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Anti-Inflammatory and Anti-Angiogenic Properties of VitD3 in Ovarian Cancer

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Abstract: Ovarian malignancies are the most complicated type among all gynecological cancers. Their etiology is yet unknown; however, they are a heterogeneous, rapidly growing, and very fatal group of cancers. Chronic inflammation and angiogenesis appear to have major contributions in the development and progression of ovarian malignancies. Angiogenesis and inflammation are involved in the pathogenesis of ovarian cancer. Vitamin D3 (VitD3) has shown to have anti-inflammatory and anti-angiogenic properties in different types of cancers. The anti-inflammatory and anti-angiogenesis effects of VitD3 on ovarian cancer are investigated in this review.

Keywords: VitD3, Ovarian cancer, Inflammation, Angiogenesis

Online publication: March 10, 2022

1. Introduction

Ovarian cancer is a malignant neoplasm of the ovaries that mainly affects postmenopausal women. Unfortunately, among all gynecological malignancies, it has the worst prognosis and the highest mortality rate ^[1]. As ovarian cancer is related to the rupture of the ovarian epithelium and the sensitivity impact of the follicular fluid with a high content of estrogens, research has suggested that the number and frequency of ovulations in a woman's lifetime are linked to her risk of developing ovarian cancer ^[2,3].

Ovarian malignancies are separated into two types. Type I cancers include low-grade endometrioid, mucinous, and clear-cell cancers, whereas type II cancers include serous cancers, which can originate de novo from the tubal and/or ovarian surface epithelium ^[2]. Surgery, as well as chemotherapy, are important in the treatment of ovarian cancer ^[2]. Unfortunately, due to its unknown cause, it may not be averted. Natural components have the potential to play a role in prophylactic or supportive treatment. According to existing evidence, there may be a relationship between ovarian cancer and nutrition. Chronic inflammation, for example, has been suggested as a contributing factor to ovarian carcinogenesis ^[4]. It has been found that women who are exposed to pro-inflammatory products have higher risk of ovarian cancer ^[5].

VitD3 is a hormone that has multiple targets ^[6], and it is involved in calcium and phosphate homeostasis ^[7]. In addition to its traditional function, it has been found that VitD3 controls the function and development of immune cells, including, dendritic cells, macrophages, B cells, and T cells, by binding to vitamin D receptors ^[8]. The anti-inflammatory property of 1,25VitD3 has been recognized as an important part of the "non-classical activities" of VitD3 ^[9-11]. Vitamin D modulates inflammatory responses by downregulating T helper 1 (Th1) cells, inhibiting the production of several pro-inflammatory cytokines, upregulating Th2

cells and regulatory T (Treg) cells, downregulating Th17 cells, and modulating antigen-presenting dendritic cells into a “tolerogenic state” [12-14].

Low vitamin D levels have therefore been linked to an increased propensity to infections and a higher chance of developing autoimmune disorders [15]. Higher levels of vitamin D have been found related to a decreased risk of developing malignancies, including ovarian cancer [16,17]. Based on a comprehensive analysis on ecologic and case-control studies, it has been proposed that increasing geographic latitude, more exposure to sun, or vitamin D supplementation can reduce the incidence or death of ovarian cancer.

A meta-analysis of four cohort studies showed an inverse association between the incidence of ovarian cancer and circulating 25(OH)D levels [18]. According to the new evidence regarding the anti-cancer effects of VitD3, this review examines the anti-inflammatory and anti-angiogenesis effects of VitD3 on ovarian cancer.

2. Anti-inflammatory property of VitD3 in ovarian cancer

Inflammatory reactions contribute to the development and progression of ovarian cancer and other cancers [19,20]. Cyclooxygenase 1 and 2 (COX-1 and COX-2) are enzymes that are involved in the production of prostaglandin and therefore regulate inflammatory response [21] (**Figure 1**). However, COX-1 is expressed permanently, differing from the expression of COX-2, which is controlled by growth factors, prostaglandins, and cytokines [21]. The increased expression of COX-2 is associated with the development of ovarian cancer, a reduction in apoptosis, increased cell expansion, and neoangiogenesis [22]. It has been suggested that stable inflammatory environments may lead to reduced levels of VitD3, which may explain why cancer is associated with low levels of circulating VitD3 [23]. Vitamin D combined with COX-2 inhibitor (celecoxib) has shown to decrease the growth rates of ovarian cancer significantly when compared to celecoxib alone [24]. The correlation between vitamin D activities and prostaglandin metabolism in ovarian carcinomas has also been discussed [24].

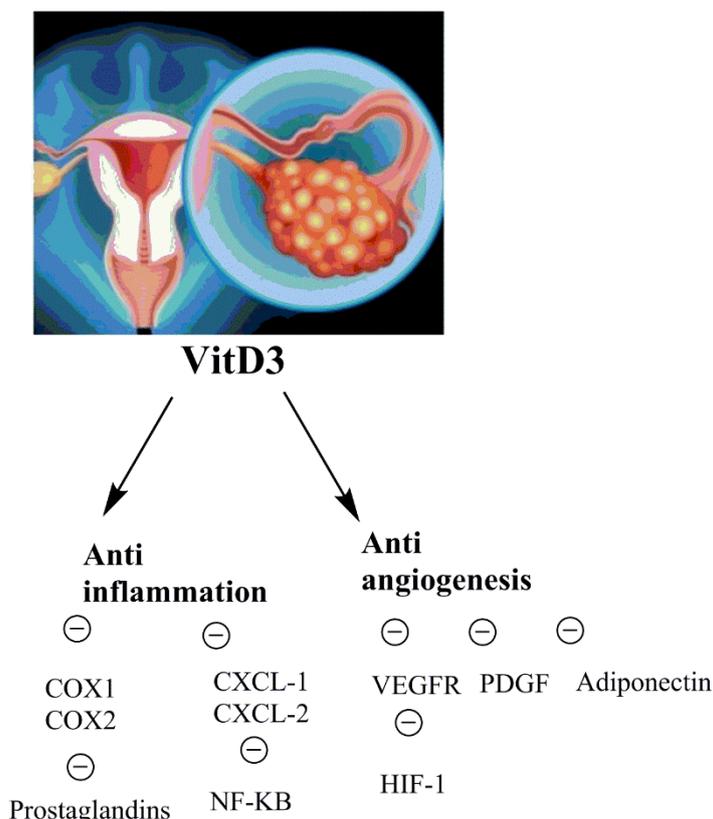


Figure 1. Anti-inflammatory and anti-angiogenic effects of VitD3 in ovarian cancer

A study that was conducted on ovarian and endometrial cancer cell lines revealed that VitD3 and progesterone can reduce the expression of CXCL1 and CXCL2 as pro-inflammatory chemokines in ovarian cells. This, in turn, leads to the downregulation of nuclear factor-kappa B (NF- κ B), which is the one of the most important transcription factors involved in tumor metastasis and inflammation [25]. The increased expression of CXCL1 and CXCL2 is associated with metastasis, angiogenesis, and tumor growth in breast and squamous cell cancers [25].

3. Anti-angiogenic property of VitD3 in ovarian cancer

Growing evidence indicates that vitamin D has a potential role in inhibiting tumor angiogenesis [29-33]. The presence of hypoxic regions within most solid tumors is a major pathophysiologic factor that regulates angiogenesis. Increased angiogenesis occurs as a cellular adaptation to hypoxia, which is regulated by hypoxia-inducible factor 1 (HIF-1). HIF-1 target genes, such as vascular endothelial growth factor (VEGF), are inhibited by 1,25(OH)₂D₃, and this molecular inhibition is mediated via a HIF-dependent pathway [34]. In a study, VitD3 decreased the growth inhibition of tumor-derived endothelial cells from vitamin D receptor (VDR) knockout mice [34]. Moreover, the loss of VDR resulted in an increase in HIF-1 α , VEGF, angiopoietin 1, and platelet-derived growth factor [34] (**Figure 1**).

4. Conclusion

The role of vitamin D in ovarian cancer has been studied, in which it has been suggested that vitamin D plays a protective and anti-cancer role. Based on relevant studies, this review suggests that vitamin D may serve as an anti-inflammatory and anti-angiogenic agent in ovarian cancer. Vitamin D may enhance anti-tumor effects, allowing for potential clinical application. Combined vitamin D and calcium supplement could be the therapeutic approach for preventing and treating ovarian cancer.

Disclosure statement

The authors declare no conflict of interest.

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Preventing Lower Extremity Deep Vein Thrombosis After Hip Fracture Surgery in Elderly Patients by Acupoint Application Combined with Pneumatic Compression Therapy

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Abstract: *Objective:* To investigate and analyze the long-term clinical effects of acupoint application combined with pneumatic compression therapy in the prevention of deep venous thrombosis after hip fracture surgery among the elderly. *Methods:* Sixty elderly patients who had undergone hip fracture surgery from February 2021 to February 2022 were selected as the research subjects. The patients were divided into two groups via drawing lots. Both the groups received nursing care, but the patients in the observation group were treated with TCM acupoint application combined with pneumatic compression therapy, whereas the control group received pneumatic compression therapy. The evaluation indicators included the patients' quality of life and complications. *Results:* The incidence of lower extremity deep vein thrombosis in the observation group was more than twice (0.3%), whereas the incidence of lower extremity complications in the control group was more than 6 times (20%). There was a significant difference between the two groups ($p < 0.05$). *Conclusion:* Traditional Chinese medicine acupoint application combined with pneumatic compression therapy is beneficial for the prevention of postoperative lower extremity deep vein thrombosis among elderly patients. In addition, the patients' overall quality-of-life scores in both physiological and psychological aspects improved significantly, which carries significant clinical reference value.

Keywords: Acupoint application; Traditional Chinese medicine; Pneumatic compression therapy; Minimally invasive surgery for hip fracture in elderly patients; Lower extremity deep vein thrombosis

Online publication: March 23, 2022

1. Introduction

In the prevention of lower extremity deep vein thrombosis after hip fracture surgery among the elderly, pneumatic compression therapy alone cannot meet the actual clinical needs, which will affect the prognosis of patients. In recent years, with the continuous development and clinical application of traditional Chinese medicine (TCM), acupoint application has emerged ^[1], which is more favorable to the prevention of postoperative complications when paired with pneumatic compression therapy for targeted nursing. This study analyzed the use of acupoint application combined with pneumatic compression therapy to explore its treatment and nursing effects.

2. Data and methods

2.1. Clinical data

Sixty elderly patients who had undergone hip fracture surgery from February 2021 to February 2022 were selected as the research subjects. The patients were divided into two groups via drawing lots. In the control group, the proportion of men to women was 13:17, their age ranged from 61 to 76, and the median age was 68.5 ± 2.28 years old; in the observation group, the proportion of women to men was 11:19, their age ranged from 62 to 77, with a median age of 60 ± 2.36 years old. The baseline data of the investigated patients had no significant difference ($p > 0.05$).

2.2. Methods

The control group received pneumatic compression therapy and nursing, which were carried out according to the following steps: upon stabilization, initiate pneumatic compression; the pressurization method of treating the lower limbs through pneumatic therapy involves applying inflation pressure to the lower limbs of the patient and gradually applying pressure to the medial side and root of the whole thigh from the sole; set the pressurization method as intermittent pressurization; the maximum inflation pressure at the pressurized part should be controlled at 180~200 mmHg; each chamber should be pressurized for 10 seconds, once in the morning and once before going to bed; the duration of each pressurization should be half an hour, and the treatment cycle should be about 10 days.

The pneumatic compression therapy received by the patients in the observation group was the same as that of the control group. On this basis, acupoint application was added to the treatment according to the following steps: first, prepare Panax notoginseng powder, pangolin, radix bupleuri, Sichuan dome, safflower, wood fragrance, Angelica sinensis, rhubarb wine, licorice, peach kernel, and trichosanthin; mix and grind the aforementioned prepared substances; mix the powdered form with alcohol and an appropriate amount of sesame oil to produce a paste that can be easily applied; place and fix the paste at the middle part of the acupoint plasters, and stick the plasters onto five acupoints (Xuanzhong, Yanglingquan, Sanyinjiao, Zusanli, and Huantiao); repeat the process each time the plasters are given to the patients; the application time should be 6 hours, and used twice a day; the cycle should be about 10 days.

During the treatment, it is important to observe the patients, especially for any systemic skin allergy, after sticking on the plasters. If there is anaphylactic shock, it needs to be removed immediately.

All the patients received the same postoperative care: (1) psychological intervention; most of the patients are elderly patients, in which after surgical treatment, they tend to stay in bed for a long time, thus affecting their limb function to a certain extent; therefore, patients often develop anxiety and other negative emotions; the attending nurses need to boost their confidence in rehabilitation, which will be conducive to their rapid recovery; (2) after surgical treatment, the nursing staffs need to regularly observe the changes in the patients' blood pressure, heart rate, and other parameters as well as conduct rounds where the patients are located at to prevent accidents; (3) since the patients' movements are restricted and their limbs are unable to function normally after the surgery, the postoperative nursing staffs need to observe the recovery of their lower limbs; they should also role the patients over and pat their backs as well as massage the patients' lower limbs, so as to reduce the incidence of lower extremity deep vein thrombosis; at the same time, patients should be informed to drink sufficient water every day; during their spare time, the nurses can assist in the recovery of the patients' respiratory function through deep breathing exercises; on the premise of following the doctor's advice, patients can be given low molecular weight heparin to avoid complications; it is worth noting that if a patient has leg swelling with non-pitting edema and an abnormal rise in temperature, it is necessary to determine whether the patient has complications of lower extremity deep vein thrombosis as soon as possible and inform the attending physician for appropriate treatment; (4) it is necessary to prepare an early rehabilitation training plan for each patient; after the surgery, it is

important to observe whether the patients' condition is stable, and then assist them in carrying out early training; at the beginning, functional activities such as standing on the hospital bed and limb flexion and extension should be encouraged, but with the recovery and improvement of the patients' lower limb, they should be encouraged to jog or walk upright, so as to promote the rehabilitation process.

2.3. Observation indicators

By using the quality-of-life score, the overall quality of life scores of the two groups of patients were observed and evaluated. The domains include the level of psychological, physiological, and social functions as well as the overall average mental state of each patient.

2.4. Statistical analysis

The statistical form of percentage (%) was adopted in this paper to directly replace the counting data, and the chi-square (X^2) values were given. The physiological function, social function, psychological function, and mental state of the patients were reflected by ($\bar{x} \pm s$). SPSS 21.0 was used to carry out the analysis, in which the chi square values, t values, and p values were analyzed. p less than 0.05 indicates statistically significant data.

3. Results

Through comparing and analyzing the complications and average quality-of-life scores of the patients in both groups, it was found that the average incidence of lower extremity deep vein thrombosis in the observation group was more than twice (0.3%), while the incidence of lower extremity complications in the control group was more than six times (20%). There was a significant difference between the two groups ($p < 0.05$). The overall quality-of-life scores of the patients in the two groups are shown in **Table 1**.

Table 1. Comparison of the quality-of-life scores between the two groups

Group	Number of cases	Psychological function	Physiological function	Social function	Mental state
Control group	30	74.12±5.35	78.45±4.52	73.33±5.24	76.43±5.54
Observation group	30	85.35±6.76	87.33±5.27	83.61±6.52	86.78±6.86
t		7.1348	7.0054	6.7313	6.4290
p		0.0000	0.0000	0.0000	0.0000

4. Discussion

Clinically, elderly hip fractures are often treated via surgery, and the symptoms can improve quickly. However, after surgery, patients often stay in bed for a long time, which increases the probability of lower extremity deep vein thrombosis [2]. However, pneumatic compression therapy alone cannot effectively prevent the occurrence of lower extremity deep vein thrombosis. This understanding has attracted great attention in clinical practice. According to traditional Chinese medicine [3], on the basis of pneumatic compression therapy, acupoint application can better prevent complications from occurring and promote the improvement of patients' quality of life. Under the combined treatment and nursing, the prognosis of patients is better [4]. This paper showed that with combined treatment and nursing, the patients' overall quality-of-life score improved significantly, which is helpful for the prevention of complications.

In short, TCM acupoint application combined with pneumatic compression therapy in the rehabilitation of postoperative elderly hip fractures and the prevention of lower extremity deep vein thrombosis has a significant value, which is worthy of clinical reference and application.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Effect of Laser Treatment Combined with Compound Xueshuantong Capsule in the Treatment of Diabetic Retinopathy

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Abstract: *Objective:* To determine the clinical value of compound Xueshuantong capsule in the treatment of diabetic retinopathy on the basis of laser treatment. *Methods:* Data were collected from 98 patients with diabetic retinopathy from February 2021 to February 2022. They were divided into two groups by drawing lots. The experimental group was treated with compound Xueshuantong capsule and laser treatment, whereas the control group was treated with laser treatment alone. *Results:* The absorption of exudation, resolution of retinal edema, and absorption of bleeding took longer in the control group; the incidence of visual acuity recovery to more than 0.5 and the patients' blood glucose levels were better in the experimental group, $p < 0.05$. *Conclusion:* For patients with diabetic retinopathy, laser treatment combined with compound Xueshuantong capsule can effectively improve the visual function and rehabilitation efficiency of patients with diabetic retinopathy as well as stabilize their blood sugar levels. It has high clinical application value.

Keywords: Laser treatment; Compound Xueshuantong capsule; Diabetic retinopathy; Clinical effect

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1. Introduction

Diabetic retinopathy is a complication of diabetes mellitus, with high incidence, multiple complications, and low cure rate. It has been reported that most diabetic patients have abnormal blood glucose levels and are prone to peripheral nerve abnormalities, gastrointestinal dysfunction, and other symptoms. With unstable blood glucose levels, complications such as retinopathy, constipation, diabetic foot, and so on may occur. Patients with diabetic retinopathy often suffer from different degrees of visual impairment. At present, the clinical effect of retinal laser treatment is unsatisfactory, thus reducing the quality of life of patients. With the progress of traditional Chinese medicine, symptomatic intervention with drugs for promoting blood circulation and removing blood stasis can effectively improve patients' clinical symptoms and gradually restore their visual function. Ninety-eight patients with diabetic retinopathy treated in February 2021 to February 2022 were included in this study. The improvement of their symptoms, visual acuity, and blood sugar levels were observed after laser treatment combined with compound Xueshuantong capsule.

2. Data and methods

2.1. Clinical data

From February 2021 to February 2022, 98 elderly patients with diabetic retinopathy were selected as the

research subjects. The patients were divided into two groups by drawing lots, with 49 patients in each group. In the control group, there were 20 male patients and 29 female patients, age ranging from 57 to 73, with a mean age of 65.19 ± 1.22 ; in the experimental group, there were 18 female patients and 31 male patients, age ranging from 58 to 72, with a mean age of 65.24 ± 1.31 . The baseline data of the patients were not statistically significant ($p > 0.05$).

Inclusion criteria: (1) approved by the Ethics Committee; (2) complete basic data; (3) normal organ function; (4) no cognitive abnormalities; (5) patients and their family members signed the informed consent form. Exclusion criteria: (1) hereditary mental disorder; (2) incomplete data; (3) mismatch with clinical diagnostic evaluation; (4) patients with coagulation dysfunction; (5) patients allergic to the experimental drug; (6) patients with poor compliance.

2.2. Methods

Prior to laser treatment, the symptoms of each patient should be evaluated, and the indications for the procedure should be determined. During laser treatment, the spot range and diameter should be adjusted, and the broadcast exposure time should be defined. The treatment should be carried out four times, once every two weeks.

For the experimental drug used in this study, compound Xueshuantong capsule (Guangdong Zhongsheng Pharmaceutical Co., Ltd.; National Drug Approval Number: Z20030017; Specification: 0.5g*60s), the patients were required to take the drug orally three times a day and three pills at a time for one week, as a course of treatment.

2.3. Observation indicators

- (1) Clinical symptoms: absorption of exudation, resolution of retinal edema, and absorption of bleeding.
- (2) Visual changes and blood glucose levels: fasting blood glucose, 2-hour postprandial blood glucose, and visual acuity.

2.4. Statistical analysis

The number of cases whose visual acuity improved to more than 0.5 were counted by %, and X^2 value was given. The bleeding absorption, exudation absorption, blood glucose levels, and the improvement of retinal edema were counted by $(\bar{x} \pm s)$. SPSS 21.0 was used to analyze the data to obtain the chi square value, t value, and p value. $p < 0.05$ indicates statistically significant data.

3. Results

3.1. Symptom improvement

After evaluation, the time for exudation absorption, retinal edema resolution, and bleeding absorption in the control group was longer ($p < 0.05$) (Table 1).

Table 1. Comparative analysis of bleeding absorption time, exudation absorption time, and retinal edema resolution time between the two groups

Group	Number of cases	Bleeding absorption (weeks)	Exudation absorption (weeks)	Retinal edema resolution (weeks)
Control group	49	3.09 ± 0.83	9.89 ± 1.46	5.34 ± 0.62
Experimental group	49	1.64 ± 0.71	8.97 ± 1.28	4.07 ± 0.69
t		9.2927	3.3167	9.5835
p		0.0000	0.0013	0.0000

3.2. Blood glucose levels and visual function

The incidence of visual acuity recovery to more than 0.5 and the measured blood glucose levels were better in the experimental group ($p < 0.05$) (Table 2).

Table 2. Comparative analysis of the incidence of visual acuity recovery to more than 0.5, fasting blood glucose levels, and 2-hour postprandial blood glucose levels between the two groups

Group	Number of cases	Incidence of visual acuity recovery to more than 0.5	Fasting blood glucose (mmol/L)	Postprandial blood glucose (mmol/L)
Control group	49	30 (61.2%)	5.05 ± 0.57	10.28 ± 1.29
Experimental group	49	48 (98.0%)	4.56 ± 0.68	8.39 ± 1.16
X^2/t		20.3538	3.8656	7.6260
p		0.0000	0.0002	0.0000

4. Discussion

Diabetes is characterized by high incidence, various complications, and low cure rate. Complications such as neurological dysfunction and gastrointestinal dysfunction may occur without proper control. Diabetic retinopathy is a common complication in the progression of diabetes mellitus. The increase of blood glucose levels can lead to retinal anoxia and ischemia, thereby reducing the visual function of patients. In severe cases, blindness may occur, lowering the patients' quality of life and increasing their stress levels [1]. Laser treatment is often used in the treatment of this disease. The clinical effects vary depending on the degree and characteristics of the condition, particularly in cases of central vein obstruction, vascular rupture, and bleeding. In traditional Chinese medicine, diabetic retinopathy is under the category of "sudden blindness." In the treatment of this condition, it is important to pay attention to promoting blood circulation to remove blood stasis, dredging meridians, and dredging collaterals. Some scholars have suggested that diabetic retinopathy is caused by blood stasis and Qi deficiency. The prescription composition of compound Xueshuantong capsule includes *Salvia miltiorrhiza*, *Panax notoginseng*, *Astragalus membranaceus*, etc. As a traditional Chinese medicine preparation, it can help reduce swelling, replenish Qi, relieve pain, remove blood stasis, cease bleeding, dredge menstruation, improve blood circulation, prevent platelet accumulation, and reduce blood viscosity [2]. Among them, *Panax notoginseng* can help with blood circulation, pulse dredging, anti-aging, and pain relief. *Astragalus membranaceus* contains antiperspirant, detoxifying, surface-strengthening, and Qi-tonifying properties. *Salvia miltiorrhiza* helps relieve menstrual pain, promote blood circulation, remove blood stasis, lower blood temperature, and reduce swelling. According to the experimental data, the exudation absorption time, bleeding absorption time, and retinal edema improvement time in the control group were worse than those of the experimental group; in addition, the incidence of visual acuity recovery to more than 0.5 and the blood glucose levels of the control group were worse than those of the experimental group ($p < 0.05$). It can be seen that on the basis of laser treatment, the use of compound Xueshuantong capsule can effectively improve the effectiveness of rehabilitation, shorten the rehabilitation cycle, alleviate the symptoms of retinal edema, restore visual function, and stabilize blood glucose levels. Modern pharmacology points out that compound Xueshuantong capsule contains total saponins of *Panax notoginseng*, which can effectively improve blood viscosity, promote blood circulation, improve blood flow in the retina, and restore retinal function [3]. According to many researchers, the use of compound Xueshuantong capsule in the treatment of diabetic retinopathy has achieved certain results on the basis of laser treatment, in which the retinal edema resolution time and hospitalization duration were shorter in the experimental group; the visual acuity score and blood sugar levels were also better in the experimental group; the data obtained were consistent with the results of this

study [4].

In conclusion, for patients with diabetic retinopathy, the combined treatment of laser therapy with compound Xueshuantong capsule can effectively improve the clinical symptoms of patients, restore their retinal function, improve their blood circulation efficiency, and stabilize their blood glucose levels. Increasing the sample size for in-depth analysis in future studies may be beneficial to improving the validity of this treatment for patients with diabetic retinopathy.

Disclosure statement

The authors declare no conflict of interest.

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Relationship between the Self-Efficacy and Mental Health of Elderly Patients with Coronary Heart Disease in Rural Hebei Province

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Abstract: *Objective:* To investigate the self-efficacy and mental health of elderly patients with coronary heart disease (CHD) in rural Hebei Province as well as to analyze the relationship between them. *Methods:* From June 2021 to December 2021, 480 elderly patients with CHD from rural areas, who had been discharged by the Department of Cardiology from three tertiary hospitals in three cities with different economic levels in Hebei Province for more than a year, were selected as the research subjects. The general self-efficacy scale (GSES) and symptom self-rating scale (SCL-90) were used to investigate the self-efficacy and mental health of these patients. SPSS 25.0 was used for data analysis. *Results:* The total mean self-efficacy score of elderly patients with CHD in rural Hebei Province was 17.18 ± 4.68 , which is lower than the international norm ($t = -32.067$, $P = 0.000$) and the national norm ($t = -28.783$, $P = 0.000$); the total average SCL-90 score was 148.64 ± 55.13 , which is higher than the national norm for adults and the reference norm for ordinary elderly people; except for hostility and psychosis, the other dimensions were significantly higher than the national norm for adults ($P < 0.05$); except for psychosis, the other dimensions were significantly higher than the reference norm for ordinary elderly people ($P < 0.05$); the self-efficacy score was found to be negatively correlated with the total SCL-90 score and the score for each dimension ($P < 0.05$). *Conclusion:* Elderly CHD patients with higher self-efficacy in rural Hebei Province have higher mental health level. It is suggested that the mental health of elderly patients with CHD in rural areas can be improved by improving their self-efficacy.

Keywords: Rural; Elderly patients; Coronary heart disease; Self-efficacy; Mental health

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1. Introduction

Coronary heart disease (CHD) is the most common cardiovascular disease. It affects the physical and mental health of elderly patients, especially those from rural areas, and brings heavy economic and disease burden to the family and society [1]. Research has shown that self-efficacy is the main factor affecting individual attitude, confidence, and behavior toward the disease, and it can affect the mental health of elderly patients with CHD through physiological processes [2]. The purpose of this study is to investigate the status quo of self-efficacy and mental health of elderly CHD patients in rural Hebei Province as well as

to analyze the relationship between the two, so as to provide a reliable basis for formulating measures to improve the mental health level of elderly patients with CHD in rural areas.

2. Research participants and methods

2.1. Participants

From June 2021 to December 2021, 480 elderly patients with CHD from rural areas, who had been discharged by the Department of Cardiology from three tertiary hospitals in three cities with different economic levels in Hebei Province for more than a year, were selected as the research subjects.

Inclusion criteria: (1) living in rural areas for ≥ 3 years; (2) diagnosed with CHD based on the diagnostic criteria of the International Society of Cardiology or via coronary angiography; (3) age ≥ 60 years old; (4) normal cognition and able to communicate; (5) informed consent given.

Exclusion criteria: (1) patients with severe visual and hearing impairments, who are unable to cooperate with the study; (2) patients with severe heart failure; (3) patients with severe arrhythmia, malignant tumors, or bone and joint diseases.

2.2. Methods

2.2.1. Data collection

This study adopted the multistage stratified cluster sampling method. First, three cities in Hebei Province were selected according to their economic conditions: Baoding (the economic level is the same as the average level of Hebei Province), Tangshan (the economic level is higher than that of Hebei Province), and Xingtai (the economic level is lower than the average level of Hebei Province) [3]. Following that, a first-class tertiary hospital in each city was selected, with a total of 532 patients screened and included through initial medical records. Data collection was carried out via telephone follow-up, and the relevant data of the patients were supplemented by consulting medical records. Cases of death (12 patients) and refusal of investigation (40 patients) were excluded by telephone interviews. There was a total of 480 successful telephone interviews, with an effective rate of 90.2%.

2.2.2. Research tools

- (1) Self-designed demographic survey: To determine the demographics, gender, age, marital status, education level, living status, per capita monthly income of the household, and other information are included.
- (2) General Self-Efficacy Scale (GSES) [4]: To evaluate the self-efficacy level, a total of 10 items, with each item having a 4-point Likert scale (no at all true = 1 point, hardly true = 2 points, moderately true = 3 points, exactly true = 4 points), adding up to a total of 40 points, are included. The higher the total score, the higher the self-efficacy level. The scale has good reliability and validity, with Cronbach's alpha = 0.870.
- (3) Symptom Checklist-90 (Scl-90) [5]: To evaluate the mental health level with 90 items and nine domains: somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. All items are rated on a 5-point Likert scale (not at all = 1, a little = 2, moderately = 3, very much = 4, extremely = 5). The higher the total score, the lower the overall mental health level. It has good reliability and validity, with Cronbach's alpha between 0.64 and 0.88.

2.3. Statistical analysis

Data analysis was performed with SPSS 25.0. General data were described in frequencies; self-efficacy and mental health levels were described in $\bar{x} \pm s$; Pearson correlation analysis was used to determine the

correlation between self-efficacy and mental health.

3. Results

3.1. Demographic data

Among the 480 elderly patients with CHD, 251 (52.3%) were male patients, and 229 (47.7%) were female patients; their age ranging from 60 to 85 years old, with a mean age of 71.18 ± 7.92 ; 339 (70.6%) patients were married, while 141 (29.4%) were divorced or widowed; the education level of 412 (85.8%) patients was of primary school level or lower, while that of 68 (14.2%) patients was of junior high school level or higher; the per capita monthly household income of 112 (23.3%) patients was below 1,000 yuan, that of 247 (51.5%) was 1,000-3,000 yuan, and that of 121 patients (25.2%) was above 3,000 yuan.

3.2. Self-efficacy

In this study, the lowest self-efficacy score was 7 points, while the highest was 30 points. The average score was 17.18 ± 4.68 points, which is significantly different from the international norm value (29.46 ± 5.33)^[6] ($t = -32.067, P = 0.000$). The result was also compared with the norm value for adults in China (28.64 ± 5.21)^[7], in which the difference was statistically significant ($t = -28.783, P = 0.000$). The results are shown in **Table 1**.

Table 1. Comparison of the subjects' self-efficacy with the international norm and national norm for adults

	Measured value (n = 480)	International norm (n = 17,553)	National norm for adults	t	P
Self-efficacy	17.18±4.68	29.46±5.33	—	-32.967	0.000
Self-efficacy	17.18±4.68	—	28.64±5.21	-28.783	0.000

3.3. Mental health

Table 2 shows that the overall average SCL-90 score of elderly patients with CHD in rural Hebei Province (148.64 ± 55.13) is higher than the national norm for adults^[8] and the reference norm for ordinary elderly people^[9]. Except for hostility and psychosis, the other dimensions were significantly higher than the national norm for adults ($P < 0.05$); except for psychosis, the other dimensions were significantly higher than the reference norm for ordinary elderly people ($P < 0.05$). The overall mental health level of the ordinary elderly was better than the national norm ($P < 0.05$). The results are shown in **Table 2**.

Table 2. Comparison of the SCL-90 scores of the subjects with the national norm for adults and reference norm for ordinary elderly people ($\bar{x} \pm s$)

Group	Total score	Somatization	Obsessive- compulsive disorder	Interpersonal sensitivity	Depression	Anxiety	Hostility	Phobic anxiety	Paranoid ideation	Psychosis
Elderly CHD patients in rural Hebei (n = 480)	148.64±55.13 ①②	1.93±0.81 ①②	1.81±0.63 ①②	1.82±0.61 ①②	1.67±0.60 ①②	1.55±0.55 ①②	1.44±0.46 ②	1.40±0.45 ①②	1.53±0.51 ①②	1.30±0.43
National adult norm (n = 1388)	129.96±38.67	1.37±0.48	1.62±0.58	1.65±0.61	1.50±0.59	1.39±0.43	1.46±0.55	1.23±0.41	1.43±0.57	1.29±0.42
Ordinary elderly reference norm (n = 24630)	118.11±34.23 ①	1.45±0.50	1.47±0.51	1.32±0.47	1.40±0.50	1.31±0.51	1.28±0.44	1.21±0.41	1.24±0.44	1.22±0.39

Note: ① Compared with the national norm for adults, $P < 0.05$; ② Compared with the reference norm for ordinary elderly people, $P < 0.05$

3.4. Relationship between self-efficacy and mental health

According to Pearson correlation analysis, the self-efficacy scores of elderly patients with CHD from rural areas in Hebei Province were negatively correlated with the total SCL-90 score and the score for each dimension ($P < 0.05$); that is, the higher the self-efficacy score, the higher the SCL-90 score, and the lower the total score and score for each dimension, the higher the mental health level. The results are shown in **Table 3**.

Table 3. Correlation analysis of the subjects' self-efficacy and mental health as well as the various domains of mental health (r)

Variable	Total score	Somatization	Obsessive-compulsive disorder	Interpersonal sensitivity	Depression	Anxiety	Hostility	Phobic anxiety	Paranoid ideation	Psychosis
Self-efficacy	-0.498**	-0.474**	-0.465**	-0.453**	-0.439**	-0.448**	-0.432*	-0.426*	-0.370*	-0.431**

Note: * $P < 0.05$; ** $P < 0.01$

4. Discussion

The self-efficacy level of middle-aged and elderly patients with CHD in this study was lower than the international norm and the national norm. In this study, 412 patients (85.8%) received primary school education or lower, and 112 patients (23.3%) have per capita monthly household income of less than 1,000 yuan, indicating that the vast majority of elderly patients with CHD have no source of income, and their families are not in good financial situation. The unique course of CHD does not only have a destructive impact on the patient's ability to work, but also contribute to the increased economic burden of patients and their families due to long-term medication and repeated hospitalizations. This causes patients to suffer both physically and mentally, resulting in the lack of confidence and hope for the future, in addition to low self-efficacy.

SCL-90 was compiled by an American psychologist in the 1970s. In 1996, the scale was used to study the mental health of the elderly in China. SCL-90 is suitable for evaluating the mental health of elderly people. In a study^[9], 100 valid samples from 315 literatures that used SCL-90 to evaluate the mental health of elderly people over a period of 10 years from 2004 to 2013 and a mental health survey using SCL-90 on 24,630 elderly people were included. The results were meta-analyzed, and the norm was determined as a reference norm for the mental health of elderly people. The results of this study showed that the mental health status of elderly patients with CHD in rural Hebei Province was worse than the national norm for adults and the reference norm for ordinary elderly people, but the overall mental health level of the general elderly was better than the national norm ($P < 0.05$). This may be due to the fact that the rich social experience of the elderly plays a strong role in promoting their psychological adjustment; hence, the overall mental health level of elderly people without disease (ordinary elderly people) is relatively high. As the course of CHD is protracted, elderly people suffering from CHD often experience repeated attacks or progressive aggravation, which not only affects their quality of life, but also increases the psychological and economic burden of their family members, thus further affecting their mental health and resulting in stress effects, such as depression, anxiety, etc.

This study found that there is a significant negative correlation between self-efficacy and mental health as well as the score for each dimension ($P < 0.05$), which is consistent with the results of local and foreign research, indicating that self-efficacy is an important aspect that affects mental health. People's behavioral choices are expressed as avoiding tasks and situations beyond their ability to undertake and perform what can be accomplished. The higher the self-efficacy level, the more vigorous their efforts, and the more they can persevere. When perseverance is converted into actual gains, there will be more psychological satisfaction and a higher mental health level^[10]. On the contrary, elderly patients with CHD in rural areas

with low self-efficacy cannot effectively cope with the stress from the disease and tend to experience negative emotions for a long time, which is not conducive to their mental health. Relevant departments can improve the self-efficacy of elderly CHD patients in rural areas through training, health education, and other means, thus ultimately improving their mental health.

Elderly patients with CHD from rural areas in Hebei Province are anxious and even feel helpless or fearful due to mental pressure. In addition, palpitations, chest discomfort, and pain caused by myocardial ischemia and hypoxia may increase the psychological burden of patients. The mental health level and self-efficacy of elderly patients with CHD in rural Hebei Province were found to be lower than the national norm. The higher the self-efficacy, the better the mental health. People with high self-efficacy are more likely to overcome difficulties and persist in self-discipline compared to those with low self-efficacy. They can generally cope with discomfort by having positive and optimistic attitudes, countering negative emotions, having confidence to overcome diseases, and also having a sense of happiness and satisfaction. Nursing staffs should be tolerant and understanding of their various psychological manifestations, showing sympathy and carrying out effective as well as reasonable guidance to help relieve tension, fear, and anxiety. Cultivating and improving the self-efficacy of elderly patients with CHD from rural areas is one of the effective ways to improve their mental health and prevent mental disorders.

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Disclosure statement

The authors declare no conflict of interest.

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Comparative Analysis of the Value of Gastroscopic Biopsy and Surgical Pathology in the Diagnosis of Gastric Cancer

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Abstract: *Objective:* To explore and analyze the diagnostic value of gastroscopic biopsy and surgical pathology in improving the diagnostic accuracy of gastric cancer. *Methods:* From May 2019 to June 2020, 80 patients with gastric cancer treated in Shuyang Xiehe Hospital were selected and divided into two groups, a control group and a study group, with 40 cases in each group, based on the examination method individually selected by the patients. The patients in the control group were investigated via gastroscopy, while those in the study group were investigated by surgical pathology. The diagnostic values of the two methods were compared and analyzed. *Results:* The diagnostic accuracy of patients in the study group was 100%, which was higher than that of the control group. The tissue type, lesion morphology, and cancer differentiation of the study group were better than those of the control group. There was significant difference between the two methods ($P < 0.05$). *Conclusion:* Surgical and pathological examination can improve the diagnostic accuracy of gastric cancer, comprehensively analyze the patient's condition, and provide corresponding theoretical basis for follow-up treatment, so that patients can obtain more active and effective treatment, reduce pain, and improve their quality of life.

Keywords: Gastric cancer; Gastroscopic biopsy; Surgical pathology

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1. Introduction

Gastric cancer is a common malignant tumor, originating from the gastric mucosal epithelium, and it can occur in different parts of the stomach. The risk factors of gastric cancer include genetics, eating habits, *Helicobacter pylori*, and other factors. Spontaneous sternal pain, epigastric discomfort, and vomiting are some of its clinical manifestations^[1]. For this disease, active treatment and intervention should be taken to reduce the occurrence of adverse events. In the early stage of gastric cancer, the clinical symptoms are atypical and often confused with gastric ulcer or other benign diseases. Therefore, missed opportunities often occur in the diagnosis of this disease, resulting in serious complications, which may be life-threatening to the patients. Therefore, clinically, the diagnosis of this disease is particularly important. Early diagnosis and early treatment can improve the quality of life of patients, reduce their pain, and promote family harmony as well as social stability. At present, the common examination methods are gastroscopic biopsy and surgical pathology. Both of these methods can achieve ideal diagnostic results for gastric cancer. In this paper, the diagnostic accuracy of gastroscopic biopsy and surgical pathology for gastric cancer is explored and discussed.

2. Data and methods

2.1. General information

From May 2019 to June 2020, 80 patients with gastric cancer treated in Shuyang Xiehe Hospital were selected and divided into two groups, a study group and a control group, with 40 cases in each group, according to the examination methods. There was no statistically significant difference in the basic data of the patients ($P > 0.05$). The basic data of the patients are shown in **Table 1**.

Table 1. Comparison of basic data between the two groups

Group	Male-female ratio	Age range (years)	Average age (years)	Mean course of disease (months)
Study group (n = 40)	22:18	40-65	52.5±2.5	16.5±5.5
Control group (n = 40)	21:19	41-66	53.5±3.5	17.5±4.5
<i>P</i>	> 0.05	> 0.05	> 0.05	> 0.05

Inclusion criteria: (1) the clinical symptoms of the patients were consistent with the indications of gastric cancer; (2) the patients and their families had given informed consent to the study.

Exclusion criteria: (1) patients with multiple organ failure, shock, cardiovascular disease, stroke, hemiplegia, diabetes, or mental disorders.

2.2. Methods

Upon admission, the patients' vital signs were monitored, and fecal occult blood test was routinely done, so as to have a preliminary understanding and judgment of the degree of their condition. The patients' past history was checked in detail, and the investigation and diagnosis were done on a specific day.

The patients in the control group were investigated via gastroscopic biopsy. The procedure was carried out according to the following steps: first, carefully observe the gastric mucosa of the patient through a gastroscope; then, record the size, degree, and distribution of the lesion in detail; following that, perform the biopsy according to the condition of the lesion; for ulcerative lesion, select the ulcer area for tissue biopsy; for the protuberant type, perform the biopsy at the apical and basal areas of the gastric mucosa; for the flat type, perform the biopsy around the gastric mucosa; for submucosal lesion, select the tissue at the central depression for biopsy. In order to improve the diagnostic accuracy, the number of tissues selected during the examination should not be less than three [2].

The patients in the study group underwent surgical and pathological diagnosis according to the following steps: make preoperative preparations, followed by routine anesthesia; select the tissues for pathological examination; if the diameter of the lesion is 0-1.0 cm, remove the whole lesion and examine pathologically; if the diameter of the lesion is greater than 1.0 cm, select typical parts of the lesion; thereafter, process the specimen, fix the specimen with 10% formaldehyde solution, and embed it in paraffin; continue by tissue sectioning and staining, and then observe the specimen under the microscope while analyzing the pathological results.

2.3. Observation indicators

The accuracy of the two methods was observed; the tissue types under the two methods were compared; the pathological types of the two methods were observed, including the rate of cases with infiltration type, ulcer type, localized ulcer type, and mass type; the differentiation degree of gastric cancer in the two groups was observed.

2.4. Statistical analysis

The data were calculated and analyzed using SPSS 23.0. The count data were expressed in n/% and X^2 test. $P < 0.05$ indicates statistical significance.

3. Results

3.1. Diagnostic accuracy

Through two different methods, the diagnostic accuracy of the study group was 100%, which was significantly higher than that of the control group ($P < 0.05$). The results are shown in **Table 2**.

Table 2. Comparison of diagnostic accuracy between the two groups (n/%)

Group	Number of cases	Undiagnosed	Diagnosed
Control group	40	10 (25)	30 (75)
Study group	40	0 (0)	40 (100)
X^2	-	-	11.4286
P	-	-	0.0007

3.2. Tissue type

Under the two different methods, there was significant difference in the tissue type between the two groups ($P < 0.05$). The results are shown in **Table 3**.

Table 3. Comparison of tissue types between the two groups (n/%)

Group	Number of cases	Adenocarcinoma	Signet ring cell carcinoma	Others
Control group	40	8 (20.0)	5 (12.5)	1 (2.5)
Study group	40	19 (47.5)	14 (35.0)	7 (17.5)
X^2	-	6.7645	5.5910	5.0000
P	-	0.0093	0.0180	0.0253

3.3. Lesion morphology

There was no significant difference in the rate of cases with ulcer type, localized ulcer type, and mass type between the study group and the control group ($P > 0.05$). The rate of cases with infiltrating type in the study group was significantly higher than that in the control group ($P < 0.05$). The results are shown in **Table 4**.

Table 4. Comparison of lesion morphology under the two examination methods (n/%)

Group	Rate of ulcer type	Rate of localized ulcer type	Rate of mass type	Rate of infiltrating type
Control group (n = 40)	6 (15.0)	5 (12.5)	10 (25.0)	3 (7.5)
Study group (n = 40)	8 (20.0)	9 (22.5)	13 (32.5)	16 (40.0)
X^2	0.3463	1.3853	0.5492	11.6652
P	0.5562	0.2392	0.4586	0.0006

3.4. Cancer differentiation

The degree of cancer differentiation of the study group was significantly better than that of the control

group ($P < 0.05$). The results are shown in **Table 5**.

Table 5. Comparison of cancer differentiation under the two examination methods (n/%)

Group	Number of cases	Poorly differentiated type	Differentiated type
Control group	40	8 (20.0)	13 (75.0)
Study group	40	17 (42.5)	23 (100.0)
χ^2	-	4.7127	5.0505
P		0.0299	0.0246

4. Discussion

Gastric cancer is a common malignant tumor seen in clinical practice. Its pathogenesis is explained by the spontaneous canceration of gastric mucosal epithelial cells. Patients with gastric cancer often present with symptoms such as epigastric discomfort, sternal pain, nausea, and vomiting. The early symptoms of gastric cancer are often confused with other gastrointestinal diseases, conferring wrong judgments and missed opportunities for treatment.

There are many risk factors of gastric cancer, including poor eating habits, *Helicobacter pylori*, genetic factors, and inflammatory diseases of the stomach. Alcoholism, smoking, and spicy food increases the burden on the stomach, leading to a series of gastric diseases and increasing the risk of cancer. Gastric mucosal inflammatory responses induced by *Helicobacter pylori* infection accelerate the reproduction of gastric mucosal epithelial cells, which eventually leads to cancer. Chronic gastritis, gastric ulcer, and other diseases have different degrees of inflammatory hyperplasia at their onset. These conditions promote inflammatory lesions at the gastric mucosal epithelium, resulting in cancer. Gene sequences and genetic factors also increase the risk of gastric cancer [3].

Gastric cancer mostly occurs in the lesser curvature of the stomach, cardia, and gastric antrum. This disease mainly affects those around 40 years old, most of which are male patients. Gastric cancer has a high mortality rate. Therefore, actively taking effective measures for intervention in the early stage of the disease, combined with chemotherapy and other measures, can improve the quality of life, prolong the life of patients, and increase the survival time to more than 5 years [4]. For patients with advanced cancer, their quality of life and survival time significantly reduce without timely treatment. Therefore, for patients with gastric cancer, intervention should be done in the early stage, but more importantly, early diagnosis is crucial.

Clinically, there are many ways to diagnose gastric cancer, such as barium meal radiographic examination, gastric fluid analysis, immunological tests, etc. These investigations can achieve ideal results to a certain extent, but there are some deficiencies in formulating reasonable and effective treatment plans. With the progress and development of intervention, the most common methods to diagnose gastric cancer are gastroscopic biopsy and surgical pathology. Gastroscopic biopsy is easy to operate, lowers the risk of injury to patients, has clear imaging, allows the surgeon to determine the location of the lesion intuitively and accurately, and has high accuracy [5]. It also provides corresponding theoretical basis for follow-up surgical treatment. However, this kind of examination has certain limitations. The field of vision of a gastroscope is small, and the pathological tissues cannot be comprehensively analyzed and judged. In order to ensure the accuracy of gastroscopic biopsy, no less than four samples of living tissues should be examined each time. The diagnosis of the pathological features of gastric mucosa is one-sided, so misdiagnosis and missed diagnosis may occur, resulting in missed opportunities for the best treatment and thus affecting the final treatment effect.

Surgical pathology involves the removal of the lesion during surgery, which will then be fixed, embedded, sectioned, stained, and finally analyzed and studied under the microscope, so as to draw relevant conclusions, make up for the shortcomings of gastroscopic biopsy, and carry out specific research and analysis of the cause for the occurrence and development of the disease, its morphology, and structure, as well as the final regression of the disease with higher accuracy.

The results of this study showed that the diagnosis made via surgical pathology had higher accuracy compared to gastroscopic biopsy. There were statistically significant differences between the two methods in terms of the degree of differentiation, lesion morphology, and tissue types ($P < 0.05$).

Gastroscopic biopsy is less harmful to patients and easier to operate. It is suitable for the preliminary screening of gastric cancer. Surgical pathology can make up for and correct the deficiencies of the former as well as improve the accuracy of diagnosing gastric cancer.

Gastric cancer, a malignant tumor disease, has serious impact on the life and health of patients. Therefore, in order to improve the treatment efficiency, early diagnosis should be strengthened. Both gastroscopic biopsy and surgical pathology have high diagnosis rate. Therefore, they are able to provide relevant theoretical basis for subsequent treatment, ensure the safety of patients, reduce the pain experienced by patients to a large extent, and improve their quality of life.

Disclosure statement

The author declares no conflict of interest.

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Genomic Signature for the Prognosis of Survival in Relation to the Tumor Microenvironment in Esophageal Adenocarcinoma

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Abstract: *Objective:* To establish a new genomic signature for the prognosis of survival in relation to the tumor microenvironment in esophageal adenocarcinoma. *Methods:* Data from The Cancer Genome Atlas (TCGA) were applied, and the stromal and immune scores of patients with esophageal adenocarcinoma (EAC) were generated through the ESTIMATE algorithm. Differentially expressed genes were obtained, and genes concerning immune prognosis were identified on the basis of these scores. Functional analysis showed that these genes were primarily involved in immunobiological processes. Additionally, CIBERSORT was used to analyze 22 subgroups of tumor-infiltrating immune cells in the tumor microenvironment. *Results:* The results of the genomic assessment shown on the Kaplan-Meier curve revealed that EAC patients with high-risk scores have the worst survival. The risk score is valid as an independent prognostic factor for the overall survival in EAC patients. The tumor microenvironment was systematically analyzed, and the immune-related prognostic biomarkers of EAC have been proposed. *Conclusion:* The expression of tumor-infiltrating immune cells and immune-related genes in EAC have been identified. Some previously overlooked genes may be used as additional biomarkers for EAC in the future.

Keywords: Esophageal adenocarcinoma; Genomic signature; Prognosis of survival; Tumor microenvironment

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1. Introduction

Esophageal cancer is one of the most common malignancies worldwide, and it has become the seventh most common cancer and the sixth leading cause of death globally ^[1]. Esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) are the two main subtypes of esophageal cancer. Esophageal adenocarcinoma, which is commonly seen in many developed countries, mainly occurs in Barrett's esophagus. In terms of its histological progress, it usually develops from epithelial metaplasia to invasive carcinoma, usually located at the distal esophagus. It is closely related to gastro-esophageal reflux and obesity ^[2]. In spite of recent progress in its treatment and diagnosis, the 5-year survival rate for esophageal adenocarcinoma is still very poor ^[3]. Therefore, a further comprehending of cancer and exploring of treatment modes are essential to improve the prognosis of EAC patients.

In recent years, people have gradually realized the function of tumor microenvironment (TME) in tumor biology. Tumor microenvironment refers to the cellular environment in which tumors are generated. It includes immune cells, endothelial cells, mesenchymal cells, inflammation agents, and extracellular matrix (ECM) [4,5]. The cells and molecules in the tumor microenvironment are dynamically changing, indicating the nature of tumor growth and mutually promoting immune absconding, tumor breeding, and metastasis [6]. In the tumor microenvironment, immune cells and stromal cells are the two main non-neoplastic components that are considered to be the focus of prognostic assessment and tumor diagnosis. Therefore, comprehending the molecular structure and usage of the tumor microenvironment is the key to control tumor evolution and immune response. The expression of unique molecular biomarkers in immune cells and stromal cells has been determined, and a tumor microenvironment prediction algorithm based on immune/stromal/ESTIMATE scores has been established [7]. On the basis of the ESTIMATE algorithm, researchers have evaluated the prognosis of many tumors and explored gene changes [8-10]. However, the value of immune/stromal scores for EAC has not been investigated in detail.

In this study, based on the exploration of the tumor microenvironment, immune-related prognostic biomarkers were traced in EAC, using both EAC cohorts of The Cancer Genome Atlas (TCGA) database and ESTIMATE algorithm.

2. Materials and methods

2.1. Data acquisition

The gene expression profiles of patients with EAC were downloaded along with clinical data on gender, age, tissue type, TNM staging, survival, and outcome from the TCGA website (<https://portal.gdc.cancer.gov/>). The selected standards were: (1) patients with EAC; (2) available overall survival (OS) data; (3) available raw count or normalized gene expression data. The downloaded data were used to calculate the stromal and immune scores via the ESTIMATE database (<https://bioinformatics.mdanderson.org/estimate/>).

2.2. Identification of differentially expressed genes (DEGs)

The TCGA cohort was stratified according to the intermediate values of the stromal/immune scores. The low- and high-risk groups of DEGs were obtained by applying the “limma” package [11]. The cut-off values for the screening of DEGs were fold change of > 2 , $P < 0.05$, and false discovery rate (FDR) of < 0.05 .

2.3. Heatmaps and Venn diagrams

The “Heatmap” R package was used to conduct heatmaps, and the “VennDiagram” package was used to generate Venn diagrams.

2.4. Bioinformatics analysis

The GO enrichment analysis of DEGs was generated by applying the “clusterProfiler” package. Meanwhile, KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway enrichment analysis was obtained by the package. The PPI network was carried out through the Metascape website (<http://metascape.org>) [12] with default parameters.

2.5. Construction of the immune-related risk signatures

The endpoint was considered as the overall survival. The model was used to perform an overall survival analysis for verification. First, a preliminary screening of genes was conducted through univariate Cox regression. Next, in order to select the prognostic genes, the least absolute shrinkage and selection operator (LASSO) Cox regression model was used [13]. The “survival” and “glmnet” R packages were used to

analyze and obtain the model. Based on the results from LASSO Cox regression, immune-related risk signatures were established for the TCGA cohort. The risk score of each patient was calculated by taking advantage of both the gene expression levels and LASSO-Cox regression coefficients. The patients were divided into low- and high-risk groups on the basis of the median risk score, and the survival rates between the two groups were estimated based on a combination of Kaplan-Meier curve and log-rank analysis. The “timeROC” package was used to perform the time-dependent receiver operating characteristic (ROC) curve of the risk scores to identify the prognostic precision of risk scores. Finally, the independent prognostic values of risk scores and other clinical features were explored using univariate and multivariable Cox analysis.

2.6. Survival analysis

Kaplan-Meier curves were applied to determine genes that could independently predict the OS of EAC patients. Kaplan-Meier curves were generated using the “survival” R package.

2.7. Evaluation of immune cell infiltration

CIBERSORT algorithm was used to calculate tumor-infiltrating immune cells [14]. CIBERSORT (<https://cibersortx.stanford.edu/index.php>) is a web tool, which has a gene expression signature matrix of 547 marker genes, applied to characterize the abundance of 22 immune cell types. The 22 immune cell subtypes include memory B cells, naive B cells, seven types of T cells, resting NK cells, activated NK cells, plasma cells, monocytes, M0-M2 macrophages, eosinophils, neutrophils, resting dendritic cells, activated dendritic cells, resting mast cells, and activated mast cells. In this study, CIBERSORT was used with a signature matrix at 1000 permutations to reckon the numbers and ranges of immune cell types in the case of transcriptome data as well as the distinctions in immune cell type composition among various groups. The results of the estimation were visualized with “barplot” and “vioplot” R packages.

3. Results

3.1. Differentially expressed gene analysis based on stromal/immune scores via the ESTIMATE algorithm

In order to explore the relationships between the gene expression profiles and the stromal/immune scores, the RNA-sequencing data of the 79 EAC cases were downloaded from the TCGA database for analysis. Among these patients, there were 11 (13.92%) female patients and 68 (86.08%) male patients. The clinical characteristics of the patients are shown in **Table 1**. Based on the ESTIMATE algorithm, these patients were divided into high-score and low-score groups according to the median values of the stromal and immune scores. The heatmaps in **Figure 1A** and **1B** revealed significant transcriptome data of the samples between the high and low stromal/immune score groups.

In addition, the Venn diagrams of differentially expressed genes (DEGs) were drawn (**Figure 1C**, **1D**, and **1E**). According to the aforementioned threshold (fold change > 2, $P < 0.05$, and false discovery rate < 0.05), 1,516 DEGs were obtained between high and low stromal groups and 988 DEGs were obtained between high and low immune score groups. Additionally, 835 genes were upregulated, and 1 gene was downregulated simultaneously between the stromal and immune score groups.

Table1. Clinical characteristics of patients with EAC in the TCGA database

Variables	Cases, N (%)
Age at diagnosis	
≤ 60	30 (37.97%)
>60	49 (62.03%)
Gender	
Female	11 (13.92%)
Male	68 (86.08%)
Pathological stage	
I	9 (11.39%)
II	22 (27.85%)
III	27 (34.18%)
IV	5 (6.33%)
NA	16 (20.25%)
TNM-T	
T0	1 (1.27%)
T1	19 (24.05%)
T2	10 (12.66%)
T3	36 (45.57%)
T4	1 (1.27%)
NA	12 (15.19%)
TNM-N	
N0	20 (25.32%)
N1	37 (46.84%)
N2	4 (5.06%)
N3	5 (6.33%)
NX	1 (1.27%)
NA	12 (15.19%)
TNM-M	
M0	51 (64.56%)
M1	5 (6.33%)
MX	9 (11.39%)
NA	14 (17.72%)

Note: NA, non-applicable

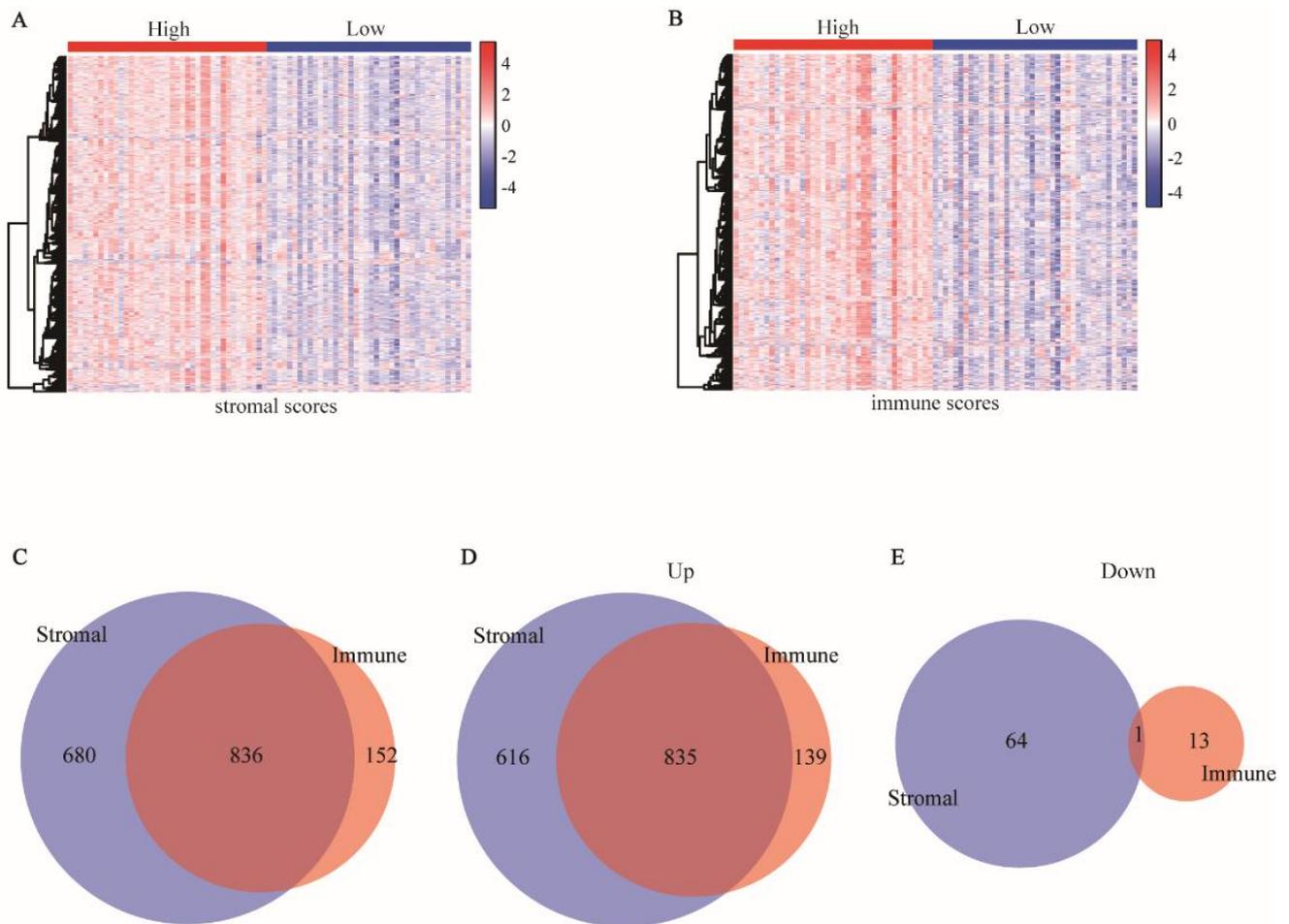


Figure 1. Stromal and immune scores of gene expression profiles in EAC; (A)(B) Heatmaps displaying distinct expressed genes according to stromal and immune scores; red marker reflects higher expression genes and blue marker reflects lower expression genes; (C)(D)(E) Venn diagrams of simultaneously differentially expressed genes drawn according to stromal and immune scores

3.2. GO and KEGG enrichment analyses for DEGs

Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses of co-DEGs using the “clusterProfiler” package were carried out to assess the differentially expressed genes on the tumor-infiltrating immune cells. The heatmap in **Figure 2A** exhibited 30 enriched terms of GO among the DEGs on the basis of biological process (BP), cellular component (CC), and molecular function (MF) for EAC cohorts; the heatmap in **Figure 2B** exhibited 15 enriched pathways of KEGG among the DEGs. Majority of these terms or pathways are related to cell activation and cell adhesion molecules (CAMs). Consistent with the GO and KEGG analyses, protein-protein interaction (PPI) networks were colored through different cluster ID (**Figure 2C**) and *P*-value (**Figure 2D**), which were generated using Metascape. As most networks from the DEGs are associated with immune response, the results indicated that the differentially expressed genes obtained according to stromal and immune scores were significant.

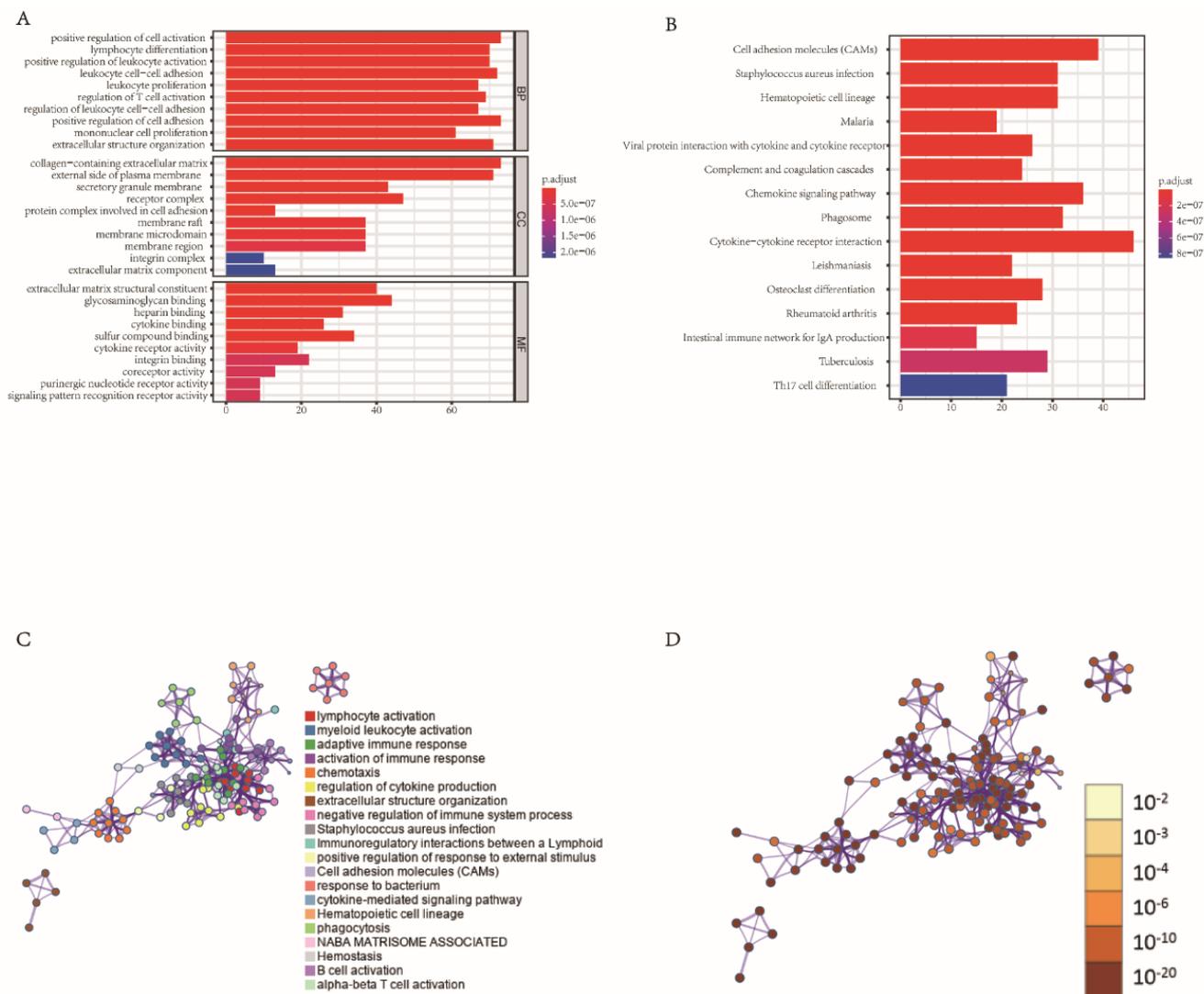


Figure 2. GO and KEGG enrichment analyses of DEGs; **(A)** GO analysis of DEGs, including biological process (BP), cellular component (CC), and molecular function (MF); **(B)** KEGG analysis of DEGs; **(C)** Protein-protein networks colored by different cluster ID; **(D)** Protein-protein networks colored by *P*-value

3.3. Establishment of genomic signature for the prognostic survival of EAC patients

According to the 836 DEGs in the stromal and immune score groups of the EAC patients, a preliminary screening was performed using Cox univariate regression to eliminate over confounding gene interference and obtain those genes that have the greatest effect on prognosis. In order to prevent the exclusion of significant genes, 29 genes with $P < 0.1$ were screened and switched to LASSO regression. The LASSO coefficient profiles of the 29 genes (**Figure 3A**) were presented, and the results from a 10-fold cross-validation were provided to determine the best value of the penalty parameter λ (**Figure 3B**).

The forest map revealed the relationship between each gene and overall survival (**Figure 3C**). Ultimately, a genomic signature with seven genes (RASGRP2, TNXB, ZBTB16, MASP1, TLR6, TNFRSF13C, and CXCL10) was selected to construct a prediction model for patients with EAC according to the gene expression levels and their regression coefficients:

$$\text{Risk score} = (0.12264 \times \text{expression level of RASGRP2}) + (-0.09632 \times \text{expression level of TNXB}) + (-0.0091 \times \text{expression level of ZBTB16}) + (-0.12716 \times \text{expression level of MASP1}) + (-0.1131 \times \text{expression level of TLR6}) + (-0.18604 \times \text{expression level of TNFRSF13C}) + (0.06844 \times \text{expression level of CXCL10})$$

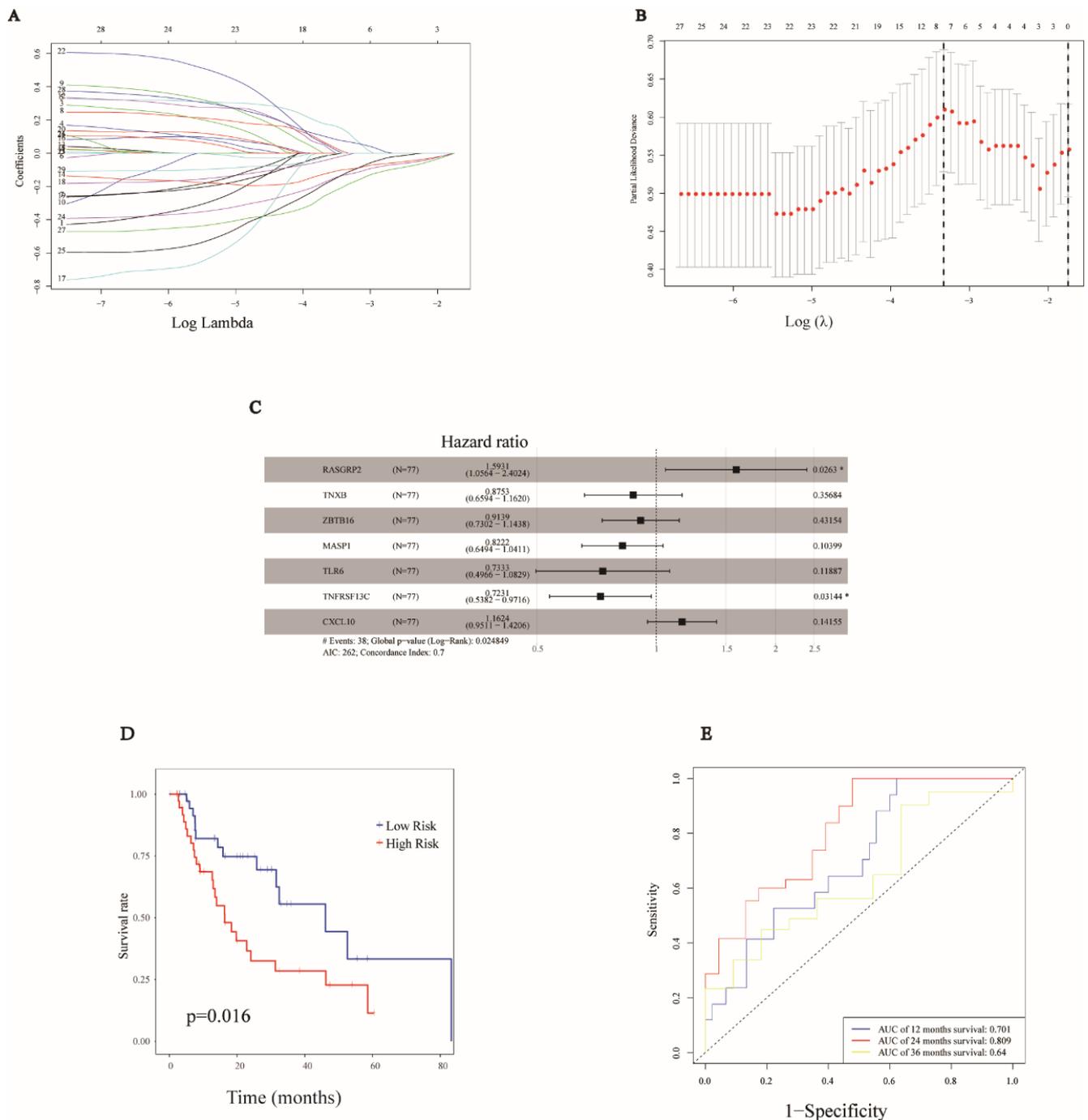


Figure 3. Establishment of genomic signature for the prognostic survival of EAC patients; **(A)** LASSO coefficient profiles of 29 genes with $P < 0.1$; **(B)** The optimal values of the penalty parameter λ determined by 10-fold cross-validation; **(C)** Association of genes with overall survival; **(D)** Kaplan-Meier curves in EAC patients; **(E)** ROC curves of 1-year, 2-year, and 3-year OS of EAC patients.

The median risk score was set as the cut-off value to divide EAC patients into low-risk and high-risk groups. The Kaplan-Meier curve revealed that low-risk patients had better survival rates ($P = 0.016$) (**Figure 3D**). Meanwhile, multivariate analysis also showed that the genomic signature with seven genes could independently predict the survival of EAC patients ($P = 0.005$, **Table 2**). The AUCs of time-dependent ROC for 1-year, 2-year, and 3-year OS of the EAC dataset were 0.701, 0.809, and 0.64, respectively (**Figure 3E**). Therefore, the ROC curve confirmed the favorable effect of risk score in exerting prognostic value for esophageal adenocarcinoma.

Table 2. Univariate and multivariate analyses of prognostic factors in EAC patients

Variables	EAC cohort			
	Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Age	0.98 (0.95-1)	0.075		
Gender	0.91 (0.32-2.6)	0.860		
Race	0.73 (0.54-0.98)	0.039	0.55 (0.31-0.97)	0.038
Tumor stage	2.5 (1.4-4.3)	< 0.001	3.16 (1.24-8.04)	0.016
Grade	2 (0.95-4.3)	0.070		
Risk score	4.8 (2-12)	< 0.001	16.83(2.35-120.36)	0.005

3.4. Survival analysis of simultaneously differentially expressed genes

In order to investigate the regulatory mechanism of EAC prognosis, Kaplan-Meier curves were generated using gene expression levels and overall survival. The study illustrated that MASP1, TNFRSF13C, and ZBTB16 were statistically significantly associated with the overall survival of EAC (**Figure 4A, 4B, and 4C**).

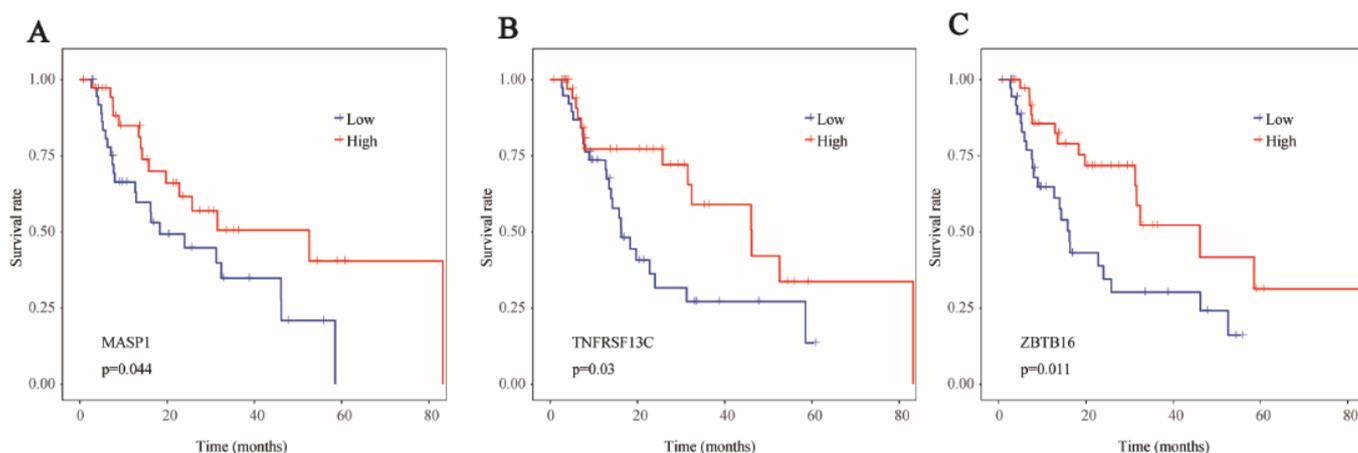


Figure 4. Correlations of immune-related DEGs with overall survival of EAC cohort; (A)(B)(C) Prognosis-related DEGs in EAC; the Kaplan-Meier survival curves were drawn based on immune-related DEGs selected from high (red line) and low (blue line) gene expression groups; log-rank test evaluated the differences with $P < 0.05$.

3.5. Immune microenvironment in EAC

In order to completely comprehend the immune and stromal signature, the proportions of immune cells in tumor tissues were determined in comparison with those in adjacent normal tissues (i.e., 79 tumor samples with EAC and 10 normal samples). As shown in **Figure 5A**, the results of CIBERSORT revealed that the infiltration levels of activated memory CD_4^+ T cells ($P = 0.046$) and resting NK cells ($P = 0.041$) were significantly higher in tumor tissues compared with normal tissues in patients with EAC; however, CD_8 T cells ($P = 0.028$), activated NK cells ($P = 0.001$), and eosinophils ($P < 0.001$) were higher in normal tissues. Moreover, the infiltration levels of naive B cells ($P = 0.015$) were relatively lower in the high-risk group compared with the low-risk group (**Figure 5B**) in EAC cohorts.

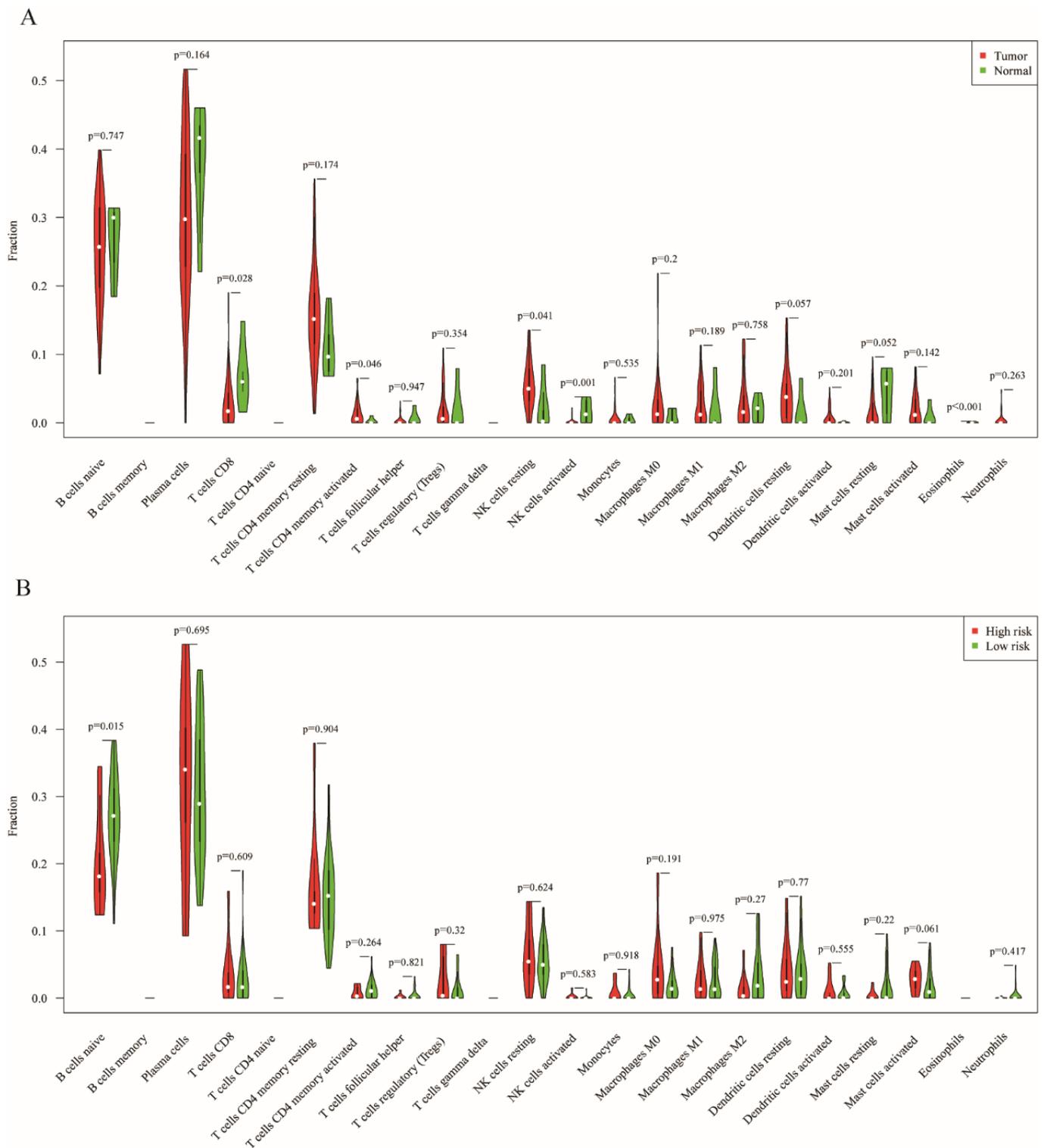


Figure 5. Infiltrated immune cells in EAC cohort using the CIBERSORT algorithm; **(A)** Differential abundance of immune infiltration between tumor tissues and normal tissues in EAC; **(B)** Differential abundance of immune infiltration between high-risk groups and low-risk groups; $P < 0.05$ is considered statistically significant.

4. Discussion

In recent years, with the improvement of treatment methods, such as radiotherapy, chemotherapy, targeted therapy, and immunotherapy, the survival of patients with esophageal cancer has improved, but the prognosis is still poor. The lack of effective prognostic biomarkers to guide the treatment of cancer is the

essential reason for the poor prognosis. A number of research studies have indicated that tumor microenvironment is a potential target for tumor therapy. First of all, cells in the tumor microenvironment, which have fewer mutations, selective pressure, and lower opportunity of developing drug resistance, are genetically more stable than cancer cells. Furthermore, owing to the lack of ability to depend on genetic mutations to conduct movement, the tumorigenicity of cells in the tumor microenvironment mainly depends on the factors in their environment. Consequently, they can be affected by the interaction of destructive environmental and other factors to drive functional changes during tumorigenesis [15]. Therefore, TCGA was used for bioinformatics analysis to identify immune-related genes in the tumor microenvironment that could predict the prognosis of EAC patients.

In order to distinguish immune-related genes and comprehend the tumor microenvironment of EAC, stromal and immune scores were obtained using the ESTIMATE algorithm. By comparing the transcriptional expression profiles of 79 EAC patients with high and low stromal/immune scores, 835 upregulated DEGs and 1 downregulated DEG were obtained. It appeared that these common DEGs are involved in crucial immune response processes, including cell activation and cell adhesion molecules (CAMs), indicating that dynamic immune microenvironments and responses in EAC might explain tumorigenesis and advancement with meaningful potential influences on the prognosis of patients.

A new method of stratifying patients according to the different immune microenvironment scores was used to identify the DEGs. The intersected genes concerning prognosis-related genes selected from the univariate Cox regression method were subjected to LASSO regression with a 10-fold cross-validation to screen out seven novel DEGs (RASGRP2, TNXB, ZBTB16, MASP1, TLR6, TNFRSF13C, and CXCL10) in EAC. In the EAC cohort, a prognostic predictive model was established based on seven genes. RASGRP2 and CXCL10 are risk immune-related genes, while TNXB, ZBTB16, MASP1, TLR6, and TNFRSF13C are protective genes. The predictive model separated the patients into high- and low-risk groups according to their median risk scores. Accordingly, the risk scores were independently associated with the prognosis of EAC patients, and the outcomes were better in the low-risk group rather than the high-risk group ($P < 0.05$).

The Kaplan-Meier survival curves revealed that MASP1, TNFRSF13C, and ZBTB16 were independently associated with prognosis.

Mannose-binding lectin (MBL) is a component in the serum that activates complement through a new way to participate in innate immunity [16]. Human MBL forms complexes with serine proteases termed MASP (MBL-associated serine protease). In the activation of the lectin channel, MBL-associated serine proteases (MASP-1, MASP-2, MASP-3, MAp-44, and MAp-19) are key elements. The serum grades of these factors have been related to low survival of several cancer types, including colorectal cancer, ovarian cancer, and cervical cancer [17-19].

BAFF receptor (BAFF-R/BR3/TNFRSF13C) is regarded as a presently discovered molecule that binds BLyS, a protein which is a part of the tumor necrosis factor (TNF) family, and has an impact on the survival and maturation of B cells [20]. A number of B-cell malignancies, for instance diffuse large B-cell lymphoma (DLBCL), express BAFF-R, and its activation promotes proliferation and survival of DLBCL cells [21-24]. ZBTB16 was first discovered in a patient with acute promyelocytic leukemia. It is an inhibitory zinc-finger transcription factor, which is a part of POZ (poxvirus and zinc finger) – Krüppel family [25,26]. ZBTB16 is involved in many different signal pathways of hematopoietic cells and solid tumors, such as cell cycle, differentiation, and programmed cell death [25,27].

In view of the activity of novel genes in the process of tumorigenesis and the marked association with the prognosis of EAC patients, they may possess the performance of new tumor biomarkers if their specific roles in EAC are known in detailed through extensive investigations.

Tumor-infiltrating immune cells have a great impact on the tumor microenvironment. When using immune checkpoint inhibitors, tumor infiltrating immune cells should be considered, because the effectiveness of immune checkpoint blockade requires immune cell infiltration [28,29]. The abundance of 22 immune cell subsets was calculated using the CIBERSORT algorithm, and the effect of tumor-infiltrating immune cells in esophageal carcinoma was illustrated. In this present study, the immune cell subsets in tumor tissues of EAC were significantly different from those in normal tissues; in EAC patients, the activated memory CD4⁺ T cells, CD8 T cells, resting NK cells, activated NK cells, and eosinophils were significantly different in tumor tissues compared with those in normal tissues; in addition, the infiltration levels of naive B cells were significantly higher in the low-risk group. The results revealed that these immune cells may play an important role in the tumor microenvironment of EAC. A meta-analysis concluded that extensive tumor-infiltrating lymphocytes (TILs) are excellent prognostic indicators for the overall survival in patients with esophageal carcinoma (ESCA) [30]. It was found that activated memory CD4⁺ T cells in tumor-infiltrating lymphocytes (TILs) widely infiltrated tumor tissues; however, CD8 T cells were universally discovered in normal tissues of EAC patients. The degree of tumor-infiltrating lymphocytes, especially activated CD8⁺ T cells in melanoma, was found to be positively correlated with a better prognosis [31]. However, in another study involving 130 patients with esophageal adenocarcinoma, CD8⁺ lymphocyte was found to have no associated with survival [32]. These results may suggest that immune cells have dual effects (host protection and tumor promotion) in different types of tumors [33,34]. Notably, it has been suggested that CD4⁺ T cells are correlated with good prognosis in patients with esophageal carcinoma [35]; however, it was found that CD4⁺ TILs are not associated with the survival of ESCA patients [30]. In the findings of this study, activated memory CD4⁺ T cells were found to be higher in tumor tissues than in normal tissues of the EAC cohort. These controversial results may be due to tissue microenvironmental factors, which may change the phenotype and function of T cells early during esophageal disease progression and may function as targets for immune intervention [36]. Further research associated with the impact of immune-infiltrating cell balance on clinical outcomes is necessary.

In recent years, it has been recognized that B cells play a very complex role in the tumor microenvironment, as some subsets of B cells may have immunomodulatory functions [37]. In this research, naive B cells were found to be associated with a low-risk score for esophageal adenocarcinoma, and it was hypothesized that they may be associated with good prognosis in patients with esophageal adenocarcinoma. However, the relationship between the subsets of B cells and the prognosis of patients with esophageal adenocarcinoma has not been defined.

Currently, the number of studies on the prognostic value of infiltrated NK cells in esophageal adenocarcinoma are very limited. In the future, more relevant studies are needed to further clarify the relationship between immune cells, such as NK, and the prognosis of esophageal adenocarcinoma.

There are several limitations in this study. First, this study was a retrospective study, in which the data of gene expression as well as clinical information were downloaded from the TCGA database; hence, selection and recall biases are inevitable. Second, the values of prognosis in EAC patients could not be fully elucidated due to the lack of comprehensive chemoradiotherapy in this study. Moreover, the present study did not rely on other available databases for external validation; thus, further investigations are required to study the mechanisms by which the immune-related prognostic genes regulate the initiation and progression of EAC.

In conclusion, the expression of tumor-infiltrating immune cells and immune-related genes in EAC have been identified. Some previously overlooked genes may be used as additional biomarkers for EAC. Further *in vivo* and *in vitro* studies are required to explore the mechanisms through which the immune cells and genes are involved in EAC progression to promote advancement in EAC treatment.

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Disclosure statement

The authors declare no conflict of interest.

Author contributions

YP and YZ designed and edited this study; LS, WQ, HG, and LL searched the databases and collected the data; YQ and MT analyzed the data and wrote the manuscript. All authors read and approved the final manuscript.

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Clinical Efficacy of Hyperbaric Oxygen Therapy at Different Pressures in the Treatment of Sudden Deafness

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Abstract: *Objective:* To analyze the efficacy of hyperbaric oxygen at different pressures in the treatment of sudden deafness. *Methods:* Eighty-two patients with sudden deafness treated in the Affiliated Hospital of Hebei University from September 2019 to September 2021 were selected as the research subjects. The patients were randomly divided into study group 1 and study group 2, and they were treated with hyperbaric oxygen on the basis of routine treatment, in which the pressure used was 1.8 ATA and 2.2 ATA, respectively. Oxygen was delivered via the pressure stabilizing mask for 60 minutes. The patients received two courses of treatment, each lasting 10 days. The changes in hearing (pure tone audiometry) and the clinical efficacy of both the groups were compared before and after treatment. The data obtained were statistically analyzed using SPSS 19.0. *Results:* The total effective rate of study group 1 was 90.00%, while that of study group 2 was 76.19%. The differences between the two groups were statistically significant ($p < 0.05$). *Conclusion:* For patients with sudden deafness treated with hyperbaric oxygen, the clinical efficacy of 1.8 ATA is more significant than that of 2.2 ATA.

Keywords: Sudden deafness; Hyperbaric oxygen therapy; Different pressures; Clinical efficacy

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1. Introduction

Sudden deafness, also known as sudden sensorineural hearing loss, has multiple causes. In this condition, hearing deteriorates in varying degrees over a short period of time, which directly affects the daily life of patients. At present, hyperbaric oxygen is mainly used in the treatment of sudden deafness. In China, there are many reports on treating sudden deafness with hyperbaric oxygen. However, there are minimal studies on the therapeutic effect of different pressures in the treatment of sudden deafness with hyperbaric oxygen [1]. In order to seek more active and effective treatment effect, this study selected several patients from the Affiliated Hospital of Hebei University as the research subjects, aiming at the clinical efficacy of using hyperbaric oxygen at different pressures in the treatment of sudden deafness, in order to provide reference for clinical practice.

2. Materials and methods

2.1. General information

Eighty-two patients with sudden deafness diagnosed and treated in the Affiliated Hospital of Hebei

University from September 2019 to September 2021 were selected as the research subjects.

Inclusion criteria: (1) patients who met the diagnostic criteria based on the “Guidelines for the Diagnosis and Treatment of Sudden Deafness (2015)” [2]; (2) hearing loss > 20 dB with at least two frequencies; (3) age > 18 years old; (4) patients with tinnitus, dizziness, and other vestibular symptoms.

Exclusion criteria: (1) patients with a history of ear disease or family history of deafness; (2) patients with recent noise exposure history; (3) patients with deafness caused by cardiovascular diseases, cerebrovascular diseases, or occupation related to the internal auditory canal; (4) patients with severe cardiac, hepatic, and renal insufficiency; (5) patients with malignant tumor, blood disease, etc.; (6) patients who had recently taken immunosuppressants; (7) patients with contraindications to hyperbaric oxygen therapy.

The patients were randomly divided into study group 1 and study group 2. In study group 1, there were 22 male patients and 18 female patients, age ranging from 21 to 65, with an average age of 46.12 ± 15.18 ; the time of onset was 3 hours ~ 30 days, with an average of 10.16 ± 6.08 days. In study group 2, there were 19 male patients and 23 female patients, age ranging from 20 to 65, with an average age of 48.16 ± 14.85 ; the time of onset was 5 hours ~ 30 days, with an average of 11.79 ± 6.07 days. There was no significant difference in gender, age, time of onset, and other general information between the two groups ($p > 0.05$).

2.2. Methods

The two groups were treated with hyperbaric oxygen on the basis of routine treatment, in which the pressure used was 1.8 ATA and 2.2 ATA, respectively. Oxygen was delivered via the pressure stabilizing mask for 60 minutes, and the patients received two courses of treatment, each lasting 10 days. The changes in hearing (pure tone audiometry) and the clinical efficacy of both the groups were compared before and after treatment.

2.3. Observation indicators

2.3.1. Clinical efficacy

The clinical efficacy of both the groups were compared, in which the “Guidelines for the Diagnosis and Treatment of Sudden Deafness” was used as a reference: “recovery” signifies that the hearing threshold of the affected frequency has completely returned to normal or reverted to its pre-onset level; “effective” signifies that the improvement level of hearing loss is between 15~30 dB; “ineffective” signifies that the improvement level of hearing loss is less than 15 dB, or a worsening condition. The total effective rate = cure rate + effective rate.

2.3.2. Severity of hearing impairment

The severity of hearing impairment was compared between the two groups, and the criteria were as follows: “mild” signifies a hearing loss ranging from 26 dB to 55 dB; “moderate” signifies a hearing loss ranging from 56 dB to 70 dB; “severe” signifies a hearing loss of more than 71 dB. Pure tone audiometry was carried out using a pure tone audiometer. Two consecutive measurements were made in a soundproof room, and the error between the two measurements was less than 5 dB.

2.4. Statistical analysis

SPSS 19.0 was used for data processing. The measurement data were expressed in $\bar{x} \pm s$, and t test was carried out. The counting data were expressed by phase logarithm, and X^2 test was carried out. Rank-sum test was used for rank data analysis. $p < 0.05$ signifies that the difference is statistically significant.

3. Results

3.1. Clinical efficacy

The total effective rate of study group 1 was 90.00%, which was significantly higher than that of study group 2 (76.19%) ($p < 0.05$), as shown in **Table 1**.

Table 1. Comparison of clinical efficacy between the two groups [n (%)]

Group	Number of cases	Recovery	Effective	Ineffective	Total effective rate
Study group 1	40	10	26	4	36 (90.00)
Study group 2	42	8	24	10	32 (76.19)
X^2					4.121
p					0.039

3.2. Hearing improvement

Before treatment, there was no significant difference in the hearing threshold between the two groups ($p > 0.05$). After treatment, the hearing threshold of both groups decreased, but the improvement of hearing threshold in study group 1 was significantly better than that in study group 2 ($p < 0.05$), as shown in **Table 2**.

Table 2. Comparison of hearing improvement between the two groups before and after treatment ($\bar{x} \pm s$, dB)

Group	Number of cases	Hearing threshold		t	p
		Before treatment	After treatment		
Study group 1	40	78.82 \pm 3.21	49.21 \pm 4.55 ^{ab}	36.069	0.000
Study group 2	42	77.68 \pm 3.89	63.06 \pm 3.68 ^a	14.812	0.000
t		1.018	18.682		
p		0.312	0.000		

Note: Compared with this group before treatment, ^a $p < 0.05$; compared with study group 2 after treatment, ^b $p < 0.05$

4. Discussion

Sudden deafness is a blood supply disorder of the inner ear caused by many factors. The disease occurs rapidly, and if it is not treated in time, it will develop into total deafness and eventually cause permanent deafness. The pathogenic causes are viral labyrinthitis and blood circulation disorders in the inner ear [3].

Hyperbaric oxygen therapy involves inhaling a high concentration of pure oxygen. This treatment rapidly increases the blood oxygen content in the human body and promotes the diffusion of oxygen to blood vessels. Moreover, it extends the diffusion distance. The improvement of capillary hypoxia reduces cellular edema [4]. The microcirculation of the inner ear improves with the increase of the speed and amount of supplied oxygen from the capillaries to the ear. In addition, hyperbaric oxygen can also improve blood viscosity. Hyperbaric oxygen can reduce vascular resistance, restore cell function, and promote the oxygen supply to cells [5]. Increasing the partial pressure of oxygen improves hypoxic and ischemic symptoms, stabilizes the heart rate and arterial blood pressure, normalizes cerebral vasoconstriction, as well as returns the function of damaged sensory cells [6]. At present, hyperbaric oxygen therapy is used for treating sudden deafness, and the pressure used is often 1.8 ATA to 2.5 ATA. However, there are minimal studies on the clinical efficacy of hyperbaric oxygen at different pressures.

The results of this study showed that the total effective rate of 1.8 ATA hyperbaric oxygen therapy in study group 1 was 90.00%, and that of 2.2 ATA in study group 2 was 76.19%. The total effective rate of study group 1 was significantly higher than that of study group 2 ($p < 0.05$). Before treatment, there was no significant difference in the hearing threshold between the two groups, ($p > 0.05$). After treatment, the hearing threshold of both groups decreased, but the improvement in study group 1 was significantly better than that in study group 2 ($p < 0.05$). This shows that hyperbaric oxygen therapy at 1.8 ATA has more significant therapeutic effect on sudden deafness, which can improve the inner ear circulation, increase the oxygen supply, and restore the patient's hearing level with an ideal effect.

In conclusion, hyperbaric oxygen therapy for sudden deafness can improve the microcirculation of the inner ear. The clinical efficacy of 1.8 ATA hyperbaric oxygen therapy is evident, and it significantly improves hearing; thus, it is worthy of clinical application.

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Disclosure statement

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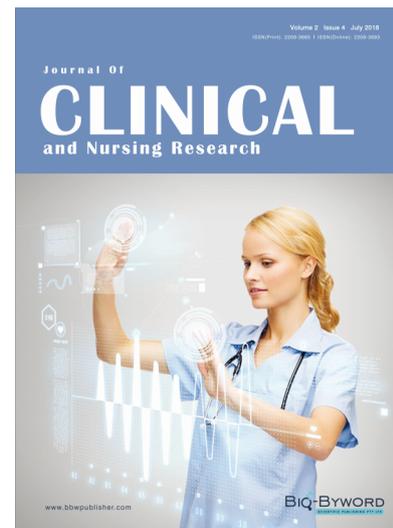
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