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HEPATOCELLULAR CARCINOMA TREATMENT; NONSURGICAL APPROACHES

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ABSTRACT

Primary liver cancer (PLC) is one of the common cancers with high incidence and poor prognosis. PLC has become one of the major diseases that causes serious harm to human health and life. In recent years, domestic and foreign researchers have studied and summarized the current status of primary liver cancer treatment, and have made great progress as well. Significant progress in terms of early diagnosis, surgical treatment, and comprehensive treatment of liver cancer results in improvement in patient's quality of life. So far, there are many available methods that can be used to improve the quality of life in these patients, but still there are many issues that need to be addressed intensively. The progress in the study of liver cancer may bring about a new hope for the treatment of liver cancer.

Non-surgical treatment plays an important role in the treatment of primary liver cancer, which includes transcatheter arterial chemoembolization, percutaneous ablation therapy, radiation therapy, chemotherapy, etc

Key Words: Primary liver cancer; Non-surgical treatments progress, Quality of life

INTRODUCTION

1. Percutaneous ablation therapy

Percutaneous ablation is a curable treatment option for small tumors, which can be used for 1. tumors with diameters less than 5 cm; 2. The number of single HCC tumors is less than three ; 3. the diameter of a single tumor is less than 3 cm in hepatocellular carcinoma patients. Tumor recurrence and survival rate after ablation is almost the same as surgical resection of the tumor which is <2 cm in diameter [1-3]. Typically, percutaneous ablation therapy includes injection of chemical substances into the tumor under ultrasound guidance. Extreme temperatures can also be used to destroy tumors.

Percutaneous ethanol injection tumor (PEIT) is another kind of percutaneous ablation therapy. Ethanol induces coagulation necrosis in the tumor cell through multiple mechanisms such as protein denaturation, thrombosis of microvasculature, cellular dehydration and so on. With less treatment costs and fewer complications, PEIT is 90% to 100% efficient in cancer treatment, precisely if tumor diameter is less than 2 cm [1]. Moreover, PEIT has a significant effect in shrinking tumor lesions, controlling and delaying tumor growth. Experiments [4] made by Omata et al showed that the survival rate of 5-year could reach 64.7% for patients whose tumor diameter <3cm and the number of tumors <3. However, the PEIT efficacy in elderly patients [5] is relatively poor (1-, 3- and 5-year survival rates were 83%, 52% and 27% respectively.

The effect of PEIT could be improved when combined with TACE. TACE-induced avascular necrosis of the tumor destroys fiber spacing inside the tumor, which contribute to the dispersion of dry ethanol and the reduction of residual tumor cells after treatment [6-7].

For the diameter of tumor > 2cm, Radiofrequency ablation (RFA) is more effective than PEIT, which can kill tumor cells by generating heat conducted by electrode alternating current [8-9].

Complete tumor destruction caused by RFA treatment is difficult to achieve especially for those tumors which are close to large vessels, sub-capsular or gallbladder, therefore orthotropic recurrence rate of tumor is higher. therefore, the insufficiency of RFA can be avoided by binding it to PEIT, resulting in complete tumor destruction. The radiofrequency treatment for tumors on the first hilar region should be done carefully to avoid damage to the bile duct. Uehara et al [10] pointed that the damage can be reduced by the formation of

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ascites because it can increase the gap between diaphragm and abdominal wall.

Because of similar indications of RFA and PEIT, Seror ea al [11] compared the differences in efficacy between RFA and PEIT, and found that 2-year overall survival rates were 91.2% and 70.8%, tumor-free survival rate were 80.7% and 68.5%, and complication rate were 15% and 6.9% respectively. Few other researches [12] showed that, the efficacy of RFA is superior to laser treatment.

The use of microwave thermal effects can cause coagulative necrosis of tumor. The effect of microwave coagulation therapy for small hepatocellular carcinoma is good. the time interval between each therapy is shorter which means more frequent treatment regimens [13], tumors less than 3 cm in diameter, can be treated by a multi-multi-point needle and other combined ways to improve the efficacy of radiation. Seki et al [14] presented the data of 68 patients with small hepatocellular carcinoma which shows that microwave treatment can be carried out laparoscopically for small tumors near the surface of the liver. The results indicated that 1, 3 and 5-year survival rates were 97%, 81% and 43% respectively. Besides, the incidence of complications is lower.

Cryosurgery – The needles are introduced into the tumor to freeze and kill the tumor cells. The temperature of superconducting tip can be reduced to -140°C in a few minutes when the argon gas released in high pressure and normal temperature. With the release of helium, the temperature can increase to 45°C. Argon-helium refrigeration has higher efficiency and more reliable efficacy compared with the traditional technique with frozen liquid nitrogen.

Other percutaneous ablation therapies include percutaneous laser hyperthermia in the tumor and high-intensity focused ultrasound et al?. Multi-point fiber laser treatment has a freezing range that can be extended under the guidance of ultrasound. Laser hyperthermia also has a hemostatic effect that can stimulate the body's immune function to kill tumors. However, currently reports have showed that multiple laser hyperthermia can be used in the treatment of multiple primary liver cancer with diameter <2 cm. High intensity focused ultrasound therapy focuses on the tumor in the liver, produces direct heat to kill tumor cells with short wave length of high-intensity ultrasound and to penetrate tissue. (However, because of the small high-intensity focused ultrasound focus area, repeated several times to operate in the treatment of tumors, absorption and reflection effects by the ribs and hollow organs of the ultrasound generated, so high-intensity focused ultrasound therapy has limiting applications.)

2. Embolization therapy

Transcatheter arterial chemoembolization (TACE) is considered to be one kind of non-surgical treatment of primary liver cancer for further development in the international context after the reports about the TACE treatment on the liver cancer by Goldstain et al [15]. The definition of TACE indications made by Chinese Society of Surgery - Liver Surgery Group as follows:

(1) Liver function belonging to class A or B;
(2) Can not be treated with surgery;
(3) Tumor recurrence after hepatectomy.

In principle, resectable liver cancer does not need interventional radiology treatment before surgery. After repeated TACE (usually 2 to 4 times) treatment, some liver cancer patients' tumors can be significantly reduced, so that they can receive non-surgical treatment, especially on the right lobe or multiple lesions. It also seizes the chance to win the radical surgery and avoid possible liver atrophy, severe decompensated liver function and other complications as well. Vogl TJ et al [16] reported that TACE can be used as one kind of preventive treatment after primary liver resection to remove residual postoperative liver tumor cells; It is not fully adapted to portal vein thrombosis, tumor volume not exceeding 70% of the whole liver, tumor remission pain caused by palliative control bleeding, and arteriovenous fistula. TACE is an important supplementary treatment to liver cancer resection and an effective treatment in the second phase of surgery for liver cancer patients. But TACE PVTT shows poor efficacy of multiple lesions distant metastases and cannot achieve satisfactory clinical effects. Therefore, it is necessary to combine TACE with surgical resection, biological therapy, Chinese medicine, etc. to eliminate tumor cells, block tumors and prolong survival time, reduce the relapse rate and achieve the purpose of long-term prevention or even cure.

1.3 Radiotherapy and chemotherapy

The current mainstream of liver cancer radiotherapy includes three-dimensional conformal radiotherapy, normal tissue complication probability (NTCP), tumor control probability (TCP). Three-dimensional conformal radiotherapy when carried out, improve safety of target radiation dose (the maximum can be increased to 90Gy). Data [17] showed that three-dimensional conformal radiation therapy could improve the interventional treatment of inoperable liver cancers and assures median survival time.

For patients, who can be treated with surgery, surgical treatment should be preferred. However, in clinical work, when 80% of primary liver cancer patients are diagnosed, they have already had intrahepatic and distant metastasis or severe cirrhosis of liver, who have lost the chance to do surgery at that time. Systemic chemotherapy, including non-surgical therapy can improve patient's quality of life or prolong survival time. Because of its side effects, the results are not satisfactory. The clinical application currently is limited to

local chemotherapy, which include transcatheter arterial chemoembolization (TACE), surgical hepatic artery catheter (HAI) and / or portal vein catheterization (PVI) chemotherapy, intraperitoneal chemotherapy. Single-agent chemotherapy includes an anthracycline antitumor drugs, fluorouracil, camptothecin, cisplatin gemcitabine etc. However, the effect is not so good, but side effects do not advocate a separate application. Currently chemotherapy regimens such as joint programs with ADM (E-ADM) and / or PDD-based; E-ADM, PDD and 5 - ECF program consisting FU; L-OHP-based joint program such as XELOX regimen [18] and GD-MOX program [19].

DISCUSSION

Among all kinds of cancers, liver cancer is a malignant disease that is difficult to treat with short survival time and high mortality. Improvement in the efficacy of liver cancer treatment relies on improvement of the basic and clinical researches, which include further understanding of the onset and development of liver cancer, individual and environmental factors, mechanism of action, mechanism of metastasis and recurrence after surgical resection of liver cancer as well as signaling mechanism such as specific antigen and genes etc. thus obtaining specific interventional means of tumor formation and growth. Another area, which required more attention is the issue related to pre-cancerous lesions. To define pre-cancerous lesions based on molecular biology and explore methods of inhibiting further development of pre-cancerous lesions, which can greatly improve the effects, in other words prevent cancer occurrence. Clinically, we should adhere to the principle of early detection and early treatment; surgery shall be the preferred treatment. To discuss surgery-centered comprehensive treatment, interventional radiology and ultrasound intervention treatment after surgery to improve disease-free survival rate; emphasis on the value of minimally invasive treatment, new methods and techniques of localized treatment, and expecting new discoveries in radiation therapy, biological therapy, physical therapy and traditional Chinese medicine therapy etc. what's more, it is necessary to synthesize and optimize the various existing methods to make an optional treatment program that is suitable for different individuals.

CONCLUSION

"Shrinking large liver tumor to smaller one" and "anti-recurrence" shall be set as the main research directions. Liver transplantation for early liver cancer should also be actively open to try. People's awareness of health care and anti-hepatitis shall be strengthened.

Conflict of interest

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