

Research Progress of Serum VEGF and FAS in Prognosis of Gastric Cancer

Hou Jianzhang^{1,*}, Zhang Shuli¹, Yuan Jianlei¹, Li Hongyan², Hou Zhenjiang²

¹Department of Hepatobiliary and Pancreatic (Minimally Invasive) Surgery, Cangzhou People's Hospital, Cancer Hospital District, Cangzhou, China

²Department of Medical Technology, Cangzhou Medical College, Cangzhou, China

Email address:

hjz3423@163.com (Hou Jianzhang)

*Corresponding author

To cite this article:

Hou Jianzhang, Zhang Shuli, Yuan Jianlei, Li Hongyan, Hou Zhenjiang. Research Progress of Serum VEGF and FAS in Prognosis of Gastric Cancer. *American Journal of Clinical and Experimental Medicine*. Vol. 11, No. 2, 2023, pp. 39-46. doi: 10.11648/j.ajcem.20231102.13

Received: March 14, 2023; **Accepted:** April 18, 2023; **Published:** April 20, 2023

Abstract: Vascular endothelial growth factor (VEGF) is an important factor to promote endothelial cell division and angiogenesis. In physiological conditions, the expression level of VEGF in human tissues is very low. Ischemia, hypoxia and many tumors can promote the synthesis and secretion of VEGF, and its expression level is related to the degree of vascularization of tumors, the proliferation, growth and metastasis of tumor cells. Fatty acid synthase (FAS) is a key enzyme for endogenous fatty acid synthesis, which is expressed at a low level in normal tissue cells, while FASN in a variety of tumor cells is continuously highly expressed to meet the energy needs of cell proliferation and the excessive demand for rapid proliferation of tumor cells to form cell membrane lipids. A large amount of research shows that VEGF and FAS play an important role in the development and development of many tumors, and the abnormally high expression in tumor tissue cells is positively correlated with serum VEGF and FAS levels, which is closely related to the prognosis of tumors. Gastric cancer (GC) is one of the most common clinical malignant tumors of the digestive tract, and its incidence and mortality have shown an increasing trend in recent years, and the prognosis is poor, seriously endangering human health. The biological properties of GC are related to the level of VEGF and FAS expression in tissues and serum. This article reviews the research progress of VEGF and FAS, their expression in GC and their prognosis.

Keywords: Vascular Endothelial Growth Factor, Fatty Acid Synthase, Serum, Gastric Cancer, Prognosis

1. Introduction

Gastric cancer (GC) is currently the most common cancer in the world and one of the most common clinical malignant tumors of the digestive tract [1]. According to Chinese cancer data in 2015, there were about 403,000 new cases and 291,000 deaths, and the incidence and mortality rate were 29.31/100,000 and 21.16/100,000, respectively, ranking second among malignant tumors, exceeding the world average by 2 times. The difference between urban and rural areas is obvious, and the incidence rate in rural areas is 1.6 times that of urban areas [2]. Because of GC having the characteristics of insidious onset, easy to miss diagnosis, easy to relapse and metastasis, the treatment effect is poor. The detection rate of early GC in China hovers only at 10% [3].

About two-thirds of patients are newly diagnosed with advanced disease, and even if cured, the rate of postoperative metastasis is high [4]. The median survival is only 3~24 months, and the 5-year survival rate is about 40% [2], which has become one of the malignant tumors that seriously threaten human health. Basic research has confirmed that the occurrence, development and metastasis of tumors largely depend on the formation of neovascularization, and various tumor cells can synthesize and secrete a variety of cytokines, among which vascular endothelial growth factor (VEGF) is an important factor to promote endothelial cell division and angiogenesis, and its expression level is closely related to the degree of blood vessels of tumors [5]. Fatty acid synthase (FAS) is a key enzyme in fatty acid synthesis and plays an important role in the synthesis of endogenous fatty acids. In normal tissue cells, FAS is expressed at a low level, while in

tumor cells FAS is highly expressed, and its expression level is positively correlated with serum FAS content. There are many commonly used Tumor markers (Tumor marker, TM), but the sensitivity and specificity are not ideal, so it is of great clinical value to find TM with an ideal prognosis for early diagnosis or monitoring. In recent years, the expression and serum content of VEGF and FAS in gastric cancer tissues have been detected clinically, which has opened up a new way for the diagnosis and prognosis monitoring of Gastric Cancer.

2. VEGF Overview

Vascular endothelial growth factor (VEGF), also known as vascular permeability factor VPF, is the present strongest factor to promote angiogenesis, VEGF is composed of two identical polypeptide chains through disulfide bond cross-linking of homodimeric glycoprotein, which plays an important role in maintaining the balance of vascular network, can not only induce and promote endothelial cell division, and then prompt the generation of new blood vessels, but also regulate the generation of blood vessels and lymphatic vessels, and that in turn increase the permeability of blood vessels and play an important role in promoting cell division and the formation of new blood vessels. Family members of human VEGF include: VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, and placental growth factor (PLGF). VEGF-A plays a leading role in regulating angiogenesis and disease, so it is directly called VEGF [6]. The first two of these are soluble secreted proteins, common forms of VEGF [5]. VEGF stimulates vascular and lymphangiogenesis by binding to one or both receptors in VEGFR1, VEGFR2, and VEGFR3 [7]. The main role of VEGF is to increase vascular permeability, promote vascular endothelial cell growth and neoangiogenesis [8], participate in the whole process of regulating normal and pathological angiogenesis. Various types of VEGF differ from their receptor binding properties and affinity and produce different biological effects. Under normal physiological conditions, the expression level of VEGF in human tissue cells is very low, and ischemia, hypoxia and many tumors can increase the synthesis and secretion of VEGF, and are closely related to the growth, metastasis and prognosis of tumors such as digestion, respiratory system and gynecology. The expression of VEGF and its receptors is influenced by a variety of factors, the most important of which are hypoxia, followed by oncogenes, tumor suppressor genes, and cytokines [9]. Hypoxia can increase the transcription and stability of VEGF mRNA, and VEGFR expression is upregulated, which enhances the biological effect of VEGF. After the improvement of hypoxic environment, the level of VEGF mRNA decreases reversibly, and the release of hypoxia-induced inflammatory mediators can increase VEGF secretion, further enhance the binding degree of hypoxia-inducible factors to VEGF genes, increase the permeability of blood vessels, and provide strong conditions for the growth, invasion and metastasis of tumor cells. Angiogenesis plays an

extremely important role in the growth and metastasis of tumors, and the expression level of VEGF is related to the degree of vascularization of tumors and the proliferation, growth and metastasis of tumor cells. Therefore, hypoxia plays an important role in the process of angiogenesis. Oncogene K-ras mutations can increase the expression of VEGF, tumor suppressor gene mutations can upregulate VEGF expression, and tumor suppressor gene p73 can inhibit the intracellular expression of VEGF. A large number of results show that VEGF plays an important role in the development and development of many tumors, and abnormally high expression of tumor tissues and serum VEGF is closely related to tumor occurrence, metastasis and poor prognosis.

3. FAS Overview

Fatty acid synthase (FAS), also known as fatty acid synthase, is a key enzyme for the synthesis of fatty acids [10], which plays a key role in the synthesis of endogenous fatty acids. FAS consists of two identical polypeptide chains connected head-to-tail to form dimers [11], forming a catalytic center of enzyme activity, which is composed of seven enzymatic activity domains such as condensation, transacylation, reduction and dehydration, which catalyze the synthesis of fatty acids by acetyl-CoA and malonic acid monoacyl-CoA. The FAS enzyme activity domain is linearly from the C terminal to the N terminus, including the enol reductase region at the C-terminus, the β -ketoesteryl reductase region, the acyl carrier protein and thioesterase region, the N-terminus β -ketoesteryl synthase region, acetic acid/malonyl monoacyl transferase, and β -hydroxyacyl dehydratase region. The distribution of FAS in normal human tissues is significantly heterogeneous, concentrated in tissues with high lipid metabolism, hormone-sensitive tissues, and cells in a proliferating state [12]. The main product of FAS is soft acid, which is one of the main components of cell membrane structure and an important substrate for cellular energy metabolism, with energy reserves, synthesis of phospholipids, participation in cell membrane structure, intracellular signal transduction and protein acylation and other functions. FAS is mainly responsible for the synthesis of endogenous fatty acids in the process of fat metabolism, and polymerizes acetyl CoA and malonyl monoacyl CoA into long-chain fatty acids to store energy in the form of triglycerides. The fatty acid metabolism of normal tissue cells mainly uses exogenous fatty acids to synthesize lipids, and the synthesis of endogenous fatty acids is at a low level, while cancer cells are different, and their self-synthesized fatty acids account for 93% of all triglycerides, further clarifying that the synthesis of endogenous fatty acids is an important source of fatty acids required for tumor cell growth [13]. Research has shown that malignant tumor cells have high expression of FAS and are not regulated by normal cell regulatory signals, and synthesize endogenous fatty acids to synthesize a large number of lipids, which is an adaptation to endogenous fatty acid synthesis and cell proliferation, and

provides lipids for the formation of cell membranes to meet the rapid proliferation of tumor cells and excessive demand for energy.

4. Detection of VEGF and FAS

The detection methods of VEGF and FAS vary according to the source and content of samples. Li Xiaojun et al. [14] used Real-Time-PCR real-time fluorescence to detect the expression level of VEGF mRNA in GC tissue, and found that the positive expression rate and content of VEGF mRNA in GC tissue were significantly higher than that of normal gastric mucosal tissue, and were closely related to lymph node metastasis and TNM staging in GC patients. Wang Haili et al. [15] used immunohistochemical SP method to detect the expression of VEGF in GC tissues, and used ELISA method to measure serum VEGF levels, and found that SVEGF levels and tissue VEGF positive expression rates were significantly higher than those in gastric ulcer group and normal control group, and serum and tissue VEGF were significantly positively correlated with VEGF in tissues ($r=0.8936$, $P<0.01$). Tumor tissue samples can be detected by immunohistochemistry for positive expression of FAS, and RT-PCR and Western-blot can detect FAS mRNA and FAS protein qualitative and relative content analysis [13]. Serum samples can be measured using the ELISA method for FAS content. Xu Yingying et al. [16] found that the expression level of FAS in colorectal cancer (CRC) tissues detected by immunohistochemistry was much higher than that of pericancerous tissues ($P<0.01$), the FAS content of CRC tissues detected by RT-PCR was significantly higher than that in pericancerous tissues ($P<0.01$), and the serum FAS content of CRC patients detected by ELISA was significantly higher than that of healthy patients. FAS is highly expressed in the tissues and serum of CRC patients, which is positively correlated with clinical stage, and those with high FAS expression have a poor prognosis. Guo Wei et al. [17] reported that the serum FAS content of positive expression of FAS protein in bladder cancer tissues was significantly higher than that of negative patients, indicating that the serum FAS content was consistent with the results of immunohistochemical detection of FAS, and the combined detection of serum and tissue FAS could improve the effective monitoring of tumors. ELISA method to detect serum FAS content is simple, rapid, and easy to promote and apply in laboratories. The results of the study showed that VEGF and FAS are abnormally highly expressed in gastrointestinal tumor tissues and serum, making them novel targets for tumor diagnosis and treatment [18, 19].

5. The Significance of Serum VEGF Level in Gastric Cancer Expression

5.1. Serum VEGF Level and Prognosis of Gastric Cancer

Patients with advanced malignant tumors are accompanied by increased endogenous secretion of VEGF, which suggests

that the prognosis of patients with elevated SVEGF level is poor. Mao Zhenbiao et al. [20] reported that the level of SVEGF in GC patients was significantly higher than that in the healthy control group, and its level was closely related to tumor size, invasion degree, TNM stage, etc. ($P<0.05$). The increased content of SVEGF indicated the metastasis and prognosis of GC. Karayiannakis et al. [21] found that the content of SVEGF in GC patients was significantly higher, which was related to TNM stage. The progression stage was significantly higher than that in the early stage. The patients with serous infiltration were significantly higher than those without serous infiltration. There was also statistical significance in the depth of venous infiltration and tumor infiltration. The level of SVEGF is also related to the recurrence of GC and the effect of chemotherapy. The recurrence rate is higher than the progression rate. The effective rate of chemotherapy is lower, and the ineffective rate is higher. It is not related to the histological type and the degree of differentiation. Zhou Haiyin et al. [22] reported that the level of SVEGF was significantly increased in patients with poorly differentiated GC, lymph node metastasis, invasion of serous layer and penetration of serous membrane, tumor greater than or equal to 5cm and clinical stage III and IV, which suggested that the level of SVEGF reflect the progression of tumor to a certain extent. Whether the level of SVEGF before surgery or the expression of VEGF in tumor tissue is closely related to tumor metastasis, stage and prognosis. Dynamic monitoring of SVEGF level can not only judge the stage and prognosis of GC, but also provide basis for judging the curative effect, recurrence and metastasis. Wang Haili et al. [15] found that SVEGF level and tissue VEGF expression in GC patients were significantly higher than those in gastric ulcer group, and there was a high consistency between serum and tissue VEGF, and there was a significant positive correlation between the two. According to SVEGF level, we can judge the positive expression of VEGF in GC tissue. Therefore, detection of SVEGF level can reflect the growth state of GC vessels. Monitoring the level of SVEGF is helpful to the diagnosis, treatment and prognosis of GC, and is of great significance to predict the invasion and metastasis of GC. Hu Min et al. [23] reported that the level of SVEGF in GC patients was significantly higher than that in the healthy control group, and the level of VEGF after surgery was significantly lower than that before surgery. The level of VEGF was closely related to the size of GC tumor, the depth of invasion, and the degree of lymph node involvement. The level of SVEGF was also significantly increased with the increase of clinical pathological stage, but the level of VEGF was not related to the degree of histological differentiation and the gender of patients. Kang Shirong and Li Jun [24] found that the preoperative VEGF level of GC patients was higher than that of the control group, and was positively correlated with MVD in GC tissue. The SVEGF level and MVD in cancer tissue were statistically different from GC infiltration depth, lymph node metastasis and histological classification, but not related to age and sex. It is suggested that the angiogenesis of GC is

closely related to the concentration of SVEGF, and its SVEGF level can be used as an important index for GC to evaluate the efficacy, recurrence, metastasis and prognosis. The level of SVEGF in GC patients was significantly higher than that in the control group (P), It has nothing to do with age, sex, degree of differentiation and other factors [25]. VEGF plays an important role in the occurrence and development of GC. Detection of serum VEGF level aims to the diagnosis of CG.

5.2. Serum VEGF Subtypes and Prognosis of Gastric Cancer

SVEGF subtypes have different prognostic values for gastric cancer. Mysliwiec *et al.* [26] reported that the content of SVEGF-A in patients with diffuse and intestinal GC was higher than that in the control group, the level of SVEGFR-2 in patients without metastasis after surgery was higher than that before surgery, and the content of SVEGF and VEGFR-2 in GC patients with lymphoma increased more significantly. Hălmăciu *et al.* [27] found that the content of SVEGF-A in preoperative GC patients was significantly higher than that in normal controls, and its level change was related to the histological type of GC, which could not be used as a prognostic factor for GC, but could be used as a marker of disease progression. Liu *et al.* [28] conducted a meta-analysis of 4794 patients with GC who underwent surgical resection, and found that both the high expression of VEGF in GC tissue and the elevated levels of VEGF, VEGF-C and VEGF-D in serum were related to the poor prognosis after GC surgery. SVEGF may be superior to tissue VEGF in predicting prognosis. Therefore, the increase of SVEGF level is an independent indicator of GC survival and tumor classification and invasion depth. Wang *et al.* [29] reported that the level of SVEGF-C in GC patients was significantly higher than that in the control group ($P=0.000$). SVEGF-C and lymphatic vessel density (LVD) were significantly increased in poorly differentiated adenocarcinoma, T3 and T4, LNM, distant metastasis and PTNM III and IV groups ($P=0.000$). The sensitivity and specificity of SVEGF-C in predicting lymph node metastasis were 82.8% and 81.8%, respectively (critical value=542.5 ng/L). The levels of SVEGF-C and LVD in VEGF-C positive group were significantly higher than those in negative group ($P=0.000$), and the level of SVEGF-C was correlated with LVD ($P=0.000$). Therefore, the levels of SVEGF-C, VEGF-C and LVD in GC patients are related to lymph node metastasis and poor prognosis. SVEGF-C may be a biomarker of GC lymph node metastasis. SVEGF-A and VEGF-C in GC patients are related to the depth of tumor invasion, lymph node and distant metastasis, and tumor TNM stage. The accuracy of combined detection in predicting lymph node metastasis of GC is higher than that of single detection [30]. Zhou Cunrong [31] and Wang Wei *et al.* [32] reported that the levels of SVEGF-C and SVEGF-D in patients with advanced GC were significantly higher than those in gastric ulcer group ($P<0.05$), With the increase of GC infiltration depth, T3~T4 group was significantly higher than T1~T2 group ($P<0.05$), and the low differentiation type was

significantly higher than the high and medium differentiation type ($P<0.05$), and the group with lymph node metastasis was significantly higher than the group without lymph node metastasis ($P<0.05$). There was no significant difference between advanced and early GC groups and between sex, tumor location and histopathological type ($P>0.05$). The high level of SVEGF-C is closely related to the invasion and lymph node metastasis of advanced GC [31], but the difference between SVEGF-D with and without lymph node metastasis is not statistically significant [32]. Therefore, the levels of SVEGF-C and SVEGF-D can be used as markers of tissue differentiation and invasion of advanced GC, but there are differences in judging whether there is lymph node metastasis before surgery. Data [33] showed that SVEGF-A, VEGF-C, VEGF-D, VEGFR-1, VEGFR-2, sVEGFR-1 in GC patients were higher than those in the control group, while serum sVEGFR-1 was lower than that in the control group. There was also significant difference between patients with different disease stages ($P<0.05$), but there was no significant difference between patients with different lesion sites ($P>0.05$).

5.3. Value of Serum VEGF Combined with Other TM in the Prognosis of Gastric Cancer

The clinical research of SVEGF combined with other tumor markers for the prognosis of GC has also been carried out. Liu Fuguo *et al.* [34] found that the levels of SVEGF and endostatin in GC patients before operation were significantly higher than those in gastritis group and control group ($P<0.01$), and both were closely related to tumor size, differentiation, depth of invasion, lymph node metastasis, distant metastasis and clinical stage ($P<0.05$). The level of SVEGF in 2 weeks after GC operation was significantly lower than that before operation, while the level of blood endostatin was higher than that before operation ($P<0.01$). It is suggested that the levels of SVEGF and Endostatin are effective indicators to evaluate the malignant behavior of GC and predict the invasion and metastasis. The content of SVEGF and p53 in GC patients is significantly correlated ($r=0.72$, $P<0.001$), which is significantly higher than that in the control group. Therefore, SVEGF and p53 can be used as an important reference index for the early diagnosis of malignant tumors, the presence or absence of metastasis, and the prognosis and survival judgment, and can be observed and guide clinical treatment [35]. The levels of SVEGF and COX-2 in GC patients were significantly higher than those in healthy people, and there was a significant positive correlation between them ($r=0.618$, $P<0.01$). The level of SVEGF and COX-2 was related to tumor size, depth of invasion, degree of differentiation, metastasis and TNM stage ($P<0.05$) [36]. It is suggested that VEGF and COX-2 play an important role in the occurrence and development of GC, and have certain value in the diagnosis, treatment and prognosis evaluation of GC. Yang Yi'e *et al.* [37] found that the serum CEA, CA724, VEGF and Endostatin levels of GC patients were significantly higher than those of gastric ulcer and normal people, and the levels of phase III and IV were significantly higher than those of phase I and II ($P<0.01$).

The sensitivity of combined detection was improved to 75%, which was significantly higher than that of single detection. Therefore, serum CEA, CA724, VEGF and Endostatin can be used for the diagnosis and prognosis of GC, and combined detection can improve the diagnostic rate. The levels of VEGF, CEA and CA724 in serum of patients with GC were significantly higher than those of benign gastric disease and normal control group ($P<0.01$), and decreased significantly after operation. Combined detection can significantly improve the sensitivity and accuracy of diagnosis ($P<0.05$), which is helpful to improve the sensitivity of GC diagnosis, and has important significance for the observation of curative effect after operation [38]. The sensitivity and specificity of serum CEA, CA199 and VEGF in the diagnosis of GC were 60%, 62% and 75%, respectively, and the specificity were 63%, 65% and 59%, respectively. The sensitivity and specificity of combined detection of CEA, CA199 and VEGF in the diagnosis of GC were 95% and 97%, respectively. The sensitivity and effective diagnostic rate were significantly higher than those of single detection, and the difference was statistically significant ($P<0.01$) [39]. Therefore, the combined detection of three indicators improves the sensitivity, specificity and effective diagnostic rate of GC diagnosis, which is of great significance to the diagnosis and efficacy monitoring of GC. Li Yumeng et al. [40] reported that serum VEGF, IL-6 and CRP in patients with GC were higher than those in the control group, and those in stage III-IV and with lymph node metastasis were higher than those in stage I-II and without lymph node metastasis ($p<0.05$). It is suggested that the development of GC is related to the levels of serum VEGF, IL-6 and CRP. The faster the disease progresses, the higher the levels of VEGF, IL-6 and CRP. Therefore, the detection of serum VEGF, IL-6 and CRP in GC patients can reflect the changes of the disease and judge the prognosis. Villarejo-Campos et al. [41] reported that the SVEGF content of GC patients decreased after tumor resection, and the survival rate of patients with significantly increased SVEGF before surgery was lower. Multivariate comprehensive analysis showed that SVEGF level was an independent prognostic factor for GC and was related to tumor type and surrounding tissue infiltration. SVEGF is positively correlated with CEA level [42]. The levels of serum VEGF, MMP-9 and endothelin in patients with GC were significantly higher than those in the control group, and were related to the clinical stage, lymph node metastasis, tumor diameter and depth of invasion of GC, indicating that all three were involved in the occurrence and development of GC [43]. The level of SVEGF in GC patients can provide prognostic information for preoperative evaluation of invasion and tumor type. The serum levels of IL-33 and VEGF-C in patients with GC were higher than those in healthy people, and those with lymph node metastasis were higher than those without lymph node metastasis ($P<0.05$) [44]. It is suggested that the high level of IL-33 in the serum of patients with GC may induce the secretion of VEGF-C and promote the lymph node metastasis of GC, which can be used as an important indicator to evaluate the prognosis of

GC. Yao Jingjing [45] detected the levels of serum IL-6, carbohydrate antigen 724 (CA724) and VEGF in patients with GC, and found that the levels of serum IL-6, CA724 and VEGF in patients with positive liver metastasis were significantly higher than those in patients with negative liver metastasis, and the levels of serum IL-6, CA724 and VEGF in patients with negative liver metastasis were significantly higher than those in the control group. The combined detection of the three indicators can effectively improve the sensitivity, specificity and coincidence rate of GC diagnosis, which has high application value for the diagnosis of GC. Liu Bing et al. [46] found that the levels of bFGF, VEGF and CE were closely related to the prognosis of GC. The lower level of bFGF, VEGF and CE suggested that the patients had a positive curative effect and a good prognosis. The curative effect of late GC was higher than that of the control group ($P<0.05$). Postoperative follow-up showed that the 3-year and 5-year survival rates were (54% vs 40%) and (36% vs 17%) respectively, with significant differences ($P<0.05$). Dong Lei et al. [47] found that the SVEGF, MMP-2 and MMP-9 levels in GC patients were significantly higher than those in the control group before operation, significantly lower than those in the control group 7 days after operation, and significantly higher in the group with lymph node metastasis than in the group without lymph node metastasis ($P<0.05$). The ROC curve analysis results showed that the sensitivity of the combined detection of the three indicators in the diagnosis of GC lymph node metastasis was 78.95%, 63.16%, 73.68% and 97.37%, respectively, and the specificity was 95.65%, 91.30%, 93.48% and 97.83%. Therefore, combined detection can be used as an effective indicator to accurately judge the lymph node metastasis of GC, and dynamic monitoring is helpful to judge the prognosis and provide basis for postoperative treatment strategies.

6. The Significance of Serum FAS Level in Gastric Cancer Expression

There is little research on the correlation between serum FAS level and GC. Kusakabe et al [48]. FAS was highly expressed in highly differentiated GC-associated gastric tubular adenoma and intestinal metaplasia, while FAS was not or low expressed in mucosa adjacent to cancer. The expression of FAS is closely related to the occurrence and development of GC, which can occur in the early stage of tumor and precancerous lesions. Ito et al [49]. Taking serum FAS=6.0ng/ml as the best critical value for diagnosis of GC, the sensitivity and specificity were 93.62% and 93.33%, respectively. Their sensitivity were higher than those of CA199 and CA724 common markers, and the serum FAS content in patients with early GC also increased. Lin Jie et al. [50] reported that the serum FAS content of GC patients [5.25 ± 0.48 ng/mL] was significantly higher than that of chronic superficial gastritis [3.24 ± 0.37 ng/mL] and healthy control group [2.82 ± 0.28 ng/mL] ($P<0.05$). Taking serum FAS=3.78ng/mL as the best critical value for diagnosis

of GC, the ROC curve analysis showed that the serum FAS [(5.83 ± 1.37) ng/mL] content of patients with GC in stage III and IV was significantly higher than that in stage I and II [(4.04 ± 0.35) ng/mL] ($P < 0.05$). Among 10 patients with preoperative serum FAS > 3.78 ng/mL, 7 patients decreased to below 3.78 ng/mL after operation ($P < 0.05$). It is suggested that the increase of serum FAS level is related to the occurrence and development of GC, and the detection of serum FAS content is helpful for the diagnosis and follow-up of GC. Li Xin [51] detected the serum FAS content of 30 patients with GC, chronic atrophic gastritis (CAG), other gastrointestinal tumors (ODT) and control group, and found that the serum FAS level of GC patients was significantly higher than that of the control group (P There was no significant difference in FAS content between ODT group and CAG group and control group ($P > 0.05$). The results showed that the serum FAS content of patients with GC was significantly higher than that of patients with CAG, but there was no significant difference between GC and ODT. Hu Liyong *et al.* [52] detected the contents of serum FAS and pepsinogen (PG) in 74 cases of GC, 45 cases of benign gastric diseases and 75 cases of healthy control group by ELISA and immunoturbidimetry. It was found that the ratio of PGI and PGI/PGII in the serum of GC patients decreased, and the serum FAS increased significantly, which was statistically significant compared with the control group ($P < 0.05$). Combined detection of PG and FAS, the area under the ROC curve was 0.972, and the sensitivity and specificity of GC diagnosis were 95.50% and 92.32%, respectively, which were higher than a couple of independent detection. It is suggested that the combined detection of serum PG and FAS can improve the diagnostic efficiency of GC and contribute to the early diagnosis of GC. To sum up, the serum FAS level is highly sensitive and specific for the diagnosis of GC, and the tumor begins to rise at the early stage. It is expected to become an indicator of early screening, diagnosis and prognosis of GC, and play an important role in the diagnosis, treatment and prevention of GC. However, the systematic research on serum FAS level and GC biological characteristics needs to be further developed.

7. Conclusion

The result is showed that VEGF and FAS are not only highly expressed in GC tissue cells, but also significantly increase in serum VEGF and FAS, and their degree is positively correlated with GC pathology and clinical stage. The changes of serum VEGF and FAS have important clinical value for the diagnosis and prognosis monitoring of GC, which provides important basis for judging the postoperative recurrence of GC and formulating individualized treatment plan, but the research results are different. TM detection plays an important role in the diagnosis and prognosis of GC, but the sensitivity and specificity of a single indicator cannot meet the needs of rapid screening. In recent years, there have been many researches on the combined detection of serum VEGF and

other TM for the diagnosis and prognosis monitoring of GC, which has improved the sensitivity and specificity of diagnosis and prognosis judgment, and open up a new way for the research of GC. However, the research on the combined detection of serum VEGF and FAS content for the diagnosis and prognosis monitoring of GC has not been reported. According to the principle of evidence-based laboratory medicine, it is imperative to screen several tumor markers such as serum VEGF, which is highly sensitive and specific for the diagnosis and prognosis of GC.

Acknowledgements

Natural Science Funding Project Cangzhou Medical College (21Z009).

References

- [1] Hou Jianzhang, Li Yong. Relationship Between the Expression of S100P in Gastric Cancer Tissue and Clinical Pathology [J]. American Journal of Clinical and Experimental Medicine, 2021, 9 (3): 55-64.
- [2] Song ZH, Xu XN, Li KL, *et al.*, Research progress on etiology of gastric cancer [J]. Chin Med J Metall Indus, 2020, 37 (5): 509-511.
- [3] Song J, Ma SJ, Luo JH, *et al.* Melatonin induces the apoptosis and inhibits the proliferation of human gastric cancer cells via blockade of the AKT/MDM2 pathway. [J]. Oncology Reports. 2018, 39 (4): 1975-1983.
- [4] Smyth EC, Nilsson M, Grabsch HI, *et al.* Gastric cancer [J]. Lancet, 2020, 396: 635-648.
- [5] Yang L, Hou JZ, Hou ZJ. Progress of vascular endothelial growth factor and its receptor in gastric cancer [J]. Chinese medical equipment, 2014, 11 (4): 68-69.
- [6] Apte RS, Chen DS, Ferrara N. VEGF in Signaling and Disease: Beyond Discovery and Development [J]. Cell, 2019, 176 (6): 1248-1264.
- [7] Karaman S, Leppänen VM, Alitalo K. Vascular endothelial growth factor signaling in development and disease [J]. Development, 2018, 145 (14): 1507-1513.
- [8] Wang X, Liu XT, Zhou ST, *et al.* Detection and Clinical Significance of Coagulation Index and VEGF in Patients with Acute Leukemia [J]. Med Rec, 2022 28 (1): 184-189.
- [9] HoU ZJ, Hou JZ. Progress of Vascular Endothelial Growth Factor and its Receptor in Esophageal Cancer [J]. Med Rec, 2010, 16 (17): 2640-2642.
- [10] Qin F, Wang XB, Gong JP. The regulatory mechanism of fatty acid synthetase expression in tumor [J]. J Med Mole Biol, 2010, 7 (5): 453-456.
- [11] LuO JX, Li CF, Cu XH, *et al.* Advances in fatty acid synthetase genes [J]. Chinese animal husbandry and veterinary medicine, 2011, 38 (6): 118-122.
- [12] Lu Z, Yang HJ, Shi Kai. Regulation of fatty acid synthetase gene expression [J]. Sichuan J Anato, 2009, 17 (2): 31-35.

- [13] Wu YX, Zhang XZ, Yu JJ, et al. Effect of silencing fatty acid synthase gene (FASN) by siRNA interference on proliferation of human esophageal cancer cells [J]. *J Clin Med Prac*, 2013, 17 (19): 7-10.
- [14] Li XJ, Zhang QH, Luo T, et al. Correlation and Significance of Peroxidase and VEGF mRNA Expression in Gastric Carcinoma [J]. *Chin J Bases Clin Gene Surg*, 2008, 15 (7): 498-502, 510.
- [15] Wang HL, Luo K, Zhang XF, et al. The Correlation between Serum VEGF level and Tissue Expression in Gastric Cancer and Their Clinical Significance [J]. *Lab Immuno-assays & Clin Med*, 2009, 16 (2): 77-78.
- [16] Xu YY, Wang ZB, Li C. The clinical discussion: expression of FAS in colorectal carcinoma tissues and relationship with clinical staging about expression in serum [J]. *Conte Med*, 2017, 23 (15): 26-28.
- [17] Guo W, Jin YS, Niu N, et al. Expression of Fas in bladder cancer and its clinical significance [J]. *Mode Onco*, 2018, 26 (24): 3990-3993.
- [18] Li HY, Zhang SL, HouJZ. The Vascular Endothelial Growth Factor's Expression in Gastric Cancer and Progress in Prognostic Research [J]. *American Journal of Biomedical and Life Sciences*, 2021, 9 (5): 239-247.
- [19] Hou JZ, Zhang SL, Yuan JL, et al. Research Progress of Fatty Acid Synthase in Digestive Tract Tumors [J]. *Scie J Public Health*, 2022, 10 (5): 214-222.
- [20] Mao ZB, Xiao MB, Huang JF, et al. Significance of Vascular endothelial growth factor in serum of patients with gastric cancer [J]. *World Chin J Diges*, 2002, 10 (10): 1220-1221.
- [21] Karayiannakis AJ, Bolanakis H, Syrigos KN, et al. Serum vascular endothelial growth factor levels in pancreatic cancer patients correlate with advanced and metastatic disease and poor prognosis [J]. *Cancer Lett*, 2003, 194 (1): 119-124.
- [22] Zhou HY, Ye GX, Wang SW, et al. Clinical study on VEGF levels in serum and tumor tissues of patients with gastric cancer [J]. *World Journal of Cancer*, 2004, 3 (4): 349-350.
- [23] Hu M, Fan ZL, Wang XH. Expression and significance of serum vascular endothelial growth factor in patients with gastric cancer [J]. *J Qinghai Med College*, 2008, 29 (1): 36-38.
- [24] Kang SR, Li J. The Determination of Serum Vascular endothelial growth factor and microvessel density in Gastric Cancer [J]. *Acta Acad Med Nei Mongol* 2009, 31 (1): 13-18.
- [25] Yin HQ, Duan Y, Xu LJ. Determination of Serum VEGF and clinical significance in patients with Stomach Carcinoma [J]. *Chin Gener Prac*, 2009, 7 (11): 1171-1172.
- [26] Mysliwiec P, Pawlak K, Bandurski R, et al. Soluble angiogenesis markers in gastric tumor patients [J]. *Folia Histo-chem Cytobiol*, 2009, 47 (1): 81-86.
- [27] Hălmăciuc I, Gurzu S, Dobreanu M, et al. The most studied VEGF molecule is VEGF-A (Vascular Endothelial Growth Factor). Its involvement in various neoplastic processes represents an intensely controversial hypothesis [J]. *Rev Med Chir Soc Med Nat Iasi*, 2012, 116 (2): 446-451.
- [28] Lei Liu, Ma XL, Xiao ZL, et al. Prognostic value of vascular endothelial growth factor expression in resected gastric cancer [J]. *Asian Pac J Cancer Prev*. 2012, 13 (7): 3089-3097.
- [29] Wang TB, Deng MH, Qiu WS. Association of serum vascular endothelial growth factor-C and lymphatic vessel density with lymph node metastasis and prognosis of patients with gastric cancer [J]. *World J Gastroenterol* 2007, 13 (12): 1794-1798.
- [30] Wu EH. Clinical study of serum VEGF-A and VEGF-C in patients with gastric cancer [D]. 2008, Master's thesis of Shanghai Jiao Tong University.
- [31] Zhou CR, Zhang MY, Wang CG, et al. Expression and significance of serum vascular endothelial growth factor C in advanced gastric carcinoma [J]. *J Sichuan Med*, 2010, 31 (11): 1587-1589.
- [32] Wang W, Wang CG, HU SC, et al. Expression and significance of serum vascular endothelial growth factor D in gastric carcinoma patients at advanced stage [J]. *Chin Trop Med*, 2010, 10 (2): 207-208.
- [33] Shen YL, Ren ZH. Changes of serum gastrointestinal hormones, Vascular endothelial growth factor and related indexes in patients with gastric cancer [J]. *Chin J Gero*, 2014, 34 (17): 6859-6860.
- [34] Liu FG, Zhou HM, Xu JM, et al. Relationship between serum levels of Vascular endothelial growth factor and Endostatin in patients with gastric carcinoma and clinical-pathological characteristics [J]. *Shandong Med*, 2009, 49 (25): 11-13.
- [35] Zhu YW, Cheng JL, Qian KQ, et al. Expression of serum VEGF and P53 in patients with gastric cancer [J]. *Mode Onco*, 2007, 15 (3): 375-376.
- [36] Zhou HC, Liu HB, Su L, et al. Serum levels of VEGF and COX-2 in gastric cancer [J]. *Mode Onco*, 2013, 21 (9): 2019-2021.
- [37] Yang YE, Meng QS, Sun XJ. Clinical significance of combined determination of serum CEA, CA724, VEGF and Endostatin in patients with gastric cancer [J]. *Med Lab & Clin*, 2010, 21 (6): 67-69.
- [38] Zhu GM, Ma L. Clinical Value of Combined Detection of Serum VEGF, CEA and CA724 in Patient with Gastric Cancer [J]. *J Mod Lab Med*, 2007, 22 (6): 83-85.
- [39] Fang YZ, Chen JG. Application of serum CEA, Cal99 and VEGF in the diagnosis of gastric cancer [J]. *J Youjiang Med College Nation*, 2009, 31 (5): 805-806.
- [40] Li YM, Ren ZHH, Zhang JW. Expression of serum interleukin-6, C-reactive protein and vascular endothelial growth factor in patients with gastric cancer and its clinical significance [J]. *J Med Forum*, 2022, 42 (5): 68-71.
- [41] Villarejo-Campos P, Padilla-Valverde D, Martin RM, et al. Serum VEGF and VEGF-C values before surgery and after postoperative treatment in gastric cancer [J]. *Clin Transl Oncol*, 2013, 15 (4): 265-270.
- [42] Bilgiç CI, Tez M. Serum VEGF levels in gastric cancer patients: correlation with clinicopathological parameters [J]. *Turk J Med Sci*. 2015, 45 (1): 112-117.
- [43] Wang SD. Changes of serum VEGF, MMP-9 and endostatin levels in patients with medical gastric cancer and their clinical significance [J]. *Shandong Med*, 2011, 51 (38): 67-68.
- [44] Xia BX, Li Fan, Xu J, et al. Expression and clinical significance of interleukin-33 and Vascular endothelial growth factor C in gastric carcinoma [J]. *Chong Qing Med*, 2016, 46 (15): 2056-2059.

- [45] Yao QQ. Clinical value of serum IL-6, CA724 and VEGF in patients with gastric cancer [J]. *Fron Med*, 2018, 8 (31): 141-142.
- [46] Liu B, Zhou F, Yang F. Serum bFGF, VEGF and CE were used to predict the efficacy of Apatinib in the treatment of advanced gastric cancer [J]. *Abstracts of the world's latest medical information*, 2020, 20 (1): 166-167.
- [47] Dong L, Xia M, Shang KX, et al. Changes and clinical significance of serum VEGF, MMP-2 and MMP 9 levels in patients with gastric cancer before and after surgery [J]. *J MolDiagn Ther*, 2020, 12 (9): 1221-1225.
- [48] Kusakabe T, Nashimoto A, HonmaK, et al. Fatty acid synthase is highly expressed in carcinoma, adenoma and in regenerative epithelium and intestinal metaplasia of the stomach [J]. *Histopathology*, 2002, 40 (1): 71-79.
- [49] Ito T, Sato K, Maekawa H, et al. Elevated levels of serum fatty acid synthase in patients with gastric carcinoma [J]. *Oncol Lett*, 2014, 7 (3): 616-620.
- [50] Lin J, Dai HF. Diagnostic significance of levels of serum fatty acid synthase in patients with gastric carcinoma [J]. *J Dalian Med Univer*, 2014, 36 (5): 475-477.
- [51] Li X. Diagnostic value of serum PG, MG7-Ag, TK1 and Fas in gastric cancer [D]. 2016, Master's degree thesis, Chengdu University of Traditional Chinese medicine.
- [52] Hli Y, Dai SC. Application value of combined detection of PG and FAS in diagnosis of gastric cancer [J]. *Int J Lab Med*, 2015, (8): 1092-1093.