Saudi Pharmaceutical Journal (2016) 24, 329–332

King Saud University

Saudi Pharmaceutical Journal

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Ablation effects of noninvasive radiofrequency field-induced hyperthermia on liver cancer cells

Kaiyun Chen [a,b,*,1], **Shuguang Zhu** [a,1], **Guoan Xiang** [b], **Xiaopeng Duan** [b], **Jiwen He** [b], **Guihua Chen** [a]

[a] *Department of Hepatology Surgery, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*
[b] *Department of General Surgery, The Second People's Hospital of Guangdong Province, Guangzhou, China*

Available online 23 April 2016

KEYWORDS

Non-invasive radiofrequency;
Ablation of liver cancer;
Clinical efficacy

Abstract To have in-depth analysis of clinical ablation effect of noninvasive radiofrequency field-induced hyperthermia on liver cancer cells, this paper collected liver cancer patients' treatment information from 10 hospitals during January 2010 and December 2011, from which 1050 cases of patients were randomly selected as study object of observation group who underwent noninvasive radiofrequency field-induced hyperthermia treatment; in addition, 500 cases of liver cancer patients were randomly selected as study object of control group who underwent clinical surgical treatment. After treatment was completed, three years of return visit were done, survival rates of the two groups of patients after 1 year, 2 years, and 3 years were compared, and clinical effects of radiofrequency ablation of liver cancer were evaluated. Zoom results show that the two groups are similar in terms of survival rate, and the difference is without statistical significance. 125 patients in observation group had varying degrees of adverse reactions, while 253 patients in control group had adverse reactions. There was difference between groups $P < 0.05$, with significant statistical significance. It can be concluded that radiofrequency ablation of liver cancer is more secure. Therefore, the results of this study fully demonstrate that liver cancer treatment with noninvasive radiofrequency field-induced hyperthermia is with safety effect and satisfactory survival rate, thus with relatively high clinical value in clinical practice.

1. Introduction

Liver cancer, liver malignant tumor, can be divided into primary and secondary ones. Primary liver malignant tumor originates from liver epithelial or mesenchymal tissue, which belongs to a serious malignant tumor (as shown in Fig. 1). Secondary liver cancer is relatively rare in comparison (Wu et al., 2015a, 2015b). Secondary or metastatic liver cancer refers to violations of the liver by malignant tumor that originates from multiple body organs (as shown in Fig. 2). In recent years, with

* Corresponding author at: Department of Hepatology Surgery, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.
E-mail address: chenkaiyunn@sina.com (K. Chen).
[1] These authors are contributed equally to this work.

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jsps.2016.04.009
1319-0164

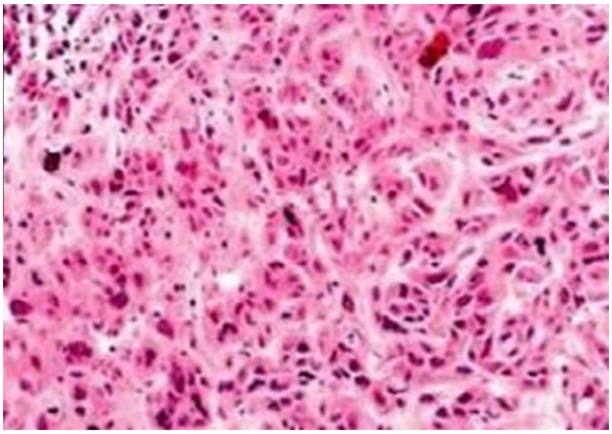

Figure 1 Primary liver cancer.

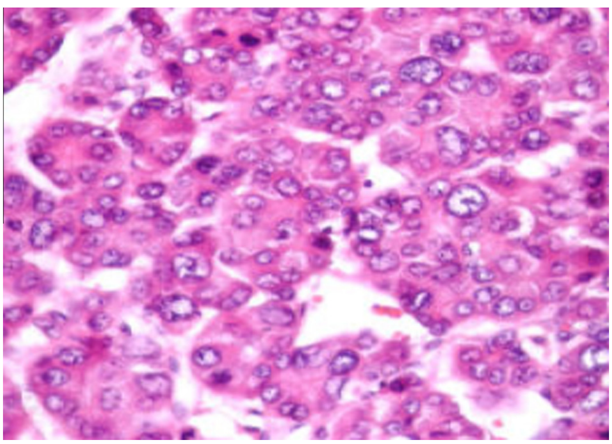

Figure 2 Secondary liver cancer.

the accelerating pace of life and the increasing bad habits in life, incidence of liver cancer in countries has increased year by year.

In clinical surgery, excision is usually adopted for liver cancer patients. But because of stealthiness of primary liver cancer, many patients in the early stages of hospitalization are diagnosed as terminal stages of cancer. In this case, there is relatively great risk for surgery, and only about 20% of patients can receive surgical treatment. But the effect after treatment is generally difficult to be satisfactory. Usually at six months after the treatment, 30% of patients will have relapse of illness (Wu et al., 2015a, 2015b; Xu et al., 2014; Han et al., 2015). With the passage of time, the recurrence rate also rises, and there are patients with metastasis and progression of the disease. It can be seen that effect of surgical treatment is difficult to make people completely satisfied, and cannot provide strong guarantee for health and safety of patients. In recent years, with continuous development of medical concepts and medical technology, radiofrequency ablation (RFA) therapy has become one of important treatment means in comprehensive treatment of liver cancer. Compared with surgical treatment, non-invasive radiofrequency ablation treatment enjoys advantages such as less trauma, safety and reliability, repeatability, and low treatment costs (He et al., 2015; Zhang et al., 2015).

Radiofrequency ablation is to insert radiofrequency electrode into the tumor tissue under ultrasound or CT guidance. Radiofrequency electrode emits radio frequency of 400 kHz, polar molecules and ions in the tumor tissue have high-speed motion vibration with the same rate as radiofrequency current, generating frictional heat which is transmitted to adjacent tissue, leading to internal temperature rise of tumor tissue, water evaporation, drying, condensation in inner and exterior cells, and thus aseptic necrosis, thereby killing tumor cells and achieving therapeutic purposes. Thus, heat of radiofrequency ablation derives from tissue surrounding electrode rather than electrode itself (as shown in Fig. 3). Under normal circumstances, under 42 °C, cells already have thermal damage. If the temperature is increased to 45 °C and lasts 3–50 h, cells will have progressive degeneration. As the temperature rises, time for irreversible cell damage is exponentially shorter. When temperature is greater than 60 °C, protein solidification occurs instantaneously, resulting in cell death. Temperature over 100 °C can cause boiling water within the tissue, evaporation and until carbonization (August et al., 2016; Sang et al., 2014). Fundamentally, lesion necrosis caused by radiofrequency ablation is different from classic "necrosis". During radiofrequency ablation, temperature of 80–110 °C can make tissue in vicinity of electrode directly freeze, which constitutes the main body of radiofrequency ablation lesion. Life structure affected by the heat energy, especially cytosolic enzyme protein, will be instantaneously solidified. This heat-induced structural variability and functional inactivation of the enzyme protein determine that radiofrequency ablation is impossible to have progressive enzymatic tissue damage or cell degradation as classic necrosis. Under the microscope, radiofrequency ablation lesion section exhibits five tissue damage reaction bands of temperature inclined curve from the center to the outer periphery: A band – electrode needle tract, carbonization or evaporation center caused by high heat production in the periphery; B band and C band – tumors or tumor adjacent to tissue paleness or reddish-brown coagulation necrosis caused by moderate heat production; D band – sharp-edged reddish or brown bleeding band caused by mild fever; and E band – outer layer of edema caused by mild fever. Generally, central region (A band) of radiofrequency ablation lesion and two outer zones (D and E band) can be confirmed based on characteristic change of tissue structure and cell components. Intermediate solidification zone (B band and C band) constitutes the main body of ablation lesions.

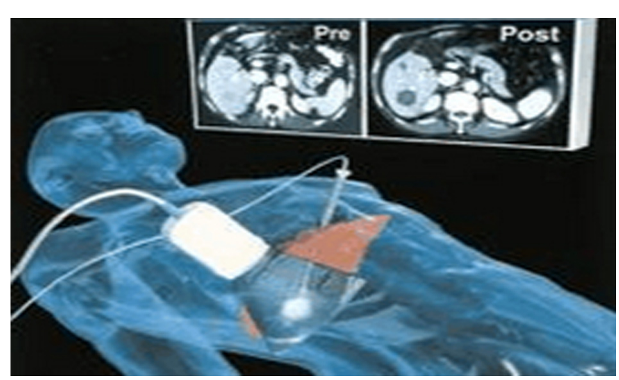

Figure 3 Liver cancer treatment model with radiofrequency ablation.

In this paper, in-depth analysis of effect of improving quality of life of patients with this treatment method is done. The result shows that radiofrequency ablation is with good effect for treatment of liver cancer. See report below for specific circumstances.

2. Materials and methods

2.1. General Information

Observation group: 1050 cases of patients, including 645 cases of male patients, 405 cases of female patients; the patients were aged between 45 and 76 years, with mean age at (58.97 ± 7.64) years; the medical records of all patients are very complete, who are not suitable for surgery or have no willingness due to various reasons, and meet RAF indication. Maximum diameter of liver lesion is 5 cm, and all patients accepted RAF treatment. This group includes 599 cases of one lesion, 288 cases with two lesions and 163 cases with three lesions. Child–Pugh classification results show that, there are 313 cases in A grade, 392 cases in B grade, and 345 cases in C grade. All cases were confirmed by serology, imaging or needle biopsy as primary liver cancer. All patients were hospitalized for the first time, untreated.

Control group: Among 500 cases of patients in the group, the maximum diameter or diameter sum is 5 cm. There are 277 cases of male, 223 cases of female; the patients were aged between 48 and 77 years, with mean age at (56.14 ± 8.12) years. There are 289 cases with one lesion, 131 cases with two lesions and 8 cases with three lesions. Child–Pugh classification results show that, there are 281 cases in A grade, 156 cases in B grade and 63 cases in C grade. All the patients received pathological diagnosis after operation.

2.2. Treatment methods

The control group takes conventional surgical treatment. Intravenous anesthesia with tracheal intubation was performed, and regular liver resection, hepatic segment resection or tumor resection were chosen according to the tumor site.

Observation group patients were treated with radiofrequency ablation. Lide LDRF-120S radiofrequency therapy instrument was used, with operating frequency at 400 KHz, to be equipped with LDRF-120S multipolar RAF electrode needle. Patients had preoperative fasting of 4–6 h, and took appropriate position under B ultrasound guidance. Then B-ultrasound detects liver cancer position. Choose the best puncture point and mark, and apply routine disinfected towel. After local infiltration anesthesia with 15% lidocaine and under ultrasonic guidance, avoid larger intrahepatic vessels and bile ducts, puncture multi-electrode needle to the tumor, expand over security border of 1 cm of maximum tumor diameter, and then start radiofrequency ablation (Qi et al., 2014; Mellotte et al., 2015). In computer automatic mode, treatment center temperature can reach 90–110e, with diameter of action range reaching electrode expansion diameter. With the increase in energy and extended treatment time, impedance increases, computer control power automatically reduces, and impedance rises to its highest before power drops to lowest. Then after radiofrequency therapeutic equipment stops working, recover sub-electrode and rotate about 30b. Open sub-electrodes and original diameter again, start ablation therapy in automatic mode and 1 treatment is completed. During treatment, use ultrasonic instrument to monitor change in echo of treatment region, take B ultrasound super echo group size for range estimate of therapeutic point, adjust electrode position if necessary, and conduct multipoint treatment until the entire tumor echo is enhanced. Finally, burn the needle to stop bleeding and prevent needle tract implantation metastasis.

2.3. Comparison methods

Through medical records, laboratory, imaging results and follow-up data collection, efficacy is evaluated. All patients received liver color Doppler ultrasonography and AFP quantitative examination every month in the first 3 months after treatment, and then reviewed liver color Doppler ultrasonography and AFP quantitative examination every two months. In case of suspicion of recurrence or local tumor progression, conduct enhanced CT or ultrasound contrast examination, and qualitative needle biopsy if necessary. In case of suspicion of tumor residue or relatively great recurrence possibility, 1–2 times of preventive TACE treatment are recommended. For patients diagnosed as recurrence or local tumor progression, TACE or TAI therapy is conducted.

Regular therapy features outpatient review, supplemented by telephone or SMS, etc. for follow-up to understand short-term and long-term efficacy. Three years' follow-up investigation was done for each patient, and survival rate at the first year, second year, and third year of patients was compared. Adverse reactions, disease metastasis and untoward effect of the two groups of patients were recorded.

2.4. Statistical methods

SPSS19.0 statistical software was used for data analysis and integration, with (n, %) to represent count data and chi-square for test. When $P < 0.05$, it indicates statistical significance.

3. Results

In comparison with survival rate of the two groups of patients, there exists no statistical significance ($P > 0.05$), with observation group respectively 85.3%, 58.3%, 36.7%; control group respectively 88%, 72%, 36%.

In observation group, 125 patients had varying degrees of adverse reactions, while in control group, 253 patients had adverse reactions. There was difference between groups $P < 0.05$, with significant statistical significance.

4. Discussion and conclusion

The results of this study show that survival rate of patients with surgical treatment and those with radiofrequency ablation are basically the same, so both schemes have desirability. However, some patients may have certain fear of and resentment toward surgical treatment in clinics, or have difficulty in bearing the treatment cost. Clinical experience has shown that radiofrequency ablation of liver cancer is a minimally invasive treatment method with relatively good efficacy, especially for

5 cm liver cancer, which can achieve nearly the same therapeutic effect as surgery. For primary liver cancer patients not suitable for or unwilling to receive surgical treatment, radiofrequency ablation is an ideal treatment method.

Acknowledgments

The research was supported by the National Natural Science Foundation of China (81201758), Science and Technology Planning Project of Guangdong Province (2012A030400055, 2011B031800184), Science and Technology projects of Guangzhou (2011J410010, 2011J4300066) and the Guangdong Province Medical Research Funds (A2012131).

References

August, D.A., Kallogjeri, D., Lewison, G., Chen, X., 2016. Nutrition support in surgical oncology. Asian Pac. J. Surg. Oncol. 2, 153–162.

Han, C.G., Zhao, W.D., Li, T.P., 2015. Application of energy spectrum CT in efficacy evaluation of lung radiofrequency ablation combined with biological treatment. J. Pract. Radiol. 13, 1362–1364, 1369.

He, M.W., Ge, W.P., Ma, J., 2015. Clinical study of protrusion of lumbar intervertebral disc with low-temperature plasma radiofrequency ablation combined with double-needle penetration ozone. Chin. J. Rehabil. Med. 30, 567–571.

Mellotte, G., Maher, V., Devitt, P.G., Shin, V.Y., Leung, C.P., 2015. Minimally invasive surgical oncology: state of the art. Asian Pac. J. Surg. Oncol. 1, 101–112.

Qi, S.Y., Li, J., Li, Y.H., 2014. Discussion of application value of carto 3-D electro-anatomical mapping system in paroxysmal supraventricular tachycardia radiofrequency ablation. Chin. Circulat. J. 17, 686–689.

Sang, Z.J., Zhu, D.W., Ji, W.Z., 2014. Treatment of rat alveolar hydatid disease with radiofrequency ablation and pathological changes. J. Intervent. Radiol. 23, 54–57.

Wu, W.W., Li, P., Wu, S.C., 2015a. Simulation and prediction of temperature control radiofrequency ablation temperature field distribution. J. Beijing Univ. Technol. 6, 789–796.

Wu, Y.H., Jiang, R., Yang, L.S., 2015b. Comparison of the mid-long-term efficacy in treating the permanent atrial fibrillation in rheumatic heart disease using monopolar vs. biopolar radiofrequency ablation concomitant cardiac valve replacement. Chin. J. Exp. Surg. 32, 1447–1450.

Xu, W., Liu, Y., Pan, P., 2014. Experimental study on optimum power of endoscopic ultrasound-guided pancreas radiofrequency ablation treatment. Chin. J. Digest. Endosc. 31, 152–154.

Zhang, Y.Y., Gu, Y.K., Huang, J.H., 2015. Experimental observation of multi-electrode radiofrequency ablation and conventional single electrode overlapping ablation effect. Nat. Med. J. China 95, 3537–3540.