ORIGINAL ARTICLE

A Multi–Center Cross–Sectional Study of The Status of Patient–Oriented Chinese Medicine Treatment of Malignant Tumors

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Abstract

Objective: To clarify the current status of traditional Chinese medicine (TCM) application and research in the field of tumor treatment, and provide reference guidance for the rational application of TCM in the treatment of tumors, multidisciplinary cooperation in tumor treatment, and improvement of TCM education. **Methods:** From July 2015 to June 2016, the patients in oncology department of four large-scale comprehensive first-class hospitals in China were selected. The general clinical data, clinical application of TCM and cognitive status data of tumor patients were obtained by using electronic medical record database combined with questionnaire to explore the clinical application of TCM in tumor treatment from the perspective of tumor patients. **Results:** The proportion of patients receiving chemotherapy (including targeted therapy) and TCM treatment was 28.7%. 16.6% of doctors were concerned that TCM combined with chemotherapy might produce adverse reactions. 20.0% of doctors think they have enough knowledge to answer questions related to TCM. 22.0% of doctors have received continuing education in TCM. During the treatment, 36.5% of patients had discussed TCM with their doctors. A total of 44.9% of doctors believe that TCM treatment is effective. **Conclusion:** The purpose of applying TCM is mainly to regulate the body's immunity, improve the symptoms such as loss of appetite, fatigue and sleep disorder, increase the effect and reduce toxicity of radiotherapy and chemotherapy. The treatment is mainly based on TCM compounds and proprietary Chinese medicines.

Keywords

TCM; malignant tumor; clinical application; literature quality evaluation

1. INTRODUCTION

According to the statistical results released by China's national center for cancer statistics in 2015, there were about 3372,175 cases of malignant tumors in China in 2011. There were 2113,048 deaths, with a mortality rate of 156.83/100,000^[1]. In February 2016, the national cancer registry published the 2015 edition of Chinese cancer statistics online in the world's top oncology journal CA: A Cancer Journal for Clinicians. The data showed that in 2015, there were about 4.3 million new cancer cases and 2.8 million death cases in China, with a significant increase compared with 2011^[2]. Another study by the national

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center for cancer statistics showed that the cumulative number of all malignant tumors in China within 5 years was about 7.49 million^[3]. Such an astonishing incidence and mortality undoubtedly put forward higher requirements and expectations for cancer prevention, diagnosis and treatment. Based on the results of similar authoritative epidemiological studies abroad and the current situation of domestic medical treatment, the questionnaire was designed. With the largest medical professional website in China as the survey platform, the study was conducted for the first time for doctors engaged in the clinical treatment of malignant tumors^[4]. Innovative online surveys of clinical application of traditional Chinese medicine (TCM) in the field of malignant tumor treatment, doctors' basic attitude to TCM, knowledge mastery, and medical practice were analyzed. A multicenter cross-sectional study of clinical epidemiology was conducted.

Through a multi-center cross-sectional study, the clinical application of TCM for cancer patients was investigated. On this basis, the differences and similarities between cancer patients and doctors in the application of TCM were preliminarily explored. It provides reference and guidance for the future rational application of TCM in the treatment of cancer and improves the doctor-patient relationship and other practical issues. At the same time, it laid a foundation for further carrying out large-scale epidemiological investigation on the clinical application of TCM in patients with malignant tumors^[5].

2. MATERIALS AND METHODS

2.1 Case Source

A cross-sectional study of clinical epidemiology was conducted to select all patients with malignant tumors in the oncology department of four large comprehensive first-class hospitals in China. Electronic medical record database and questionnaire were used to obtain the general clinical data of patients, clinical application and cognition data of TCM, so as to understand the popularity of clinical application of TCM. Chi-square test and logistic regression model were used before and after respectively for univariate and multivariate analysis to explore the related factors of TCM treatment for tumor patients. A questionnaire for clinicians engaged in tumor treatment was designed to compare and analyze the data of TCM application between patients and doctors. From July 1, 2015 to June 30, 2016, all inpatients in the oncology department at the four centers were selected.

2.2 Data Collection

Inclusion criteria: Age ≥ 18 years. Patients were diagnosed as a malignant tumor with a clear history of treatment. The Eastern Cooperative Oncology Group (ECOG) has a performance status (PS) score of ≤ 2 points. The patient has certain reading ability and can understand the questions and answer them. Patients are informed and agree to participate in the study voluntarily.

Exclusion criteria: Those who fill out incomplete surveys or do not meet the requirements. Patients with mental illness or unwillingness to cooperate. Patient families do not agree with their participants. First hospitalization.

2.3 Questionnaire Design

A large number of related foreign literatures have been read, and similar studies that have been carried out abroad have been referred to. Based on the current medical conditions in China, a research working group and an expert consulting group were set up to design the questionnaire. The research working group proposed the survey, and the expert advisory group qualitatively evaluated the survey content. After several discussions and revisions, the survey questionnaire was finally determined. Oncologists are also included in each center to understand the doctor's application of TCM. The questionnaire for doctors has a different basic information design than the patient, but the survey content is consistent and the language expression is slightly different.

2.4 Basic Situation

Age, gender, education background, ECOG-PS score, tumor type, time of first diagnosis, previous treatment, current hospitalization treatment, clinical stage, type of medical insurance, annual family income.

Communication and cognition: Patients consult the doctor about the problems of TCM. Doctors take the initiative to discuss the situation of TCM with patients and the basic attitude towards the use of TCM.

2.5 Sample Size Calculation

All data were entered using Epidata 3.0, and subject data was collected and organized using Microsoft Excel 2007. The sample size based on the overall probability and its confidence interval were calculate. With reference to the proportion of TCM

applications, it is expected that the proportion of TCM applications in this cross-sectional study will also be 40%. The allowable error is 5%. The α is taken as 0.05. The calculated sample size is 384.

2.6 Statistical Methods

Statistical descriptions include percentages, mean $\pm$ standard deviation, and 95% confidence intervals. The distribution of categorical variables is described by frequency and percentage, and the distribution of continuous variables is described by mean and standard deviation.

The t-test was used to compare the measurement data between the two groups. The Chi-square test was used to compare the rates between the two groups. The nonparametric test analysis was used to analyze the grade data.

For the analysis of influencing factors for tumor patients using TCM, single factor analysis followed by logistic regression analysis were used. The baseline information of tumor patients and other relevant factors were used as influencing factors for univariate analysis. According to the results of univariate analysis, all factors that meet $P < 0.25$ are selected as independent variables in the binary classification logistic regression model (where age and gender must be included, regardless of whether the univariate analysis results meet $P < 0.25$) and the outcome of the event is used as the dependent variable. The independent variable introduction standard is 0.05, and the exclusion standard is 0.10.

The difference was statistically significant with $P < 0.05$. Statistical analysis of each data was performed in SPSS 21.0 (SPSS Inc., Chicago, Illinois, USA) statistical software.

3. RESULTS

3.1 General Data

During the study observation period, a total of 729 tumor patients were included in the study. The average age was 59.3 ± 11.7 years. There were 384 male patients (52.7%). Among them, 189 were lung cancer (25.9%), 146 were colorectal cancer (20.0%), and gastric cancer was 125 cases (17.1%). 66.8% of the patients had a high school or middle school educational background, and 21.4% had a college educational background or above. The mean course of disease was 24.0 ± 32.7 months. Clinical stage III patients were 141 (19.3%) and stage IV patients were 390 (53.5%). The ECOG-PS score was 1 point in 521 patients (71.5%). Surgery was performed in 574 patients (78.7%) and chemotherapy was performed in 551 patients (75.6%). 159 (21.8%) had local health insurance.

The clinicians in the oncology department of the four centers were screened, and the inclusion criteria were doctors' willingness and final completion of the questionnaire. The exclusion criteria are doctors who have been in hospital for less than one year. Finally, fifty-two participants were included, with an average age of 34.0 ± 5.9 years. Thirty-four were male (65.4%). The mean clinical working time was 7.0 ± 5.6 years.

3.2 Clinical Application and Cognition of TCM

According to the TCM doctor's advice and prescription in the electronic medical record system of each center, as well as the clinical use of TCM filled in by the patients in the questionnaire, after accounting, the proportion of TCM clinical application in tumor patients after the diagnosis of malignant tumor is 59.7% (435/729). Among 294 cancer patients who were not treated with TCM, when asked why they were not treated with TCM, thirty-three patients said they did not believe in TCM (11.2%), one hundred and thirty-eight patients showed no knowledge of TCM (46.9%), the doctors of the seventy-two patients objected to the use of TCM (24.5%), twenty-seven patients were worried about side effects of Chinese medicine (9.2%), and twenty-seven patients were not treated with TCM for other reasons (9.2%).

Proprietary Chinese medicine (64.8%) and herbal medicine (57.9%) were the most commonly used TCM treatments. Fatigue (39.1%) and loss of appetite (20.9%) were the most common clinical indications for TCM use. 26.7% of tumor patients received TCM treatment in addition to chemotherapy, including targeted therapy. When combined with chemotherapy, 4.4% (19/435) of tumor patients had adverse reactions. "Regulating immunity and strengthening physique" (57.7%) and "relieving uncomfortable symptoms" (48.5%) were the main therapeutic purposes of TCM.

88.3% of the patients believed that TCM was effective in tumor treatment. In the course of treatment, 40.9% of tumor patients said that doctors had discussed TCM with them. 62.5% of cancer patients said they had consulted their doctors about TCM. In the 163 patients who had not been consulted about TCM, seventy-three patients said their time was limited, fifty-seven

patients had no recollection of TCM treatment, fourteen patients had no knowledge of TCM, seven patients had rejected the use of TCM, and twelve patients had no consultation for other reasons. 35.6% cancer patients said their doctors encouraged them to use TCM when they had received or considered it.

Based on this, the patient's and doctor's survey data are compared. The results show that there are some differences between the two in terms of the purpose of Chinese medicine treatment, the choice of specific treatment methods and indications, and the identification of clinical efficacy (Table 1).

Table 1 Clinical application and cognition of TCM in cancer patients

Item	Patient (n = 435)	Doctor (n = 52)	P
	Yes (%)	Yes (%)	
Chinese patent medicine	282 (64.8)	35 (67.3)	0.723
Chinese herbal medicine	252 (57.9)	40 (76.9)	0.008
TCM	65 (14.9)	20 (38.5)	< 0.0001
Fatigue	170 (39.1)	38 (73.1)	< 0.0001
Loss of appetite	91 (20.9)	34 (65.4)	< 0.0001
Feel sick and vomit	63 (14.5)	17 (32.7)	0.001
Sleep disorder	35 (8.0)	30 (57.7)	< 0.0001

Note: TCM: traditional Chinese medicine.

3.3 Univariate Analysis of Tumor Patients Using TCM

The age (< 59 years, ≥ 59 years), gender (male, female), education (primary and below, middle school, university and above), patient time (< 24 months, ≥ 24 months), clinical stage of cancer (early, advanced), local medical insurance (with and without), and annual household income (< 200,000, ≥ 200,000) is taken as predictive factors. Univariate analysis was performed on patients using TCM treatment. Factors meeting the $P < 0.25$ in univariate analysis were included in the logistic regression model for multivariate analysis. Age and gender were included in the regression model regardless of the results. The results are detailed in Table 2.

Table 2 Univariate analysis of tumor patients using TCM

Predictive factors	Cancer patients treated with Chinese medicine	
	Yes (%)	P*
Age		0.001
< 59	207 (47.6)	
≥ 59	228 (52.4)	
Gender		0.067
Male	217 (49.9)	
Female	218 (50.1)	
Duration of illness (month)		0.208
< 24	290 (66.7)	
≥ 24	145 (33.3)	
Clinical stage of tumor*		0.017
Early stage	104 (23.9)	
Advanced stage	331 (76.1)	

* Early stage includes stage I and II; progressive stage includes stage III and IV; TCM: traditional Chinese medicine.

3.4 Multivariate Analysis of Tumor Patients Using TCM

Table 3 shows the results of multivariate analysis of tumor patients using TCM. According to the results of odd ratio (OR)

values, age (< 59 years), females, education level of primary school and below, and annual family income ($\geq$ 200,000) are the relevant factors for the use of TCM for cancer patients.

Table 3 Multivariate analysis of tumor patients using TCM

Predictive factors	Cancer patients treated with Chinese medicine		P
	OR	95% CI	
Age ($\geq$ 59 vs. < 59 years)	0.67	0.49-0.92	0.016
Gender (female vs male)	1.41	1.02-1.95	0.035
Duration of illness ($\geq$ 24 vs. < 24 months)	1.26	0.90-1.76	0.19
Clinical stage of tumor (Advanced vs early stage)*	1.38	0.97-1.98	0.075
Local health insurance (no vs. yes)	0.74	0.50-1.08	0.12

* Early stage includes stage I and II; progressive stage includes stage III and IV; TCM: traditional Chinese medicine; OR: odd ratio; CI: confidence interval.

4. DISCUSSION

This study was mainly conducted for cancer patients, and the most important data obtained was that the clinical application rate of TCM was 59.7%. This data is lower than 83% from a single-center cross-sectional survey conducted by Fudan University Cancer Hospital in 2012^[6-8]. At the same time, it is higher than the 40% obtained by the national survey, and is closer to the data of other foreign surveys. The main reasons for the gap between the two studies in China are as follows: (1) The clinical stage of 72.8% of the patients included in this study was advanced, and the average disease duration was 24 months. Patients in the middle and advanced stages often experience a longer battle with tumors than patients in the early stages, and are more likely to have dissatisfaction with the current “standard treatment”, so they are more likely to receive Chinese medicine treatment. (2) The excessive use of Chinese medicine obtained from single-center research conducted by Fudan University’s Cancer Hospital may be associated with the combination of TCM and western medicine in China, which has attracted more cancer patients to receive TCM treatment. In addition, the reference value of the research results is limited. (3) The data on the proportion of TCM use obtained in the first part is estimated by clinicians. According to the experience of previous epidemiological studies of the same type, the data estimated by doctors is often lower than that of patients the actual situation.

From the results of this study, Chinese medicine is widely used in cancer treatment. Chinese herbal medicine and proprietary Chinese medicine are the most commonly used Chinese medicine treatments. Fatigue and loss of appetite are the most common clinical indications for patients using TCM. “Regulating immunity, enhancing physical fitness” and “alleviating discomfort” are the main purposes of TCM treatment^[9]. It involves multiple links such as preventing recurrence and metastasis after surgery, alleviating various symptoms, increasing efficiency and reducing toxicity, and improving quality of life. The above data reflects the basic situation of domestic Chinese medicine treatment of tumors, and the advantages and development direction of TCM treatment of tumors.

In terms of safety evaluation, although only 4.4% of tumor patients had adverse reactions, the incidence of adverse reactions reported by doctors was only 5.8% by considering that 26.7% of patients received TCM treatment while chemotherapy. Therefore, the safety issue in the combined application of Chinese medicine and chemotherapy cannot be ignored^[10]. From a safety perspective, we still advocate that the timing of treatment of Chinese herbal medicine and proprietary medicines should be staggered with that of chemotherapy, and the treatment of Chinese herbal medicine and proprietary medicines after chemotherapy or at intervals were arranged to the extent possible. As for acupuncture, massage, diet therapy and other non-drug treatments, there are no reports of related adverse reactions. Under the guidance of doctors, it can be applied throughout the entire process of tumor treatment.

Cross-sectional studies, also known as status studies, describe the basic characteristics and disease or treatment of patients in a certain range of people within a certain period of time^[11]. It is the most widely used method in clinical epidemiology. A cross-sectional study is the preferred method for describing the clinical application of a drug or therapy. Considering that comprehensive top three hospitals are better represented in different types of hospitals, this study chose to conduct cross-

sectional studies in comprehensive top three hospitals.

There are many limitations to this study. Firstly, although the results of more than 700 tumor patients were included in this study, the study was limited to four large comprehensive tertiary hospitals in China and failed to be used in oncology hospitals, secondary hospitals, and community hospitals. The center is set up for extensive sampling, and there are some interference factors and influencing factors. The results may not fully represent the overall situation of the whole country, and it will be further verified by conducting epidemiological surveys of large samples with multiple centers and diversification nationwide in the future. Secondly, due to limited objective conditions, the research content is limited, and many issues related to the treatment of tumors by TCM have not been included in the survey, and many issues involved in the research have not been able to conduct in-depth investigations.

In conclusion, according to the results of this multi-center cross-sectional study, Chinese medicine is widely used in the treatment of malignant tumors and can run through the entire process of tumor treatment. The main purpose of its treatment is to regulate immunity, enhance physique and relieve discomfort. The treatment is mainly made of proprietary Chinese medicines and Chinese herbal medicines.

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