sciendo
10.2478/AMB-2025-0006

ORIGINAL ARTICLE

THE ROLE OF ALBUMIN-TO-FIBRINOGEN AND FIBRINOGEN-TO-PREALBUMIN RATIOS IN THE DEVELOPMENT OF OVARIAN CARCINOMA

V. Racheva[1], I. Dekova[2], Z. Gorcheva[3], T. Semova[4], D. Dimitrov[4], E. Petkova[5]

[1]Clinical Laboratory, University Hospital „Sv. Marina“ Pleven, Medical University – Pleven, Bulgaria
[2]Department of Hepatobiliary and Pancreatic Surgery at the First Clinic of University Hospital „Dr. G. Stranski – Pleven“, Medical University – Pleven, Bulgaria
[3]Clinic of Internal Medicine, University Hospital „Sv. Marina“ Pleven, Medical University – Pleven, Bulgaria
[4]Obstetrics and Gynaecology, University Hospital „Sv. Marina“ Pleven, Medical University – Pleven, Bulgaria
[5]Department of Midwifery care, Faculty of Health Care, Medical University – Pleven, Bulgaria

Abstract. *Ovarian carcinoma (OC) has the highest mortality among gynecological carcinomas in developed countries. Many authors have drawn attention to fibrinogen-to-prealbumin (FPR) and albumin-to-fibrinogen (AFR) ratios and demonstrated that low AFR values and high FPR values correlate with an increased risk of mortality and recurrence of carcinoma and may be promising prognostic markers for malignant diseases. As emerging biomarkers, FPR and AFR have significant advantages due to their availability, cost-effectiveness, and reliability.*

Key words: *ovarian carcinoma, prealbumin, albumin, fibrinogen, ratios, prognosis*

Corresponding author: *Valeria Z. Racheva, tel: +359889228102, e-mail: v_ra4eva22@abv.bg*

ORCID: *0000-0001-7777-7713*

Received: *17 September 2024;* ***Accepted:*** *08 October 2024*

INTRODUCTION

Morbidity and mortality from oncological diseases are increasing rapidly worldwide. Prognosis for patients with such diseases remains poor and their 5-year survival rate is only 67% [1].

Ovarian carcinoma is one of the deadliest malignancies in women. Worldwide, the incidence rate is 6.6 cases per 100,000 people and the mortality rate is 4.2 cases per 100,000 people [2]. Lack of screening, late diagnosis caused by unclear and nonspecific symptoms and high recurrence rate (70-80%) influence its poor prognosis [3, 4] and its low five-year survival rate ~ 45% [5, 6].

Routinely used approaches for the diagnosis of ovarian carcinoma are transvaginal ultrasonography and determination of the concentration of carcinoma antigen 125 (CA 125) in the blood [7, 8]. They do not have high specificity and sensitivity, which prevents the correct analysis of the obtained results and is associated with the low survival of patients [9].

In order to improve survival from this disease, it is necessary to identify both new markers for its early detection and new prognostic factors to improve risk stratification.

Many researchers prove that nutrition, inflammation and coagulation play an important role in the progression of oncological diseases [10].

Numerous studies have confirmed that serum albumin (Alb), prealbumin (preAlb) and plasma fibrinogen (Fib) are involved in the regulation of the onset and devel-

opment of various tumors. Their role in the coagulation cascade and in reflecting the nutritional status of the person is recognized. They provide information about the presence of local and systemic inflammation associated with the presence of a tumor [11-13].

More and more studies prove that the levels of albumin, prealbumin and fibrinogen are closely related to the prognosis of tumors [14-16].

Albumin is the most abundant protein in human plasma, accounting for more than 50% of total serum protein [17]. It is mainly synthesized by hepatocytes. It is involved in the maintenance of colloid osmotic pressure, the transport of nutrients and the metabolism of toxic substances and plays a key role in acute and chronic inflammation of the body [18]. Alb level is an important nutritional index for carcinoma patients [19]. In patients with advanced or metastatic malignant diseases, serum albumin concentrations decrease regardless of malnutrition [20].

Prealbumin is a negative acute phase protein. It is synthesized by the liver and has a short half-life of about two days and a smaller serum pool than albumin. Its main functions are to bind and transport endogenous proteins and small molecules. It reflects patients‘ recent dietary intake rather than their overall nutritional status [21]. It shows changes due to malnutrition in a significantly short period of time and is therefore considered a major nutritional index for detecting high-risk patients [22]. Prealbumin is also known as transthyretin and is involved in the regulation of the synthesis and transport of vitamin A and thyroxine [23]. Its serum concentration can be affected by various factors, such as dietary intake, inflammatory state, liver disease, endocrine disease. However, many studies have demonstrated that low preoperative preAlb levels are an independent poor prognostic factor for survival [24].

Fibrinogen is a plasma glycoprotein with a molecular mass of 340 kDa and consists of three pairs of polypeptide chains, α-, β- and γ-chains [25]. It is factor 1 in the coagulation cascade, is synthesized by the liver, and has a half-life of four to six days. Under the action of thrombin, Fib is transformed into fibrin, which plays a central role in thrombosis [26, 27]. As a protein in the acute phase of inflammation, Fib is increased in coagulation-related diseases, surgery, infections, trauma, and tumors [28]. Numerous studies have shown that it is related to the level of inflammation, to the processes of proliferation of malignant tumor cells, metastases and formation of an inflammatory microenvironment [29]. There is evidence that Fib levels are significantly associated with the prognosis of various tumors [30]. Several studies have reported that higher preoperative fibrinogen level is associated with tumor development and indicates poor prognosis [10] and low survival in carcinoma [29].

Role of coagulation in the progression of oncological diseases

The appearance and development of various malignant tumors are often accompanied by various coagulation disorders. Activation of factors by the coagulation system leads to hypercoagulability, which is associated with malignant tumor proliferation and metastasis [31]. Studies have shown that about 50% of patients with tumors that have not metastasized and 90% of patients with metastatic tumor have disorders of coagulation function [32, 33].

There is ample evidence that the presence of malignant tumors significantly increases the level of Fib, which increases blood viscosity and leads to hypercoagulation [34]. Therefore, Fib can be considered as a key factor for tumor metastasis [35].

Role of nutrition in the progression of oncological diseases

Patients with malignant tumors often suffer from malnutrition and progressive weight loss. This creates a vicious circle in which the protective abilities of the immune system are weakened, the risk of infection increases and the proliferation and development of tumor cells is accelerated. This causes deterioration of the patient‘s condition and quality of life [36]. Alb level is a sensitive nutritional index [37]. Tumor cell proliferation requires an increase in albumin uptake for cells to maintain their metabolic functions, leading to a decrease in Alb storage capacity and in turn hypoalbuminemia [38].

A large number of studies have shown that hypoalbuminemia is closely related to the occurrence of various postoperative complications [39] and prolongation of the time required for tissue repair. These complications lead to a poor prognosis [15, 40].

Prealbumin is more sensitive to changes in protein-energy status than albumin, and its concentration reflects recent dietary intake rather than overall nutritional status [41]. Therefore, preAlb concentration can be considered primarily as a marker for patients who need nutritional monitoring [42]. Low preAlb concentration is an independent risk factor associated with poor postoperative survival [43].

Role of inflammation in cancer progression

The inflammatory response plays an important role in tumor progression. The tumor microenvironment includes stromal cells, cytokines, and tumor cells that are associated with inflammation [44]. They stimulate

the appearance and development of tumors and inhibit the ability of the immune system to kill the tumor and ultimately affect the patient's survival rate [45-47]. Increasing evidence suggests that markers of systemic inflammatory response correlate with long-term survival of various tumors [48, 49] and serve as a prognostic factor [50-53]. Multiple studies have shown that serum preAlb levels change when inflammation and tissue damage occur [54]. The tumor induces the release of various pro-inflammatory factors, inhibits the synthesis of Alb and reduces its amount. Thus, the change in Alb levels is directly proportional to the patient's level of inflammation [55]. A decrease in Alb concentration enhances the tumor-associated inflammatory response and leads to the release of cytokines that contribute to tumor progression [56]. Therefore, serum levels of Alb and preAlb not only represent the nutritional status of the body, but also reflect the degree of inflammation in the body. Fib increases with systemic inflammation. The infiltration of inflammatory cells increases the secretion of interleukin-6 (IL-6), IL-21 and IL-33. This secretion increases the intensity of the systemic inflammatory response and affects the recovery and survival of patients [57, 58].

Although many studies have shown that Alb, preAlb, and Fib are related to the prognosis and treatment effect of cancer patients, some scientists question the accuracy and effectiveness of using them alone [59].

Increasing evidence suggests that preoperative fibrinogen-to-prealbumin (FPR) and albumin-to-fibrinogen (AFR) ratios are markers that can simultaneously reflect a patient's inflammation, coagulation, and nutritional status and have prognostic value in many solid tumors [60], such as ovarian carcinoma [61], esophageal carcinoma [62], breast carcinoma [63], gastric carcinoma [36] and non-small cell lung carcinoma.

OBJECTIVE

The aim of our study was, by determining the AFR and FPR ratios in women with proven ovarian carcinoma, to assess to what extent they may be factors predicting the development and prognosis of ovarian carcinoma.

MATERIALS AND METHODS

Sixty women with histopathological biopsy-proven ovarian carcinoma participated in our study. The patients underwent surgery and were hospitalized in the Gynecology Clinic of the „Sv. Marina" UMBAL Pleven in the period 01.2020-11.2020. The average age of the patients was 57.67 years (age range 29-83 years).

In all patients, we took venous blood from v. brachialis in 2 Greiner Vacuette tubes – one without anticoagulant to separate serum, the other with trisodium citrate anticoagulant (9:1) to separate citrate plasma. After centrifugation of the blood at 3500 rpm (revolutions per minute) for 15 minutes, the separated serum was used to determine the concentrations of albumin and prealbumin, and the separated citrated plasma was used to determine the concentration of fibrinogen. We did all the research in the Clinical Laboratory of the „Sveta Marina" UMBAL Pleven. We determined the albumin concentration by a colorimetric method with bromocresol green on a biochemical analyzer AU 480 Beckman Coulter. Prealbumin concentrations were determined by immunoturbidimetric method on the same biochemical analyzer AU 480 Beckman Coulter. We measured the plasma concentration of fibrinogen with thrombin reagent of Dutch diagnostic according to the Claus method on an automatic coagulometer Coagulazer 100.

All patients in the study gave written informed consent.

The patients were staged according to the classification of the International Federation of Obstetrics and Gynecology FIGO, which led to the formation of 3 working groups:

1) group 1 – 19 patients with ovarian carcinoma in stage I according to FIGO (mean age 51.1 years and age range 29-72 years);

2) group 2 – 19 patients with ovarian carcinoma in stage II according to FIGO (average age 58.6 years and age range 40-77 years);

3) group 3 – 22 patients with ovarian carcinoma in stage III according to FIGO (average age 62.5 years and age range 42-83 years).

There were no FIGO stage IV patients among the patients in our study.

From the data in the patients' medical records, we obtained information about concomitant malignancies, liver diseases leading to impaired liver function, autoimmune and hematological diseases. The presence of such diseases were the criteria for excluding patients from our study.

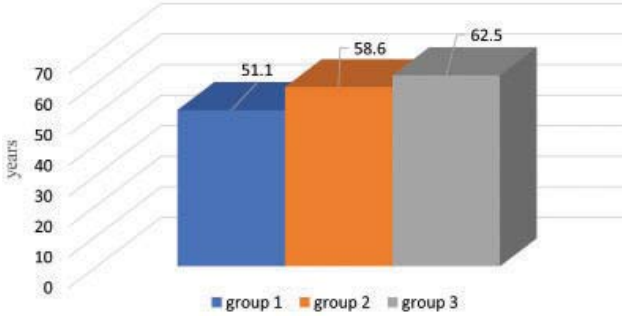

Fig. 1. Mean age of the patients in the three groups

RESULTS

We determined the concentrations of albumin, prealbumin and fibrinogen in all (n = 60) patients. We adopted the reference values for each of the studied parameters, according to the recommendations of the manufacturers of the reagents used:

For albumin 35-52 g/l; for prealbumin 0.2-0.4 g/l; for fibrinogen 2.0-4.0 g/l

We calculated mean concentration and standard deviation (Mean ± SD) for each of the three parameters in the three groups.

We determined albumin-to-fibrinogen (AFR) and fibrinogen-to-prealbumin (FPR) ratios in all patients (n = 60).

We calculated mean concentration and standard deviation (Mean ± SD) for AFR and FPR in the three groups.

Table 1. Mean concentrations of albumin, prealbumin and fibrinogen in the three groups.

Parameter	Mean ± SD		
	1st group – I stage	2nd group – II stage	3rd group – III stage
Albumin g/l	40.59 ± 4.05	37.05 ± 5.27	31.45 ± 4.51
Prealbumin g/l	0.25 ± 0.05	0.16 ± 0.06	0.14 ± 0.06
Fibrinogen g/l	3.07 ± 0.48	3.74 ± 0.68	5.14 ± 1.15

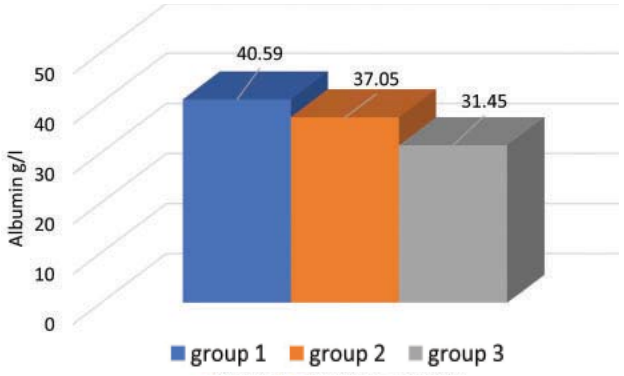

Fig. 2. Mean albumin concentration in the three groups

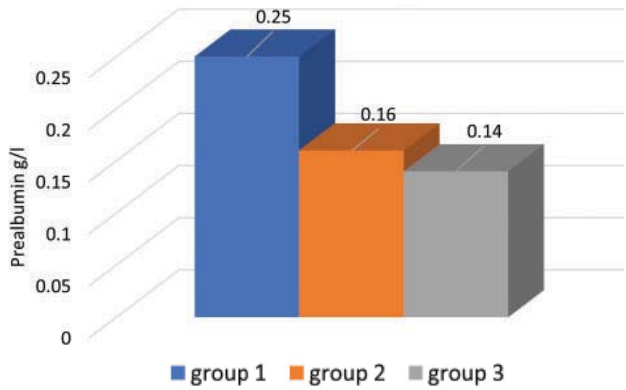

Fig. 3. Mean prealbumin concentration in the three groups

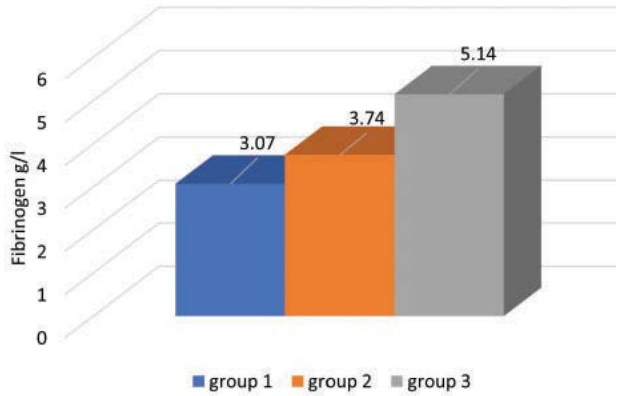

Fig. 4. Mean concentration of fibrinogen in the three groups

Table 2. Mean values of AFR and FPR.

Parameter	Mean ± SD		
	1 group – I stage	2nd group – II stage	3rd group – III stage
AFR	13.47 ± 2.00	10.19 ± 2.18	6.35 ± 1.26
FPR	12.78 ± 2.97	28.24 ± 20.49	47.97 ± 30.28

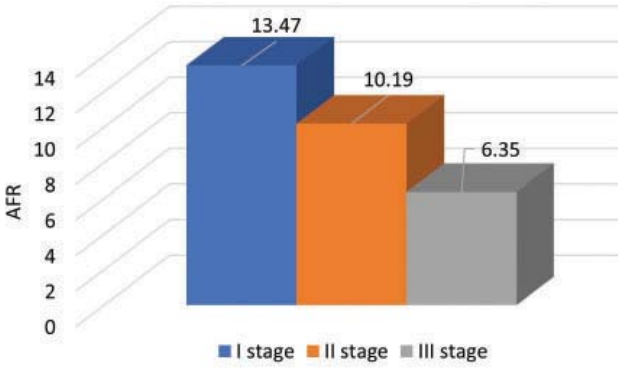

Fig. 5. Mean values of AFR in the three groups of patients

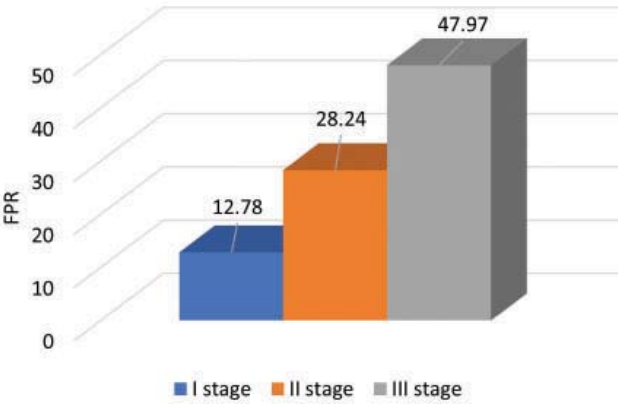

Fig. 6. Mean values of FPR in the three groups of patients

We used the statistical program ANOVA calculator to compare the AFR and FPR ratios in the three groups and to follow their statistical significance.

Our results showed the presence of statistical significance between carcinoma stage and the ratios:

The p-value comparing the AFR ratio in the three groups was < 0.00001. The result is statistically significant at $p < 0.05$.

The p-value comparing the FPR ratio in the three groups was < 0.000011. The result is statistically significant at $p < 0.05$.

We set out to determine which AFR and FPR values would predict ovarian carcinoma progression.

Based on our finding that, as ovarian carcinoma progresses, albumin and prealbumin concentrations decrease below the lower reference limit, and fibrinogen concentration increases above the upper reference limit, we determined:

- Value for AFR = 8.75, according to lower reference limit of albumin 35 g/l and upper reference limit of fibrinogen 4 g/l.
- Value for FPR = 20, according to upper reference limit of fibrinogen 4 g/l and lower reference limit of prealbumin 0.20 g/l.

According to our determined values for AFR and FPR, we found that in patients with first-stage ovarian carcinoma (n = 19) there was none with AFR < 8.75 and FPR > 20. In patients with second-stage disease (n = 19) 4 had AFR < 8.75 and 14 of them had FPR > 20. In the patients in the third stage of the disease (n = 22), all had AFR < 8.75 and 20 of them had FPR > 20.

DISCUSSION

Many researchers have analyzed Fib, Alb and preAlb levels in cancer patients. Their studies proved that Fib levels in carcinoma patients were higher, while Alb and preAlb levels were lower than reference values [29, 64].

Hu WH et al. found that hyperfibrinogenemia and hypoalbuminemia were frequently observed in patients with carcinoma, especially in the presence of metastases [65]. There is evidence that high level of Fib and low level of Alb and preAlb are important prognostic factors influencing the progression of oncological diseases [66-68].

Our results confirm all these analyses.

In our study, we found that in the group of patients in stage I, the mean values of the concentrations of the three proteins were within reference limits. In the stage II group of patients, the mean values of Alb and Fib concentrations were within reference limits, but the mean preAlb concentration was below the lower reference limit. In the group of patients in stage III, the mean values of all three proteins were outside the reference limits.

We found that as the stage of carcinoma progresses, the levels of Alb and preAlb decrease, and the concentration of Fib increases.

Alb, preAlb and Fib levels are closely related to FPR and AFR ratios. According to various studies, FPR and AFR are prognostic markers that have great prospects for clinical application. Many reports have demonstrated that low AFR values and high FPR values are associated with an increased risk of mortality and recurrence of multiple malignancies [36, 62-63, 69, 70].

We also confirmed this evidence and found that low preoperative AFR values and high preoperative FPR values correlated with advancing carcinoma stage.

Determining FPR and AFR ratios has multiple advantages. Albumin, prealbumin, and fibrinogen are available in the medical records of most patients with carcinoma. Moreover, the test method is easy to conduct, affordable and safe. Measurements are inexpensive and reproducible. The time for examination and obtaining the results is short, which allows a timely preliminary assessment of the patient‘s condition and gives greater opportunities to adjust the treatment.

CONCLUSION

Ovarian carcinoma is a devastating disease and patients have a poor prognosis. Therefore, research is needed to identify prognostic factors to help improve the risk and lifestyle stratification of these patients.

In our opinion, AFR and FPR are two cost-effective and effective biomarkers for monitoring the progression of ovarian carcinoma as well as guiding patients to receive an optimal therapeutic regimen.

Conflict of Interest Statement: *The authors declare no conflicts of interest related to this work.*

Funding: *The authors did not receive any financial support from any organization for this research work.*

Ethical statement: *This study has been performed in accordance with the ethical standards as laid down in the Declaration of Helsinki.*

Informed Consent from Participants: *Informed consent was obtained from all participants included in the study.*

REFERENCES

1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics. 2016, 66:271-89.
2. World Cancer Research Fund International. Ovarian cancer statistics [Internet]. 2024 [cited 2024/02/10]. Available from: https://www.wcrf.org/cancer-trends/ovarian-cancer-statistics/.
3. Stewart C, Ralyea C, Lockwood S. Ovarian cancer: an integrated review. InSeminars in oncology nursing. 2019, 35:151-156.
4. Fan C, Reader J, Roque DM. Review of immune therapies targeting ovarian cancer. Current treatment options in oncology. 2018, 19:1-21.
5. Webb PM, Jordan SJ. Epidemiology of epithelial ovarian cancer. Best practice & research Clinical obstetrics & gynaecology. 2017, 41:3-14.
6. Zhang Y, Luo G, Li M, et al. Global patterns and trends in ovarian cancer incidence: age, period and birth cohort analysis. BMC cancer. 2019, 19:1-4.
7. Saorin A, Di Gregorio E, Miolo G, et al. Emerging role of metabolomics in ovarian cancer diagnosis. Metabolites. 2019, 10:419.
8. Kim J, Park EY, Kim O, et al. Cell origins of high-grade serous ovarian cancer. Cancers. 2018, 12:433.
9. Guo L, Wang J, Li N, et al. Peptides for diagnosis and treatment of ovarian cancer. Frontiers in Oncology. 2023, 5:1135523.
10. Chen S, Yan H, Du J, et al. Prognostic significance of preresection albumin/fibrinogen ratio in patients with non-small cell lung cancer: A propensity score matching analysis. Clinica chimica acta. 2018, 482:203-8.
11. Allin KH, Bojesen SE, Nordestgaard BG: Inflammatory biomarkers and risk of cancer in 84,000 individuals from the general population. Int J Cancer. 2016, 139:1493-1500.
12. Nazha B, Moussaly E, Zaarour M, et al. Hypoalbuminemia in colorectal cancer prognosis: nutritional marker or inflammatory surrogate?. World J Gastrointest Surg. 2015, 7:370-377.
13. Zhou J, Hiki N, Mine S, et al. Role of prealbumin as a powerful and simple index for predicting postoperative complications after gastric cancer surgery. Ann Surg Oncol. 2017, 24:510-517.
14. Cai W, Kong W, Dong B, et al. Pretreatment serum prealbumin as an independent prognostic indicator in patients with metastatic renal cell carcinoma using tyrosine kinase inhibitors as first-line target therapy. Clin Genitourin Cancer. 2017, 15:437-446.
15. Miura K, Hamanaka K, Koizumi T, et al. Clinical significance of preoperative serum albumin level for prognosis in surgically resected patients with non-small cell lung cancer: comparative study of normal lung, emphysema, and pulmonary fibrosis. Lung Cancer. 2017, 111:88-95.
16. Huang W, Wang S, Zhang H, et al. Prognostic significance of combined fibrinogen concentration and neutrophil-to-lymphocyte ratio in patients with resectable non-small cell lung cancer. Cancer Biol Med. 2018, 15:88-96.
17. Loftus TJ, Brown MP, Slish JH, et al. Serum levels of prealbumin and albumin for preoperative risk stratification. Nutr Clin Pract. 2019, 34:340-348.
18. Li XF, Wang X, Lu WJ, et al. Relationship between fibrinogen/albumin ratio and coronary collateral circulation in patients with chronic total occlusion. Henan Med Res. 2020, 29:589.
19. Miao Y, Li S, Yan Q, et al. Prognostic significance of preoperative prognostic nutritional index in epithelial ovarian cancer patients treated with platinum-based chemotherapy. Oncol Res Treat. 2016, 39:712-719.
20. Deme D, Telekes A. Prognostic importance of albumin in oncology. Orv Hetil. 2018, 159:96-106.
21. Lu J, Xu BB, Zheng ZF, et al. CRP/prealbumin, a novel inflammatory index for predicting recurrence after radical resection in gastric cancer patients: post hoc analysis of a randomized Phase III trial. Gastric Cancer. 2019, 22:536-545.
22. Zhang L, Zhang J, Wang Y, et al. Potential prognostic factors for predicting the chemotherapeutic outcomes and prognosis of patients with metastatic colorectal cancer. J Clin Lab Anal. 2019, 33:22958.
23. Smith SH. Using albumin and prealbumin to assess nutritional status. Nursing. 2017, 47:65-66.
24. Ma YQ, Zhang YQ, Liu DL, et al. Correlation analysis of postoperative albumin changes and complications in elderly patients with gastric cancer with normal preoperative serum albumin level. Clin Oncol China. 2020, 47:823.
25. Shafer JA, Higgins DL, Lewis SD. Steady state kinetics for the thrombin catalyzed sequential release of fibrinopeptides A & B from human fibrinogen. InFed. Proc. 1982, 41:654.
26. Sun YR, Gao XY, Lu ZJ, et al. Predictive efficacy of preoperative plasma fibrinogen to albumin ratio for adverse cardiovascular events in patients with NSTE-ACS after PCI. Shandong Med. 2020, 60:81.
27. Kavitha S, Sridhar MG, Satheesh S. Periprocedural plasma fibrinogen levels and coronary stent outcome. Indian Heart J. 2015, 67:440-443.
28. Ahn HJ, Baker SK, Norris EH, et al. Inflaming the Brain. Neuron. 2019, 101:991-993.
29. Perisanidis C, Psyrri A, Cohen EE, et al. Prognostic role of pretreatment plasma fibrinogen in patients with solid tumors: a systematic review and meta-analysis. Cancer Treat Rev. 2015, 41:960-970.
30. Ji R, Ren Q, Bai S, et al. Prognostic significance of pretreatment plasma fibrinogen level in patients with digestive system tumors: a meta-analysis. Int J Biol Markers. 2018, 33:254-265.
31. Marco P, Marco A. Biomolecular markers in cancer-associated thromboembolism. Med Clin Barc. 2015, 144:21-25.
32. Zhang D, Zhou X, Bao W, et al. Plasma fibrinogen levels are correlated with postoperative distant metastasis and prognosis in esophageal squamous cell carcinoma. Oncotarget. 2015, 6:38410-38420.
33. Jain A, Zhang Q, Toh HC. Awakening immunity against cancer: a 2017 primer for clinicians. Chin J Cancer. 2017, 36:67.
34. Zhu L, Zhang JQ. Clinical analysis of coagulation and fibrinolysis indexes in patients with malignant tumor and relevant nursing countermeasures. Thrombosis Hemostasis. 2016, 22:588.
35. Zhang J, Li SQ, Liao ZH, et al. Prognostic value of a novel FPR biomarker in patients with surgical stage II and III gastric cancer. Oncotarget. 2017, 8:75195-75205.
36. Virizuela JA, Camblor-álvarez M, Luengo-Pérez LM, et al. Nutritional support and parenteral nutrition in cancer patients: an expert consensus report. Clin Transl Oncol. 2018, 20:619-629.
37. Daniele A, Divella R, Abbate I, et al. Assessment of nutritional and inflammatory status to determine the prevalence of malnutrition in patients undergoing surgery for colorectal carcinoma. Anticancer Res. 2017, 37:1281-1287.
38. Moujaess E, Fakhoury M, Assi T, et al. The Therapeutic use of human albumin in cancer patients' management. Crit Rev Oncol Hematol. 2017, 120:203-209.
39. Filip B, Scarpa M, Cavallin F, et al. Postoperative outcome after oesophagectomy for cancer: nutritional status is the missing ring in the current prognostic scores. Eur J Surg Oncol. 2015, 41:787-794.
40. Xu Q, Yan Y, Gu S, et al. A novel inflammation-based prognostic score: the fibrinogen/albumin ratio predicts prognoses

of patients after curative resection for hepatocellular carcinoma. J Immunol Res. 2018:4925498.
41. Ingenbleek Y, Young VR: Significance of transthyretin in protein metabolism. Clin Chem Lab Med. 2002, 40:1281-91.
42. Shenkin A. Serum prealbumin: is it a marker of nutritional status or of risk of malnutrition?. Clinical chemistry. 2006, 52:2177-9.
43. Sun F, Peng HX, Gao QF, et al. Preoperative circulating FPR and CCF score are promising biomarkers for predicting clinical outcome of stage II-III colorectal cancer patients. Cancer Manag Res. 2018, 10:2151-2161.
44. Mills JC, Samuelson LC. Past questions and current understanding about gastric cancer. Gastroenterology. 2018, 155:939-944.
45. Che Y, Wang J, Li Y, et al. Cisplatin-activated PAI-1 secretion in the cancer-associated fibroblasts with paracrine effects promoting esophageal squamous cell carcinoma progression and causing chemoresistance. Cell Death Dis. 2018, 9:759.
46. Bakker E, Qattan M, Mutti L, et al. The role of microenvironment and immunity in drug response in leukemia. Biochim Biophys Acta. 2016, 1863:414-426.
47. Isella C, Terrasi A, Bellomo SE, et al. Stromal contribution to the colorectal cancer transcriptome. Nat Genet. 2015, 47:312-319.
48. Dolan RD, McSorley ST, Park JH, et al. The prognostic value of systemic inflammation in patients undergoing surgery for colon cancer: comparison of composite ratios and cumulative scores. Br J Cancer. 2018, 119:40-51.
49. Jagadesham VP, Lagarde SM, Immanuel A, et al. Systemic inflammatory markers and outcome in patients with locally advanced adenocarcinoma of the oesophagus and gastro-oesophageal junction. Br J Surg. 2017, 104:401-407.
50. Berzigotti A, Reig M, Abraldes JG, et al. Portal hypertension and the outcome of surgery for hepatocellular carcinoma in compensated cirrhosis: a systematic review and meta-analysis. Hepatology. 2015, 61:526-536.
51. Kozasa K, Mabuchi S, Komura N, et al. Comparison of clinical utilities of the platelet count and platelet-lymphocyte ratio for predicting survival in patients with cervical cancer: a single institutional study and literature review. Oncotarget. 2017, 8:55394-55404.
52. Wu Y, Zhou D, Zhang G, et al. Preoperative serum platelet-lymphocyte ratio as a prognostic factor in cholangiocarcinoma patients after radical resection: a retrospective analysis of 119 patients. Gastroenterol Res Pract. 2019:8506967.
53. Wu CC, Li SH, Lu HI, et al. Inflammation-based prognostic scores predict the prognosis of locally advanced cervical esophageal squamous cell carcinoma patients receiving curative concurrent chemoradiotherapy: a propensity score-matched analysis. PeerJ. 2018, 6:5655.
54. Lv Y, Zhang J, Liu Z, et al. A novel inflammation-based prognostic index for patients with esophageal squamous cell carcinoma: neutrophil lymphocyte ratio/prealbumin ratio. Medicine :e14562.
55. Wei XL, Wang FH, Zhang DS, et al. A novel inflammation-based prognostic score in esophageal squamous cell carcinoma: the C-reactive protein/albumin ratio. BMC Cancer. 2015, 15:350.
56. Wei SH, Wang Y, Ye ZS, et al. Relationship between preoperative serum albumin level and clinicopathological features and prognosis of patients with gastric stump cancer. Chin J Gen Surg. 2018, 33:828.
57. Huynh PT, Beswick EJ, Coronado YA, et al. CD90(+) stromal cells are the major source of IL-6, which supports cancer stem-like cells and inflammation in colorectal cancer. Int J Cancer. 2016, 138:1971-1981.
58. Li Y, Shi J, Qi S, et al. Correction to: IL-33 facilitates proliferation of colorectal cancer dependent on COX2/PGE2. J Exp Clin Cancer Res. 2020, 39:15.
59. Graf ME, Sookthai D, Johnson T, et al. Pre-diagnostic plasma concentrations of Fibrinogen, sGPIIb/IIIa, sP-selectin, sThrombomodulin, Thrombopoietin in relation to cancer risk: findings from a large prospective study. Int J Cancer. 2018, 143:2659-2667.
60. Li SQ, You XH, Sun F, et al. Albumin to fibrinogen ratio and fibrinogen to pre-albumin ratio are economical, simple and promising prognostic factors for solid malignancy. 2019, 11:2036-2036.
61. Zhang WW, Zhang ZW, He L. Analysis of prognostic factors in 342 patients with ovarian cancer undergoing surgery. Chin J Cancer Prev Treat. 2019, 26:1288-1295. 10.16073/j.cnki.cjcpt.2019.17.11
62. Tan Z, Zhang M, Han Q, et al. A novel blood tool of cancer prognosis in esophageal squamous cell carcinoma: the fibrinogen/albumin ratio. J Cancer. 2017, 8:1025-1029.
63. Hwang KT, Chung JK, Roh EY, et al. Prognostic influence of preoperative fibrinogen to albumin ratio for breast cancer. J Breast Cancer. 2017, 20:254-263.
64. Huang J, Wang Y, Yuan Y, et al. Preoperative serum prealbumin as an independent prognostic indicator in patients with localized upper tract urothelial carcinoma after radical nephroureterectomy. Oncotarget. 2017, 8:36772-36779.
65. Hu WH, Cajas-Monson LC, Eisenstein S, et al. Preoperative malnutrition assessments as predictors of postoperative mortality and morbidity in colorectal cancer: an analysis of ACS-NSQIP. Nutr J. 2015, 14:91.
66. Suzuki T, Shimada H, Nanami T, et al. Hyperfibrinogenemia is associated with inflammatory mediators and poor prognosis in patients with gastric cancer. 2016, 46:1394-1401.
67. Han WX, Chen ZM, Wei ZJ, Xu AM. Preoperative pre-albumin predicts prognosis of patients after gastrectomy for adenocarcinoma of esophagogastric junction. World J Surg Oncol. 2016, 14:279.
68. Liu BZ, Tao L, Chen YZ, et al. Preoperative Body Mass Index, Blood Albumin and Triglycerides Predict Survival for Patients with Gastric Cancer. PLoS One. 2016, 11:0157401.
69. Tominaga T, Nonaka T, Sumida Y, et al. The C-reactive protein to albumin ratio as a predictor of severe side effects of adjuvant chemotherapy in stage III colorectal cancer patients. PLoS One. 2016, 11:0167967.
70. Sun DW, An L, Lv GY. Albumin-fibrinogen ratio and fibrinogen-prealbumin ratio as promising prognostic markers for cancers: an updated meta-analysis. World journal of surgical oncology. 2020, 18:1-5.