# One Case of Ovarian Cancer Combined with Ascites Treated by the Cancer Emerging Medical System

Song Ziyun<sup>1</sup>, Zhang Yutian<sup>2,\*</sup>

<sup>1</sup>Chengde Medical College, Chengde, Hebei, 067000, China <sup>2</sup>Chengde Hospital of Traditional Chinese Medicine, Chengde, Hebei, 067000, China \*Corresponding author

*Keywords:* Ovarian cancer; integrated traditional Chinese and western medicine; Cancer Emerging Medical System

**Abstract:** This article reported a successful case of ovarian cancer combined with by ascites due to cirrhosis treated by Professor Zhang Yutian using the method of Cancer Emerging Medical System for achieving dual benefits in terms of survival quality and survival time. The article explains Professor Zhang Yutian's innovative thoughts of Cancer Emerging Medical System. What 'more, it explored the immense potential of integrated traditional Chinese and western medicine in the treatment of cancer.

### 1. Introduction

In traditional Chinese medicine, tumors can be seen in the category of disease names such as "Zheng Ji", "Accumulation", corresponding to specific diseases, and are also called such as "Milk Rock", "Choking Diaphragm" and "Lung Accumulation" [1]. Modern medicine believes that tumors are neoplasms formed by the loss of normal regulation of their growth at the genetic level by local tissue cells under the long-term synergistic effect of various tumorigenic factors inside and outside the body, resulting in abnormal proliferation of cells [2]. According to statistics, an estimated 19. 3 million new cancer cases and nearly 10 million cancer deaths occurred worldwide in 2020, and nearly half of new cancer cases and 58. 3% of cancer deaths occurred in Asia [3]. With the development of the times, cancer has increasingly become the main cause of death and an important obstacle to prolonging life expectancy. At present, western medicine has surgical treatment, chemotherapy, radiotherapy, biological therapy, interventional therapy, and so on. Cancer treatment is more and more accurate and efficient, but there are still problems such as high toxicity, poor prognosis of malignant tumors, and drug resistance in clinical practice. For patients with advanced diseases, single Western medicine treatment has been unable to meet the needs of patients, integrated traditional Chinese and Western medicine treatment can better achieve efficacy and improve the quality of life of patients. Professor Zhang Yutian of Chengde Hospital of Traditional Chinese Medicine has rich experience in the treatment of malignant tumors. Cancer Emerging Medical System and its immune reconstitution system proposed by him enrich the theory of integrated traditional Chinese and Western medicine in the treatment of malignant tumors and have practical reference significance for the clinical treatment of malignant tumors.

Cancer Emerging Medical System and its immune reconstitution system are brand-new theories

and treatment methods for cancer treatment based on integrated traditional Chinese and Western medicine for cancer that Professor Zhang Yutian led his medical team to invent after 9 years of research. CEMS is the abbreviation of Cancer Emerging Medical System, which refers to the use of traditional Chinese medicine (TCM) throughout the whole process under the guidance of the overall concept of TCM and the idea of syndrome differentiation and treatment, based on the theory of TCM syndrome differentiation, according to the patient's gender, age, physical fitness and pathological type of the disease, degree of disease development, development trend, planned, scientific and reasonable use of modern medical means, from the pathology, psychology, pharmacology of integrated traditional Chinese and western medicine to treat tumors, and from all aspects of the body and mind comprehensive rehabilitation, as well as strengthen preventive health care, TCM health preservation, control of precancerous lesions, to achieve the purpose of improving the cure rate of cancer and reducing the occurrence of cancer. The concept of Professor Zhang Yutian 's new pulse system is summarized from a case of ovarian cancer with cirrhosis ascites.

#### 2. Case data

Dong Shumei, female, 55 years old, visited the local hospital due to abdominal distension on October 14, 2022, and was considered to have posthepatitic cirrhosis and ascites after perfecting relevant auxiliary examinations. After symptomatic treatment, the symptoms were not relieved, and abdominal effusion was increased than before. Later, the patient visited Peking University First Hospital on November 22, and ascites cytology sent for pathology revealed a malignant epithelial tumor. Immunolabels suggest the female reproductive system's origin. The patient was discharged after symptomatic treatment. He presented to our hospital on January 3, 2023, weighing 57 kg. CT (2023. 01. 04) in our hospital showed a large amount of fluid shadows in the abdominopelvic cavity. Multiple low-density shadows were observed in the liver, some with less clear boundaries, gallbladder wall thickening, and punctate dense shadows in the neck of the gallbladder. Multiple soft tissue density mass shadows were observed in the pelvic cavity, with unclear boundaries between partial and peritoneum, and the shape of the uterus was less regular. TCM diagnosis: syndrome accumulation spleen and kidney yang deficiency Western medicine diagnosis: 1. Ovarian epithelial cancer peritoneal metastasis 2. Abdominal effusion 3. Viral hepatitis B posthepatitic cirrhosis. Therefore, after perfecting the relevant auxiliary examinations, Professor Zhang Yutian formulated the diagnosis and treatment plan for the patient according to the syndrome differentiation of CEMS 's theory, adopted under the guidance of the theory of syndrome differentiation of TCM, using Western medicine therapy such as harmonic scalpel, chemotherapy, immunotherapy and other direct hit lesions, adding traditional Chinese medicine decoction and external treatment of traditional Chinese medicine to protect the patient's righteousness and improve immunity, supplemented by psychological counseling and mindfulness training.

The first course of treatment began on January 5, carving diagnosis showed: that the patient had oligoconiosis, generalized weakness, yellow skin, ecchymosis and petechiae, dry mouth, abdominal distension, difficulty in falling asleep, normal urination and defecation, pale red tongue, yellow gray greasy fur, and weak pulse. Patients' quality of life score (Karnofsky performance status) was 60 points. He was given a decoction of Bushen Zhuyang Decoction, prescription: Astragalus membranaceus 35 g, Atractylodes macrocephala 15 g, Bupleurum chinense 15 g, Radix Paeoniae Alba 15 g, Radix Astragali 15 g, Radix Eucommiae 15 g, Hedyotis diffusa 15 g, Radix Pseudostellariae 30 g, Radix Rehmanniae 15 g, Herba Epimedii 15 g, Curculigo 15 g, Caulis Spatholobi 15 g, Radix Angelicae Sinensis 15 abdominal paracentesis and ascites drainage were performed with the consent of the family to reduce the effusion. Docetaxel 120 mg intravenous drip + carboplatin injection 500 ng intraperitoneal perfusion + recombinant human endostatin 60 mg

intraperitoneal perfusion were administered for 1 cycle on chemotherapy. After chemotherapy, the patient developed IV °bone marrow suppression complicated with systemic inflammatory response, infectious fever, and thrombocytopenia, and was given symptomatic treatment such as blood raising, blood transfusion, anti-inflammation, and fluid replacement. Symptomatic treatments such as acid suppression and hemostasis were given due to severe gastrointestinal reactions with gastrointestinal bleeding. The patient had severe bone marrow suppression and continued to be given traditional Chinese medicine decoction for righting vital energy. At the same time, the patient was given 0. 9% Sodium Chloride Injection 250ml + Kangai Injection 40 mL ivgtt qd for supplementing qi and antitumor; external treatment of traditional Chinese medicine with auricular point application to enhance systemic immunity; plaster application of Wenyang Yiqi Xiao zhang and improvement of appetite; in vitro high-frequency hyperthermia for warming yang and dispersing cold to relieve pain. The symptoms of bone marrow suppression were relieved, the quality of life score was 90 points, and high-intensity focused ultrasound thermal ablation of ovarian lesions was given after various indicators were stable.

On February 4, 2023, a reexamination of CT showed multiple soft tissue density mass shadows in the pelvic cavity, some of which were poorly demarcated from the peritoneum, and the shape of the uterus was irregular. Compared with 2023.01.04 CT, peritoneal nodules and adnexal masses were significantly reduced. On February 5, 2023, a comprehensive reexamination showed that the tumor markers were significantly decreased, the lesions were significantly smaller than before, and the efficacy was evaluated as PR. Considering severe bone marrow suppression after previous chemotherapy, chemotherapy was no longer considered. The patient was given targeted therapy with nilaparib tosylate capsules 0. 22 orally once daily for 1 cycle and was discharged after the condition was improved. During the second course of treatment on 19 February 2023, the patient complained of improved mental status at home and was admitted to the hospital to continue targeted therapy. The patient experienced bone marrow suppression again during the administration of Nilaparib Capsules in Cycle 2. Considering the patient's intolerance, the targeted drug was discontinued and the patient was treated with traditional Chinese medicine for 1 cycle. This TCM treatment follows the previous external treatment, and the TCM decoction is adjusted according to the patient's current main symptoms. The patient complained of hot flashes and night sweats, which were severe every night, easy to wake up at night, and normal urination and defecation. Tongue red moss yellow, cracked, pulse string thin. According to the symptoms of deficiency of both yin and yang, the prescription was adjusted: Radix Astragali 10g, Rhizoma Atractylodis Macrocephalae 15g, Bear Bile Powder 0. 6g, Fried Semen Ziziphi Spinosae 15g, Radix Polygoni Multiflori 15g, Radix Pseudostellariae 15g, Radix Dioscoreae 15g, Radix Achyranthis Bidentatae 15g, Radix Eucommiae 15g, Radix Rehmanniae 15g, Herba Epimedii 15g, Radix Aconiti 10gAfter medication, the symptoms of yin deficiency were relieved, combined with Shenmai injection and other anti-tumor treatment. On February 4, 2023, a reexamination of CT showed a less regular uterine shape. Compared with 2023. 02. 20CT, abdominopelvic effusion was absorbed, enlarged lymph node shadows were observed in the abdominal cavity, periaortic region, and pelvic cavity, and the rest had no significant change. After treatment, the patient became mentally well and was discharged with improved condition.

Four months later, the patient was admitted to our hospital regularly to complete the treatment plan. On July 25, the patient came to our hospital for reexamination and showed a stable condition, without obvious contraindications. On August 9, 2023, the patient began to be given traditional Chinese medicine treatment mainly combined with pianluzumab immunotherapy for 4 cycles. During this period, the patient developed a depressed mood and pessimistic negative mentality due to changes in the condition and drug effect. Therefore, the patient was given positive psychological rehabilitation treatment. After treatment, the patient's mood improved, and the patient was

discharged after the condition was stable. Later, the patient continued regular admission for rehabilitation treatment. Now CT showed that the primary lesion disappeared, the tumor indicators gradually returned to normal, the patient had excellent mental status, ruddy complexion, sufficient anti-cancer confidence, the condition was well controlled, the primary tumor showed no recurrence, and the Karnofsky score was 100 points, basically reaching the normal state.

#### 3. TCM is the way and Western medicine is the operation

The beginning of integrated traditional Chinese and Western medicine can be traced back to Sun Simiao 's dispute to absorb the essence of ancient Indian Vedic medicine into medicine [4], but in recent years, there has been a continuous flow between traditional Chinese medicine and western medicine, and some scholars believe that the difficulty of integrated traditional Chinese and western medicine lies in their incommensurability, and the combination between the two requires a long innovation process [5]. Professor Zhang Yutian innovatively put forward CEMS and cleverly combined traditional Chinese medicine with Western medicine. CEMS emphasizes TCM as the way and Western medicine as the operation, that is, taking TCM as the core, taking the overall concept of TCM and syndrome differentiation and treatment as the guiding principle, TCM and all other therapies are integrated and complement each other, and TCM runs through the whole treatment process. ¿Lizhai Shen Er Bian has a cloud: "The larger side of the road is called the way, the smaller side called the operation. "Chinese medicine treatment of people, the body as an environmental system, more macroscopic; Western medicine symptomatic, the symptoms of continuous subdivision of research, more microscopic. Integrative Chinese and Western medicine have both macroscopical and microscopic, can treat specimens, and is an excellent match.

In the above cases, Professor Zhang Yutian regarded the patient, the patient, and the environment, and the patient and the society as an organic whole, and believed that ovarian cancer suffered by this patient was a tumor formed due to the deficiency of yang qi in the human body caused by factors such as long-term poor living state, the disharmony between yin and yang, the yin and cold agglomeration, phlegm-dampness blocking collaterals, and qi stagnation and blood stasis. Under the guidance of the overall concept of treatment, the patient was advanced ovarian cancer, "Lingshu • Kouwen" said: "where the evil, is insufficient. "The essence of cancer is the state of deficiency of yang qi and accumulation of yin and cold, and the patient has been ill for a long time, deficiency of vital gi causes the extreme, so its constitution is a deficiency of cold, that is, deficiency syndrome, so first give the prescription of tonifying the kidney and assisting yang, adjust the patient's constitution; "urgent treatment of symptoms, slow treatment of the root cause. "The patient suffered from ascites, so abdominal paracentesis was performed to treat the symptoms urgently. The human body is regarded as an organic whole, and chemotherapy and harmonic scalpel are given to the patients while traditional Chinese medicine complements the vital qi of the human body so that the patients can tolerate the attack. When the patients have adverse reactions, western medicine is immediately used for symptomatic treatment, supplemented by external treatment of traditional Chinese medicine to relieve the patient's pain. In addition, pay attention to the overall relationship between people the environment, and society, timely give psychological counseling to patients, adjust the patient's diet, and promote the rehabilitation of patients. The advantage of Western medicine is to treat tumor lesions, mainly to treat symptoms, and the advantage of traditional Chinese medicine is to invigorate the spleen and kidney, enhance systemic immunity, reduce toxic side effects, and improve the cancer environment, mainly to cure the disease. The progress of modern medicine has deepened the understanding of human health status from a microscopic point of view, and traditional Chinese medicine has always emphasized integrity in the process of recognizing diseases and people for thousands of years and avoids the error of "blind person

touching image" for modern medicine [6]. Therefore, CEMS advocates "traditional Chinese medicine as the road, western medicine as the operation", taking into account the macro of traditional Chinese medicine and the micro of Western medicine, promoting the integration and innovation of integrated traditional Chinese and Western medicine.

#### 4. TCM Characteristics

## 4.1. TCM Therapy Based On Syndrome Differentiation

Today, scholars have their views on the etiology and pathogenesis of tumors. Some people believe that "a deficiency of vital qi into tumors", emphasizing the relationship between the formation of tumors and deficiency of vital qi [7]; others believe that the cancer virus is the key to the occurrence and development of tumors [8]; others are responsible for phlegm-turbid resistance [9]. Professor Zhang Yutian believes that cancer is due to long-term bad living habits, bad eating habits, poor psychological status, but also other carcinogenic factors, leading to the body Yang deficiency, promoting cell differentiation of the source power is insufficient, Yin and Yang disharmony, caused by yin and cold agglomeration, phlegm-dampness blocking collaterals, qi stagnation, and blood stasis, resulting in the formation of a tumor. It believes that "cancer" is a state, is a state of imbalance between the internal organs of the human body and nature. Cancer environment first, then cancer cells. In order to prevent, control and ultimately cure cancer, it is not only necessary to kill cancer cells, but also to change the "cancer state". This means changing the soil in which the cancer cell grows, that is, the "cancer environment". In this case, the patient was newly diagnosed with yang deficiency, so a large number of drugs to replenish yang and qi were given in the formula, "Lingshu • All Diseases Origin" said: "The beginning of the accumulation, get cold is born", the formation of tumors is based on the environment of insufficient yang, vin-cold accumulation, and phlegm, blood stasis, and finally tumor formation, "yang, vin formation", therefore, for the treatment of cancer patients, can first start from warming yang, invigorating the spleen and kidney, improving the patient's immunity, and improving the patient' cancer environment." In practical clinical practice, blindly supplementing yang is not allowed, and it needs to be flexible, individualized, and treated based on syndrome differentiation. For example, in the above case, the patient experienced symptoms of yin deficiency such as hot flashes and night sweats during the second course of treatment. At this time, the patient belongs to both yin and yang deficiency syndrome, and the root cause is that the patient is undergoing chemotherapy. If you excessively attack evil qi, it will consume Yin fluid. Therefore, we adjusted the formula and added nourishing yin drugs. However, the patient's Yang deficiency constitution has not improved, and even Yang deficiency and Yin deficiency occurred. Therefore, the entire formula needs to complement Yin and Yang, and be combined with the correct medication. Professor Zhang Yutian advocates in the application of prescriptions: on the one hand, we should make extensive use of traditional Chinese medicine's syndrome differentiation and treatment to coordinate yin and yang, qi and blood. On the other hand, we should use traditional Chinese medicine decoctions to clear heat and detoxify, promote blood circulation and remove blood stasis, which can directly inhibit tumor growth. This not only improves physical fitness and enhances immunity, but also reduces toxic side effects and complications.

## 4.2. External Treatment of TCM

"Theoretical Diaowen" says: "The rationale of external treatment, that is, the rationale of internal treatment, the medicine of external treatment, that is, the medicine of internal treatment, the law of different. "External treatment, like internal treatment, is also used under the guidance of TCM

syndrome differentiation, and external treatment has unique features to supplement the shortcomings of internal treatment. In the above cases, the acupoint application of Wenyang Yiqi Tongluo was selected for external treatment; most scholars today believe that acupoint application achieves the purpose of treatment through acupoint stimulation and drug absorption at specific sites under the guidance of the overall concept [10]. Direct administration on the body surface avoids the multi-link inactivation encountered by digestive tract absorption and some toxic and side effects caused by some internal medicine, especially for some patients with advanced cancer, vital qi is weak and intolerant to attack, internal medicine alone has poor efficacy, and external application of traditional Chinese medicine has more advantages. In this case, the patient had a deficiency of vital qi, so Qihai, Guanyuan, and Zusanli Wenyang were selected to replenish qi and invigorate the spleen. The patient had clinical abdominal distension and Zhongwan and Tianshu were added to reduce gastrointestinal reactions. The specific drugs were selected as products of large heat and warming yang, such as dried ginger 20g, cinnamon 20g, aconite 10g, and clove 10g, with strong penetration and very good efficacy. In addition, this case also used in vitro high-frequency hyperthermia, which heated Qihai, Guanyuan, and other acupoints according to the disease control temperature to achieve the purpose of warming yang qi, dispersing cold and removing dampness, to treat a series of chronic diseases caused by deficiency of yang qi and accumulation of yin cold, such as tumors.

External treatment of TCM in CEMS includes CEMS acupuncture, plaster application, medicinal moxibustion, massage, scraping, cupping, hyperthermia, etc., which provides a guarantee for the treatment of complications and complications of cancer patients and reduces the recurrence and metastasis of patients. Professor Zhang Yutian attaches importance to internal and external treatment and believes that external treatment is a major feature of traditional Chinese medicine. It has a long history and obvious curative effect and is worthy of inheritance and development, especially for such chronic diseases of tumors, internal and external treatment, and more unexpected curative effects.

#### 4.3. Rehabilitation Therapy

"The disease comes like a mountain, the disease goes like a filament", the tumor does not use the disappearance of the lesion as the standard of cure, with the development of medical technology, the implementation of humanistic intervention for cancer patients has become a new medical development trend [11], in clinical practice, not only pay attention to the cure of the patient's physical disease but also pay attention to psychogenic rehabilitation. Studies have shown that psychological status is closely related to tumors, such as chronic psychological stress affecting the body's endocrine system, thereby accelerating the occurrence and development of tumors [12].

CEMS advocates continuous conditioning of physical fitness for patients for 2-3 years to achieve comprehensive rehabilitation of the mind. In this case, the patient had experienced a depressed mood or even loss of anti-cancer confidence and other manifestations, Chinese medicine says, "seven emotions cause disease", the adverse psychological state may aggravate the patient's condition, therefore, it is necessary to early detect the patient's psychological problems and carry out a series of psychological rehabilitation treatment for the patient. From the clinical findings, most cancer patients have emotional problems, long-term emotional depression, negativity will cause physical damage, so, regulating mood is the most important part of rehabilitation treatment. The new Mai system has established a cancer rehabilitation school, through the course of positive psychology, so that patients maintain a comfortable mood. These include confidence transmission — cancer-cured patients assist, set an example — anti-cancer stars, rehabilitation training camps, and qigong, meditation, and brain field training to improve concentration and control. We cultivate

good habits in diet, exercise, emotions, and other aspects in patients through a complete set of behavioral and personality training, improving their quality of life and family life.

## 5. Summary

In conclusion, from this case and its experience, CEMS has a high reference significance for the treatment of cancer patients. It first uses TCM treatment to improve immunity and physical status and lay the foundation for in-depth treatment. In cancer patients' body yin and yang imbalance, Yang Qi can not be fixed; for some patients after multiple chemoradiotherapy physical weakness, and immune disorders; classification confirmed the first with CEMS Chinese medicine decoction, combined acupuncture, plaster, and other means of immune environment improvement, synchronous cancer rehabilitation school psychological counseling, traditional cultural education, Chinese medicine health education, and other enhanced immune environment improvement, for further cancer treatment to lay a good physical foundation and good psychological state. Then integrated traditional Chinese and Western medicine treatment, rapid elimination of solid tumors, scattered cancer cell accumulation, and simultaneous in vivo immune environment repair. Chemoradiotherapy and HIFU, microwave ablation, radiofrequency ablation, argon-helium knife, radiotherapy particle implantation, photodynamic therapy, endoscopic radiofrequency ablation, magnetic rotation therapy, and other techniques were used in combination with traditional Chinese medicine and traditional Chinese medicine techniques. Use Western medicine technology to quickly eliminate solid tumors, use the macro-dialectical theory of traditional Chinese medicine to guide the application of technology, and reduce the physical damage to patients and immune system damage. The use of traditional Chinese medicine technology and traditional Chinese medicine can achieve sensitization and synergism, reduce the dosage, reduce the patient's physical damage, reduce alopecia, vomiting, leukopenia, and other treatment complications, and quickly restore the patient's immunity. Solve superficial tumors with CEMS 43 °needle, Xiaozheng Zhitong ointment, and other matching products. When the tumor is under control, the complications of the patient will be treated through Chinese medicine technology and supporting Chinese medicine prescriptions and plasters such as Fuzheng Xiaozheng Pill, combined with acupuncture and moxibustion to dredge the meridians. Secondly, through the supporting courses of rehabilitation schools, patients can undergo physical and psychological reconstruction, ultimately achieving a transition from clinical cure to lifelong cure, which can truly restore their physical health and benefit millions of households.

## Acknowledgements

Major Project of Science and Technology Cooperation Center of Traditional Chinese Medicine, Academy of Chinese Medical Sciences (20210301).

#### References

- [1] Hu Dongjian, Yang Xudong, Zhao Zhiheng. To investigate the treatment of tumor with fire needle based on "Yang Hua Qi, Yin Sheng" [J]. Journal of Tianjin University of Traditional Chinese Medicine, 2021, 40 (05): 578-582.
- [2] Wang Guanjun, He Jie. Oncology Synopsis [M]. People's Medical Publishing House, 2013.
- [3] Sung H, Ferlay J, Siegel R L, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortalityworldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2021.
- [4] Jia Yunbin, Wei Jianglei. Thinking about Integrated Traditional Chinese and Western Medicine [J]. Shi Zhen, Sinopharm, 2011, 22 (02): 479-481.
- [5] Zhang Yupeng. From the Incommensurability of Paradigm to View the Relationship between Chinese and Western Medicine [J]. Chinese Journal of Basic Medicine of Traditional Chinese Medicine, 2016, 22 (03): 326-327 + 341.
- [6] Huang Jianbo, Zhang Guangji. Source and Innovative Development of Overall Concept of Traditional Chinese Medicine [J]. Chinese Journal of Traditional Chinese Medicine, 2020, 35 (01): 35-38.

- [7] You Jie, Liu Jiaxiang. Liu Jiaxiang's Academic Thought on Fuzheng Treating Cancer [J]. Chinese Journal of Traditional Chinese Medicine, 2011, 29 (08): 1829-1831.
- [8] Yang Yong, Yang Lin, Yu Mingwei, et al. Cancer Toxin Yin and Yang Differentiation [J]. Journal of Traditional Chinese Medicine, 2016, 57 (17): 1522-1523.
- [9] Yang Yuxing, Wei Pinkang. Wei Pinkang's Clinical Experience in Treating Digestive System Tumors from Phlegm [J]. Shanghai Journal of Traditional Chinese Medicine, 2008 (07): 16-18.
- [10] Zhang Xiaoming, Pang Qiaoling. Mechanism of Acupoint Application Therapy [J]. Chinese Folk Medicine, 2005 (08): 18-19.
- [11] Huang Shiying, Chen Shuang, Jiang Mei. Exploration of TCM in tumor psychotherapy [J]. Journal of Traditional Chinese Medicine Oncology, 2023, 5 (05): 7-12.
- [12] Li Yangyang, Chen Xuesong. Research Progress on the Effect of Chronic Psychological Stress on Cancer [J]. Chinese Oncology, 2020, 29 (06): 458-462.