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Cancer

Review

Progress in the treatment of ovarian cancer with traditional Chinese medicine and western medicine

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Highlights

- Traditional Chinese medicine can promote the recovery of postoperative patients with ovarian cancer and reduce the side effects of postoperative chemotherapy or radiotherapy.

Editor's Summary

At present, the treatment of ovarian cancer is still mainly surgery. In recent years, traditional Chinese medicine has played an important role in the adjuvant treatment of ovarian cancer.

Abstract

Ovarian cancer is one of the female genital malignant tumors. Because its early clinical symptoms are not obvious and there is no specific early diagnosis method, about 70% of patients are in advanced stage (stage III-IV) at the time of diagnosis. Ovarian cancer mortality is the highest in female reproductive system tumor. According to the 2017 edition of the National Comprehensive Cancer Network (NCCN) published in the "Ophthalmic Cancer Clinical Practice Guide", the main treatment plan is surgery-based, postoperative adjuvant chemotherapy and other comprehensive treatment. Ovarian cancer is similar to "*Jia Ju*" in traditional Chinese medicine. In recent years, traditional Chinese medicine has been widely used in clinical practice. Postoperative patients with Chinese medicine, acupuncture, *et al.* promote rapid recovery, and traditional Chinese medical methods can also reduce the side effects caused by radiotherapy and chemotherapy.

Keywords: Ovarian cancer, Treatment, Integrated Chinese and western medicine

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Introduction

Ovarian cancer is one of the female genital malignant tumors. Because its early clinical symptoms are not obvious and there is no specific early diagnosis method, about 70% of patients are in advanced stage (stage III-IV) at the time of diagnosis. Ovarian cancer mortality is the highest in female reproductive system tumors [1]. According to the 2017 edition of the National Comprehensive Cancer Network (NCCN) published in the "Ophthalmic Cancer Clinical Practice Guide" [2], the main treatment plan is surgery-based, postoperative adjuvant chemotherapy and other comprehensive treatment. Ovarian cancer is similar to "*Jia Ju*" in traditional Chinese medicine. In recent years, traditional Chinese medicine has been widely used in clinical practice. Postoperative patients with Chinese medicine, acupuncture, *et al*. promote rapid recovery, and traditional Chinese medical methods can also reduce the side effects caused by radiotherapy and chemotherapy. This article reviews the research progress of traditional Chinese and western medicine for ovarian cancer as follows.

Surgical treatment

Once ovarian cancer is diagnosed, the current mainstream treatment perspective is surgery. The implementation of surgery can not only treat patients with advanced ovarian cancer but also perform a comprehensive FIGO staging for patients with early ovarian cancer [3]. Inaccurate FIGO staging will affect the subsequent adjuvant treatment of ovarian cancer, which in turn affects the prognosis of patients [4]. Therefore, surgery is an essential treatment for patients with ovarian cancer.

Principle of surgery

Before 2017, for patients with stage IB, because of bilateral tumors in both ovaries, there is no recommendation for the preservation of fertility. In the first edition of the NCCN ovarian cancer guidelines in 2017, it was pointed out that for women with low-potential tumors, germ cell tumors, or malignant stromal cell tumor types, tumor stage was staged at IA and IB, and women with fertility requirements can be treated with unilateral, bilateral salpingo-oophorectomy plus comprehensive staging of fertility preservation surgery [2]. Patients who retain the uterus can use assisted reproductive technology for fertility in the future. For patients with stage II-IV non-reservable fertility and available surgical treatment, "abdominal exploration + total hysterectomy + double attachment resection + cytoreductive tumor surgery" should be performed. Reziwan Guli *et al*. [5] reviewed 36 cases of early ovarian cancer, 18 cases underwent laparoscopic surgery, and 18 cases underwent open surgery. The operation time, intraoperative blood transfusion, and the number of intraoperative lymph node resections in the two groups were no significant differences in postoperative complications and postoperative chemotherapy ($P > 0.05$). However, it was concluded that laparoscopic surgery is less traumatic than open surgery and has little effect on immune function, which is more conducive to healthy recovery. It is worth promoting in clinical use.

Tumor cell depletion surgery

For patients with advanced stage, tumor depletion should be performed, and the tumor tissue that can be removed should be removed as much as possible. The volume of residual lesions after tumor cell depletion is the most important prognostic factor in patients with advanced ovarian cancer [3]. The NCCN ovarian cancer guidelines clearly state that cytoreductive surgery should minimize residual tumor lesions by < 1 cm, preferably removing all visible lesions. Guli Jianati *et al*. [6] used neoadjuvant chemotherapy combined with interval cytoreductive surgery for patients with advanced ovarian cancer. The results showed that the 5-year survival rate of patients who underwent cytoreductive surgery was 26.7%, and the 5-year survival rate of the combined group was 60.0%, indicating a significantly prolonged of patients' overall survival.

Controversy about lymph node dissection in advanced patients

There is controversy about whether or not systemic lymphadenectomy is performed during surgery for patients with advanced ovarian cancer. Those who oppose systemic lymph node dissection believe that lymph node dissection increases their risk such as lymphocytosis, pain, infection, and retroperitoneal implantation. Studies have shown that systemic pelvic and para-aortic lymphadenectomy does not prolong the overall survival (OS), but can slightly prolong the patient's progression-free survival (PFS) (level of evidence A) [3]. Scholars who insist on systemic lymph node dissection believe that lymph node dissection is beneficial for prognosis. Suk-Joon Chang *et al*. [7] performed lymph node dissection on 135 of 189 patients, of which 101 patients were found positive lymph node nodules, 87 patients were found lymph nodes > 1 cm, and the proportion in positive lymph nodes was as high as 86.1%. The positive rate in the experimental group was 64.4%, which was considered to be beneficial to the prognosis of patients. Bachmann

et al. [8] studied patients with advanced patients and concluded that the positive rate of lymph nodes could be used to guide the decision of lymph node dissection in the case of incomplete cytoreductive surgery, and to estimate the prognosis of patients with advanced stage.

Chemotherapy

The first-line chemotherapy regimen in ovarian cancer is platinum combined with paclitaxel, which can be treated by intravenous chemotherapy or intraperitoneal infusion chemotherapy [9].

Chemotherapy in stage I patients

No postoperative adjuvant therapy is required for patients with stage IA and IB grade G1 or pathological serous/endometrial carcinoma as determined by comprehensive staging. Patients with stage IA and IB, and graded G2 ovarian cancer can be followed up clinically or given intravenous chemotherapy with paclitaxel / carboplatin for 3-6 cycles. For IA and IB G3 grade, clear cell carcinoma or IC grade should continue to receive 3 to 6 cycles of chemotherapy after surgery. Data suggest that patients with poor cell differentiation may benefit more after receiving 6 cycles of chemotherapy [2].

Chemotherapy in patients with advanced stage

For patients with stage II-IV surgery and resection, 6 cycles of chemotherapy should be given after cytoreductive surgery [3]. However, there is no uniform standard for screening patients with neoadjuvant chemotherapy, and there is still controversy about the order of use of cytoreductive surgery and neoadjuvant chemotherapy. The NCCN guidelines indicate that a gynecological oncologist should evaluate patients with large or inoperable masses and follow by a histological biopsy. Three to four cycles of neoadjuvant chemotherapy can be performed before the cytoreductive surgery. This can reduce the tumor burden to varying degrees, providing opportunities for subsequent satisfactory cytoreductive surgery [10].

Radiation therapy

In ovarian malignancies, anaplastic cell tumors occur in younger patients and are sensitive to radiotherapy. However, pelvic irradiation can affect the endocrine function of the ovaries and lead to loss of fertility. Therefore, chemotherapy is more often used after surgery. Radiotherapy is only suitable for elderly patients without fertility requirements, and patients who have other serious diseases cannot receive chemotherapy [11]. For patients with advanced tumor masses, total abdominal radiotherapy is no longer the primary treatment or consolidation option [2]. About 60% to 70% of patients with pelvic radiotherapy will develop radiation enteritis, which may lead to congestion, edema, and necrosis of the intestinal mucosa as the course of treatment progresses, followed by intestinal reactions. Radiotherapy can damage the surrounding normal tissue, making the tissue gap unclear and losing the chance of surgery [12].

Traditional Chinese medicine understanding of ovarian cancer

Ancient records of “ovarian cancer”

Traditional Chinese medicine practitioner linked ovarian cancer with the name of the Chinese medicine disease "*Zheng Jia*, *Shi Zheng*, and *Jia Ju*". "*Su Wen*" (*453 B.C.-221 B.C.*) believes that the location of ovarian cancer is on *Renmai* and *Dumai*. "*Golden Chambers*" (*200 A.D.-210 A.D.*) proposed that *Biejia Pills* and *Guizhi Fuling Pills* can be used to treat ovarian cancer. Zhang Jing-Yue, a doctor of the *Ming Dynasty*, systematically and comprehensively discussed the symptoms in the “*Jingyue Quanshu Women's Regulations*” (*1368 A.D.-1644 A.D.*), which has a greater impact on future generations. Zeng Yu-Yan *et al*. [13] summarized the etiology and pathogenesis of the disease as "*Qi* stagnation and *Blood* stasis, cold blood clotting sputum". Zhu Yuan-Yuan *et al*. [14] found out that the primary method of Zhang Jing-Yue in treating ovarian cancer is mainly to regulate *Qi*, and relieves the symptoms of the patients.

Chinese medicine for the treatment of ovarian cancer

Liu Dan-Dan *et al*. [15] summed up the modern Chinese medicine doctors for the pathogenesis of ovarian cancer, which mainly based on the virtual standard, the whole body is virtual, the local is evil, and the pathological products such as *Qi*, *Blood*, *Tan*, and *Yin* are mainly stagnation. Liu Wei *et al*.[10] believes that Chinese medicine can improve the quality of life and reduce the quality of patients with ovarian cancer by promoting *Qi* and *Blood*, regulating *Yin* and *Yang*, and promoting the repair of cancer cells and apoptosis of cancer cells. We have included 60 patients with *Qi*-deficiency and *Blood* stasis type ovarian cancer after surgery. They were randomly divided into a treatment group (anti-tumor soup + chemotherapy) and a control group (chemotherapy alone), 30 cases in each group, according to the established protocol. Finally, it is concluded that Yiliu *Decoction* can improve the quality of life of postoperative chemotherapy patients with *Qi* deficiency and *Blood* stasis type ovarian cancer.

Moreover, *Yiliu Decoction* can prevent and reduce the bone marrow suppression, liver and kidney dysfunction, nausea and vomiting and other toxic side effects caused by paclitaxel + carboplatin (TP) chemotherapy [16-17]. Yang Bo-Jun *et al*. [18] studies the effect of *Fufang* Daqiqi *Decoction* combined with cisplatin on the expression of Bcl-2/Bax in subcutaneous xenografts of nude mice. The results showed that the tumor weight reduction of cisplatin combined with traditional Chinese medicine group was lower than other groups. Furthermore, RT-PCR showed that the expression of Bax mRNA of cisplatin combined with Chinese medicine group was lower than other groups. In the future, traditional Chinese medicine still has a lot of room for controlling ovarian cancer to reduce chemo-resistance, metastasis and enhance the quality of life of patients. It can be used to assist patients with post-operative, post-chemotherapy and palliative treatment.

Acupuncture for the treatment of ovarian cancer after chemotherapy

With the development of integrated Chinese and Western medicine, in recent years, acupuncture, warm acupuncture, acupoint injection and other methods have been applied to reduce the related side effects after chemotherapy for ovarian cancer. Fu Ya-Hong and Chi Chun-Yan [19] conducted warm acupuncture on the patients taking *Zusanli* and *Sanyinjiao* points after chemotherapy. The results showed that acupuncture treatment was used to treat leukopenia after chemotherapy for malignant tumors. Zhao Xi-Xin *et al*. [20] found the mechanisms of acupuncture anti-chemotherapy bone marrow suppression and leukocyte promotion is to promote the release of bone marrow cells into peripheral blood, prolong leukocyte life, by increasing serum colony stimulating factor activity. Tian Yan-Ping *et al*. [21] studied the acupoints of Hegu , Yangxi, Waiguan, Shousanli, Quchi, Taichong, Zusanli, Yanglingquan, Qihai and Honglong, and found that the neurotoxicity after warm acupuncture treatment is significantly lower than patients receiving neurotropin. It is well known that the rest of the time for patients with advanced ovarian cancer is inseparable from chemotherapy. Many patients cannot continue treatment because of serious chemotherapy complications. Acupuncture, warm acupuncture and acupoint injection can be used for the treatment of chemotherapy complications and reduce complications, which may provide patients with a good quality of life.

Conclusion

In summary, patients with ovarian cancer should be treated with surgery after diagnosis, which not only has a therapeutic effect on early surgery but also can be comprehensively staged. Tumor cytoreductive surgery for patients with advanced ovarian cancer has a positive effect on prognosis. However, even if we follow the NCCN guidelines for strict treatment, the 5-year survival rate of patients with advanced ovarian cancer is only 30% to 40% [22]. Although Chinese medicine has a long history, it has certain advantages in controlling the side effects of chemotherapy. However, how to explore and exert the Chinese medicine to prolong the survival rate of patients with ovarian cancer is still a considerable challenge.

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