Does Albumin Level Change the Strength of the Memorial Sloan Kettering Cancer Center Nomogram Used to Predict 5-year Survival in Patients with Colon Cancer?

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ABSTRACT

Objective: To test the efficacy of including albumin in the Memorial Sloan Kettering Cancer Center (MKSCC) nomogram (MSKCC+A) on predicting the overall survival.

Study Design: Descriptive study.

Place and Duration of Study: Ankara Training and Research Hospital & Ataturk Training and Research Hospital, Turkey, in 2020, on patients who were operated between 2009 and 2014 to confirm the 5-year survival results.

Methodology: Patients who underwent R0 resection for colon cancer were evaluated. For each patient in the cohort, the 5-year probability of survival was calculated and compared with actual, using the AJCC (American Joint Committee on Cancer), MSKCC and MSKCC+A estimation systems obtained using logistic regression. The performance of the estimation methods was evaluated by the ROC analysis.

Results: Two hundred and thirty-nine patients were studied. When the patients with more than 5-year overall survival were compared, the AJCC, MSKCC, and enhanced MSKCC survival scores were significantly higher. AUC = 0.699 for the AJCC staging system, AUC = 0.702 for the MKSCC nomogram, and AUC = 0.777 when the albumin level was added to the MKSCC system.

Conclusions: The use of the MSKCC overall survival nomogram in patients with colon cancer appears useful for both clinicians and patients. The prognostic power of this calculator was found to be further enhanced by including the preoperative serum albumin level as an extra variable in the nomogram.

Key Words: *Nomograms, Neoplasm grading, Survival, Colon cancer, Serum albumin.*

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INTRODUCTION

Colorectal cancer is a potentially curable disease, which should be treated in a multidisciplinary fashion.[1] When the diversity of this disease is in anatomic location, pathologic stage, genetic background and biologic behaviour are considered. It is obvious that the treatment of colorectal cancer should be individualised for each patient. Decision making for the right combination of therapy must be based on multitude factors, one of which is the pathologic stage of the disease.

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However, even the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) system, which is the gold standard in cancer staging,[2] has flaws in predicting survival and therefore helping in decision making.[2,3] For this reason, individualised prognostication models have been proposed as alternative prognostic tools for cancer patients.[2]

Moreover, referred to as nomograms by some researchers, these are the pictorial representations of complicated mathematical formulas predicting overall or disease-free survival.[4] These models have the advantage of using multiple variables for each patient that helps better and more individualised predictions than conventional staging and scoring systems. One of the models proposed for colorectal cancer to predict overall survival is the system that was designed by Weisner *et al*. in Memorial Sloan Kettering Cancer Center (MSKCC), which can be found as an automatic calculation tool readily available online.[5,6] This model was proven by its developers to be a more accurate predictor of 5-year overall survival than the 7th edition

of AJCC; and also was externally validated as an effective prognostication model.[7] Over other prognostication models for colorectal cancer, this tool has the advantage of being the only nomogram using variables widely available in all clinical settings.[5] All these easily accessible variables individually were previously shown to influence overall and disease-free survival after colon cancer.[5]

Preoperative albumin level is another routinely tested variable that was shown to influence the overall survival of colorectal cancer patients, but was not included in the MSKCC prediction tool.[5,8]

This study aimed to test the impact of incorporation of this marker into the original MKSCC nomogram in predicting overall survival.

METHODOLOGY

Hospital records of 271 colon cancer patients with AJCC stage I to III, who underwent R0 resection between January 2009 and January 2014 in the General Surgery Departments of Ankara Training and Research Hospital & Ataturk Training and Research Hospital, Turkey, were retrospectively reviewed in 2020. The patients who died in the early postoperative period (within 30 days postoperatively), patients with non-primary colon cancers, and non-adenocarcinoma tumors, and cases that the pathologic examination did not reveal any lymph nodes, were excluded. The patients, whose preoperative albumin levels or information essential for the MSKCC nomogram were missing, were also excluded from the study. After the exclusions, the study analysis was restricted to 239 patients.

Every patient in the cohort was referred to the Oncology Department at the time of discharge from the Hospital, and the patients decided to be appropriate for adjuvant therapy by the oncologists, received chemotherapy after discharge. Thereafter, the patients were followed up at regular intervals by the Surgery and Oncology Departments. The follow-up schedule was as follows: Once in three months for the first three years, once in six months the following two years, and once in a year thereafter. The patients who were lost to follow-up were tracked for survival or the date of death *via* the central population registry system. Thus, the data of the observed overall survival of every patient in the study's patient cohort was acquired.

The AJCC stages of the included patients were recorded from their pathology and hospital reports. The following information, which are essential for the MSKCC nomogram, were also recorded: Age of diagnosis, gender, T-stage, tumor grade (well, moderately or poorly differentiated), total number of regional lymph nodes evaluated, and number of positive lymph nodes. In addition to these variables, the preoperative albumin level for each patient was also recorded. The observed overall survival was defined as the time interval from the day of surgery until the day of death or the last day of follow-up.

Three probability scores – as percentages – for 5-year overall survival, using three prediction systems, were assigned to each patient in the cohort. First, the estimated survival of every patient according to the AJCC staging system, using the observed overall survival rates for colon cancer stages as stated in the 7th edition of the AJCC cancer staging manual was determined.[9] Second, the 8th edition of the manual was not used since the observed survival rates were not referred in this edition. Then the predicted overall survival for each patient using the MSKCC online system was calculated.[6] Thirdly, an overall survival probability for each patient in the cohort was calculated by enhancement of the predicted MSKCC nomogram probability *via* adding the impact of preoperative serum albumin level to the overall survival probability by using logistic regression. The cutoff point of 3.5 g/dl was acknowledged for albumin level. The higher levels were accepted normal; and the lower levels were accepted as low. The impact of preoperative serum albumin level was calculated by Cox regression in this cohort. After overall survival scores for each patient were predicted using these three methods, the predictive accuracy of the methods was compared according to the observed overall survival in the patient cohort. The performance of the three prediction methods was evaluated by the area under the receiver operating characteristic curve (AUC), which was later converted to concordance index, a number between 0.5 and 1, indicating a random prediction and perfect concordance, respectively.

All the qualitative variables were expressed as counts and percentages; whereas, all the measurable variables that conformed to a non-normal distribution were expressed as median and IQR. Distribution of the variables was measured using Kolmogorov-Smirnov test. Non-parametric variables were analysed using the Mann-Whitney U-test. The performance of the three prediction methods was evaluated by the area under the receiver operating characteristic curve (AUC), which was later converted to concordance index. The univariate and multivariate analyses were performed using Cox regression. Survival analysis was performed using the Cox-regression analysis. IBM SPSS version 22.0 programme was used for the statistical analyses. A p-value of less than 0.05 was used to determine the level of significance.

RESULTS

The clinical characteristics of the 239 patients, comprising the present cohort, are summarised in Table I. The univariate analysis revealed that age ($p < 0.001$), T-stage ($p < 0.001$), N stage ($p < 0.001$), AJCC-stage ($p < 0.001$), lymph node positivity ($p = 0.027$), albumin level ($p < 0.001$), survival ratios according to AJCC manual ($p < 0.001$), survival ratios according to MSCC nomogram ($p < 0.001$), and survival ratios according to MSKCC nomogram enhanced with albumin ($p < 0.001$) were significantly associated with 5-year overall survival; whereas, gender, tumor location, tumor size, total number of examined lymph nodes, and differentiation of the tumor were not. According to the multivariate analysis, survival ratios according to MSKCC nomogram enhanced with albumin ($p = 0.023$), and survival ratios according to AJCC ($p < 0.001$) were significantly associated with 5-year overall survival (Table II).

Table I: Descriptive Analysis of the Patient Cohort (n=239).

		Median (IQR) / n (%)
Age (year)		64.77 (16.56)
Sex	Male	135 (56.5%)
	Female	104 (43.5%)
Follow up (month)		65.00 (0.43)
5 Years survival	(-)	96 (40.2%)
	(+)	143 (59.8%)
Albumin	˂3.5 g/dL	73 (30.5%)
	≥3.5 g/dL	166 (69.5%)
Albumin (g/dL)		3.80 (0.80)
MSKCC surv. score (%)		0.69 (0.23)
AJCC surv. score (%)		0.61 (0.21)
Positive LN (n)		0.00 (2.00)
Total exemined LN (n)		11.00 (11.00)
Tumor size (cm)		4.50 (2.70)
Tumor side	Right	75 (31.4%)
	Left	49 (20.5%)
	Sigmoid	99 (41.4%)
	Transverse	16 (6.7%)
T stage	T1	1 (0.4%)
	T2	33 (13.8%)
	T3	135 (56.5%)
	T4a	55 (23.0%)
	T4b	15 (6.3%)
N stage	N1a	31 (13.0%)
	N1b	34 (14.2%)
	N1c	7 (2.9%)
	N2a	24 (10.0%)
	N2b	20 (8.4%)
Tumor differantion	Poor	31 (13.0%)
	Moderate	148 (61.9%)
	Well	60 (25.1%)
AJCC stage	1	28 (11.7%)
	2A	72 (30.1%)
	2B	18 (7.5%)
	2C	7 (2.9%)
	3A	3 (1.3%)
	3B	75 (31.4%)
	3C	31 (13.0%)
	4A	4 (1.7%)
	4B	1 (0.4%)

AJCC Stage: Cancer Stage according to 7th edition of American Joint Committee on Cancer manual; LN: Lymph Node; AJCC Score: survival score according to 7th edition of American Joint Committee on Cancer manual; MSKCC Score: survival score according to Memorial Sloan Kettering Cancer Center nomogram

When the patients with more than 5-year overall survival were compared to the patients who died within the first five postoperative years, the AJCC ($p < 0.001$), MSKCC ($p < 0.001$), and MSKCC nomogram enhanced with albumin survival scores ($p < 0.001$) were significantly higher (Table III). According to Cox-regression, higher survival scores of all of the three systems were associated with higher overall survival (Table II).

The predictive efficiency of the AJCC TNM staging system, the MSKCC nomogram and the MSKCC nomogram with the addition of the impact of albumin levels were assessed by calculating the AUC. All the three systems were acceptably effective in predicting 5-year overall survival (Figure 1). Among the three systems, predicting overall survival according to the AJCC stages was the least reliable method, having a concordance index of 0.699 (0.631-0.767, 95% CI). MKSCC nomogram was slightly more effective than this method with a concordance index value of 0.702 (0.635-0.770, 95% CI). When impact of the preoperative albumin level was added to the MKSCC system using logistic regression, the prediction performance represented by concordance index increased to 0.777 (0.718-0.836, 95% CI).

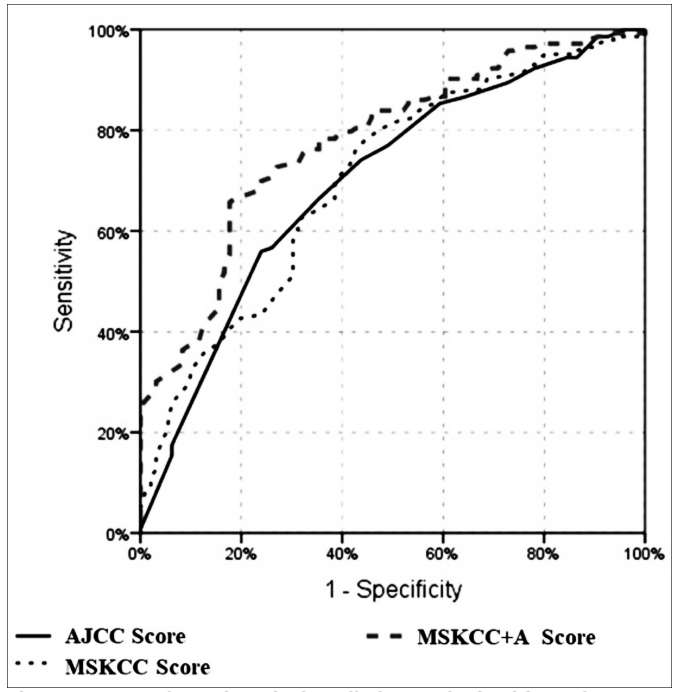

Figure 1: Comparison of survival prediction methods with receiver operating characteristic analysis (graphic).
AJCC score: Survival score according to 7th edition of American joint committee on cancer manual; MSKCC score: Survival score according to memorial sloan kettering cancer center nomogram; MSKCC+A score: Survival score according to memorial sloan kettering cancer center nomogram with albumin added.

DISCUSSION

Realising the advantages of individualised prognostication in patients with malignancy, and the inadequacy of the 7th edition of AJCC TNM system in personalised survival prediction in colon cancer, Weiser *et al*. proposed a new prognostic model less than a decade ago.[5] They demonstrated that replacing the N-stage variable with the number of totally harvested lymph nodes and the number of metastatic lymph nodes provided higher prognostic power than using a system solely based on T and N stages. They improved further on this system by adding tumor grade, patient age and gender. This simple personal prognostication system had the advantage of using easily accessible variables that were registered even in non-specialised centres and being more superior to the AJCC system in personal survival prediction.[5] This nomogram was later validated in a different patient group by a separate group of researchers;[7] and in a recent study, it was shown to perform better in discrimination for overall survival as compared to AJCC 7th edition in an Australian patient cohort.[10] Depending on the demonstrated efficacy of this nomogram, the first intention of this study was to investigate its prognostic power in a patient population which is distinct from previous populations, both ethnically and geographically.

The results of the present study proved, in its own patient population, the MSKCC nomogram to be a better predictor of survival when compared with the AJCC results.

Table II: Results of univariate and multivariate logistic regression analyses of parameters.

	Univariate Model			Multivariate Model		
	HR	% 95 CI	p	HR	% 95 CI	p
Sex	0.835	0.575-1.211	0.342			
Age	1.031	1.015-1.048	<0.001			
TM location	1.111	0.904-1.365	0.318			
TM size	0.959	0.874-1.052	0.377			
T stage	1.713	1.270-2.312	<0.001			
N stage	1.615	1.284-2.031	<0.001			
AJCC stage	1.826	1.362-2.448	<0.001			
Positive LN	1.023	1.002-1.043	0.027			
Total LN	0.997	0.979-1.015	0.721			
Tumor differantion	0.996	0.732-1.356	0.981			
Albumin	0.342	0.235-0.498	<0.001			
AJCC score	0.059	0.020-0.176	<0.001	0.043	0.020-0.094	<0.001
MSKCC score	0.052	0.021-0.128	<0.001			
MSKCC+A score	0.043	0.020-0.094	<0.001	1.403	1.047-1.879	0.023

Cox Regression. TM: Tumor; AJCC Stage: Cancer Stage according to 7th edition of American Joint Committee on Cancer manual; LN: Lymph Node; AJCC Score: survival score according to 7th edition of American Joint Committee on Cancer manual; MSKCC Score: survival score according to Memorial Sloan Kettering Cancer Center nomogram; MSKCC+A Score: survival score according to Memorial Sloan Kettering Cancer Center nomogram with albumin added.

Table III: Comparison of predicted scores of patients who achieved and did not achieve 5-year survival.

	Patients who did not achieved 5-year survival		Patients who achieved 5-year survival		p
	Median	Range	Median	Range	
AJCC score	0.52	0.13 – 0.74	0.67	0.18–0.79	<0.001
MSKCC score	0.62	0.14 – 0.89	0.74	0.11 – 0.94	<0.001
MSKCC+A score	0.45	0.07 – 0.83	0.75	0.05 – 0.89	<0.001

Mann-whitney u test. AJCC Score: survival score according to 7th edition of American Joint Committee on Cancer manual; MSKCC Score: survival score according to Memorial Sloan Kettering Cancer Center nomogram; MSKCC+A Score: survival score according to Memorial Sloan Kettering Cancer Center nomogram with albumin added.

In this study, the observed survival rates of the 7th edition of the AJCC were used to predict the overall survival of the patients in different TNM stages.[9] The 8th edition of the staging system was not used since the manual that was published in 2016 did not include the observed overall survival rates for different colon cancer stages; and it had only minor modifications compared with the 7th edition.[11] A recent study that was performed after the publication of the 8th edition also used the 7th edition for comparison with the discriminatory power of several nomograms.[10]

The second intention of the study was to search an approach to increase its prognostic power without depriving it of its uncomplicated nature. The easiest route to this second intention was to incorporate the impact of a known prognostic factor in cancer patients, to the individual predictions made by the MSKCC nomogram using logistic regression. Serum albumin level is one such variable whose low levels are known to be a risk factor for the mortality and other poor conditions in various clinical situations.[12] Serum albumin level is already known to correlate with postoperative morbidity and mortality in patients with colon cancer and to be associated with overall survival in advanced colon cancer.[13,14] Moreover, this parameter was previously found to be an independent prognostic factor for survival in various cancers including colorectal cancer.[8,15-18] Rather an inflammatory marker than a nutritional one among patients with colorectal cancer,[8] albumin is used for calculating modified Glasgow prognostic score, whose prognostic value has been confirmed in primary operable colorectal cancer patients.[19-21] Therefore, in the present study, the authors sought to enhance the effectiveness of MSKCC nomogram using the serum albumin values.

The present study demonstrates that the incorporation of the prognostic impact of preoperative albumin levels to the predictions made by MSKCC nomogram can strengthen its prognostic power. Indeed, according to the results of this study, the difference between the prognostic power of this new prognostic calculation and the original MSKCC nomogram is even greater than that between MSKCC nomogram and AJCC system. At this point, it needs to be emphasised that a new modified version of the MSKCC nomogram was not proposed by the authors in this study, since the patient number would be highly inadequate for such an objective. What was done was simply enhancing its prognostic power by calculating the impact of addition of preoperative albumin levels' prognostic power. This was done to show the improvement that can be provided by such a small modification. Depending on the positive results that were achieved, incorporation of this widely studied parameter to the MSKCC nomogram or any nomogram used in colon cancer patients as a variable can be proposed. For this purpose, a larger cohort of patients will be required in future studies that will be carried out for this purpose.

Improved survival prediction provided by this simple modification may be of great value both for the clinicians and the patients in making treatment decisions. The greatest expected impact may be on the decision of adjuvant chemotherapy decision, whose major determining factor is still AJCC TNM stage of the tumor.[22] An increase in the N-stage rises the AJCC-stage of the patient, which necessarily does not correlate with patient survival.[23,24] For instance, N+ tumors without distant organ metastases are classified into stage III, which may have a better prognosis than some stage

II tumors depending on the T-stage.[23,24] It was reported that patients with stage IIIA tumors fare better than patients with stage IIA and stage IIB tumors.[5] However, although N+ patients routinely receive chemotherapy, some high-risk stage II patients with T3 or T4 tumors are followed without adjuvant therapy.[22] This decision making for chemotherapy in patients with stage II colon cancer is a highly individualised action, which requires patient-physician discussion regarding the potential risk of adjuvant therapy compared to its potential benefits.[22] Currently, the factors that need to be taken into consideration include number of lymph nodes analysed after surgery (<12), poor prognostic features (such as poorly differentiated histology, lymphatic/vascular invasion, bowel obstruction, perineural invasion, localised perforation, status of the margins); and genetic characteristics of the tumor such as microsatellite instability or mismatch repair gene status.[22] Incorporating all of these parameters to a survival prediction calculator would result in much more refined predictions; but would end up in a rather complicated model. In the authors' opinion using a simple prediction model such as the MSKCC nomogram enhanced with serum albumin levels together with scrutiny of aforementioned considerations would benefit the clinicians and patients for better selection for cytotoxic chemotherapy. This may help increase adjuvant therapy's effectiveness, increasing the overall survival of colon cancer patients.

In addition to making better treatment decisions, enhanced selection of high-risk patients may be of value in surveillance planning. Using the estimates of an effective and simple survival calculation model together with the presence or absence of high-risk factors may ease the selection of patients in need of closer follow-up.

Another advantage of estimating prognosis may be building up of a stronger relationship between the physicians and the patients. As the patients raise questions about prognosis from the time of diagnosis, the inability of the clinicians to accurately predict is cited as an important barrier to patient--physician communication.[14,25] An effective model predicting survival tailored to individual patient factors is thus, a valuable tool for clinicians[14] and one for the patients to assist in planning their future.[5]

Lastly, more accurate prognostication may aid in designing clinical trials and patient selection.[14] This may help avoid imbalance between patient arms, especially in small trails; and can also help in identifying patients for trails where poor prognosis may warrant treatment escalation.[14]

The strength of this study lies in its validation of a previously used nomogram in a patient cohort that is ethnically, sociologically, and geographically distinct from the previous populations it was validated in. This nomogram has the strength of using data elements widely available from tumor registries and is more effective in predicting overall survival than AJCC TNM system. In this study, it is also proposed that addition of another widely studied variable can improve the prognostic power of the MSKCC nomogram.

It can be considered as a limitation of the study to propose a new nomogram including the variables of the MSKCC nomogram plus preoperative albumin level; however, the study population is not adequate for such a proposition.

CONCLUSIONS

Using MSKCC overall survival nomogram for predicting survival in patients with colon cancer seems feasible and useful for both clinicians and patients. The prognostic power of this calculator can further be enhanced by incorporating preoperative serum albumin level as an extra variable to the nomogram without depriving it of its uncomplicated nature. However, a future study with adequate number of patients is required to achieve this goal.

ETHICAL APPROVAL:
All data collections and analyses were carried out with the approval of the local Institutional Ethics Committee (Approval date/No. 07.02.2019/02-15). The study protocol confirmed the ethical guidelines of the 1975 Declaration of Helsinki as reflected in approval by the Ethics Committee.

PATIENTS' CONSENT:
As the study was designed retrospectively, data was collected from clinical archive after ethical approval.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
MK: Study design, data collection, literature review, writing and statistical analysis.
BOB, MOY, RHG: Drafting of work, data collection, editing, final review and correspondence.
All authors have critically reviewed the manuscript.

REFERENCES

1. Kozak VN, Khorana AA, Amarnath S, Glass KE, Kalady MF. Multidisciplinary clinics for colorectal cancer care reduces treatment time. *Clin Colorectal Cancer* 2017; **16(4)**:366-71. doi: 10.1016/j.clcc.2017.03.020.
2. Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: More than meets the eye. *Lancet Oncol* 2015; **16(4)**:e173-e80. doi: 10.1016/S1470-2045(14)71116-7.
3. Gunderson LL, Jessup JM, Sargent DJ, Greene FL, Stewart AK. Revised TN categorization for colon cancer based on national survival outcomes data. *J Clin Oncol* 2010; **28(2)**:264. doi: 10.1200/JCO.2009.24.0952.
4. Grimes DA. The nomogram epidemic: Resurgence of a medical relic. *Annals Internal Med* 2008; **149(4)**:273-5. doi: 10.7326/0003-4819-149-4-200808190-00010.
5. Weiser MR, Gonen M, Chou JF, Kattan MW, Schrag D.

Predicting survival after curative colectomy for cancer: Individualising colon cancer staging. *J Clin Oncol* 2011; **29(36)**:4796. doi: 10.1200/JCO.2011.36.5080.

6. Prediction tools: Colorectal cancer nomograms: Overall survival probability following surgery available from: URL: http://www.mskcc.org/nomograms/colorectal/overall_survival_probability.
7. Liu M, Qu H, Bu Z, Chen D, Jiang B, Cui M, *et al.* Validation of the memorial sloan-kettering cancer center nomogram to predict overall survival after curative colectomy in a Chinese colon cancer population. *Ann Surg Oncol* 2015; **22(12)**:3881-7. doi: 10.1245/s10434-015-4495-2.
8. Nazha B, Moussaly E, Zaarour M, Weerasinghe C, Azab B. Hypoalbuminemia in colorectal cancer prognosis: Nutritional marker or inflammatory surrogate? *World J Gastro Surg* 2015; **7(12)**:370. doi: 10.4240/wjgs. v7.i12.370.
9. Hari DM, Leung AM, Lee JH, Sim MS, Vuong B, Chiu CG, *et al.* AJCC cancer staging manual 7th edition criteria for colon cancer: Do the complex modifications improve prognostic assessment? *J Am College Surgeons* 2013; **217(2)**:181-90. doi: 10.1016/j.jamcollsurg.2013.04.018.
10. Jorissen RN, Croxford M, Jones IT, Ward RL, Hawkins NJ, Gibbs P, *et al.* Evaluation of the transferability of survival calculators for stage II/III colon cancer across healthcare systems. *Int J Cancer* 2019; **145(1)**:132-42. doi: 10.1002/ijc.32100.
11. Weiser MR. Ajcc 8th edition: Colorectal cancer. *Ann Surg Oncol* 2018; **25(6)**:1454-5. doi: 10.1245/s10434-018- 6462-1.
12. Kim S, McClave SA, Martindale RG, Miller KR, Hurt RT. Hypoalbuminemia and clinical outcomes: What is the mechanism behind the relationship? *Am Surg* 2017; **83(11)**: 1220-7. doi: 10.1177/000313481708301123.
13. Chiang J, Chang C, Jiang S, Yeh C, You J, Hsieh P, *et al.* Preoperative serum albumin level substantially predicts postoperative morbidity and mortality among patients with colorectal cancer who undergo elective colectomy. *Eur J Cancer Care* 2017; **26(2)**:e12403. doi: 10.1111/ecc.12403.
14. Sjoquist KM, Renfro LA, Simes RJ, Tebbutt NC, Clarke S, Seymour MT, *et al.* Personalising survival predictions in advanced colorectal cancer: The ARCAD nomogram project. *J Natl Cancer Inst* 2018; **110(6)**:638-48. doi: 10.1093/ jnci/djx253.
15. Heys S, Walker L, Deehan D, Eremin O. Serum albumin: A prognostic indicator in patients with colorectal cancer. *J Royal Coll Surg Edinburgh* 1998; **43(3)**:163-8.
16. Boonpipattanapong T, Chewatanakornkul S. Preoperative carbryonic antigen and albumin in predicting survival in patients with colon and rectal ccinoemarcinomas. *J Clin Gastroenterol* 2006; **40(7)**:592-5. doi: 10.1097/00004836-200608000-00006.
17. Onate-Ocana LF, Aiello-Crocifoglio V, Gallardo-Rincon D, Herrera-Goepfert R, Brom-Valladares R, Carrillo JF, *et al.* Serum albumin as a significant prognostic factor for patients with gastric carcinoma. *Ann Surg Oncol* 2007; **14(2)**:381-9. doi: 10.1245/s10434-006-9093-x.
18. Lam P, Leung M, Tse C. Identifying prognostic factors for survival in advanced cancer patients: A prospective study. *Hong Kong Med J* 2007; **13(6)**:453.
19. Dolan RD, Lim J, McSorley ST, Horgan PG, McMillan DC. The role of the systemic inflammatory response in predicting outcomes in patients with operable cancer: Systematic review and meta-analysis. *Sci Rep* 2017; **7(1)**:16717. doi: 10.1038/s41598-017-16955-5.
20. Liu Y, He X, Pan J, Chen S, Wang L. Prognostic role of glasgow prognostic score in patients with colorectal cancer: Evidence from population studies. *Sci Rep* 2017; **7(1)**:6144. doi: 10.1038/s41598-017-06577-2.
21. Park JH, Fuglestad AJ, Køstner AH, Oliwa A, Graham J, Horgan PG, *et al.* Systemic ınflammation and outcome in 2295 patients with stage I-III colorectal cancer from scotland and norway: First results from the scotscan colorectal cancer group. *Ann Surg Oncol* 2020; **27(8)**:2784-94. doi: 10.1245/s10434-020-08268-1.
22. Benson AB, Venook AP, Al-Hawary MM, Cederquist L, Chen YJ, Ciombor KK, *et al.* NCCN guidelines insights: Colon cancer, version 2.2018. *J National Comprehensive Cancer Network* 2018; **16(4)**:359-69. doi: 10.6004/jnccn.2018.0021.
23. Kong X, Li J, Cai Y, Tian Y, Chi S, Tong D, *et al*. A modified TNM staging system for non-metastatic colorectal cancer based on nomogram analysis of SEER database. *BMC Cancer* 2018; **18(1)**:50. doi: 10.1186/s12885-017-3796-1.
24. Kim MJ, Jeong SY, Choi SJ, Ryoo SB, Park JW, Park KJ, *et al*. Survival paradox between stage IIB/C (T4N0) and stage IIIA (T1-2N1) colon cancer. *Ann Surg Oncol* 2015; **22(2)**: 505-12. doi: 10.1245/s10434-014-3982-1.
25. Mack JW, Smith TJ. Reasons why physicians do not have discussions about poor prognosis, why it matters, and what can be improved. *J Clin Oncol* 2012; **30(22)**:2715-7. doi: 10.1200/JCO.2012.42.4564.