Cancer Research Journal
2022; 10(3): 55-60
http://www.sciencepublishinggroup.com/j/crj
doi: 10.11648/j.crj.20221003.11
ISSN: 2330-8192 (Print); ISSN: 2330-8214 (Online)

Glasgow Prognostic Score as a Prognostic Factor for Survival in Chinese Elderly Patients with Colorectal Cancer

Zi-Jian Li†, Qi An†, Jian Cui, Tao Yu, Guo-Ju Wu*

Department of General Surgery, Department of Gastrointestinal Surgery, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China

Email address:

13501359939@163.com (Guo-Ju Wu)

*Corresponding author

† Zi-Jian Li and Qi An are co-first authors.

To cite this article:

Zi-Jian Li, Qi An, Jian Cui, Tao Yu, Guo-Ju Wu. Glasgow Prognostic Score as a Prognostic Factor for Survival in Chinese Elderly Patients with Colorectal Cancer. *Cancer Research Journal*. Vol. 10, No. 3, 2022, pp. 55-60. doi: 10.11648/j.crj.20221003.11

Received: December 12, 2021; **Accepted**: June 14, 2022; **Published**: July 5, 2022

Abstract: To investigate the predictive value of Glasgow Prognostic Score (GPS) for the postoperative complications and survival in elderly patients with colorectal cancer (CRC) undergoing radical resection. These participants in Beijing Hospital between February 2009 and November 2011 were included and classified into three groups according to GPS. The GPS was constructed based on C-reactive protein and serum albumin. Univariate and multivariate analyses evaluating predictors of long-term survival were performed. 137 participants were enrolled, including 58 (42.3%) with GPS=0, 64 (46.7%) with GPS=1 and 15 (11.0%) with GPS=2. High GPS group patients were associated with older age ($P < 0.001$), higher levels of BMI ($P = 0.002$), higher rate of postoperative complications ($P < 0.001$), lymph node metastasis ($P < 0.001$), higher levels of CEA ($P < 0.001$), CA199 ($P = 0.031$), as well as more advanced tumor depth and TNM stage ($P < 0.001$). The 5-year survival rate was 40.9% and 5-year disease-free rate was 51.8%. Univariate and multivariate analyses revealed that GPS, CA199, TNM stage and BMI were independent risk factors of overall survival. Moreover GPS, CA199, TNM stage and BMI were independent risk factors of disease-free survival. The GPS was an independent biomarker to predict long-outcomes of elderly CRC patients undergoing radical resection.

Keywords: Colorectal Cancer, Glasgow Prognostic Score, Elderly, Survival Outcomes

1. Introduction

Colorectal cancer (CRC) is the third most common malignancy worldwide and the second leading cause of cancer-related death [1]. Approximate 1.93 million new cases were diagnosed in 2020 [2]. Currently, therapeutic strategies for CRC are determined by the tumor stage and patients' condition. Curative colorectal resection, chemotherapy, radiotherapy, immunotherapy as well as targeted therapy are effective therapeutic regimens. Nevertheless, high postoperative recurrence and metastasis rates remain a serious problem, and improving 5-years overall survival (OS) and disease-free survival (DFS) still a serious challenge. Hence, it is of great importance to explore novel indicators to predict the prognosis of CRC patients after surgery.

Increasing evidence indicates that the systemic inflammatory response plays a critical role in carcinogenesis. Cancer-related inflammation can influence cell proliferation, cell survival, angiogenesis, tumor cell migration, invasion, metastasis, and inhibition of adaptive immunity [3]. It's an independent risk factor for the development of tumor and is associated with worse prognosis in many malignancies [2, 4-6]. The original Glasgow Prognostic Score (GPS) was developed as a prognostic score in metastatic non-small cell lung cancer [7] and is composed of C-reactive protein (CRP) and albumin, both of which may reflect the underlying inflammatory condition and nutritional status [2]. Accumulating studies have showed the utility of the GPS as an indicator of survival outcomes for various cancers [8-11]. Due to systemic comorbidities and decreased physical and physiological functions, elderly patients are at high risks for morbidity and mortality and have poor prognosis. The predictive value of GPS in the elderly CRC patients remains unclear.

We aimed to evaluate and validate the relationship between preoperative GPS and long-term outcomes in Chinese elderly CRC patients undergoing radical resection. The results may provide a further insight into the association between preoperative GPS and prognosis of CRC patients.

2. Material and Methods

2.1. Patients

In this retrospective study, data were collected from 137 elderly patients with CRC who underwent curative operation at Department of General Surgery, Beijing Hospital, between February 2009 and November 2011. The inclusion criteria were as follows: (1) patients were diagnosed as advanced CRC based on imaging finding; (2) colorectal cancer confirmed by preoperative pathological examinations; (3) treatment without preoperative radiotherapy; (4) no serious surgical contraindications; (5) the age over 60 years old. The exclusion criteria were as follows: (1) multiple primary colorectal cancer; (2) incomplete clinical data; (3) emergency surgery. The patients' clinicopathological factors included age, gender, body mass index (BMI), tumor location, tumor characteristics, TNM stage, the results of laboratory tests such as CEA, CA199, CRP, albumin, operative characteristics and survival outcomes.

The optimal cutoff values for continuous variables were defined as old age (> 65 years old), underweight (BMI < 18.5 kg/m^2), and abnormal CEA level (CEA > 6 ng/mL), and abnormal CA199 level (CA199 > 37 ng/mL). The GPS was defined based on the presence of hypoalbuminemia (< 3.5 g/dL) and elevated CRP (> 10 mg/L) as follows: If both were abnormal, the score was 2; if either was abnormal, the score was 1; if not, the score was 0 [12].

2.2. Clinical Outcomes

Postoperative complications were graded using the Clavien-Dindo classification [13]. Patients were followed up at 3-month intervals. Recurrence was confirmed by clinical examinations. Overall survival (OS) was calculated from the time of surgery to the period of death from any cause or the last follow-up. Disease-free survival (DFS) was defined as the time from surgery to the time of cancer recurrence or death from any cause. The patients were continuously followed up until April 2016 or death, whichever occurred first.

2.3. Statistical Analysis

Statistical analyses were performed using SPSS software, version 26.0 (IBM Corporation). Group data were compared using Pearson's chi-square test. The associations between survival outcomes and clinicopathological characteristics were analyzed using Cox proportional hazard models. All independent variables significantly associated with survival outcomes in the univariate analysis were included in the multivariate analysis. The survival curves were generated by the R package (survminer). P-values < 0.05 were considered statistically significant.

3. Results

3.1. Patient Characteristics

A total of 137 patients were enrolled in this study. The clinical characteristics are shown in Table 1. The study population comprised 83 (60.6%) males and 54 (39.4%) females, with 82 (59.9%) of patients were above 65 years. Twenty-eight (21.8%) patients had stage I- II CRC, 44 (34.3%) had stage III-IV CRC. Tumor located in the colon in 83 cases (60.6%) and in the rectum in 54 cases (39.4%). All patients received standard surgery.

Table 1. *Clinicopathological characteristics of enrolled patients.*

Characteristic	Total (n=137)
Sex, n (%)	
Male	83 (60.6)
Female	54 (39.4)
Age at diagnosis, n (%)	
≥65 years old	82 (59.9)
<65 years old	55 (40.1)
BMI, n (%)	
< 18.5 kg/m^2	19 (13.9)
≥18.5 kg/m^2	118 (86.1)
CEA, n (%)	
≥6 ng/mL	52 (38.0)
<6 ng/mL	85 (62.0)
CA199, n (%)	
≥37 ng/mL	28 (20.4)
<37 ng/mL	109 (79.6)
Primary tumor location, n (%)	
Colon	83 (60.6)
Rectum	54 (39.4)
Histological type, n (%)	
Well/Moderately differentiated	113 (82.5)
Poor differentiated	24 (17.5)
Tumor depth, n (%)	
T1-T2	20 (14.6)
T3-T4	117 (85.4)
Lymph node metastasis, n (%)	
Negative	76 (55.5)
Positive	61 (44.5)
Metastasis, n (%)	0 (0)
TNM stage, n (%)	
I-II	75 (54.7)
III-IV	62 (45.3)
Postoperative complications, n (%)	
Clavien-Dindo grade 3 or higher	17 (12.4)
Glasgow Prognostic Score, n (%)	
0	58 (42.3)
1	64 (46.7)
2	15 (11.0)

3.2. Correlation Between GPS and Clinicopathological Characteristics

Patients were stratified into three groups according to GPS, 58 patients with a GPS of 0 (42.3%), 64 patients with a GPS of 1 (46.7%) and 15 patients with a GPS of 2 (11.0%) (Table 2). High GPS group patients were associated with older age (P < 0.001), higher levels of BMI (P = 0.002), higher rate of postoperative complications (P < 0.001), lymph node metastasis (P < 0.001), and higher levels of CEA (P < 0.001), CA199 (P = 0.031), as well as more advanced tumor depth and

TNM stage ($P < 0.001$). There was no statistical difference in sex, tumor location, and histological type.

Table 2. *The relationship between GPS and clinicopathological characteristics in enrolled patients.*

Characteristic	GPS			*P* value
	0 (n=58)	1 (n = 64)	2 (n = 15)	
Sex, n (%)				0.578
Male	38 (65.5)	36 (56.3)	9 (60.0)	
Female	20 (34.5)	28 (43.8)	6 (40.0)	
Age at diagnosis, n (%)				< 0.001
≥65 years old	18 (31.0)	52 (81.3)	12 (80.0)	
<65 years old	40 (69.0)	12 (18.7)	3 (20.0)	
BMI, n (%)				0.002
< 18.5 kg/m^2	2 (3.5)	12 (18.8)	5 (33.3)	
≥18.5 kg/m^2	56 (96.6)	52 (81.3)	10 (66.7)	
CEA, n (%)				< 0.001
≥6 ng/mL	10 (17.2)	36 (56.3)	6 (40.0)	
<6 ng/mL	48 (82.8)	28 (43.8)	9 (60.0)	
CA199, n (%)				0.026
≥37 ng/mL	6 (10.3)	19 (29.7)	3 (20.0)	
<37 ng/mL	52 (89.7)	45 (70.3)	12 (80.0)	
Primary tumor location, n (%)				0.157
Colon	31 (53.4)	40 (62.5)	12 (80.0)	
Rectum	27 (46.6)	24 (37.5)	3 (20.0)	
Histological type, n (%)				0.088
Well/Moderately differentiated	52 (89.7)	51 (79.7)	10 (66.7)	
Poor differentiated	6 (10.3)	13 (20.3)	5 (33.3)	
Tumor depth, n (%)				0.018
T1-T2	13 (22.4)	7 (10.9)	0 (0)	
T3-T4	45 (77.6)	57 (89.1)	15 (100)	
Lymph node metastasis, n (%)				< 0.001
Negative	42 (72.4)	31 (48.4)	3 (20.0)	
Positive	16 (27.6)	33 (51.6)	13 (80.0)	
Metastasis, n (%)	0 (0)	0 (0)	0 (0)	1.000
TNM stage, n (%)				< 0.001
I-II	42 (72.4)	30 (46.9)	3 (20.0)	
III-IV	16 (27.6)	34 (53.1)	12 (80.0)	
Postoperative complications, n (%)				< 0.001
Clavien-Dindo grade 3 or higher	3 (5.2)	10 (15.6)	11 (73.3)	

3.3. Prognostic Value of Glasgow Prognostic Score for Survival

The median follow-up time for all patients was 43 months (range 1-86 months). During the follow-up period, 81 events (59.1%) of death were observed in this study population. Disease recurrence was detected in 66 patients (48.2%).

Univariate analysis revealed that OS was significantly associated with the age ($p = 0.015$), BMI ($p = 0.011$), CEA ($p = 0.048$), CA199 ($p < 0.001$), lymph node metastasis ($p < 0.001$), TNM stage ($p < 0.001$), postoperative complications ($p < 0.001$), and GPS ($p < 0.001$). In multivariate analysis, BMI (HR = 0.551; 95%CI: 0.304-0.996) was found to be a predictor of improved OS. While CA199 (HR = 2.060; 95%CI: 1.264-3.357), TNM stage (HR = 1.837; 95%CI: 1.145-2.948) and GPS (1, HR = 2.314; 95%CI: 1.309-4.090; 2, HR =5.296; 95%CI: 2.528-11.095) as independent predictors of poor OS (Table 3).

Univariate and multivariate analysis demonstrated BMI (HR = 0.358; 95%CI: 0.184-0.696), CA199 (HR = 1.732; 95%CI: 1.010-2.970), TNM stage (HR = 4.168; 95%CI: 2.365-7.346) and GPS (1, HR = 1.495; 95%CI: 0.818-2.734; 2, HR =3.434; 95%CI: 1.555-7.584) as independent predictors of DFS (Table 4).

The 5-year OS and DFS rates were significantly poorer in the high GPS group than in the other groups (GPS=2 vs. GPS=1 vs. GPS=0: 26.7% vs. 26.6% vs. 67.2%, $p < 0.001$; and 0% vs. 32.8% vs. 63.8%, $p < 0.001$, respectively) (Figure 1).

Table 3. *Univariate and multivariate analyses of predictive factors for overall survival.*

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex (Female)	1.189 (0.765-1.848)	0.441		
Age at diagnosis (≥65 years old)	1.817 (1.125-2.932)	0.015		0.634
BMI (≥18.5 kg/m^2)	0.482 (0.275-0.848)	0.011	0.551 (0.304-0.996)	0.048
CEA (≥6 ng/mL)	1.555 (1.004-2.408)	0.048		0.722
CA199 (≥37 ng/mL)	2.840 (1.760-4.582)	< 0.001	2.060 (1.264-3.357)	0.004
Primary tumor location (Rectum)	0.911 (0.582-1.427)	0.685		

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Histological type (Poor)	1.516 (0.897-2.563)	0.121		
Tumor depth (T3-T4)	1.745 (0.840-3.627)	0.136		
Lymph node metastasis (Positive)	2.232 (1.436-3.468)	< 0.001		0.525
TNM stage (III-IV)	2.331 (1.498-3.628)	< 0.001	1.837 (1.145-2.948)	0.012
Postoperative complications	2.937 (1.691-5.102)	< 0.001		0.616
Glasgow Prognostic Score (1)	3.197 (1.854-5.513)	< 0.001	2.314 (1.309-4.090)	0.004
Glasgow Prognostic Score (2)	7.723 (3.830-15.572)	< 0.001	5.296 (2.528-11.095)	< 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio.

Table 4. *Analyses of predictive factors for disease-free survival.*

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex (Female)	1.048 (0.643-1.708)	0.851		
Age at diagnosis (≥65 years old)	1.477 (0.890-2.453)	0.131		
BMI (≥18.5 kg/m^2)	0.428 (0.233-0.788)	0.006	0.358 (0.184-0.696)	0.002
CEA (≥6 ng/mL)	1.700 (1.048-2.759)	0.032		0.946
CA199 (≥37 ng/mL)	2.312 (1.362-3.925)	0.002	1.732 (1.010-2.970)	0.046
Primary tumor location (Rectum)	1.053 (0.645-1.721)	0.836		
Histological type (Poor)	1.907 (1.095-3.319)	0.023		0.351
Tumor depth (T3-T4)	2.288 (0.987-5.304)	0.054		
Lymph node metastasis (Positive)	4.181 (2.491-7.015)	< 0.001		0.405
TNM stage (III-IV)	4.466 (2.644-7.541)	< 0.001	4.168 (2.365-7.346)	< 0.001
Postoperative complications	3.093 (1.679-5.699)	< 0.001		0.445
Glasgow Prognostic Score (1)	2.467 (1.384-4.398)	0.002	1.495 (0.818-2.734)	0.192
Glasgow Prognostic Score (2)	7.290 (3.492-15.220)	< 0.001	3.435 (1.555-7.584)	0.002

Abbreviations: CI, confidence interval; HR, hazard ratio.

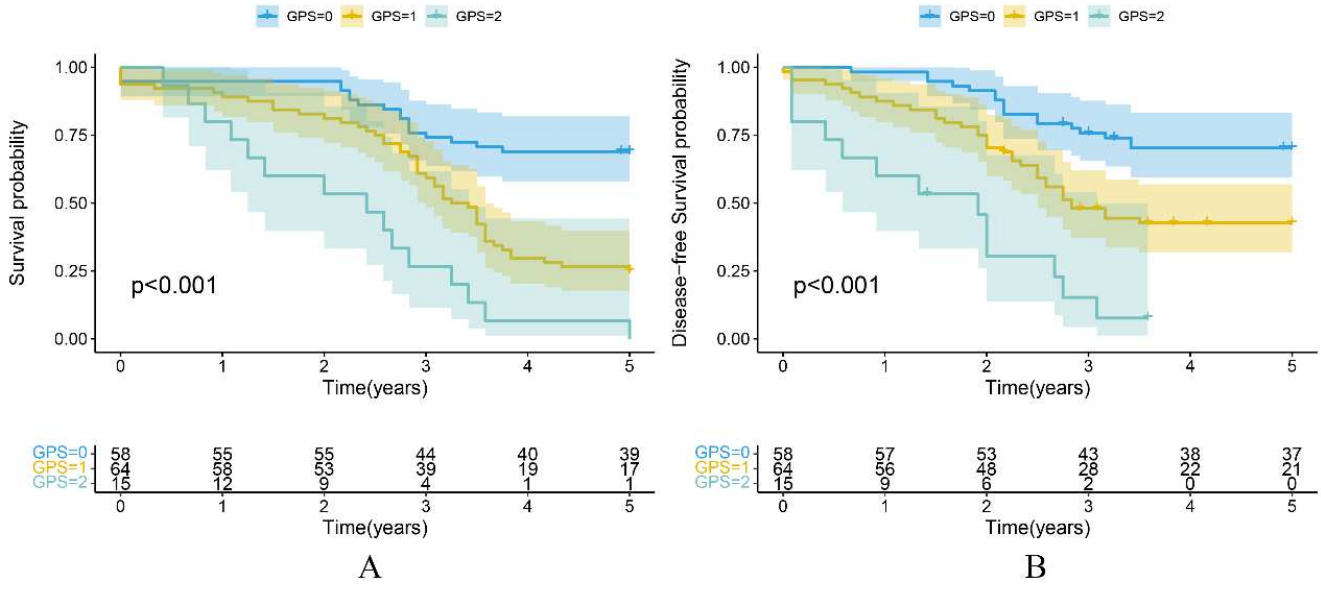

Figure 1. *The overall survival (A) and disease-free survival (B) of patients with different GPS.*

4. Discussion and Conclusion

In the present study, we found that preoperative GPS was significantly associated with OS and DFS of CRC patients in univariate and multivariate analyses. We found the GPS was significantly higher in patients with older age, lower BMI, lymph node metastasis, higher levels of CEA and CA199 and advanced TNM stage. No significant difference could be detected among the GPS groups when sex, tumor location, and histological type were analyzed.

Inflammation has an important role in the initiation and progression in colorectal cancer [14]. It could modify the tumor microenvironment that permits the progression and metastasis of tumor cells and correlate with response to therapy [15]. A combination of inflammation-related indicators has a significant potential in predicting the initiation and development of tumors and patient prognosis. CRP is a positive acute-phase inflammatory reactant synthesized by the liver and a marker of systemic inflammation [16]. And CRP

has been perceived as an independent biomarker to predict survival outcome in various cancers, including colorectal cancer [17], breast cancer, cervical cancer [18], bone neoplasms [19], lung cancer [20] and urologic cancer [21]. While as a major protein synthesized by the liver, albumin is a negative acute phase reactant related to inflammation. The albumin level is decreased in cancer patients due to malnutrition and systemic inflammation. Hypoalbuminemia correlates with poor prognosis of the many malignancies, such as adrenocortical carcinoma [22], prostate cancer [23], pancreatic ductal adenocarcinoma [24], and gastric cancer [25]. CRP and albumin levels are the two markers that represent a balance between inflammation and nutritional status [8]. The pathophysiological background of the GPS is the intensity of systemic inflammation and decreasing nutritional status elicited by consumptive character of an underlying malignant disease [10]. The calculation of the GPS is an extremely cost-effective and readily available tool to predict survival in cancer patients.

Compared with other types of cancer, patients with CRC have been found higher rate of malnutrition due to its local effects on bowel function from obstruction and malabsorption. In our study, low BMI was significantly associated with shorter OS and DFS. Because malnutrition can impede the effects of anticancer therapies. Huong et al. [26] found that nutritional intervention could improve outcomes in colon cancer patients receiving chemotherapy. Therefore, it is important to provide effective nutritional intervention for oncology patients, particularly CRC patients. Elderly patients always have poor prognosis owing to systemic comorbidities and decreased physical and physiological functions. As shown in this study, patient age was related with the GPS, but wasn't associated with survival outcomes. While Tamai et al. [6] proposed that elderly patients with chronic inflammation, C-reactive protein/albumin ratio (CAR) maybe a useful prognostic marker. What's more, Yu et al. [27] found that CAR is an effective predictor for anastomotic leak in elderly patients. TNM stage has been validated as indicators to evaluate CRC prognosis before patients undergo treatment. Our current study showed that advanced TNM stage is an independent predictor of poor OS and DFS. Studies have confirmed that CEA has independent prognostic value in CRC, and that preoperatively elevated CEA was correlated with worsened outcomes [28]. Koper-Lenkiewicz et al. [29] found that CA199 could affect the CRP concentration. In present study we found that serum CEA and CA199 levels were related with the GPS and prognosis of CRC patients.

There are several limitations to our study. One of the main limitations of the current study was the relatively small number of patients and its single-center, retrospective design, which made the data may not be fully convincing. And we didn't get the detailed adjuvant therapy of all patients, which may influence our results. Therefore, a multi-center, prospective, large scale well-designed studies are needed.

In conclusion, the present study demonstrated that GPS, an inflammation-based score, is a useful marker in predicting the prognosis of CRC patients who received curative surgery.

References

[1] 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.

[2] Liao CK, Yu YL, Lin YC, et al. Prognostic value of the C-reactive protein to albumin ratio in colorectal cancer: an updated systematic review and meta-analysis. *World J Surg Oncol*. May 1 2021; 19 (1): 139. doi: 10.1186/s12957-021-02253-y.

[3] Choi KW, Hong SW, Chang YG, et al. Inflammation-based score (Glasgow prognostic score) as an independent prognostic factor in colorectal cancer patients. *Annals of surgical treatment and research*. 2014; 86 (6): 309-313. doi: 10.4174/astr.2014.86.6.309.

[4] He L, Li H, Cai J, et al. Prognostic Value of the Glasgow Prognostic Score or Modified Glasgow Prognostic Score for Patients with Colorectal Cancer Receiving Various Treatments: a Systematic Review and Meta-Analysis. *Cell Physiol Biochem*. 2018; 51 (3): 1237-1249. doi: 10.1159/000495500.

[5] Hong T, Shen D, Chen X, Cai D, Wu X, Hua D. A novel systematic inflammation related index is prognostic in curatively resected non-metastatic colorectal cancer. *Am J Surg*. Sep 2018; 216 (3): 450-457. doi: 10.1016/j.amjsurg.2017.07.021.

[6] Tamai K, Okamura S, Makino S, et al. C-reactive protein/albumin ratio predicts survival after curative surgery in elderly patients with colorectal cancer. *Updates Surg*. Mar 6 2021; doi: 10.1007/s13304-021-01011-9.

[7] Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *Br J Cancer*. 2003; 89 (6): 1028-1030.

[8] Qu G, Wang D, Xu W, Wu K, Guo W. The Systemic Inflammation-Based Prognostic Score Predicts Postoperative Complications in Patients Undergoing Pancreaticoduodenectomy. *Int J Gen Med*. 2021; 14: 787-795. doi: 10.2147/ijgm.S299167.

[9] Minohara K, Matoba T, Kawakita D, et al. Novel Prognostic Score for recurrent or metastatic head and neck cancer patients treated with Nivolumab. *Sci Rep*. 2021; 11 (1): 16992. doi: 10.1038/s41598-021-96538-7.

[10] Gebauer N, Mengler B, Kopelke S, et al. Prognostic impact of nutritional and inflammation-based risk scores in follicular lymphoma in the era of anti-CD20 targeted treatment strategies. *J Cancer Res Clin Oncol*. 2021; doi: 10.1007/s00432-021-03758-5.

[11] Imai H, Kishikawa T, Minemura H, et al. Pretreatment Glasgow prognostic score predicts survival among patients with high PD-L1 expression administered first-line pembrolizumab monotherapy for non-small cell lung cancer. *Cancer Med*. 2021; doi: 10.1002/cam4.4220.

[12] Yu YL, Fan CW, Tseng WK, et al. Correlation Between the Glasgow Prognostic Score and the Serum Cytokine Profile in Taiwanese Patients with Colorectal Cancer. *Int J Biol Markers*. Jun 2021; 36 (2): 40-49. doi: 10.1177/17246008211022769.

[13] Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004; 240 (2): 205-213. doi: 10.1097/01.sla.0000133083.54934.ae.

[14] Triantafillidis JK, Nasioulas G, Kosmidis PA. Colorectal cancer and inflammatory bowel disease: epidemiology, risk factors, mechanisms of carcinogenesis and prevention strategies. *Anticancer Res*. Jul 2009; 29 (7): 2727-37.

[15] Gaiani F, Marchesi F, Negri F, et al. Heterogeneity of Colorectal Cancer Progression: Molecular Gas and Brakes. *Int J Mol Sci*. 2021; 22 (10) doi: 10.3390/ijms22105246.

[16] Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *The Journal of clinical investigation*. 2003; 111 (12): 1805-1812.

[17] Lumachi F, Basso SMM, Santeufemia DA, Ermani M, Lo Re G, Chiara GB. Preoperative serum C-reactive protein and its prognostic significance in patients with stage III-IV colorectal cancer. *Anticancer Res*. 2014; 34 (12): 7263-7266.

[18] Han X, Liu S, Yang G, et al. Prognostic value of systemic hemato-immunological indices in uterine cervical cancer: A systemic review, meta-analysis, and meta-regression of observational studies. *Gynecol Oncol*. 2021; 160 (1): 351-360. doi: 10.1016/j.ygyno.2020.10.011.

[19] Li W, Luo X, Liu Z, Chen Y, Li Z. Prognostic value of C-reactive protein levels in patients with bone neoplasms: A meta-analysis. *PLoS One*. 2018; 13 (4): e0195769. doi: 10.1371/journal.pone.0195769.

[20] Moik F, Zöchbauer-Müller S, Posch F, Pabinger I, Ay C. Systemic Inflammation and Activation of Haemostasis Predict Poor Prognosis and Response to Chemotherapy in Patients with Advanced Lung Cancer. *Cancers (Basel)*. 2020; 12 (6) doi: 10.3390/cancers12061619.

[21] Tamura K, Osawa T, Takeuchi A, et al. External validation of the albumin, C-reactive protein and lactate dehydrogenase model in patients with metastatic renal cell carcinoma receiving second-line axitinib therapy in a Japanese multi-center cohort. *Jpn J Clin Oncol*. 2021; 51 (5): 810-818. doi: 10.1093/jjco/hyaa264.

[22] Zhang F, Liu Z, Liang J, et al. Association between preoperative serum albumin and prognosis in patients with adrenocortical carcinoma after primary resection: a retrospective study. *BMC Cancer*. Aug 26 2021; 21 (1): 961. doi: 10.1186/s12885-021-08689-5.

[23] Pan J, Wang J, Wei Y, et al. Combination of body mass index and albumin predicts the survival in metastatic castration-resistant prostate cancer patients treated with abiraterone: A post hoc analysis of two randomized trials. *Cancer Med*. Aug 20 2021; doi: 10.1002/cam4.4205.

[24] Arima K, Yamashita Y-i, Hashimoto D, et al. Clinical usefulness of postoperative C-reactive protein/albumin ratio in pancreatic ductal adenocarcinoma. *The American Journal of Surgery*. 2018/07/01/ 2018; 216 (1): 111-115. doi: https://doi.org/10.1016/j.amjsurg.2017.08.016.

[25] Yamashita K, Ushiku H, Katada N, et al. Reduced preoperative serum albumin and absence of peritoneal dissemination may be predictive factors for long-term survival with advanced gastric cancer with positive cytology test. *European Journal of Surgical Oncology (EJSO)*. 2015/10/01/ 2015; 41 (10): 1324-1332. doi: https://doi.org/10.1016/j.ejso.2015.05.021.

[26] Huong LT, Phuong DT, Anh DK, et al. Nutritional Intervention Improves Nutrition Outcomes in Stomach and Colon Cancer Patients Receiving Chemotherapy: Finding from a Quasi-Experiment in Vietnam. *Healthcare (Basel)*. Jul 4 2021; 9 (7) doi: 10.3390/healthcare9070843.

[27] Yu Y, Wu Z, Shen Z, Cao Y. Preoperative C-reactive protein-to-albumin ratio predicts anastomotic leak in elderly patients after curative colorectal surgery. *Cancer Biomark*. 2020; 27 (3): 295-302. doi: 10.3233/cbm-190470.

[28] Lehtomäki K, Mustonen H, Kellokumpu-Lehtinen P-L, et al. Lead Time and Prognostic Role of Serum CEA, CA19-9, IL-6, CRP, and YKL-40 after Adjuvant Chemotherapy in Colorectal Cancer. *Cancers (Basel)*. 2021; 13 (15) doi: 10.3390/cancers13153892.

[29] Koper-Lenkiewicz OM, Dymicka-Piekarska V, Milewska AJ, Zińczuk J, Kamińska J. The Relationship between Inflammation Markers (CRP, IL-6, sCD40L) and Colorectal Cancer Stage, Grade, Size and Location. *Diagnostics (Basel)*. Jul 31 2021; 11 (8) doi: 10.3390/diagnostics11081382.