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Research article

Effects of Taichi and Cardiac Health, Ejection Fraction among Cancer Patients: A Pilot Study (TICHEFCAP)

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Abstract

Background: A particular chemotherapy, such as Adriamycin or Trastuzumab, has been reported to cause worsening cardiac functions. Previous studies showed that Tai chi may enhance some favorable cardiovascular effects with a better quality of life. Nonetheless, there is inadequate evidence to prove Tai chi as a standard of care for cardiac health, and ejection fraction, especially in cancer patients. **Objective:** To investigate the effects of Tai chi for cardiac health and ejection fraction in cancer patients. **Methods:** A single-blinded, non-randomized controlled trial was conducted in 30 cancer patients who were sent for echocardiogram before receiving either Adriamycin or Trastuzumab and allocated into either Tai chi or control group. Primary outcomes were LV systolic function and global longitudinal strain (GLS) measured by one blinded cardiologist. Whilst, secondary outcomes included the quality of life measurement by FACT-G score and distress thermometer scale. **Results:** Data of 18 cancer patients were analyzed (9 patients in each group). For primary outcomes, LV systolic function was increased by 1.44±1.74 % in Tai chi group and decreased by 1.11±4.91 % in control group (p-value = 0.161). When adjusted for confounding factor, the Tai chi group had 4.37% improvement in LV systolic function when compared with the control group (p=0.087). Whereas, GLS was improved by 0.56±1.51 in the Tai chi group and worsened by 0.67±3.46 in the control group (p-value = 0.301). Tai chi also yielded a better quality of life demonstrated by higher post treatment FACT G score (5.25±16.21 in the Tai chi group and 2.56±5.85 in the control group, p-value = 0.647). Nonetheless, distress thermometer scale was lower in the Tai chi group, with the difference of 0.56±2.79 in the tai chi group and -0.11±1.54 in the control group (p-value = 0.538). **Conclusion:** Tai chi demonstrates favorable outcomes in the improvement of cardiac function (LV systolic function and GLS), with trend of higher quality of life among cancer patients receiving cardiotoxic chemotherapy agents.

Keywords: Tai chi, GLS, LV systolic function, Chemotherapy, Cancer patients

Introduction

Cancer has been a leading cause of death worldwide for decades. In 2012, there were 14.1 million patients diagnosed with cancer globally, with a trend to be 23.5 million individuals in 2030, similar to Thailand. Whilst, the beneficial mainstay of cancer treatment is chemotherapy despite inevitable side effects physically and spiritually. One of the most concerning chemotherapy's complications is myocardial dysfunction and heart failure[1]. One of the current criteria for

diagnosis of cancer therapeutics–related cardiac dysfunction (CTRCD) according to ESC guideline is a decrease >10 % of LVEF to below normal limit or reduction of global longitudinal strain (GLS) >15% from baseline. GLS is an esta-blished echocardiographic modality used in tracking of myocardial deformation[1]. Peak GLS appears to be the most consistent parameter for assessing early reduction in subclinical myocardial dysfunction[2], especial-ly in CTRCD.

Particular chemotherapy agents, such as anthracyclines and HER2 receptor antagonist, are highly associated with cardiotoxicity from earlier reports[3]. A study showed that heart failure usually occurs within 5-72 weeks after HER2 receptor antagonist. Also, asympto-matic LV dysfunction can occur within 6-132 weeks and might return to baseline within 191 days or around 6-7 months after drug discontinuation. In anthracycline group, the risk of symptoms and LV dysfunction depends on accumulated doses. For example, doxorubicin 400 mg/M2 has 3-5% chance of LV dysfunction, while a dose of 550 mg/M2 has 7-26% chance of LV dysfunction[3]. At present, there are still no effective interventions confirmed to prevent CTRCD. Nonetheless, previous studies proposed that aerobic exercise can prevent the deteriora-tion of heart function. In 2011, Haddadzadeh MH performed a RCT in patients with coronary artery disease to compare between exercise and control groups. After 12 weeks, the exercise group significantly had an increase in LV systolic function compared to the control group (46.9 %± 5.9 to 61.5 % ± 5.3 in the exercise group and 47.9% ± 7.0 to 47.6 % ± 6.9 in the control group, P=0.001)[4]. Aerobic exercise is recommended as a method for cardio protection and heath-promotion in cancer patients following the guideline[1]. However, practicing aerobic exercise requires a combination of physical and mental fitness. During chemotherapy session, most patients suffer from the deterioration of physical and mental health, resulting in reluctant to exercise. Thus, an exercising alternatively with lower intensity may be more suitable and persuasive for patients. Since 18th century AD, Tai chi has been proved for its benefits and safety among millions of Chinese people practicing this meditative exercise, with flowing and low intensity movements to help maintain their well-being. Additionally, Tai chi has recently been introduced to other parts of the world and virally gained popularity. Not only in healthy people, the benefits in various diseases have but also been reported in previous study for those with cancer, osteoarthritis, heart failure and chronic obstructive pulmonary diseases[5–9]. In cancer patients, a number of studies have suggested that Tai Chi can improve aerobic capacity, muscle strength, QOL, etc[3,10].

In 2014, a review by Hartley L from 13 studies on Tai chi in preventing cardio-vascular disease showed inconclusive results on isometric exercise's effective-ness[11]. In 2017 Shirley S M Fong[12] conducted RCT in 54 breast cancer survivors, with an improve-ment in blood oxygenation and quality of life observed after 3 months of Tai chi. Meanwhile, the efficacy of Tai chi on cardiovascular prevention was noted in previous studies, most of which were done in those with other diseases or post chemotherapy. To date, there have been few studies on Tai chi among cancer patients in Thailand. Hence, this pilot study was designed and conducted to investigate Tai chi's effectiveness and its application in Thai cancer patients during CMT

Objectives

Primary outcome: To study the effects of Tai chi for the improvement of LV systolic function and global longitudinal strain (GLS).

Secondary outcomes: To measure the spiritual and physical effectiveness of Tai chi, such as quality of life by FACT-G score and distress thermometer scale described in supplement data, as well as BW, BMI, and vital sign.

Materials and methods

Subjects

Patients at Chulabhorm Hospital who were sent from oncologists before receiving either Adriamycin or Trastuzumab between October 2018 and January 2020 were recruited. The participants would be enrolled according to the inclusion criteria and the signed written informed consent. The Inclusion criteria were 1) Diagnosed with breast cancer or lymphoma, 2) Planning to receive or now receiving either Adriamycin or Trastuzumab during follow-up period, 3) Aged 18-80 years, 4) No physical limitation prohibiting the exercise, as well as able to balance and poise without equipment, 5) Agreeing to communicate routinely by phone and message, 6) Willing to engage in the exercise as planned, and 7) Having no clinical diagnoses of mental disorders.

Exclusion criteria included 1) Distance metastasis in crucial organ such as brain, 2) Diagnosed with DVT or PE or on current anticoagulant 3) Baseline LV dysfunction (defined as LVEF <53 %) or severe structural heart disease such as valve pathology, 4) Low quality echocardiogram image such as poor window, frequent arrhythmia, 5) Difficulty in communication or self-practice such as no cell phone, no internet, no VDO player, and 6) High risk of bleeding or coagulopathy.

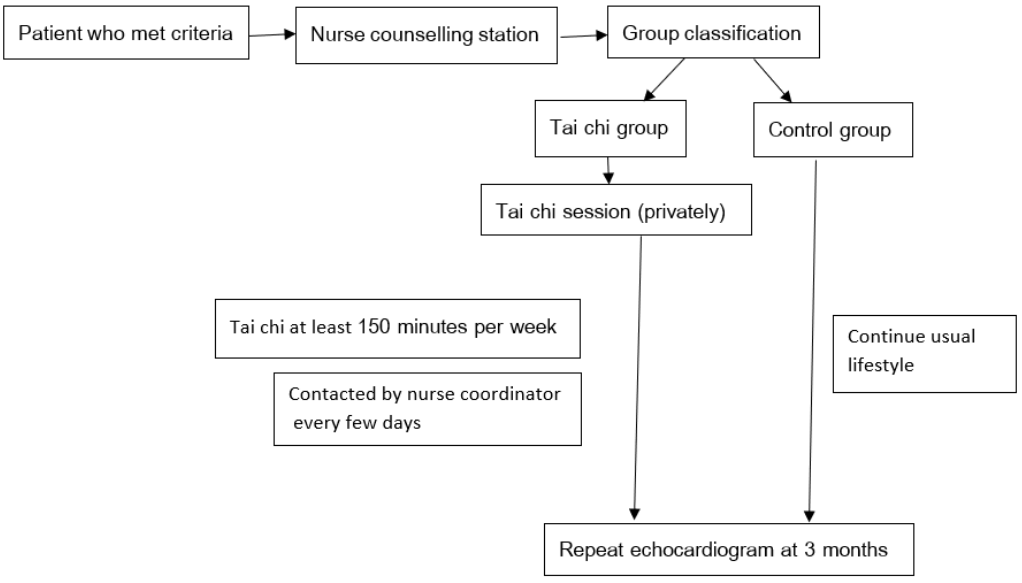

Figure 1: Protocol flow diagram

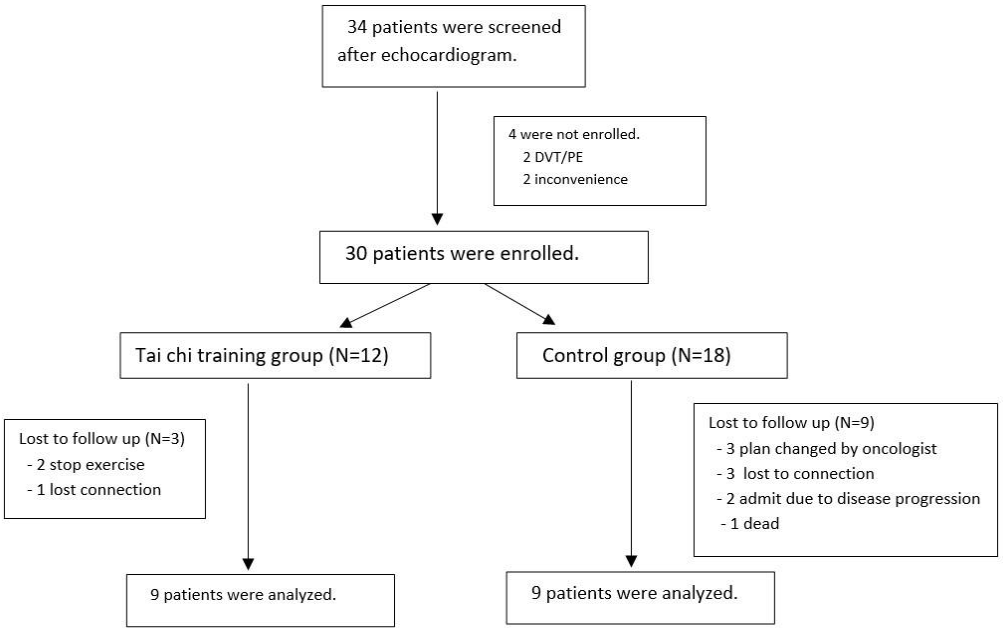

Figure 2: Flow diagram

Protocol

The protocol was reviewed and approved by Human Research Ethics Committee of Chulabhorn Research Institute (Project code: 035/2561). The protocol team of study comprised of 12 Counselling nurses who passed Tai chi workshop training with postures proved by Tai chi master, and 3) Nurse coordinators who communicated with patients by telephone and message to ensure that Tai chi should be done as planned.

After the echocardiogram, all parameters were measured. The patients were sent to see the counselling nurses for data collection, with a short course about Tai chi and how to practice. With the filled out FACT-G and distress thermometer form, the patients then independently decided whether they would participate and which group they wanted to join in. Next, a team of nurses arranged one practice session demonstrating and correcting the postures for patients in Tai chi group individually. The Tai chi group was sent home with CD and youtube link of the practice media. They were contacted every few days to assure the Tai chi practice approximately 150 minutes per week. All the participants should record their exercise by phone and send to the nurse coordinators for verification. The control group was also contacted every week asking about their well-beings. Every patient continued treatment according to the oncologist's plan without any interruption. After 3 months, all patients were called back for echocardiogram.

Intervention

There were 18 forms of Tai Chi postures as in the supplement.

Statistical analysis

Demographic data or category data were presented in frequency and percentage. Whilst, continuous data were described in mean ± SD. Normality of distribution was tested by Shapiro-Wilk normality test. Pre and post treatment was compared by paired t-test. Group comparison was done by independent t-test for continuous data and fisher's exact test for category data. Regression analysis was used to control confounding factors.

Results

A total of 30 patients were enrolled and 18 of them were analyzed at second visit (9 patients in each group). Baseline characteristics were shown in Table 1. Most subjects were female with breast cancer, while only few were lymphoma receiving Adriamycin. Participants who chose Tai chi tended to be with more cardiovascular risk (DM, HT, DLP), higher BMI, and totally unemployed. Bassline LV function and GLS was similar in both groups. Tai chi group was noted with lower quality of life according to higher distress thermometer and lower FACT-G. After intervention, the Tai Chi group was likely to have 1.44% higher LV function by compared to 1.11% lower in the control group, with no statistical significance as shown in figure 2. Furthermore, after the adjusted baseline confounding factor, there was a percentage change in the Tai chi group with improvement of 4.37% in LVEF (p-value = 0.087).

Table 1: Baseline characteristics

Baseline	Total patients (N=30)	Tai chi group (N=9)	Control group (N=9)	p-value**
Age (years)	54.23 ± 11.90	56.67 ±7.86	52.00 ±10.70	0.307
Female	24 (80.0)	7 (77.8)	8(88.9)	1.000
Employed	11 (36.7)	0 (0.0)	5(55.56)	0.029
Breast cancer	22 (73.3)	7(77.8)	8(88.9)	1.000
Cancer stage				0.603
1	8(26.7)	2(22.2)	3(33.3)	
2	7(23.3)	2(22.2)	1(11.1)	
3	10(33.3)	3(33.3)	5(55.6)	
4	5(16.7)	2(22.2)	0(0.0)	
Hypertension	1(26.7)	4 (44.4)	1 (11.1)	0.294
Diabetes	4(13.3)	2(22.2)	0(0.0)	0.471
Dyslipidemia	6(20.0)	2(22.2)	0(0.0)	0.471
Trastuzumab	11 (36.7)	5(55.6)	6(66.7)	1.000
Herb	7(23.3)	1(11.1)	4(44.4)	0.294
Smoke	0(0.0)	0(0.0)	0(0.0)	1.000
Alcohol	7(23.3)	0(0.0)	0(0.0)	1.000
Body weight (Kg)	66.31 ±16.32	69.31 ±21.19	60.13 ±9.19	0.251
BMI (kg/m^2)	26.19 ± 6.00	27.88 ±8.08	24.24 ±2.90	0.221
SBP (mmHg)	120.10 ±15.63	119.44 ± 13.60	119.00 ±15.07	0.948
DBP (mmHg)	70.13 ±12.85	69.22 ±15.23	71.00 ±8.83	0.766
Pulse (/min)	82.53 ±12.99	77.00 ±9.97	77.44 ±7.16	0.915
Baseline LVEF (%)	64.30±3.94	64.67 ±4.15	63.33 ±3.93	0.495
Baseline GLS	-17.17 ±8.06	-20.11 ±2.76	-20.33 ±2.83	0.868
Follow up time (days)	159.50±55.23	117.67±37.55	183.33±51.44	
FACT-G score	81.79±14.59	76.63±19.06	82.56±12.72	0.457
Distress thermometer scale	2.31±2.28	3.44±2.35	1.33±1.41	0.035

*GLS = Global longitudinal strain, SBP = systolic blood pressure, DBP = diastolic blood pressure

** p-value comparing Tai chi group and control group

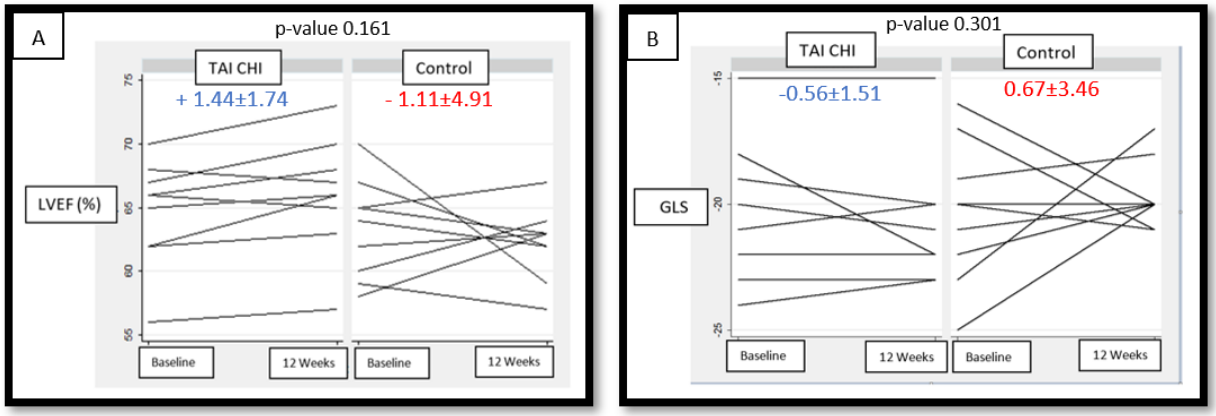

Figure 3: Primary outcomes. (A) Change in LV systolic function baseline to 12 weeks, (B) Change in GLS from baseline to 12 weeks

Table 2: Secondary outcome

Outcome	Tai chi group(N=9)	Control group (N=9)	p-value
Difference in FACT-G score	5.25±16.21	2.56±5.85	0.647
Difference in distress thermometer scale	0.56±2.79	-0.11±1.54	0.538
Difference in BMI*	-0.51±1.46	0.11±1.45	0.382

*Difference defined as second time value minus first time value

For secondary outcome, the Tai chi group tended to have better quality of life after intervention following the higher difference in FACT-G score of 5.25±16.21 compared to 2.56±5.85 in the control group (p-value = 0.647). When look into each part of the questionnaire, the difference was driven by the emotional well-being and function well-being part. On the contrary, difference in distress thermometer scale was better in the control group (increase by 0.56±2.79 in the Tai chi group and decrease by -0.11±1.54, p-value = 0.538) as shown in Table 2. Tai chi also yielded the benefit in losing weight, illustrated by a decrease in BMI of 0.51±1.46 in the Tai chi group, but an increase in BMI of 0.11±1.45 in the control group (p-value = 0.382).

Discussion

Despite no statistical significance, our pilot study showed that Tai chi could be effective in cancer patients who received high risk cardiotoxic chemotherapy towards the enhancement of their cardiac heath by increasing LV systolic function and improving GLS. Our finding supported prior studies in which Tai chi exhibits the improvement in cardiac capacity among cancer patients[12–15]. All participants in the Tai chi group satisfied with the outcome of Tai chi exercise to make them feel stronger. They would want to continue practicing Tai chi even after completing chemotherapy. The intervention required high cooperation and willingness, thus this controlled the participants' allocation and force to do Tai chi, resulting in low compliance. Nonetheless, it was still

necessary in a large amount of patients, which should be feasible in further non pilot study. Main reasons that some participants participated were that they were overweight and wanted to lose weight, which was obviously noted in baseline characteristics of higher BMI in the Tai chi group. Whilst, those in the control group refused Tai chi exercise due to: 1) Time, which was explainable by the higher employment rate in the control group at baseline, 2) Being afraid of trying new things due to negative attitudes. A few patients, though having cancer, they didn't want to do anything, which was compatible to baseline of higher FACT-G and distress thermometer scale.

The variability between FACT-G score and distress thermometer score, despite non-significant, could be caused by the difference in specifications. Both questionnaires, as in the detailed supplement, were created and widely used for the evaluation of cancer patients, especially when involving each patient's mental problems. FACT-G score has become a more descriptive questionnaire with Cronbach's coefficient alpha of 0.89[16] and 0.83 in Thai version[17]. Distress thermometer scale implemented by NCCN also has been a screening tool with a scale of 0-10. Thus, we believed that Tai chi could improve the quality of life.

Tai chi is a safe exercise training since no adverse events reported previously by Wayne PM in 2014[14]. The study reviewed 153 Tai chi studies, with 50 studies reported on Tai chi's non-vital, no additional treatment side effects. In the meantime, there was no side effect reported in our study.

In conclusion, the result of our pilot study suggested that Tai chi could have a positive influence on cardiac health and functions, as well as the quality of life among cancer patients receiving adriamycin or trastuzumab. Giving this favorable finding in our small pilot study, further research should be warranted to confirm its significance and future implementation of this practice in routine protocols. Moreover, additional larger sample size RCT to monitor the practice within the hospital should be applied for practice guideline development.

Whereas, our study has several limitations. As a pilot study, a small group of patients should be expected. A multicenter study or longer period of enrollment is also needed for further future study if a larger number of patients is required. Additionally, the non-randomization method of our study has to be adjusted for the confounding factors during analysis. Importantly, the inability to blind patients could not be done because our assignment needed participants' acknowledgment; however, we did blind the interpreter. Since most of the participants were inconvenience to come for practicing at the hospital, the evaluation for compliance was implemented by narrative from the participants. For more accuracy, the in-hospital exercise monitoring is recommended for future study.

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