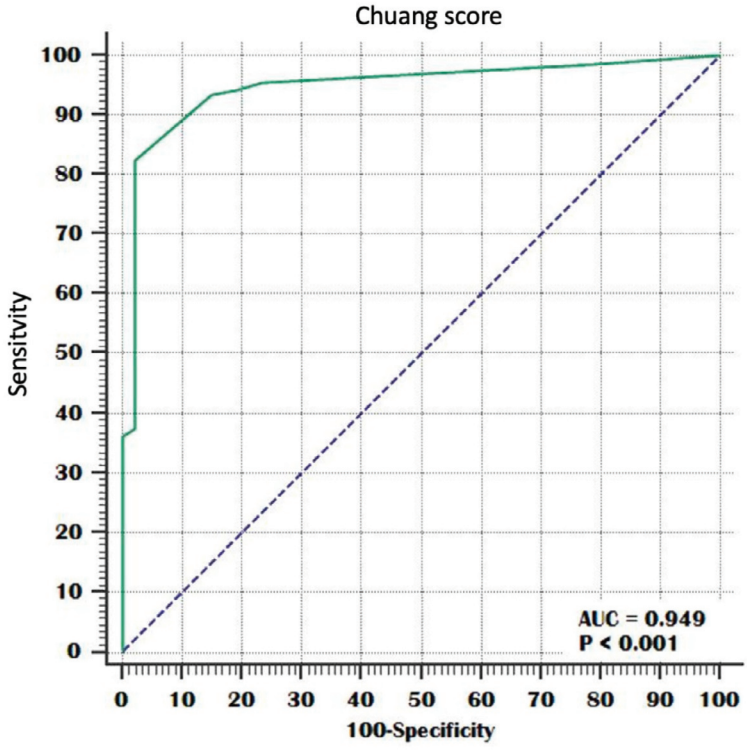

Figure 2. This figure shows the receiver-operating characteristic curve for mortality prediction in patients with metastatic gastric cancer using the Chuang's Prognostic Scale.
AUC: Area under curve

this situation. Hence, careful survival assessment and adequate general condition appraisal will aid both MRP and patients in selecting therapies in harmony and avoiding either helpful or dangerous treatments.[9-11]

Despite this significance, physicians overestimate the chances of survival. Practical and straightforward scales are required to achieve better results.

The area under the curve and concordance index was used to assess the prognostic precision of the palliative performance scale, palliative prognostic score, and MRP survival prediction in a prospective study with pre-planned secondary analysis that included 204 patients with advanced cancer. According to the results, the four methods might be applied to palliative care units for patients with advanced cancer to predict prognosis.[13]

CPS is a simple and effective prognostic model that has been proven to predict the survival outcome of 356 Taiwanese patients with terminal cancer. When the CPS cut-off was less than 3.5, and the accuracy was 0.6, a prediction of two-week survival was provided.[6]

In an alternative study, the CPS's ability to predict survival in patients with advanced cancer was assessed. The survival analysis suggested a median OS of 103 days. These findings showed that the CPS may be applied to the advanced cancer prognosis.[14]

In a prospective study by Alsirafy et al., 36 patients with mCRC were included. Patients with a score of ≤5 survived for 149 days, while those with a score of >5 survived for 61 days. The authors concluded that CPS might define the patients with mCRC who were less likely to benefit from PST.[15]

Additionally, 221 patients with metastatic breast cancer, who had received three or more PST lines, participated in the study. Compared with 21.3% of patients with a score of ≥5.7, 86.2% of patients with a score of ≤5.7 survived for more than three months. The outcomes were assumed using CPS in survival prediction for this type of patient.[5]

The main points of limitation in the research were the single-arm, single-center design and the lack of any comparison with other scores.

Conclusion

Patients with mGC who have undergone two or more lines of PST frequently exhibit signs of disease aggressiveness and progression, accompanied by a deterioration in overall health and performance status. Notably, individuals presenting with high CPS scores at baseline experience diminished survival rates, indicating that PST yields minimal benefits in prolonging their lives. Consequently, employing the CPS model as a straightforward and practical tool facilitates selecting optimal supportive care. This approach minimizes the risk of unnecessary toxicity for patients unlikely to benefit from further aggressive treatment, thus aligning therapeutic efforts with realistic outcomes.

Acknowledgment

I sincerely thank the medical oncology team for their invaluable support and collaboration.

Funding

None declared.

Authors' Contribution

All the authors contributed to the design of the study, analysis of data, drafting and reviewing it, approval for publishing, and were included in all aspects of the work. Questions related to the accuracy or integrity of the work were appropriately investigated and resolved.

Conflict of Interest

None declared.

References

1. Sexton RE, Al Hallak MN, Diab M, Azmi AS. Gastric cancer: a comprehensive review of current and future treatment strategies. *Cancer Metastasis Rev.* 2020; 39(4):1179-203. doi: 10.1007/s10555-020-09925-3.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424. doi: 10.3322/caac.21492. Erratum in: *CA Cancer J Clin*. 2020;70(4):313.

3. Ren J, Dai Y, Chao F, Tang D, Gu J, Niu G, et al. A nomogram for predicting the cancer-specific survival of patients with initially diagnosed metastatic gastric cancer. *Clin Med Insights Oncol.* 2022;16:117955 49221142095. doi: 10.1177/11795549221142095.
4. Kopecky K, Monton O, Rosman L, Johnston F. Palliative interventions for patients with advanced gastric cancer: a systematic review. *Chin Clin Oncol*. 2022;11(6):47. doi: 10.21037/cco-22-102.
5. Mohammed AA, Al-Zahrani O, Elsayed FM, Elshentenawy A. Prediction of survival outcome using Chuang's prognostic scale in metastatic breast cancer. *Indian J Palliat Care.* 2021;27(1):43-6. doi: 10.4103/IJPC.IJPC_97_20.
6. Chuang RB, Hu WY, Chiu TY, Chen CY. Prediction of survival in terminal cancer patients in Taiwan: constructing a prognostic scale. *J Pain Symptom Manage*. 2004;28(2):115-22. doi: 10.1016/j.jpainsymman.2003.11.008.
7. Bashiri A, Ghazisaeedi M, Safdari R, Shahmoradi L, Ehtesham H. Improving the prediction of survival in cancer patients by using machine learning techniques: experience of gene expression data: a narrative review. *Iran J Public Health.* 2017;46(2):165-72.
8. Ghosn M, Tabchi S, Kourie HR, Tehfe M. Metastatic gastric cancer treatment: Second line and beyond. *World J Gastroenterol.* 2016;22(11):3069-77. doi: 10.3748/wjg.v22.i11.3069.
9. Kottorou A, Dimitrakopoulos FI, Tsezou A. Non-coding RNAs in cancer-associated cachexia: clinical implications and future perspectives. *Transl Oncol.* 2021;14(7):101101. doi: 10.1016/j.tranon.2021.101101.
10. Rosania R, Chiapponi C, Malfertheiner P, Venerito M. Nutrition in patients with gastric cancer: an update. *Gastrointest Tumors*. 2016;2(4):178-87. doi: 10.1159/000445188.
11. Yarema R, Ohorchak M, Hyrya P, Kovalchuk Y, Safiyan V, Karelin I, et al. Gastric cancer with peritoneal metastases: Efficiency of standard treatment methods. *World J Gastrointest Oncol.* 2020;12(5):569-81. doi: 10.4251/wjgo.v12.i5.569.
12. Butow PN, Clayton JM, Epstein RM. Prognostic awareness in adult oncology and palliative care. *J Clin Oncol.* 2020;38(9):877-84. doi: 10.1200/JCO.18.02112.
13. Hui D, Ross J, Park M, Dev R, Vidal M, Liu D, et al. Predicting survival in patients with advanced cancer in the last weeks of life: How accurate are prognostic models compared to clinicians' estimates? *Palliat Med.* 2020;34(1):126-33. doi: 10.1177/0269216319873261.
14. Al-Zahrani AS, El-Kashif AT, Mohammad AA, Elsamany S, Alsirafy SA. Prediction of in-hospital mortality of patients with advanced cancer using the Chuang Prognostic Score. *Am J Hosp Palliat Care*. 2013;30(7):707-11. doi: 10.1177/1049909112467362.
15. Alsirafy SA, Zaki O, Sakr AY, Farag DE, El-Sherief WA, Mohammed AA. The use of the Chuang's Prognostic Scale to predict the survival of metastatic colorectal cancer patients receiving palliative systemic anticancer therapy. *Indian J Palliat Care.* 2016;22(3):312-6. doi: 10.4103/0973-1075.185043.