Effects of a six-month Tai Chi Qigong program on arterial hemodynamics and functional aerobic capacity in survivors of nasopharyngeal cancer

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Abstract

Purpose: Survivors of nasopharyngeal cancer (NPC) often sustain cardiovascular complications after conventional cancer treatments. Tai Chi (TC) Qigong training may be a viable way to improve peripheral circulatory status and aerobic capacity in this population. The objective of this study was to evaluate the effects of a 6-month TC Qigong training program on blood flow velocities and resistance, palmar skin temperature and functional aerobic capacity in survivors of NPC.

Methods: Twenty-five and 27 survivors of NPC volunteered to join the intervention group (mean age: 55.4±7.5 years) and control group (mean age: 58.7±9.5 years), respectively. The intervention group underwent a TC Qigong training program - the modified 18 Forms TC Internal Qigong - for 6 months, while the control group received no training. Peripheral arterial blood flow velocities and resistance, palmar skin temperature and functional aerobic capacity were measured by a Doppler Ultrasound machine, an infrared thermometer and six-minute walk test, respectively. All outcomes were assessed at baseline, mid-intervention (3-month), post-intervention (6-month) and follow-up (12-month) periods.

Results: The TC Qigong group had higher diastolic blood flow velocity (p=0.010), lower arterial blood flow resistance (p=0.009) and higher palmar skin temperature (p=0.004) than the control group after TC Qigong training. However, only the diastolic blood flow velocity was higher in the TC Qigong group than in the control group during the no-training follow-up period (p=0.032). Additionally, an improvement in functional aerobic capacity was found in the intervention group after TC Qigong training (p<0.008) but not in the control group over time (p>0.008).

Conclusions: TC Qigong training may improve peripheral circulatory status and functional aerobic capacity among people treated for NPC. However, this is only a pilot study and future definitive trials are needed to confirm the results.

Implications for Cancer Survivors: TC Qigong may have enormous potential as a rehabilitation intervention for survivors of NPC to improve arterial hemodynamics and functional aerobic capacity.

Keywords

Head and Neck Neoplasms; Mind-Body Therapies; Cardiovascular System; Physical Fitness

Introduction

Cardiovascular complications are common after conventional cancer treatments, namely chemotherapy and radiotherapy. For example, the chemotherapeutic agent 5-fluorouracil, which is commonly used to treat nasopharyngeal carcinoma (NPC) [1], can induce arterial spasm and interfere with endothelial function, increase blood thrombogenic properties, increase blood viscosity and transit time and lead to cardiac dysfunction. If it is administered with concomitant radiation therapy, the risk of these vascular complications increases [2]. Radiotherapy itself can also cause accelerated atherosclerosis, particularly in the major vessels [3]. Therefore, the hemodynamics and aerobic capacity in NPC patients and survivors may be compromised following these aggressive cancer treatments.

We are specifically concerned with survivors of NPC, as NPC is endemic in Southeast Asia, Southern China and North Africa, and the incidence rate is high (25 to 50 per 100,000) [4]. NPC may occur at any age, but is usually seen in the 15 to 25 age range, or in the fourth to fifth decade [1]. As NPC therapies have advanced, the survival rate of these relatively young individuals is now high (five-year survival rate: 55%-90%) [1]. A large number of survivors of NPC of different ages may therefore suffer from the residual cardiovascular complications brought on by conventional cancer treatments.

Tai Chi (TC) Qigong, an oriental exercise which combines the movements of Tai Chi and the essence of Qigong (meditation, visualization and breathing techniques), has become increasingly popular among survivors of cancer [5, 6]. Several studies have investigated the effects of these mind-and-body exercises – TC, Qigong and TC Qigong – in managing the cardiovascular changes that result from cancer treatments or aging [5, 7-9]. The randomized controlled study design of Lu et al. [7] demonstrated that TC can improve arterial compliance (i.e., the change in the volume of an artery with a change in pressure) [10] in the elderly. The authors did not, however, measure the change in blood flow, which is essential to the supply of oxygen and nutrients to tissues and cells [11, 12]. Certain studies in China have reported that Qigong training can improve microcirculation by accelerating blood flow and raising skin temperature, and can also change the viscosity of blood and increase the elasticity of blood vessels in cancer patients [8]. Our research team reached the same conclusion, finding that TC Qigong exercise improved blood flow velocities and decreased blood flow resistance in survivors of breast cancer who had received chemotherapy and/or radiotherapy [5]. Using the six-minute walk test (6 MWT) to measure cardiovascular fitness and functional capacity in survivors of breast cancer, Mustian et al. [9] suggested that short-term TC training can improve functional aerobic capacity. Based on the existing evidence, we hypothesized that TC and Qigong training may lower arterial resistance, optimize arterial and cutaneous blood flow, thereby increase skin temperature, and improve aerobic capacity in survivors of cancer. Among the many different forms of TC and Qigong, the modified 18 Forms TC Internal Qigong was selectively tested in this study because evidence suggests that this TC Qigong form could improve blood flow velocities in cancer survivors [5]. No study to date has specifically examined the potential cardiovascular benefits associated with the modified 18 Forms TC Internal Qigong training in survivors of NPC. Therefore, the purpose of this study was to determine the effects of a 6-month TC Qigong training program on blood flow velocities and resistance, palmar skin temperature and functional aerobic capacity in survivors of NPC.

Methods

Participants

We carried out a single-blinded, non-randomized controlled clinical trial. A convenience sample of survivors of NPC was recruited from a medical clinic and a local cancer self-help group between November 2012 and January 2013. The sampling frame included about 200 survivors of NPC. Approximately 60 individuals volunteered to participate in the study, and were screened by a medical doctor prior to participation. They were required to fulfill the following inclusion criteria: (1) had a history of NPC (Epstein-Barr virus-DNA and biopsy test results were positive at diagnosis); (2) had completed conventional medical care at a hospital and were medically stable; (3) were between 40 and 85 years old and had an expected survival time of over one year; (4) were Cantonese and resided in Hong Kong; and (5) had normal cognitive and sensory functions. The exclusion criteria were: (1) still receiving active cancer treatments (e.g., chemotherapy, radiotherapy or traditional Chinese medicine) or rehabilitation during the study period; (2) had chronic disease (e.g., poorly controlled diabetes mellitus or hypertension, or symptomatic orthostatic hypotension); (3) had significant neurological (e.g., a history of stroke), musculoskeletal (e.g., recent fracture), cardiopulmonary (e.g., a history of myocardial infraction or chronic obstructive pulmonary disease) or peripheral vascular disorders that might affect test performances; (4) unable to ambulate independently; (5) took regular anti-hypertensive medication or diuretics; or (6) were smokers. Ethical approval was obtained from the Ethics Committees of the University of Hong Kong and the Hong Kong Institute of Education. Written informed consent was also obtained prior to data collection. All procedures were conducted according to the Declaration of Helsinki concerning human experiments.

Intervention

Participants in the TC Qigong group underwent a training program for 6 months (1.5 hours per session, one session per week) at the Nature Health Qigong Association. Six months of TC Qigong training, which is a kind of aerobic exercise, was needed to elicit improvement in aerobic capacity [13]. A Chinese Healthy Qigong Association certified TC Qigong instructor and an assistant instructor supervised each training session. The TC Qigong training protocol was modified from the 18 Forms Tai Chi Internal Qigong form [6] by a medical doctor and a Qigong master. The protocol is presented in Table 1. This TC Qigong protocol aims to bring the body and mind into balance and to relieve the residual side effects of radiotherapy in survivors of NPC. It places emphasis on meditation and coordinated breathing, together with slow and smooth TC movements [6]. Participants were instructed to report any adverse symptoms during or after the TC Qigong training. They were also asked to maintain their perceived exertion at very light to fairly light levels (i.e., Borg scale ranging from 9 to 12) during practice [11].

Home exercises (using the same TC Qigong form) were prescribed to increase the exercise frequency to three times per week (excluding the TC Qigong class days). The TC Qigong instructor or assistant instructor checked the participants' compliance to this home program every week. The control group received no TC Qigong training, but continued to receive hospital care if necessary.

Outcome measurements

All physical outcomes were measured by a physiotherapist and a trained assistant who were blinded to the subject group before the initiation of the TC Qigong program (pre-test), after 3 months of TC Qigong training (mid-intervention test), immediately after the training ended (post-test) and 6 months after the cessation of TC Qigong training (follow-up test). The hemodynamics assessment procedures took place at the clinic of our co-investigator (Dr. W.S. Luk). The ambient temperature was kept at 22˚C in the assessment room. The six-minute walk test was conducted in a corridor outside the clinic. At pre-test, participants were also asked to provide their demographic characteristics and medical history (Table 2). The baseline physical activity level of each participant was estimated by asking him/her what physical activity he or she was most actively engaged in during a typical week over the past year. The physical activity level [metabolic equivalent (MET) hours per week] was then calculated based on the reported exercise intensity (light, moderate or hard), duration (hours/time), frequency (times/week), and the MET value of the activity according to the Compendium of Physical Activities (Table 2) [14]. Each participant, regardless of grouping, then underwent the following assessments in sequence.

Blood flow velocities and arterial resistance

These outcome parameters reflect the circulatory status, and were measured with the participant in a resting state, sitting on a chair. A plinth was used to support the participant's dominant forearm at about heart level [5]. Arterial blood flow velocities during both systole and diastole phases of the heart were assessed by a Doppler Ultrasound machine (Sonovit CV-30, Schiller AG, Switzerland). This machine has been validated and shown to have good test-retest reliability (ICC=0.76) [15, 16]. A distal part of the radial artery was selected as the measurement site because it is superficial and relatively parallel to the skin surface [17]. The ultrasound transducer, operating at 8 MHz, was fixed at 45° relative to the skin surface in the distal radius region, and was opposite to the direction of blood flow (i.e., pointing proximally). To facilitate the transmission of ultrasound waves, aqueous gel was applied to the skin surface before applying the probe. Both the maximum systolic Doppler frequency and minimum diastolic Doppler frequency were monitored continuously and in real time. When the values of these two parameters became stable over four consecutive Doppler waveforms, they were recorded [15, 16]. The maximum systolic and minimum diastolic Doppler frequencies were then inserted into the following equation to calculate the maximum systolic arterial blood flow velocity (SV) and minimum diastolic arterial blood flow velocity (DV), respectively:

$$F_D \text{ (kHz)} = [f_o \text{ (kHz)} \times 2 \times v \text{ (cm/s)} \times (\cos \Theta)] / c \text{ (cm/s)},$$

where F_D is either the maximum systolic or minimum diastolic Doppler frequency; f_o is the transducer frequency (8MHz); v is the arterial blood flow velocity (SV or DV); Θ is the Doppler angle (45°); and c is the velocity of ultrasound in blood (154,000 cm/s) [18]. The resistance index (RI), representing peripheral blood flow resistance, was derived from the following equation:

RI = (Maximum systolic blood flow velocity – Minimum diastolic blood flow velocity)/Maximum systolic blood flow velocity.

Lower RI values (close to 0) correspond to lower blood flow resistance (continuous blood flow) and higher RI values (close to 1) correspond to higher blood flow resistance (systolic blood flow) [19]. SV, DV and RI were used for analysis.

Palmar skin temperature

To study the hemodynamics of the hand, palmar skin temperature was also assessed. With participants maintaining the same seated posture as mentioned above, the skin temperature was taken twice from the center of the palm (an acupuncture point: Láo gong, PC8) [20] of the dominant hand using an infrared thermometer (Hygenia HST101, Great Eastern Healthcare Ltd., Hong Kong). The measurement range of the device is 32.0˚C-42.9˚C with 0.1˚C precision. The measurement calibration accuracy is ±0.2˚C at 35.5˚C-42˚C and ±0.3˚C at 32.0˚C-35.4˚C [21]. Previous studies have found infrared thermometric measurements of skin temperature in the hand to be reliable (inter-rater reliability: ICC=0.80) [22]. Any moisture was removed before the infrared measurements were taken, as this can interfere with the results [23]. The average palmar skin temperature (˚C) of the two trials was used for analysis.

Functional aerobic capacity

The 6 MWT, a valid and optimal measure of physical endurance in survivors of cancer [9], was conducted according to the guidelines of the American Thoracic Society [24]. Each participant was instructed to walk independently along a 30-meter walkway, and to go as far as possible in six minutes. Walking was self-paced and rests were allowed if necessary. The total distance walked (meters) was recorded. Longer distances covered indicated higher levels of functional aerobic capacity [24]. Participants were also asked to describe the degree of fatigue they felt at the end of the walk. The test-retest reliability of the 6 MWT has been reported to be good ($0.88<r<0.94$) in older adults [25].

Statistical analysis

All statistical analyses were performed using IBM Statistical Package for the Social Sciences version 20.0 software (IBM, Armonk, NY, USA). The normality of continuous data was first checked using the Kolmogorov-Smirnov test. Independent t-tests (for continuous data) and chi-square tests (for nominal data) were used to compare the demographic and baseline characteristics of the TC Qigong group and the control group. To deal with missing data, the intention-to-treat principle was applied; that is, for participants who withdrew early from the study, the last recorded observation was carried over to the subsequent assessments. To test the overall time-by-group interaction effects of TC Qigong training, and to avoid the probability of inflating type I errors, a two-way, repeated measures multivariate analysis of covariance (MANCOVA) (time x group), incorporating all outcome variables, was conducted. If there were significant between-group differences in body height or any of the outcome variables at baseline, the baseline data for the outstanding outcome variables were treated as covariates. Effect sizes (partial eta-squared) were also calculated and values of 0.14, 0.06 and 0.01 represent large, medium and small effects, respectively [26].

After the multivariate analysis, univariate analyses were performed as necessary, using one-way repeated measures analysis of variance (ANOVA), then post-hoc paired t-tests with Bonferroni corrections were applied to each outcome measure. Independent t-tests were also used to compare all of the outcome parameters of the two groups. The significance level was set at 0.05 (two-tailed) and corrected using Bonferroni's method, specifically for the paired t-tests (i.e. alpha=0.008 due to six pairwise comparisons), to maintain an overall type one error rate of 5%.

Results

Fifty-two survivors of NPC met the inclusion criteria and were deemed eligible to participate in the study. Twenty-five participants joined the TC Qigong group and the rest (n=27) joined the control group. Of these, 17 (32.7%) dropped out; 11 from the TC Qigong group and 6 from the control group. Although the attrition rate was slightly higher than expected, the reasons for dropping out were not related to the TC Qigong intervention, and were similar between the two groups (from the TC Qigong group: busy work schedule n=4, illness n=2 and unable to commit the time n=5; from the control group: busy work schedule n=1, unable to commit the time n=1, travelled overseas n=1 and lost to follow up n=3). Thirty-five participants (TC Qigong group n=14, control group n=21) completed the study. No significant differences in baseline characteristics or outcome measures were found between those who dropped out and those who stayed in the study ($p>0.05$) (not shown). Moreover, no adverse training or testing effects were reported by the participants. The average attendance rate of the TC Qigong class reached 90%.

Comparison of baseline characteristics

No significant between-group differences were identified in any of the demographic or outcome variables at baseline ($p>0.05$) (Tables 2 and 3). Therefore, multivariate analysis of variance (MANOVA) instead of MANCOVA was performed.

Changes in blood flow velocities and arterial resistance

The MANOVA results revealed no significant time-by-group interaction effect ($p=0.243$), time effect ($p=0.167$) or group effect ($p=0.736$) for the maximum systolic blood flow velocity (Table 3). However, for the minimum diastolic blood flow velocity, a significant group effect ($p=0.021$) and time effect ($p=0.040$) were identified, although the time-by-group interaction effect was not significant ($p=0.158$). Between-group differences were found at post-test and follow-up. Participants in the TC Qigong group demonstrated 170.5% ($p=0.010$) and 148.3% ($p=0.032$) faster diastolic blood flow velocities than the control group after 6 months of TC Qigong training and 6 months after the cessation of TC Qigong training, respectively. In addition, the diastolic blood flow velocity dropped by 56.6% ($p=0.007$) from the mid-intervention test to the follow-up test in the no-training controls. No significant change in diastolic blood flow velocity was noted in the TC Qigong group over time ($p=0.113$) (Table 3).

No significant interaction effect of time x group ($p=0.135$) or time ($p=0.137$) was found in the arterial resistance index (RI). The group effect was, however, significant ($p=0.027$). Further analysis using independent t-tests revealed that the RI recorded in the TC Qigong group was 18.5% ($p=0.009$) lower than that of the control group immediately after the 6-month TC Qigong training. No significant between-group difference was found at other time points, including the follow-up test ($p>0.05$) (Table 3).

Changes in palmar skin temperature

The multivariate analysis showed a significant time-by-group interaction (*p*=0.004), indicating that overall, the TC Qigong training program induced a higher palmar skin temperature than no training throughout the 12-month study period. Post-hoc analyses revealed that the mean palmar skin temperature increased by 3.2% from pre-test to post-test (*p*=0.001) in the TC Qigong group, while no significant change was detected in the control group over time (*p*=0.331). In fact, the mean palmar skin temperature recorded in the TC Qigong group was 2.6% higher than that of the control group at post-test (*p*=0.004) (Table 3).

Changes in functional aerobic capacity

A significant time-by-group interaction effect (*p*=0.009) and time effect (*p*=0.025), but a non-significant group effect (*p*=0.810), were found for the 6 MWT. The total distance covered within the six-minute period after TC Qigong training (at post-test) was significantly longer than that of the pre-test (*p*=0.007) and mid-intervention test (*p*=0.003) distances. However, this improvement in walking distance was not observed in the follow-up test (*p*>0.05) or in the control group over time (*p*=0.123) (Table 3). All participants reported slight fatigue after the six-minute walk.

Discussion

Blood flow velocities and arterial resistance

The results generally supported our hypothesis that TC Qigong training may reduce arterial blood flow resistance and enhance blood flow velocity in survivors of NPC. Specifically, we found that the intervention group had lower blood flow resistance and higher diastolic blood flow velocity than the control group after TC Qigong training. In addition, the diastolic blood flow velocity was higher in the intervention group than the control group during the no-training follow-up period. A decrease in diastolic blood flow velocity was detected in the control group but not the TC Qigong group over time. These findings are similar to those of our previous study, which showed that TC Qigong training could reduce blood flow resistance and increase blood flow velocity concomitantly in survivors of breast cancer [5].

Why would TC Qigong training induce such favorable vascular outcomes? Several physiological studies suggest the following mechanisms. First, the TC Qigong-trained participants may have had better arterial compliance, which is defined as the change in arterial blood volume due to a given change in arterial blood pressure [10]. The arteries of the TC Qigong-trained participants may have become more elastic (ready to distend) in response to pressure, so blood flow resistance decreased and blood flow velocity increased [7]. Second, vascular resistance may have decreased after TC Qigong training, as it may enhance the integration of hypothalamic responses, resulting in homeostasis of the sympathetic and parasympathetic nervous systems (Qigong psychoneuroimmunology theory) [27]. This may regulate the vasoconstriction and vasodilation of the peripheral arteries more effectively, and hence optimize vascular resistance and blood flow [17]. Third, the viscosity of blood may have changed after TC Qigong training [8], thereby increasing the blood flow velocity. Further studies should explore this theory by examining the effect of TC Qigong training on the viscosity of blood.

Interestingly, we found that the diastolic blood flow velocity, but not the systolic blood flow velocity, was higher in the intervention group than in the control group after TC Qigong training and during the follow-up period. The exact mechanism for this is not known, but it is possibly because peripheral vascular resistance is exclusively associated with diastolic blood flow [28]. Therefore, any change in vascular resistance after TC Qigong training may not affect systolic blood flow.

Palmar temperature

As expected, palmar skin temperature increased significantly (3.2%) following the TC Qigong intervention, whereas the control group showed no significant change. Although this increase was small, it was well above the estimated measurement error level (0.6%-0.9%), indicating that the observed change reflected an actual improvement and was not due to chance. The TC Qigong-trained participants in fact had a 2.6% higher palmar skin temperature than their non-trained counterparts at post-test. The magnitude of increase in palmar skin temperature recorded in this study was smaller than that reported in the Qigong exercise trial of Kuan et al. [29] In their study, older adults who underwent a 12-week Qigong program had a 7.8% increase in distal skin temperature, measured at the index finger, whereas the control group increase was only 0.3%, resulting in a significant between-group difference. Kuo et al. [30] found that palmar skin temperature increased by 2.1% during Qigong training, compared to a resting state, in younger adults.

Taken together, these results show that TC Qigong or Qigong training may lead to an increase in the distal upper limb skin temperature of adults, including survivors of NPC.

The increase in palmar skin temperature after TC Qigong training was associated with enhanced endothelial-dependent dilation in skin vasculature and improved cutaneous microcirculation (i.e., blood flow in the capillaries) [31]. Theoretically, increased cutaneous blood flow should in turn increase oxygen and nutrient supplies to tissues and cells, improve the removal of waste products from cells, strengthen metabolism and achieve an overall anti-tumor effect [8, 12]. However, no prospective intervention study has demonstrated such a link. Further research is required to explore the relationship between blood flow and biopsy results or incidents of cancer recurrence among survivors of NPC. Although palmar skin temperature increased (presumably due to improved cutaneous blood flow) at post-test, the increase was transient and was not detected 6 months after the TC Qigong exercise was terminated. Our results suggest that the long-term and regular practice of TC Qigong may be necessary to sustain this beneficial effect.

Functional aerobic capacity

This study used the 6 MWT as a measure of functional capacity, specifically aerobic capacity, in survivors of NPC [9]. The baseline mean walking distance was 281 m in the TC Qigong group and 296 m in the control group, both of which were far lower than the distances achieved by age-matched healthy elderly people (460m-609m) [32]. A significant improvement in mean walking distance was observed in the TC Qigong group after the 6-month TC Qigong training (9.6%), but not in the control group. Although there was still a big difference between the norm (460 m-609 m) and the post-intervention walking distance (308 m) in the TC Qigong group, our findings generally imply that TC Qigong training may improve aerobic fitness in survivors of NPC. This is consistent with our hypothesis and a previous study in which a 12-week TC training program improved the 6 MWT distance among survivors of breast cancer [9]. The survivors of breast cancer participating in the study of Mustian et al. covered 636 m in the 6 MWT after TC training [9]. Although the absolute distance covered by these participants was longer than that covered by participants in our study after TC/Qigong training, the actual percentage improvement in walking distance was less in theirs (4.4%) than in ours (9.6%). This could be explained by the difference in the intervention duration. TC/Qigong training is considered to be aerobic in nature [33, 34]. Our study required participants to undergo 6 months of TC Qigong, whereas the participants in the Mustian et al. study underwent just 3 months of aerobic exercise (TC) [9]. According to the American College of Sports Medicine recommendations for aerobic exercise training, the first 1.5 months of aerobic exercise is initial conditioning, with progressive training and improvement occurring over the subsequent 4 to 8 months [13]. Our participants spent longer in the improvement stage, and therefore may sustain a greater improvement in aerobic fitness. We also followed this up and assessed aerobic capacity after 12 months, and found no difference between the two groups. The fitness levels of the TC Qigong-trained participants may have decreased 6 months after the cessation of the training.

Limitations

While the results are promising, there are certain limitations to our study. The participants were a self-selected group, who, given the transparent nature of the study, were interested in exploring TC Qigong as a cancer rehabilitation option. These individuals may have been more motivated or physically more capable. Therefore, the significant changes in outcomes may be related to the psychological or physical attributes of the participants rather than the effects of the TC Qigong training [26]. A randomized controlled trial should be carried out to confirm the positive effects of the TC Qigong intervention. A second limitation was the somewhat high attrition rate, which may have introduced some bias into the findings. Further studies may consider giving incentives to the participants to improve the completion rate [26] as well as increasing the sample size.

Conclusion

This novel pilot study showed that TC Qigong training may generally improve peripheral circulatory status and functional aerobic capacity among people treated for NPC. TC Qigong could be a safe and well-accepted form of exercise, with enormous potential as a therapeutic intervention for optimizing arterial hemodynamics and improving aerobic capacity after treatment for NPC. However, this is only a small-scale pilot study and future definitive trials are needed to confirm the results.

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Conflict of interest

The authors declare that they have no conflicts of interest with respect to the authorship or publication of this paper.

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Table

Table 1. Tai Chi Qigong training protocol

Exercise type	**Frequency**	**Intensity**	**Duration**
Warm-up: Jogging		Mild sweating	5 minutes
18 Forms Tai Chi Internal Qigong:			40 minutes
1. Raising the arms and pressing down			
2. Opening the chest			
3. Painting a rainbow from side to side			
4. Separating the clouds with two arms			
5. Rolling the arms in a horse-riding stance			
6. Rowing the boat			
7. Carrying a ball in front of the shoulders			
8. Turning around to look at the moon			
9. Twisting the waist and pushing the palms			
10. Cloud hands in a horse-riding stance			
11. Scooping the sea and searching the sky			
12. Pushing waves in walking stance			
13. Flying dove spreads its wings			
14. Punching in horse stance	TC Qigong	Rating of	

15. Flying like wild geese 16. Rotating a flying wheel 17. Stepping whilst bouncing a ball 18. Pressing down to balance the chi	session: once per week; and home-practice: 3 times per week	perceived exertion: very light-fairly light	
Additional exercises for survivors of NPC:			40 minutes
1. Crossing the arms in front of the chest and curling up the body			
2. Hands behind neck			
3. Olfactory stimulation (breathing in slowly and deeply, imagine smelling a flower)			
4. Inner ear stimulation (use hands to compress the ears externally)			
5. Oral and swallowing training (swallow saliva bit by bit)			
6. Mouth-opening exercise and making sounds with the throat			
Cool-down: Gentle whole-body stretching		Mild tension of muscles	5 minutes

Note: All movements were practiced in sequence. Participants learned one to two new movements per session progressively.

Table 2. Demographic characteristics of the participants

	TC Qigong group (n=25)	**Control group (n=27)**	***P***
Age (year)	55.4±7.5	58.7±9.5	0.172
Sex (men/women, n)	12/13	16/11	0.416
Weight (kg)	59.5±15.1	56.8±10.5	0.451
Height (cm)	163.2±9.1	161.5±8.1	0.496
Body mass index (kg/m^2)	22.3±5.0	21.7±3.3	0.640
NPC stage at diagnosis [35]			
Stage I (n, %)	5 (20%)	2 (7.4%)	
Stage II (n, %)	5 (20%)	7 (25.9%)	
Stage III (n, %)	11 (44%)	15 (55.6%)	
Stage IV (n, %)	4 (16%)	3 (11.1%)	
Post-NPC duration (year)	12.5±7.1	8.4±9.7	0.094
History of NPC treatment			
Radiotherapy only (n, %)	17 (68%)	9 (33.3%)	
Radiotherapy and chemotherapy (n, %)	7 (28%)	18 (66.6%)	
Radiotherapy, chemotherapy and surgery (n, %)	1 (4%)	0 (0%)	

Hypertension (n, %)	5 (20%)	4 (14.8%)	0.621
Diabetes mellitus (n, %)	4 (16%)	2 (7.4%)	0.333
Habitual physical activity level before intervention (MET hours per week)	13.9±14.1	14.9±14.5	0.795

NPC, nasopharyngeal carcinoma; MET, metabolic equivalent.

Mean ± standard deviation presented for continuous variables.

*p<0.05 for between-group comparisons.

Table 3. Outcome measurements

	TC Qigong group (n=25)				Control group (n=27)				Group x Time interaction		Group effect		Time effect	
	Pre	Mid	Post	FU	Pre	Mid	Post	FU	Effect size	*P*	Effect size	*P*	Effect size	*P*
Blood flow velocities and arterial blood flow resistance (radial artery)														
Maximum systolic velocity (cm/s)	26.75±9.12	23.45±10.28	24.99±9.04	23.37±9.39	24.09±9.21	25.58±8.42	23.95±9.69	22.07±9.02	0.028	0.243	0.002	0.736	0.034	0.167
Minimum diastolic velocity (cm/s)	5.86±5.26	3.61±5.67	5.14±5.58[a]	3.65±4.48[a]	3.39±4.48	3.39±3.12	1.90±2.00	1.47±1.97[c]	0.036	0.158	0.102	0.021*	0.060	0.040*
Resistance index	0.81±0.16	0.82±0.29	0.75±0.29[a]	0.86±0.16	0.87±0.13	0.85±0.14	0.92±0.09	0.93±0.12	0.039	0.135	0.094	0.027*	0.039	0.137
Skin temperature														
Middle of the palm (˚C)	34.64±1.40	35.17±1.34	35.76±0.47[a,b]	35.08±1.21	35.14±1.12	35.30±0.70	34.86±1.40	35.33±0.90	0.094	0.004*	<0.001	0.974	0.036	0.149

Functional aerobic capacity														
Six-minute walk test (m)	281.00± 57.66	288.00± 51.32	308.00 ±62.72[b,c]	305.20± 65.90	296.48 ±53.17	287.04 ±50.98	285.19 ±50.34	299.63± 59.71	0.084	0.009*	0.001	0.810	0.068	0.025*

Pre, Pre-test (baseline); **Mid,** Mid-intervention test (3-month); **Post,** Post-test (6-month); **FU,** Follow-up test (12-month).

Mean ± standard deviation presented for continuous variables.

Effect sizes are in partial eta-squared.

Between groups:

[a]Denotes a difference significant at $p<0.05$ when compared with the control group.

Within group:

[b]Denotes a difference significant at $p<0.008$ when compared with pre-test values.

[c]Denotes a difference significant at $p<0.008$ when compared with mid-intervention test values.

(Alpha was adjusted to 0.008 because of six paired comparisons.)

Group by time interaction, group and time effects:

*Denotes a difference significant at $p<0.05$.