

Evaluation of Quality of Life in Patients Treated with Traditional Chinese Medicine

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Abstract: The worldwide clinical implementation of Traditional Chinese Medicine (TCM) is increasing as complementary therapy to Western Medicine. This development leads to an increasing demand to evaluate not only the scientific proof of efficacy, but also to measure the quality of life (QOL) concepts specific to TCM.

This article attempts to 1) review the relevant published literature (indexed in Medline) on the evaluation of QOL in patients treated with TCM, 2) compare QOL of patients treated with Western Medicine and TCM and 3) describe the limitations of the literature and future research directions.

Overall, the approach of TCM as a model of system biology appears to improve QOL and may be worth integrated into conventional Western Medicine.

Keywords: Traditional Chinese Medicine (TCM), Quality of Life (QOL), complementary therapy, western medicine.

1. TRADITIONAL CHINESE MEDICINE (TCM)

1.1. Definition

A modern understanding of Chinese Medicine (CM) regards TCM as a model of system biology with the objective of a holistic therapy of diseases. Diagnosis in TCM is based on a system of clinical signs, sensations and findings designed to assess the functional vegetative state of the patient. Therapy includes vegetative and central nervous reflex interventions such as acupuncture and Chinese manual therapy (*Tuina*), traditional vegetative biofeedback exercises (*Taichi* and *Qigong*), which consist of meditative breathing and movement exercises. The main therapeutic method, however, is Chinese phytopharmacology and dietetics, which includes administration of plants [1, 2], minerals, and other products, as well as Chinese functional food.

1.2. History

Although the actual origin of CM remains unclear, it seems that CM has a history of more than 5000 years [3].

The oldest written sources are the *I Ging* (Book of Changes) and the *Huangdi Neijing* (Yellow Emperor's Classic on Internal Medicine) dating back over 2300 years. The first contains mathematical knowledge of binary numbers [4] (yang and yin as I/0) which was decoded by the mathematician Gottfried Wilhelm Leibniz (1646-1716), the latter is comparable in importance to the Hippocratic Corpus in Greek medicine [5].

The term "Traditional Chinese Medicine" (TCM) originally describes the modern practice of CM as a result of widespread reforms that took place after 1950 in the People's Republic of China. This included the need of quick distribution of the methodology, resulting in a certain reduction of the theoretical background.

The term "Classical Chinese medicine" (CCM) often refers to medical practices that are based on theories and methods dating from before the fall of the Qing Dynasty (1911) [6].

"Integrated Chinese Medicine" or integrated TCM refers to more comprehensive recom compilations based on CCM and the current *status quo* of methodologies. The theoretical basis of such recom compilations, e.g. the "*Heidelberg Model of TCM*" [2, 4] are mathematical models on vegetative regulation inherent in the classical *corpus medicus*. By this approach, certain technical terms like yin, yang and the

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phases can be translated as vegetative functional terms. This may be considered crucial for the integration of TCM in Western health care systems and research.

1.3. Distribution

Western Medicine, like any other *corpus medicus*, has limitations in diagnostic and therapeutic success [7]. This is why 60 to 80 % of the chronically ill search for complementary treatment methods such as acupuncture [8-13]. In fact, according to the World Health Organization, in many developed countries, 70-80% of the population has used some form of alternative or complementary medicine (e.g., acupuncture) [14]. The report from a Consensus Development Conference on Acupuncture held at the National Institutes of Health in 1997 stated that acupuncture is being “widely” practiced—by thousands of physicians, dentists, and other practitioners—for relief or prevention of pain and for various other health conditions. According to the 2002 National Health Interview Survey—the largest and most comprehensive survey of complementary and alternative medicine use by American adults to date—an estimated 8.2 million U.S. adults had ever used acupuncture, and an estimated 2.1 million U.S. adults had used acupuncture in the previous year [15]. In the year 2003, Chinese Medicine, including its products and services, had an estimated turnover of 3,2 billion €, which is roughly 40 € per citizen of Germany per year [2].

1.4. Clinical Studies on Acupuncture in Otorhinolaryngology

Diseases in Otorhinolaryngology offer a wide range of possible application of TCM. In one of our first studies, we could show that additional use of acupuncture on top of non-steroidal anti-inflammatory drugs effectively reduced post-tonsillectomy pain [16]. Nevertheless, major challenges in clinical acupuncture studies remain the design of (I) double blinding and (II) appropriate placebo controls [17].

Double blinding is the scientific gold standard in pharmaceutical studies. As acupuncture is a complex procedure, it is difficult to design studies in which both the acupuncturist and patient are blinded to the treatment.

Recently, we could meet these standardized, scientific requirements in a controlled, double-blinded acupuncture study with the “*Heidelberg double-blinding array*”. We confirmed a significant decongestant efficacy of a specific *verum* acupuncture to a non-specific control acupuncture and a non-acupuncture standard medication group for the improvement of nasal breathing [18].

1.5. TCM and Phytopharmacology

Medicinal herbs have played an important role in Western medicine from ancient to modern times. However, medicinal plants gradually lost their importance as pharmaceutical synthetic chemistry progressed in Western countries during the 20th century. Currently, there is a revival of interest in medicinal plants and an increasing scientific interest in phytochemicals as chemical lead compounds for the generation of semi-synthetic derivatives [19-21].

Hundreds of botanical, animal, and mineral preparations were categorized in traditional Chinese pharmacopoeias

starting millennia ago. TCM plants provide an enormous variety of drugs based on thousands of years of tradition [22, 23]. Consequently, it can be assumed that by this time many ineffective prescriptions have disappeared from the system of TCM thereby significantly improving the prospects for identifying novel active constituents from TCM-plant prescriptions [24]. Among anticancer agents, camptothecin, paclitaxel, vincristine, and indirubin are developed from *Camptotheca acuminata*, *Taxus chinensis*, *Catharanthus roseus*, and *Baphicacanthus cusia*, respectively, although the original plants were not used traditionally to treat cancer [20].

2. QUALITY OF LIFE (QOL)

2.1. Definition

The World Health Organization (WHO) defines quality of life (QOL) as the individual perception of the position in life within the context of the culture and value systems and in relation to individual goals, expectations, standards and concerns [25].

QOL can be differentiated in the assessment of general and health-related QOL, which both are regarded as a multidimensional construct [26]. According to Lawton *et al.* [27], four main aspects belong to QOL: objective environment, competence of behavior (including health), perceived QOL and psychological well-being (including life satisfaction) [27].

2.2. Measures of QOL

Among the various possibilities to assess QOL, two questionnaires have been applied in the majority of QOL-assessments in patients treated with TCM.

The World Health Organization Quality of Life Survey (WHOQOL-100) is a standard QOL assessment questionnaire consisting of 100 questions. By this test, the overall QOL and the general health perceptions are assessed. The WHOQOL was developed especially to be a cross-cultural measurement tool. It has demonstrated excellent reliability and validity [28, 29]. Chinese [30], Danish [31], and Portuguese [32] translations have subsequently been tested and confirmed good reliability and validity.

The SF-36 is a multi-purpose, short-form health survey with 36 questions. It consists of a profile of functional health and wellbeing scores, as well as general physical and mental health self-assessments. Accordingly, the SF-36 has shown to be useful in surveys of the general population and specific subpopulations, thereby comparing the relative burden of diseases in order to evaluate the health benefits offered by a wide range of different treatments [33]. The SF-36 has been translated for use in more than 40 countries [34, 35].

3. INTRODUCTION OF QOL ASSESSMENT IN TCM

As TCM is a medical system with proper diagnostic key symptoms and signs, the development of health-related Quality of life (HRQOL) assessments specific to TCM was mandatory. For this purpose, the Chinese Quality of Life Instrument (ChQOL) was developed, which is a TCM-specific self-report health status instrument. The ChQOL is a 50 item-questionnaire, which comprises aspects of health, which are not well covered by the existing generic health

related QOL scores, such as the WHOQOL-100 and the SF-36. The ChQOL categorizes physical aspects of health in two domains, the physical form domain and the mental domain. Moreover, it contains a domain on emotion that covers various kinds of moods. This domain gathers information, which belongs to the affective self-perception in nature. Other psychological mechanisms, for example, self-esteem, that are more cognitive are however not included [36].

Speaking of the limitations, there is less overlapping in the WHOQOL-100 and the ChQOL at the domain level. There is even less overlapping between SF-36 and ChQOL. However, the combination of ChQOL and WHOQOL-100 or SF-36 is claimed to provide a wider range of information on people's health. Due to methodological limitations, the structure of the ChQOL was not able to fully reflect the concept of health in TCM. As an example, although the pulse diagnosis is one of the principle findings in TCM, it could not be included in the ChQOL [36].

The content of ChQOL was shown to be valid in the context of TCM for Cantonese speaking Chinese independent of spoken dialect and health care system [37].

In the USA, a structured assessment instrument was developed for use in clinical trials of acupuncture and other Chinese medical therapies. It is using an interdisciplinary approach. Under the guidance of two group process facilitators, and in order to establish whether the assessment instrument was consistent with accepted CM diagnostic categories (face validity) and included the full range of each concept's meaning (content validity), a panel of TCM expert clinicians convened and their responses were organized using the Delphi process, an iterative, anonymous, idea-generating and consensus-building process. An aggregate rating measure was obtained by taking the mean of mean ratings for each question across all 10 experts. The assessment instrument, called TEAMSI-TCM (Traditional East Asian Medicine Structured Interview, TCM version) uses the pattern differentiation model characteristic of TCM. This modular, dynamic version was specifically designed to assess women, with a focus on gynecologic conditions; with modifications it can be adapted for use with other populations and conditions. TEAMSI-TCM is a prescriptive instrument that guides clinicians to use the proper indicators, combines them in a systematic manner, and generates conclusions. In conjunction with treatment and training it may serve to increase inter-rater reliability and inter-trial reproducibility in CM clinical trial [38].

4. EVALUATION OF QOL IN TCM

4.1. Otorhinolaryngology & Pulmonology

An acupuncture-like transcutaneous nerve stimulation method (Codetron) without invasive needles was developed to mimic acupuncture treatment. In a Phase I-II study, the effectiveness of Codetron in treating radiation-induced xerostomia in head-and-neck cancer patients was examined. Xerostomia symptoms were assessed by a five-item xerostomia symptom questionnaire with a Visual Analogue Scale and QOL was evaluated using the Head and Neck Radiotherapy Questionnaire (QOL-RTI) [39]. A significant improvement in whole saliva production and related symptoms was noted at 3 and 6 months after treatment

completion, respectively. However, no statistically significant change in the QOL evaluation compared with baseline was observed [40].

An Austrian group of investigators assessed lung function and QOL by the Pediatric Asthma Quality of Life Questionnaire [41] in asthmatic school-age children. In a randomized, placebo-controlled, double-blinded pilot study, patients were treated with laser acupuncture and oral probiotic drops (living non-pathogenic *Enterococcus faecalis*). Patients of the control group were treated with a laser pen, which did not emit laser light and were given placebo drops. No additional beneficial effects of TCM treatment was seen on forced expiratory volume in 1 s (FEV1), QOL and use of rescue medication in children with intermittent or mild persistent bronchial asthma [42].

Neumeister *et al.* [43] investigated the effect of acupuncture in patients with chronic obstructive pulmonary disease (COPD) on QOL with the Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ) [44], pulmonary function measures and inspiratory mouth occlusion pressures (MOP) in a prospective randomized and placebo-controlled pilot study. Patients receiving *verum* acupuncture improved significantly with FEV1, residual volume (RV) and total lung capacity (TLC). There was an improvement of large magnitude in QOL and a trend of lower demand of the respiratory pump. In the placebo group, only a slight improvement of QOL, a deterioration of lung function parameters and a trend of higher demand of the respiratory pump were observed.

4.2. Oncology

The emotional distress of a diagnosis of cancer and the persistent side effects while having treatment significantly compromise patients' QOL [45]. As a consequence, those diagnosed with cancer are increasingly seeking out supportive and complementary therapies as adjuncts to medical treatment in their efforts to cope with their illness and promote healing. Cancer patients are frequent users of complementary medicine, 91% of cancer patients diagnosed with cancer in the United States [46] use some form of complementary medicine when receiving usual medical treatment. While some patients hope these will impact on survival, many are using these methods to improve their QOL.

Over the last three decades, there has been a growing consensus among health care providers and researchers that efficacy of therapeutic intervention should be evaluated by its impact on both quantity and quality of life [47]. In oncology or palliative care, QOL assessment is even more important in determining treatment benefit when survival advantage is limited and other aspects of the patients' life are more important [48]. It may also provide valuable clinical data to support treatment decisions for the patient and doctor to decide on the best treatment options.

Mistletoe extracts have been applied to cancer patients for several decades. The influence of a standardized mistletoe extract (sME) on QOL in breast, ovarian and non-small cell lung cancer patients was investigated in a prospective randomized controlled clinical study. QOL improved significantly for patients who were complementarily treated with sME, as determined by the

questionnaires FLIC (Functional Living Index-Cancer), Traditional Chinese Medicine Index and the KPI (Karnofsky Performance Index) in comparison to the control group [49].

The European Organization for Research and Treatment of Cancer (EORTC) developed cancer-specific core questionnaires, one common to patients with various sites of primary tumor, and also site-specific questionnaires for the measurement of QOL of patients with cancers of specific sites of the body. The EORTC QLQ-C30 was proved to have good reliability and validity [3-8]. The EORTC QLQ-C30 has been translated into traditional Chinese (Mandarin spoken in Taiwan) and validated in Taiwan [9-12]. The EORTC QLQ-OV28 was designed as a supplement to the EORTC QLQ-C30 for the use in ovarian cancer clinical trials and related studies [13] and has been used in a study assessing QOL for patients after pelvic exenteration [14]. Cultural differences between Taiwan and China seem not to influence EORTC QLQ-OV28. The reliability and validity of the Taiwan Chinese Version of the EORTC QLQ-OV28 on patients with ovarian cancer in Taiwan was confirmed [50].

QOL of cancer patients is often diminished due to the side effects of treatment and symptoms of the disease itself. TCM provides *Qigong*, a Chinese meditative practice in combination with slow gentle body movements and controlled breathing techniques, is supposed to promote the circulation of *qi* within the human body, and enhance a practitioner's overall health [1]. Oh *et al.* [51], indicate that *Qigong* with usual medical treatment is able to improve QOL (measured with the EORTC QLQ-C 30) of cancer patients and reduce inflammation (measured with the c-reactive protein) in cancer patients. However, the results were not statistically significant between treatment and control groups, most probably due to small sample size.

The success of cancer chemo- and radiotherapy is mainly measured in terms of disease-free survival, whereas QOL is often separated from survival. This may be inadequate, and the full potential of beneficial treatment effects should be taken into account. Hence, health-related quality of life (HRQL) represents an outcome, which also has to be incorporated in randomized, controlled clinical trials. This has been considered not only as relevant from the patient's perspective gaining cure from the disease, but also from a health policy level. The old "Who should pay?" dilemma is even more pressing in economically critical times, where decisions have to be made, how much a society is able to pay for expensive therapies [52].

Survival analyses, *e.g.*, Kaplan-Meier statistics, measure two health states: dead or alive. Such mortality-based statistics do not consider morbidity of surviving cancer patients. The overall survival time of cancer patients can be divided into time with toxicity, time without symptoms and toxicity (TWiST), and time after systemic relapse (REL) [53]. Various health outcome models have been proposed focusing on QOL of cancer patients, such as quality of wellbeing (QWB), quality-adjusted life years (QALY), or health years equivalent (HYE) [54].

While these models may be generally considered in medicine, the Q-TWiST method has been proposed for use in cancer trials. Q-TWiST describes the quality-adjusted

time without symptoms and toxicity. It integrates side effects and benefits of adjuvant cancer therapy by determination of mortality, morbidity, and duration of different health states in a single number [55-60].

Q-TWiST is a well-established method in clinical oncology. Its value for TCM has, however, not been elucidated yet. From our point of view, the performance of Q-TWiST-based clinical trials integrating TCM in cancer therapy is one of the most thriving and attractive challenges in therapy research today. As recently reviewed [61], there is mounting evidence that TCM reduces side effects associated with cancer chemo- and radiotherapy. Therefore, measuring Q-TWiST using TCM would greatly foster the integration of TCM in standard cancer treatment regimens.

In this context, two general TCM categories may be discussed, which are suitable for setting up Q-TWiST-based clinical trials:

1. **Phytotherapy:** A recent meta-analysis showed that *Astragalus*-based herbal remedies improved response to chemotherapy and reduced therapy-related side effects by stimulation of macrophages and natural killer cells as well as inhibition of T-helper cell type 2 cytokines [62]. A total of 34 randomized clinical trials ($n=2815$ patients) with platinum-based chemotherapy for non-small cell lung cancer were included in the meta-analysis. In 12 trials ($n=940$ patients), a reduced risk of death at 12 months appeared. Better response to chemotherapy was found in 30 trials ($n=2472$ patients). Injection of the Chinese *Ai Di* remedy improved life quality in four trials ($n=257$ patients) as measured by Karnovsky index.
2. **Acupuncture** is widely used in TCM for pain treatment, a major side effect of cancer therapy, *e.g.* in Otorhinolaryngology. The value of acupuncture was re-evaluated in a meta-analysis, which included 11 randomized controlled trials, two non-randomized trials and 8 case studies [63]. The authors found that acupuncture, electro-acupuncture, and massage therapy indeed significantly relieved pain of cancer patients. Typical side effects of cancer chemotherapy are nausea and vomiting. As described in another meta-analysis considering 11 clinical trials ($n=1247$ patients), acupuncture-point stimulation, electro-acupuncture, and acupressure reduced the incidence of acute vomiting, but not acute or delayed nausea severity as compared to control [64].

5. CONCLUSIONS

Screening the literature, indexed in Medline, few relevant studies have adequately addressed the evaluation of QOL in patients treated with TCM. Reports in the literature have been conflicting, with some studies finding deterioration in QOL and some finding stability or improvement in QOL over time.

Given the fact that QOL reflects patients' perceptions of their health state, QOL is an especially pertinent issue on which to focus. Before concluding anything regarding QOL two premises are, however, important to note. First, it is important to utilize a well-validated measure of QOL in order to compare QOL in patients treated with TCM.

Second, due to the relatively small number of studies concerning this issue, any interpretation of the impact of TCM on QOL must be tentative.

Finally, recommendations are difficult to make based on the research. There have been no prospective studies in which patients have been randomly assigned to Western treatment or TCM treatment only. Despite the limitations of the current research, we can draw a tentative conclusion. In sum, the approach of TCM as a system biology appears to improve QOL and may be worth integrated into conventional Western Medicine.

6. PERSPECTIVES

Future research concerning the evaluation of QOL in patients treated with TCM should include prospective and multi-center studies, which would allow comparative analysis of QOL. Also, studies measuring the impact of various TCM treatment methods on QOL should be undertaken, as there appear to be adverse reactions from traditional herbal medicine.

Ideally, these studies would assist Western physicians as well as patients in the process of decision making whether to implement TCM in the Western treatment modalities as an add on treatment to conventional cancer therapy.

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