來源文章

太極拳鍛練用於肺癌患者因接受化療產生的疲勞副作用：隨機對照試驗

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摘要

現狀（前後關係）：太極是中國傳統能促進健康的運動。它已被證明可以增強精神健康和改善心理狀況。

目標：我們旨在評估太極運動對肺癌患者在進行化療中產生的疲勞副作用的有效性。

方法：我們進行了太極拳運動的隨機試驗，並以低衝擊運動作為控制干預的對照組。為這2個研究組進行為期12週，每次1小時的練習。練習每隔一天進行一次。主要最終目的是觀察多項疲勞症狀簡化表（MFSI-SF）的總分變化。次要最終目的是觀察MFSI-SF的五個子量表得分的變化。2組的所有評估在三個時間點重複，T0：首次化療療程前。T1：第3個化療療程前。T2：第4個化療療程結束時。

結果：在2012年1月至2014年12月期間，96名患者參加了該試驗。在6和12週時，與對照組相比，太極拳組的MFSI-SF總分較低（59.5±11.3相對於vs.66.8±11.9，P <0.05; 53.3±11.8對比vs.59.3±12.2，P <0.05）。在6週時，與對照組比較。太極組有較低的MFSI-SF一般子量表得分（18.1±4.6對比20.4±4.5，P <0.05）和物理子量表得分（17.5±4.4對比19.1±4.5，P <0.05）並有較高的MFSI-SF活力分量表評分（14.5±3.3對比11.6±3.4，P <0.05）。但在太極拳組和對照組的情緒分量表（20.2 3.6與20.0 3.5，P> 0.05）和精神分量表（18.2 4.0與18.9 3.9，P> 0.05）之間沒有顯著差異。在12週時，MFSI-SF子量表評分顯示與六週時相同的趨勢。

結論：太極是一種用於治療並能有效的干預正在接受化療的肺癌患者與因癌症所產生的相關疲勞症狀。特別是用於減少一般疲勞和身體疲勞以及增加活力。 J Pain Symptom Manage2016; 51：504e511。 2016美國臨終關懷和症狀減輕治療學院。發布者Elsevier Inc.保留所有權利。

關鍵詞

肺癌，癌症相關疲勞(CRF)，太極運動，化療

介紹

根據國家綜合癌症網絡，癌症相關疲勞（CRF）被定義為與癌症或癌症治療相關的身體，情感和/或認知疲勞或疲勞的持續主觀感覺。CRF是癌症患者的常見症狀。已經報導在診斷時約50%-75%的癌症患者中有此症狀，並且在接受放射治療的患者中患病率增加至80%-96%，而接下來受化療的患者中的患病率增加至60%-93%。CRF是降低總體患者與健康相關的生活質量的滿意度的強有力和獨立的預測因子。

CRF管理包括藥理學和非藥物學干預。雖然有越來越多的證據表明精神興奮劑在臨床上有意義的水平提供能改善CRF，但也與造血生長因子增加的不良結果相關。因此，這些藥物不能再被推薦用於治療CRF。運動治療是最常用於CRF的非藥物干預。 Meta分析證實運動能夠顯著降CRF。

太極拳是中國傳統的能促進健康的運動。它是一種容易去緩和身體，低至中等強度的身體鍛煉形式。太極拳已被發現對帕金森病和慢性心力衰竭有積極影響，能改善慢性阻塞性肺疾病患者的肺功能和活動耐受性，並改善平衡和減少老年人的跌倒。它也被證明可以增強精神健康和改善心理狀況，包括減少老年抑鬱症，減少焦慮，和提高自我身體機能。太極拳也被發現對癌症患者有積極的影響。 Mustian等人報導稱，乳腺癌患者經12週的太極拳練習，能在與健康相關的生活質量和自我評價從基本程度改善到等級6。Zhang 等人發現太極拳可以改善非小細胞肺癌患者術後的免疫系統功能。 16週的太極拳干預能造成CD55影響的顯著減弱。Fong等人也發現氣功和太極拳訓練可以改善鼻咽癌患者的外周循環狀態和功能性含氧量的能力。一項包括13項隨機對照試驗的綜合分析表明，太極拳對癌症患者的癌症特異性生活質量、疲勞、免疫功能和皮質醇水平能產生積極影響。最近發現，在三個月的隨訪中太極可以降低乳腺癌患者的CRF 。然而，太極拳尚未被作為降低接受化療的肺癌患者CRF的干預措施。在本研究中，我們旨在評估太極運動對CRF在這個人群中的有效性。

方法

實驗規劃

這是一項前瞻性，隨機對照的干預試驗，評估將太極拳運動使用於正在接受化療的肺癌患者。經醫院倫理委員會批准。所有患者都有書面知情同意書。

資格標準和排除標準

資格標準如下：

1）通過臨床評估證實肺癌診斷，如：胸部X線，計算機斷層掃描或組織學檢查;
2）接受每21天為1個週期，2-4療程以cisplatin為基礎的化療;
3）年齡大於18歲;
4）東方腫瘤合作組織功能狀況0-3;
5）願意參加太極拳運動或低衝擊運動。

排除標準如下：

1）阻力訓練禁忌症患者，如中度至重度心力衰竭;
2）化療前已經參加太極拳運動;
3）無法完成疲勞評分評估;
4）參加者不能堅持太極拳運動或低衝擊運動。

招聘和隨機化

2012年1月至2014年12月，在我們醫院接受化療的肺癌患者參加了本次研究。患者隨機分配到太極拳運動組或低衝擊運動對照組1：1。隨機化通過計算機生成的隨機數來完成。第三方人員由招聘人員進行配置。

干預/介入

在太極練習組中，參與者練習了簡約的楊氏風格太極拳，是由經驗豐富的太極拳教練在社區和教學DVD教授的。八個簡易太極動作包括：1）開始招式（雙手上升到肩膀水平），2）彎腰，3）

側身橫向移動臂，4）移動手，5）對角步，6）站在一條腿上，7）踩踏，8）關閉招式（雙手落在一邊，左腿拉到右腿）。每次練習都包括五到十分鐘的暖身，其次是太極拳練習。在練習中，參與者注意運動協調和呼吸調節。
在低衝擊運動組中，參與者進行手臂，頸部和腿部圓圈，隨後伸展上下肢肌肉組以及深部腹部呼吸。當患者從化療反應中恢復時，太極拳運動和低衝擊運動的干預均在家里或社區進行。在21天的化療週期中的第10天開始鍛煉。太極拳運動和低衝擊運動每隔一天練習一次，早上八點至十點之間。
運動程序如圖1所示。
運動實施僅為住院化療的患者提供。如果參與者無法進行太極拳運動或低衝擊運動，他們被排除在研究之外。

與癌症相關的疲勞的結果
主要結果是多種疲勞症狀清單簡化表（MFSI-SF）的總分來顯示。 MFSI-SF是一個30項目的自我評估報告，旨在評估疲勞的五個經驗導出的尺度：一般疲勞，身體疲勞，情緒疲勞，精神疲勞和活力。每個六項目子量表都闡述了過去一周內經歷過各種疲勞描述的程度。用五點刻度來反應，從0=沒有，到4=非常。可以通過從四個疲勞子量表的總和中減去活力子量表得分來計算總疲勞評分。 MFSI-SF在疲勞評估中有效，Cronbach a為總量綱，子量表範圍為0.83～0.92。次要結果是MFSI-SF的五個子量表的分數：一般疲勞，身體疲勞，情緒疲勞，精神疲勞和活力。
在患者住院化療時的三個時間點進行MFSI-SF的評估：第一個評估為化療療程之前。T1為：第三個化療療程之前。T2為：第四個化療療程結束時。 MFSI-SF評估計劃在化學療法療程的第1天，第43天和第85天進行。當化療週期延遲時，MFSI-SF評估也會相應推遲。MFSI-SF評估指標也**如圖1所示**。

統計分析
人口統計學和基線變量之間的組間差異用分類變量的卡方檢驗進行了測試。通過重複測量的混合線性模型比較MFSI-SF評分。 P <0.05被認為是顯著的。所有統計分析使用IBM SPSS，版本19.0（IBM Corp.，Armonk，NY）進行。

結果
參與者的基準特徵
2012年1月至2014年12月，96名患者參加了本次試驗。招募和隨機化流程圖**如圖2所示**。其中有5位患者隨機分組後，1位分配到太極拳組（n = 1）和4位分配到低衝擊運動組（n = 4），因為他們不再感興趣，隨機化後立即退出。**表1**總結了隨機化後91例患者的基線數據。患者平均年齡為62.8歲，7.47%為男性。兩組之間基線特徵平衡良好，兩組比較均有統計學差異（P> 0.05）。太極組與對照組之間平均MFSI-SF總分和五個子量表評分也相似（**表2**，T0）。

MFSI-SF總分
第六週時，因為無法忍受化療，太極拳組失去了5名患者，對照組失去3名患者。由於化療，MFSI-SF總分與基線相比，顯著增加。然而，與對照組相比，太極組的MFSI-SF總分則較低（59.5±11.3VS.66.8±11.9，P <0.05）。

第12週時，太極拳組失去4名患者（3名因忍受不了化療，1人死亡）。對照組失去5例（3例忍受不了化療，2例死亡）。太極拳組與對照組相比MFSI-SF總分仍然較低
（53.3±11.8vs.59.3±12.2，P <0.05）。
表2和圖3顯示了兩組MFSISF總分數從基線到第6周和第12週的變化。

MFSI-SF量表分數
在六週時間內，與對照組相比，太極拳組的MFSI-SF普通子量表（18.1±4.6vs對比20.4±4.5，P <0.05）和物理子量表（17.5±4.4vs對比19.1±4.5，P <0.05）的評分得分較低；MFSI-SF活力子量表（14.5±3.3vs對比11.6±3.4，P <0.05）評分得分較高。在太極拳組與對照組之間，情緒分量表（20.2±3.6vs對比20.0±3.5，P> 0.05）和心理分量表（18.2±4.0vs對比18.9±3.9，P> 0.05）得分無顯著差異。
第12週時，與對照組比較，太極拳組依舊有較低的MFSISF總分子量表評分（17.5±4.4，19.2±4.6，P <0.05）與物理子量表評分（15.1±4.6 b = 17.1±4.5，P <0.05），以及更高的MFSI-SF活力子量表評分（15.0±3.5，12.6±4.9，P <0.05）。再一次的，在太極組與對照組之間，在情緒子量表（19.1±3.9對比19.3±3.5，P >0.05）與心理分量表（16.6±3.7對比16.3±3.6，P> 0.05）中沒有發現顯著差異。
表2和圖4顯示了兩個組對於五個MFSI-SF子量表得分，從基底線至六周和十二週的變化。

討論
CRF常見於癌症患者。即使在早期非小細胞肺癌倖存者中，CRF的患病率為57%。在6-12週的隨訪，我們的隨機對照干預試驗發現，與對照組相比，太極拳組的MFSI-SF總分低於對照組。(59.5 ±11.3 vs. 66.8 ±11.9, P < 0.05; 53.3 ± 11.8 vs. 59.3 ± 12.2, P < 0.05, respectively.)。結果顯示，太極拳是治療肺癌化療患者CRF的有效干預措施。 CRF的機制尚不清楚，但可能包括5-HT神經遞質失調，迷走神經傳入激活，肌肉和ATP代謝改變，下丘腦前列腺素腎上腺（APH）軸功能障礙，晝夜節律紊亂和細胞因子失調。在1989年的一項研究中，太極拳的實踐增加了心率以及尿液中的去甲腎上腺素排泄，降低了唾液中的皮質醇濃度，降低了緊張、抑鬱、憤怒、疲勞、混亂和焦慮狀態。參與者感覺更加活躍，被情緒干擾較少。Lu 等人發現，太極拳的短期效果是增強迷走神經調節，並將交感神經平衡傾向於降低交感神經調節。林等人和Lu等人也發現，太極拳運動可以改善老年人的肌肉力量。太極拳運動可以有效調節APH軸，曲線下皮質醇面積（P = 0.02），和皮質醇變化（r = 0.74; P <0.05）。Irwin等人報導了只有在太極拳練習組裡發現，白細胞介素-6和腫瘤壞死因子組合的toll樣受體4活化單核細胞產生的總體降低（P <0.02）。以及降低白細胞介素-6（P = 0.07）和腫瘤壞死因子（P <0.05）。根據這項研究，我們發現太極可以通過增加迷走神經調節，改善肌肉力量，調節APH軸和減少一些細胞因子來減少CRF。這些可能是太極拳能有效干預CRF的原因。我們的研究結果發現，與對照組比較，太極拳練習組有較低的MFSI-SF總分子量表（18.1 ± 4.6對比vs.20.4 ± 4.5，P <0.05）和物理子量表評分（17.5 ± 4.4對比vs19.1 ± 4.5，P <0.05）。較高的MFSI-SF活力子量表評分（14.5 ± 3.3對比vs.11.6 ± 3.4，P <0.05）。但情緒評分（20.2 ± 3.6對比vs.20.0 ± 3.5，P> 0.05）和精神評分（18.2 ± 4.0對比vs18.9 ± 3.9，P> 0.05）卻沒有顯著的不同。然而，其他一些研究發現太極拳運動可能會影響心理社會地位。Taylor-Piliae等報導說，經過12週的太極拳運動計劃，皆表明心理社會狀態的統計學上的改善（P

<0.05），特別是情緒（h2 = 0.12），感覺壓力（h2 = 0.13）。我們的研究沒有發現太極拳和低衝擊運動組之間的情緒和心理分數的差異。也許低影響的運動也可以改善情緒和精神疲勞的影響。

這項研究有一些限制。首先，我們只有研究接受化療的參與者12週的時間，所以太極拳對於肺癌患者的長期有效性仍有待確定。第二，這是一個“開放標籤”的行為干預試驗。參與者知道他們被分配到哪個組。因此，不可能蒙蔽參與者或是收集數據的人。
總之，我們的初步研究結果表明，太極拳是治療肺癌化療患者的有效干預措施，特別是減少一般身體疲勞和增加活力。所以有必要使用較大的臨床樣本的長期研究來證實和擴大本研究的結果。

圖3。太極拳組和對照組（低衝擊運動）（MFSI-SF）各個總分（治療前：P> 0.05。治療後6週：P <0.05。治療後12週：P <0.05）
誤差條表示標準偏差。

圖4。太極拳組和對照組（低衝擊運動）在3個時間點的多項疲勞症狀簡化表（MFSI-SF）的五個子量表。
a）總分子量表：治療前：P> 0.05。治療後6週：P <0.05。治療後12週：P <0.05。
b）物理子量表：治療前：P> 0.05。治療後6週：P <0.05。治療後12週：P <0.05。
c）活力子量表：治療前：P> 0.05。治療後6週：P <0.05。治療後12週：P <0.05。誤差條表示標準偏差。

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Original Article

Tai Chi Exercise for Cancer-Related Fatigue in Patients With Lung Cancer Undergoing Chemotherapy: A Randomized Controlled Trial

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Abstract

Context. Tai Chi is a traditional Chinese health-promoting exercise. It has been shown to enhance mental health and improve psychological condition.

Objectives. We aimed to assess the effectiveness of Tai Chi exercise for cancer-related fatigue in patients with lung cancer undergoing chemotherapy.

Methods. We conducted a randomized trial of Tai Chi exercise as compared with low-impact exercise as a control intervention. Exercises were practiced every other day, a one-hour session for 12 weeks for each of the study groups. The primary end point was a change in total score of the Multidimensional Fatigue Symptom Inventory—Short Form (MFSI-SF). Secondary end points were changes in five subscale scores of the MFSI-SF. All assessments were repeated at three time points, T0: before first course of chemotherapy; T1: before third course of chemotherapy; and T2: at the end of the fourth course of chemotherapy.

Results. Between January 2012 and December 2014, 96 patients were enrolled in this trial. At six and 12 weeks, the Tai Chi group had a lower MFSI-SF total score compared with the control group (59.5 ± 11.3 vs. 66.8 ± 11.9, $P < 0.05$; 53.3 ± 11.8 vs. 59.3 ± 12.2, $P < 0.05$). At six weeks, the Tai Chi group had lower MFSI-SF general subscale scores (18.1 ± 4.6 vs. 20.4 ± 4.5, $P < 0.05$) and physical subscale scores (17.5 ± 4.4 vs. 19.1 ± 4.5, $P < 0.05$), and higher MFSI-SF vigor subscale scores (14.5 ± 3.3 vs. 11.6 ± 3.4, $P < 0.05$), compared with the control group. But no significant differences were found in emotional subscale (20.2 ± 3.6 vs. 20.0 ± 3.5, $P > 0.05$) and mental subscale (18.2 ± 4.0 vs. 18.9 ± 3.9, $P > 0.05$) scores between the Tai Chi group and the control group. At 12 weeks, the MFSI-SF subscale scores showed the same trends as at six weeks.

Conclusion. Tai Chi is an effective intervention for managing cancer-related fatigue in patients with lung cancer undergoing chemotherapy, especially for decreasing general fatigue and physical fatigue, and increasing vigor. J Pain Symptom Manage 2016;51:504—511.

Key Words
Lung cancer, cancer-related fatigue, Tai Chi exercise, chemotherapy

Introduction

According to the National Comprehensive Cancer Network, cancer-related fatigue (CRF) is defined as a persistent subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment.[1] CRF is a common symptom among patients with cancer. It has been reported in approximately 50%—75% of cancer patients at the time of diagnosis, and the prevalence increases to 80%—96% in patients undergoing chemotherapy and to 60%—93% in patients receiving radiotherapy.[2] CRF is a strong and independent predictor of decreased overall patient satisfaction and health-related quality of life.[3]

CRF management includes pharmacologic and non-pharmacologic interventions.[4] Although there is increasing evidence that psychostimulant agents

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provide improvement in CRF at a clinically meaningful level, the hemopoietic growth factors are associated with increased adverse outcomes. Therefore, these drugs can no longer be recommended in the treatment of CRF.[5] Exercise treatment is the most commonly used nonpharmacologic intervention for CRF. Meta-analyses have confirmed that exercise was able to significantly reduce CRF.[6,7]

Tai Chi is a traditional Chinese health-promoting exercise. It is an easily modifiable, low-to-moderate intensity form of physical exercise. Tai Chi has been found to have positive effects on Parkinson's disease[8] and chronic heart failure,[9] improves lung function and activity tolerance in patients with chronic obstructive pulmonary disease,[10] and improves balance and reduces falls in older adults.[11] It also has been shown to enhance mental health and improve psychological conditions, including reducing geriatric depression,[12] reducing anxiety,[13] and enhancing self-efficacy.[14] Tai Chi also has been found to have positive effects in cancer patients. Mustian et al. reported that Tai Chi exhibited improvements in health-related quality of life and self-esteem from baseline to six and 12 weeks in breast cancer survivors.[15] Zhang et al. found Tai Chi Chuan can improve immune system function in postsurgical non−small cell lung cancer survivors. A 16-week Tai Chi intervention caused significantly attenuated CD55 expression.[16] Fong et al. also found Qigong and Tai Chi training may improve peripheral circulatory status and functional aerobic capacity among survivors of nasopharyngeal cancer.[17] A meta-analysis that included 13 randomized controlled trials concluded that Tai Chi had positive effects on cancer-specific quality of life, fatigue, immune function, and cortisol level of cancer patients.[18]

Recently, it has been found Tai Chi can decrease CRF in breast cancer survivors at three-month follow-up.[19] However, Tai Chi has not been tested as an intervention for reducing CRF in patients with lung cancer undergoing chemotherapy. In the present study, we aimed to assess the effectiveness of Tai Chi exercise for CRF in this population.

Methods

Study Design

This was a prospective, randomized, controlled intervention trial evaluating Tai Chi exercise in patients with lung cancer undergoing chemotherapy. It was approved by the Ethics Committee of our hospital. All patients gave written informed consent.

Eligibility Criteria and Exclusion Criteria

Eligibility criteria were as follows: 1) lung cancer diagnosis confirmed by clinical assessment, chest X-ray, computed tomography, or histological examination; 2) receiving 2−4 courses of cisplatin-based chemotherapy for a 21-day cycle; 3) age ≥ 18 years; 4) Eastern Cooperative Oncology Group Performance Status 0−3; and 5) willing to participate in Tai Chi exercise or low-impact exercise. Exclusion criteria were as follows: 1) patients with contraindications for resistance training, such as moderate-to-severe heart failure; 2) already participating in Tai Chi exercise before chemotherapy; 3) unable to complete fatigue score assessment; and 4) participants cannot insist on Tai Chi exercise or low-impact exercise.

Recruitment and Randomization

Between January 2012 and December 2014, patients with lung cancer undergoing chemotherapy in our hospital were enrolled in our study. Patients were randomly allocated 1:1 to the Tai Chi exercise group or low-impact exercise control group. Randomization was accomplished by computer-generated random number. Allocation was performed by third-party personnel uninvolved in recruitment.

Interventions

In the Tai Chi exercise group, participants practiced a simplified Yang style.[20] Tai Chi was taught by experienced Tai Chi instructors in the community and by instructional DVD. The Eight-Form Easy Tai Chi included the following: 1) commencing form (both hands rise to shoulder level); 2) curving back arms; 3) stepping sideways and moving arms; 4) moving hands; 5) diagonal strides; 6) standing on one leg; 7) stepping and pushing; and 8) closing form (both hands fall to the side, left leg drawn to the right leg).[21] Each session included five to 10 minutes of warm-up, followed by Tai Chi practice. In the practice session, participants paid attention to movement coordination and regulated breathing.

In the low-impact exercise group, participants practiced arm, neck, and leg circles, followed by stretches for upper and lower body muscle groups along with deep abdominal breathing.

Both Tai Chi exercise and low-impact exercise interventions were performed at home or in the community when patients recovered from their chemotherapy response. The exercises began on the 10th day during the 21-day chemotherapy cycle. Both Tai Chi exercise and low-impact exercise were practiced every other day, for one hour in the morning, between approximately 8:00 to 10:00 AM. The exercise program is shown in the Figure 1.

Exercise implementation was offered to patients hospitalized for chemotherapy. If the participants were unable to perform Tai Chi exercise or low-impact exercise, they were excluded from the study

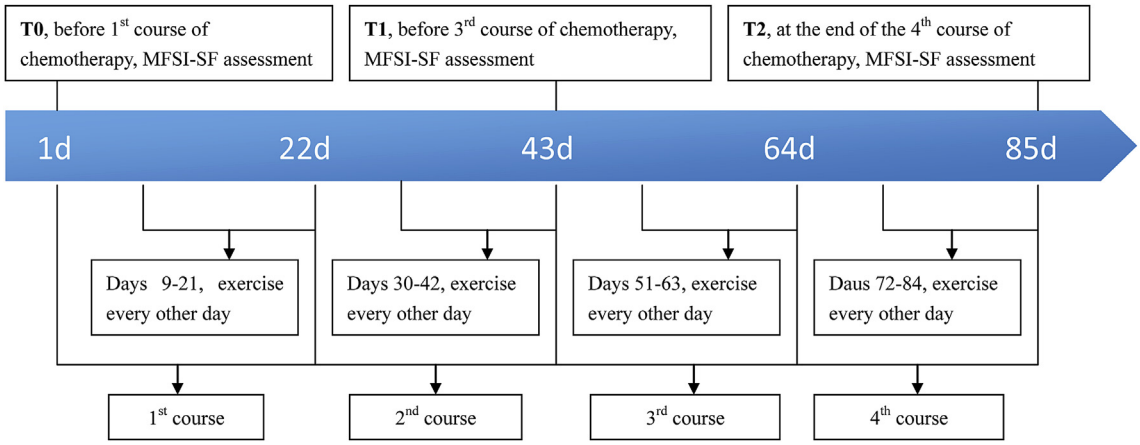

Fig. 1. Timeline for Tai Chi exercise or low-impact exercise in chemotherapy courses. MFSI-SF = Multidimensional Fatigue Symptom Inventory—Short Form.

Cancer-Related Fatigue Outcomes

The primary outcome was total score of the Multidimensional Fatigue Symptom Inventory—Short Form (MFSI-SF). The MFSI-SF is a 30-item self-report measure designed to assess five empirically derived dimensions of fatigue: general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor. Each six-item subscale addresses the degree to which

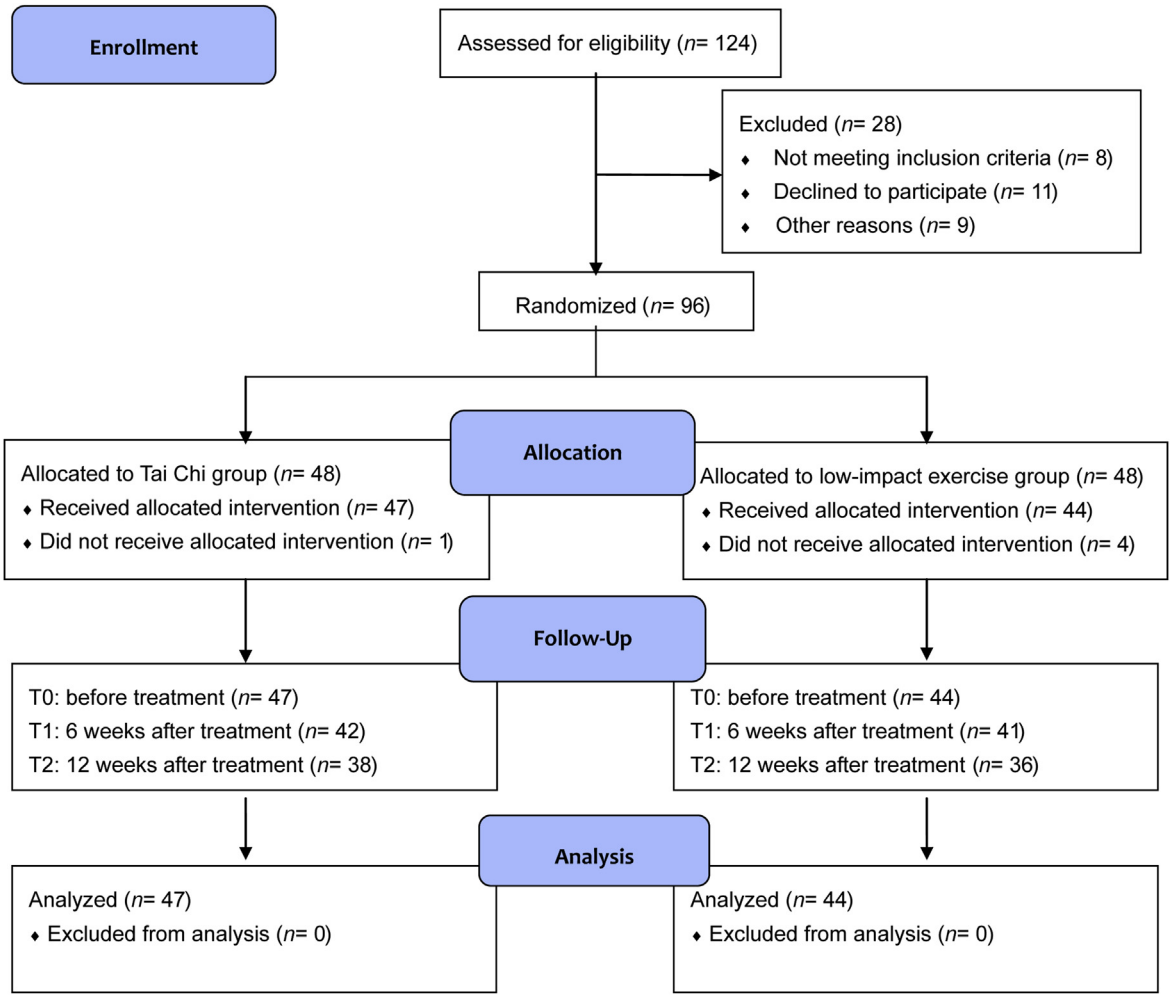

Fig. 2. Flow of participants through each stage of the trial.

Table 1
Baseline Characteristics of Study Participants by Randomized Group

Characteristic	Tai Chi ($n = 47$)	Control ($n = 44$)	χ^2	P
Age			0.321	0.571
≤60	25	26		
≤60	22	18		
Gender			0.823	0.364
Male	37	31		
Female	10	13		
Education			0.963	0.618
≤Sixth grade	29	30		
Junior high or high school	12	11		
≥College	6	3		
Marital status			1.248	0.264
Single	8	4		
Not single	39	40		
Type of lung cancer			0.165	0.685
NSCLC	38	37		
SCLC	9	7		
Stage			0.435	0.933
I	2	1		
II	4	4		
III	10	11		
IV	31	28		
Smoking status			0.008	0.930
Nonsmoker	25	23		
Smoker	22	21		
Performance status			0.538	0.764
0	24	25		
1	15	11		
2	8	8		
Chemotherapy regimens			0.180	0.914
DDP + NVB	20	20		
DDP + GEM	18	17		
DDP + Vp16	9	7		
Chemotherapy response			0.158	0.691
CR + PR	28	28		
SD + PD	19	16		

NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer; DDP = cisplatin; NVB = vinorelbine; GEM = gemcitabine; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease.

various descriptors of fatigue have been experienced in the past week. Responses are made on a five-point scale, ranging from 0 = not at all to 4 = extremely. A total fatigue score may be calculated by subtracting the vigor subscale score from the sum of the four fatigue subscales. The MFSI-SF is effective in fatigue assessment, with the Cronbach α of the total scale and subscales ranging between 0.83 and 0.92.[22,23] The secondary outcomes were the scores on the five subscales of the MFSI-SF: general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor.

The MFSI-SFs were assessed when patients were admitted to the hospitalized chemotherapy at three time points: T0: before the first course of chemotherapy; T1: before the third course of chemotherapy; and T2: at the end of the fourth course of chemotherapy. The MFSI-SF assessments were scheduled on the first day, 43rd day, and 85th day of the chemotherapy course. When the chemotherapy cycle was delayed, the MFSI-SF assessments also were postponed. The MFSI-SF assessment schedule also is shown in Figure 1.

Statistical Analyses

Between-group differences in demographic and baseline variables were tested with a chi-square test for categorical variables. MFSI-SF scores were compared by mixed linear model for repeated measures. $P < 0.05$ was considered significant. All statistical analyses were performed using IBM SPSS, version 19.0 (IBM Corp., Armonk, NY).

Results

Baseline Characteristics of Participants

Between January 2012 and December 2014, 96 patients were enrolled in this trial. A recruitment and randomization flow chart is shown in Figure 2. Five patients assigned to the Tai Chi group ($n = 1$) and low-impact exercise control group ($n = 4$) withdrew immediately after randomization because they were no longer interested. Table 1 summarizes baseline data for the 91 patients after randomization. Patients had a mean age

Table 2
Fatigue Scores Over Time in the Two Groups

MFSI-SF	Group	T0: Before Treatment		T1: Six Weeks After Treatment		T2: 12 Weeks After Treatment	
		n	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
Total score	Tai Chi	47	46.0 (11.6)	42	59.5 (11.3)[a]	38	53.3 (11.8)[a]
	Control	44	46.8 (12.2)	41	66.8 (11.9)	36	59.3 (12.2)
General fatigue	Tai Chi	47	15.3 (3.8)	42	18.1 (4.6)[a]	38	17.5 (4.4)[a]
	Control	44	15.5 (3.6)	41	20.4 (4.5)	36	19.2 (4.6)
Physical fatigue	Tai Chi	47	14.6 (4.1)	42	17.5 (4.4)[a]	38	15.1 (4.6)[a]
	Control	44	14.5 (3.9)	41	19.1 (4.5)	36	17.1 (4.5)
Emotional fatigue	Tai Chi	47	18.4 (3.2)	42	20.2 (3.6)	38	19.1 (3.9)
	Control	44	17.5 (3.3)	41	20.0 (3.5)	36	19.3 (3.5)
Mental fatigue	Tai Chi	47	15.3 (4.2)	42	18.2 (4.0)	38	16.6 (3.7)
	Control	44	14.6 (4.1)	41	18.9 (3.9)	36	16.3 (3.6)
Vigor	Tai Chi	47	16.8 (3.5)	42	14.5 (3.3)[a]	38	15.0 (3.5)[a]
	Control	44	16.1 (3.4)	41	11.6 (3.4)	36	12.6 (4.9)

[a]Compared with control group (low-impact exercise) $P < 0.05$.

of 62.8 years, and 7.47% were male. Baseline characteristics were well balanced between the two groups ($P > 0.05$). The mean MFSI-SF total score and five subscale scores at baseline were also similar between the Tai Chi group and the control groups (Table 2, T0).

MFSI-SF Total Score

At six weeks, the Tai Chi group lost five patients, and the control group lost three patients, all because of intolerance to chemotherapy. The MFSI-SF total score significantly increased compared with baseline because of chemotherapy. However, the Tai Chi group had a lower MFSI-SF total score compared with the control group (59.5 ± 11.3 vs. 66.8 ± 11.9, $P < 0.05$).

At 12 weeks, the Tai Chi group lost four patients (three because of chemotherapy intolerance, and one died). The control group lost five patients (three were intolerant to chemotherapy, and two died). The Tai Chi group also had a lower MFSI-SF total score compared with the control group (53.3 ± 11.8 vs. 59.3 ± 12.2, $P < 0.05$).

Table 2 and Figure 3 show the changes from baseline to six and 12 weeks in the two groups for MFSI-SF total score.

MFSI-SF Subscale Scores

At six weeks, the Tai Chi group had lower MFSI-SF general subscale scores (18.1 ± 4.6 vs. 20.4 ± 4.5, $P < 0.05$) and physical subscale scores (17.5 ± 4.4 vs. 19.1 ± 4.5, $P < 0.05$), and higher MFSI-SF vigor subscale scores (14.5 ± 3.3 vs. 11.6 ± 3.4, $P < 0.05$), compared with the control group. No significant differences were found in emotional subscale (20.2 ± 3.6 vs. 20.0 ± 3.5, $P > 0.05$) and mental subscale (18.2 ± 4.0 vs. 18.9 ± 3.9, $P > 0.05$) scores between the Tai Chi group and the control group.

At 12 weeks, the Tai Chi group also had lower MFSI-SF general subscale scores (17.5 ± 4.4 vs. 19.2 ± 4.6, $P < 0.05$) and physical subscale scores (15.1 ± 4.6 b = vs. 17.1 ± 4.5, $P < 0.05$), and higher MFSI-SF vigor subscale scores (15.0 ± 3.5 vs. 12.6 ± 4.9, $P < 0.05$), compared with the control group. Again, no significant differences were found in emotional subscale (19.1 ± 3.9 vs. 19.3 ± 3.5, $P > 0.05$) and mental subscale (16.6 ± 3.7 vs. 16.3 ± 3.6, $P > 0.05$) scores between the Tai Chi group and the control group.

Table 2 and Figure 4 show changes from baseline to six and 12 weeks in the two groups for the five MFSI-SF subscale scores.

Discussion

CRF is commonly found in patients with cancer. Even in early-stage non−small cell lung cancer survivors, the prevalence of CRF is 57%.[24] Our randomized controlled intervention trial found that the Tai Chi group had a lower MFSI-SF total score compared with the control group at six- and 12-week follow-up

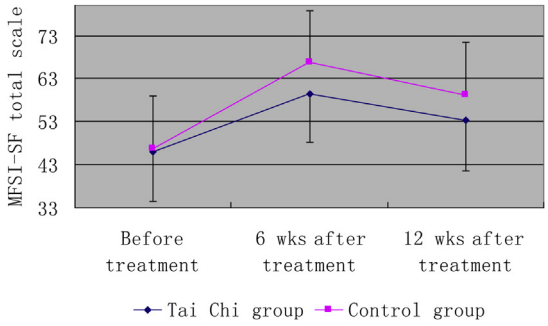

Fig. 3. Multidimensional Fatigue Symptom Inventory−Short Form (MFSI-SF) total score in Tai Chi group and control group (low-impact exercise) at three time points (before treatment: $P > 0.05$; six weeks after treatment: $P < 0.05$; 12 weeks after treatment: $P < 0.05$). *Error bars* indicate the standard deviation.

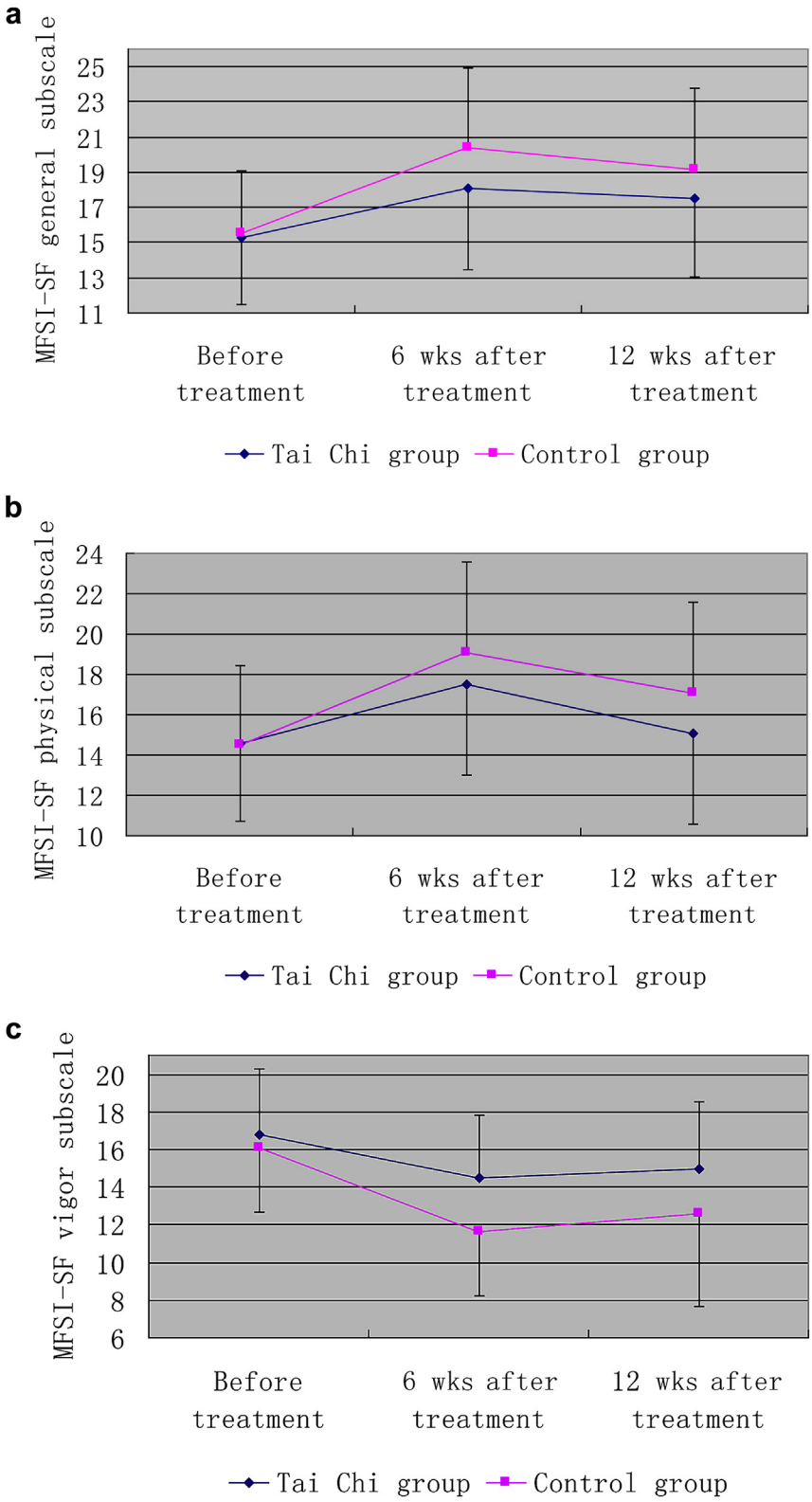

Fig. 4. Five subscales of Multidimensional Fatigue Symptom Inventory—Short Form (MFSI-SF) in Tai Chi group and control group (low-impact exercise) at three time points. a) General subscale: before treatment: $P > 0.05$; six weeks after treatment: $P < 0.05$; 12 weeks after treatment: $P < 0.05$. b) Physical subscale: before treatment: $P > 0.05$; six weeks after treatment: $P < 0.05$; 12 weeks after treatment: $P < 0.05$. c) vigor subscale: before treatment: $P > 0.05$; six weeks after treatment: $P < 0.05$; 12 weeks after treatment: $P < 0.05$. *Error bars* indicated the standard deviation.

(59.5 ± 11.3 vs. 66.8 ± 11.9, $P < 0.05$; 53.3 ± 11.8 vs. 59.3 ± 12.2, $P < 0.05$, respectively.) The results showed Tai Chi was an effective intervention for managing CRF in patients with lung cancer undergoing chemotherapy. The mechanisms for CRF are still unclear, but possibly include 5-HT neurotransmitter dysregulation, vagal afferent activation, alterations in muscle and ATP metabolism, hypothalamic–pituitary–adrenal (APH) axis dysfunction, circadian rhythm disruption, and cytokine dysregulation.[25] In a 1989 study by Jin, the practice of Tai Chi increased heart rate and noradrenaline excretion in urine, and decreased salivary cortisol concentration, tension, depression, anger, fatigue, confusion, and state anxiety. The participants felt more vigorous, and they had less total mood disturbance.[26] Lu et al. found the short-term effect of Tai Chi was to enhance vagal modulation and tilt the sympathovagal balance toward decreased sympathetic modulation.[27] Lin et al. and Lu et al. also found that Tai Chi exercise can improve muscle strength for older people.[28,29] Tai Chi exercise can effectively regulate the APH axis, with lower cortisol area under the curve ($P = 0.02$),[30] and cortisol change ($r = 0.74$; $P < 0.05$).[31] Irwin et al. reported levels of toll-like receptor-4-activated monocyte production of interleukin-6 and tumor necrosis factor combined had an overall reduction ($P < 0.02$), and interleukin-6 ($P = 0.07$) and tumor necrosis factor ($P < 0.05$) individually in the Tai Chi group.[32] According to this research, we found Tai Chi can decrease CRF by enhancing vagal modulation, improving muscle strength, regulating the APH axis, and reducing some cytokines. These may be the reasons why Tai Chi is an effective intervention for CRF.

Our results found that the Tai Chi group had lower MFSI-SF general subscale scores (18.1 ± 4.6 vs. 20.4 ± 4.5, $P < 0.05$) and physical subscale scores (17.5 ± 4.4 vs. 19.1 ± 4.5, $P < 0.05$), and higher MFSI-SF vigor subscale scores (14.5 ± 3.3 vs. 11.6 ± 3.4, $P < 0.05$), but no significant differences were found in emotional (20.2 ± 3.6 vs. 20.0 ± 3.5, $P > 0.05$) and mental (18.2 ± 4.0 vs. 18.9 ± 3.9, $P > 0.05$) subscale scores, compared with the control group. However, some other studies found Tai Chi exercise could affect psychosocial status. Taylor-Piliae et al. reported that following a 12-week Tai Chi exercise program, all measures of psychosocial status were statistically improved ($P \leq 0.05$), especially in mood ($\eta^2 = 0.12$), and perceived stress ($\eta^2 = 0.13$).[33] Our study did not find differences in emotional and mental scores between the Tai Chi and low-impact exercise groups. Perhaps low-impact exercise also can improve the emotional and mental effects of fatigue.

There are some limitations in this study. First, we followed participants undergoing chemotherapy for only 12 weeks, so the long-term effectiveness of Tai Chi in patients with lung cancer remains to be determined. Second, this was a behavioral intervention, "open label" trial. The participants knew to which group they had been assigned. Therefore, it was impossible to blind the participants or data collector.

In conclusion, our preliminary findings indicate that Tai Chi is an effective intervention for managing CRF in patients with lung cancer undergoing chemotherapy, especially for decreasing general and physical fatigue and increasing vigor. Longer term studies with larger clinical samples are warranted to confirm and expand the findings of this study.

Disclosures and Acknowledgments

All authors declare no potential conflicts of interest.

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