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ORIGINAL ARTICLE

Multimodal exercise ameliorates exercise responses and body composition in head and neck cancer patients receiving chemotherapy

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Abstract

Background Studies have found that many chemotherapy drugs will produce multiple side effects and complications in cancer patients, especially in the case of the cardiovascular disease. This study was intended to investigate whether the exercise training intervention could improve the body composition and exercise responses of patients with head and neck (H&N) cancer who are receiving chemotherapy.

Methods This is a randomized controlled trial. Eighty-four H&N patients were assigned to sedentary group or exercise group. The data were collected pretraining and posttraining, where the body composition, heart rate (HR), blood pressure (BP), rate-pressure product (RPP), and exercise capacity were measured.

Results Our data reported that body weight and body mass index were decreased after 8 weeks of chemotherapy in the sedentary group but not in the exercise group. The decreased visceral fat and the increased skeletal muscle rate had been found in the exercise group after 8 weeks of training. In addition, in the exercise group, the HR, HR recovery, BP, BP recovery, RPP, and minutes walking distance were better than the sedentary group. Results from this study suggested exercise training significantly improved exercise responses and body composition.

Conclusion These findings suggested that exercise can help to promote cardiopulmonary fitness and exercise capacity for H&N cancer patients undergoing chemotherapy.

Keywords Head and neck cancer · Exercise training · Exercise responses · Chemotherapy · Body composition

Abbreviations

H&N head and neck
HR heart rate
BP blood pressure
RPP rate-pressure product

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Introduction

Malignant neoplasms have been the top leading cause of death in Taiwan for more than 30 years [4]. In the case of head and neck (H&N) cancer, most chemotherapy treatments involve the use of cisplatin and uracil-tegafur or a single use cisplatin. Anti-cancer medications used to kill cancer cells also affect the body's normal tissue because the anti-cancer drugs are acting on any fast splitting cells, such as bone marrow, gastrointestinal mucosa, the reproductive system, and hair follicle cells, all of which go through fast cell division. The side effects from cancer treatment can occur immediately or within a few hours after treatment, thereby reducing the quality of life [24].

Chemotherapy drugs are already one of the main medical treatments to help cancer patients fight cancer cells [29]. It is well known that chemotherapy drugs not only poison cancer cells but also affect normal cells, leading to tissue or organ damage. However, chemotherapy drugs have been significantly associated with an elevated risk of cardiovascular dysfunction, which may impair the fitness levels and impair the cardiopulmonary fitness [27]. Navidi et al. also reported that 4-week chemotherapy represses the cardiopulmonary fitness in cancer patients [17]. Chemotherapy drugs cause the body to experience high levels of oxidative stress, which affect the cardiovascular system and lead to myocardial cell apoptosis and death caused [2]. The cardiotoxicity includes asymptomatic systolic or diastolic left ventricle dysfunction, which can lead to dilated cardiomyopathy and ultimately to heart failure [14].

Exercise has been shown to be effective in improving the health of many patients who have chronic diseases, such as chronic bronchitis, heart disease (heart failure or coronary artery disease), osteoporosis, depression, cancer [10, 23]. According to the College of Sports Medicine (ACSM), patients need regular exercise to improve health problems, reduce morbidity, reduce depression, increase cardiorespiratory endurance, reduce mortality, and increase bone density and muscle strength [8, 9, 18]. Currently, most studies on exercise intervention have focused on breast cancer patients [20]. Mohamady et al. indicated that after receiving chemotherapy, breast cancer patients given 12 weeks of moderate intensity aerobic exercise were found to have increased hemoglobin and erythrocytes and improvement in anemia [16]. In addition, exercise intervention has been shown to improve cancer-related fatigue and increase psychological comfort [26].

H&N cancer patients are more likely to receive radiation therapy or flap repair surgery and often have shoulder and neck or oral joint mobility reduction problems. Past research, however, has focused on shoulder and neck and oral issues or joint mobility [3], rather than systemic exercise. In addition, studies in cancer patients in the past had involved exercise prescriptions that mainly comprise aerobic exercise and resistance exercise, so a combination of muscle strength training and aerobic exercise training as a multi-mode exercise treatment intervention requires more relevant research support. At last, previous cancer-related studies were focused on the investigation of the exercise effects in patients with completion of cancer treatment such as chemotherapy. The effect of exercise intervention on patients receiving chemotherapy is limited. Mishra et al. reported that exercise training improves health-related quality of life in cancer patients during active chemotherapy [15]. This study was designed to answer whether 8-week exercise intervention could provide positive effects of exercise responses on patients receiving chemotherapy.

Methods

Study participants

This current study was a randomized, controlled, parallel-group trial. The participants for this study were collected from the population of the outpatient clinic in the Hematology and Oncology Department at National Cheng Kung University Hospital (NCKUH), Tainan, Taiwan, from 2016 to 2017. The sample size was referred by previous cancer exercise studies [6, 11]. All participants were assigned to either the sedentary group or the exercise group. The inclusion criteria included (1) ≧20 years old with H&N cancer, (2) H&N cancer diagnosed by pathology, cytology, or imaging, (3) no serious complications, (4) no brain tumor metastasis, and (5) no history of mental illness. The exclusion criteria included (1) those who could not sign the consent, (2) neurological disorders (e.g., stroke), (3) pregnant or lactating women, (4) severe psychiatric disorders (e.g., bipolar disorder and schizophrenia), (5) musculoskeletal disorders that limited mobility (e.g., myopathy, amputation), (6) severe organ failure, and (7) clinically determined to have a survival rate of less than 3 months. All procedures were approved by the ethical committee of National Cheng Kung University Hospital Institutional Review Board, Tainan, Taiwan (B-ER-105-102). After explaining all the experimental procedures in detail, including the possible risks and benefits, each participant provided written consent to participate in the study. A detailed flow of the participants throughout the study is presented as Fig. 1.

Six-minute walk test

The 6-min walk test is an objective evaluation of multifunction exercise capacity and exercise responses. The 6-min walk test site involves walking 30 m on a flat floor where this specific distance is required. The starting and ending points are marked, and the participant continues walking for 6 min [12]. All participants could walk in accordance with their walking speed and were instructed as to the distance range. Before the test, blood pressure (BP), heart rate (HR), oxygen saturation, and rate of perceived exertion (RPE) scores were collected. All participants were measured for their peak in BP, HR, oxygen saturation, and RPE scores throughout the test. A minute and 3 min after the test was completed, the parameters were measured for recovery. In addition, the total number of meters for all of the participants was calculated.

Study protocol for the exercise intervention

The exercise group in this study was undergoing chemotherapy and 8 weeks of exercise intervention. The exercise was divided into two categories: aerobic exercise and resistance exercise for at least 3 days a week. Before the exercise training intervention, the

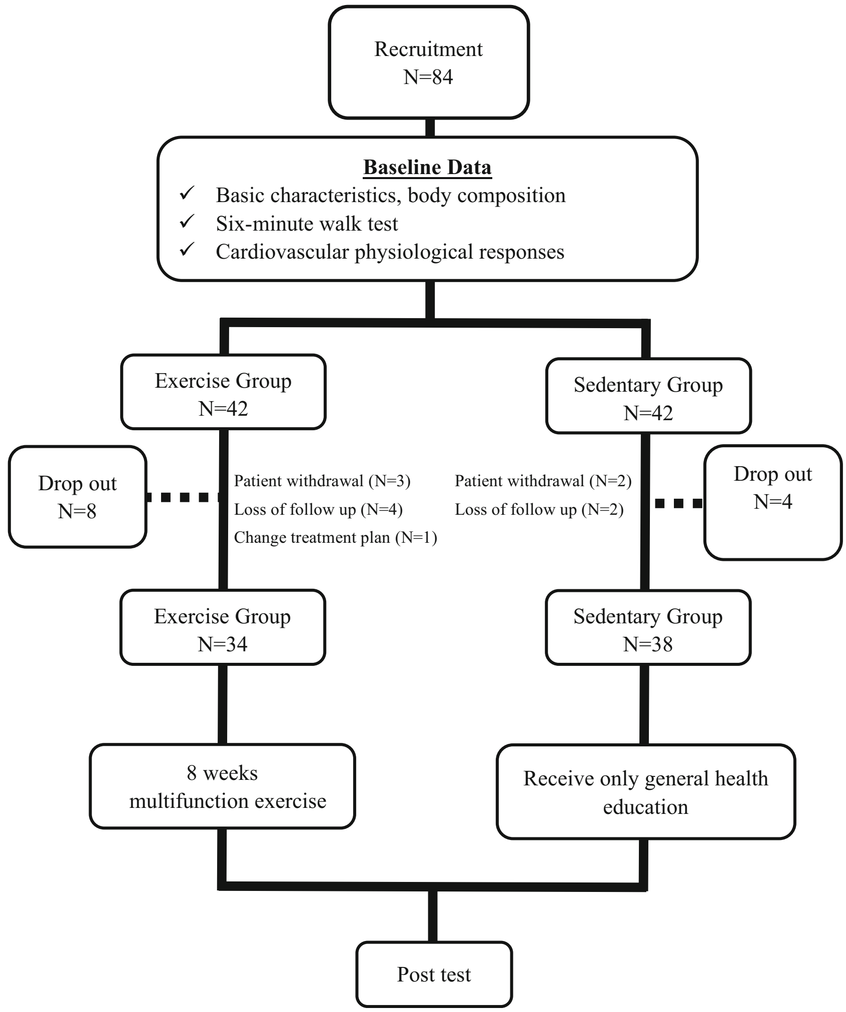

Fig. 1 Recruitment of subjects

participants in the exercise group learned gentle warm-up exercises used in walking or stepping with simple limb movements. Before each exercise warm-up session, the cardiovascular physiological responses, including resting BP, resting HR, resting SpO_2, resting RPE, and maximum HR were measured, prior to the aerobic training. The training intensity of the exercise group was based on the American College of Sports Medicine's cancer patient guidelines: using moderate intensity exercise training, with the intensity of the maximum HR ranging between 60 and 70%, where the maximum HR calculation formula is usually 220 minus the age [5]. Each week for 3 days, a training time of 40 to 50 min included a 5-min warm up, aerobic exercise training for 30 min, and a 5-min cool down. Resistance exercise is used more for training the upper and lower limbs (relatively large muscles), and includes such exercises as shoulder flexion, extension, abduction, elbow flexion and exercise, hip flexion, extension, abduction, knee flexion, and extension using TheraBand at the intensity of Rated Perceived Exertion (RPE) scale from "Somewhat heavy" to "Heavy." Ten different resistance exercises were performed in every training. Each exercise consists of ten repetitions for one set, three sets per training, with one repetition lasting 3 s. Controls were not asked about self-reported exercise.

Statistical analysis

Data were expressed as mean ± standard deviations. Baseline and changes in values after exercise were also compared within group by using a paired *t* test, and the comparison between the sedentary group and exercise group was performed using a Student's independent *t* test with significance level set at 0.05. All analyses were done using SPSS version 22.0 (Ins., Chicago, IL, U.S.A.).

Results

Basic characteristics and body composition of the sedentary group and exercise group at baseline

A total of 84 H&N cancer patients participated in this study, for whom the baseline characteristics of the patients were shown in Table 1. No significant differences were found in age, height,

Table 1 Basic characteristics in sedentary group and exercise group at baseline

Basic characteristics	Sedentary group ($N = 38$)	Exercise group ($N = 34$)	p value
Gender			
Female	8	7	–
Male	30	27	–
Risk factor			
Smoke	17	17	–
Drink	23	22	–
Age (year)	54.8 ± 9.7	52 ± 10.7	0.249
Height (m)	1.6 ± 0.1	1.6 ± 0.1	0.56
Body weight (kg)	59.1 ± 11.3	60.6 ± 10.1	0.61
BMI (kg/m^2)	22.3 ± 3.8	22.4 ± 2.9	0.87
Body composition			
Body Fat (%)	24.1 ± 6.3	23.6 ± 6.3	0.74
Visceral fat	8.2 ± 5.5	7.9 ± 4.7	0.85
Skeletal muscle rate	31.8 ± 4.6	32.1 ± 3.8	0.75
Drugs			
Chemotherapy drugs			
Aldesleukin	1	0	
Cisplatin	29	29	
Carboplatin	1	0	
Gemcitabine	0	1	
Medroxyprogesterone	1	7	
Uracil-Tegafur	12	0	
Target drug			
Cetuximab	2	1	

Student's independent t test was used. $p < 0.05$

weight, and body mass index (BMI), body fat, visceral fat, or musculoskeletal rates ($p > 0.05$). The cancer types for the patients were shown in Table 2, The basic clinical variables were equivalent in this study. Our subjects were assessed prior to beginning chemotherapy for collecting the baseline data. The post training data were evaluated after exercise training. In Table 3, we revealed that basic characteristics and body composition in the sedentary and exercise group at pre/post training revealed that there were no significant differences between the baseline characteristics and body composition of the sedentary and exercise groups. However, the body weight and BMI were significantly reduced in the sedentary group; the visceral fat was reduced in the exercise group; the skeletal muscle rates were significantly increased in the exercise group after 8 weeks of training.

Blood pressure in sedentary and exercise groups

After exercise training, results from 6-min walk test suggested that significant differences between the two groups in resting SBP (sedentary vs. exercise group: 116 ± 15.6 vs.104.2 ± 11.1; $p < 0.05$), resting DBP (sedentary vs. exercise group: 75.8 ± 10.3 vs. 61.9 ± 8.9; $p < 0.05$), resting 1-min DBP (sedentary vs. exercise group: 77.8 ± 11.4 vs. 67.4 ± 9.8; $p < 0.05$), resting 3-min SBP (sedentary vs. exercise group: 113.1 ± 15.2 vs. 101.3 ± 15.8; $p < 0.05$), resting 3-min DBP (sedentary vs. exercise group: 78.5 ± 10 vs. 61.2 ± 12.7; $p < 0.05$), resting MAP (sedentary vs. exercise group: 89.2 ± 11.1 vs. 76 ± 8.5; $p < 0.05$), resting 1-min MAP (sedentary vs. exercise group 90.1 ± 12 vs. 82.2 ± 10; $p < 0.05$), and resting 3-min MAP (sedentary vs. exercise group: 90 ± 10 vs. 74.6 ± 13.1; $p < 0.05$), we found no significant differences between the two groups in terms of peak SBP (sedentary vs. exercise group: 124.1 ± 17.7 vs. 129.9 ± 27.3; $p = 0.28$), peak DBP (sedentary vs. exercise group: 80.2 ± 11.8 vs. 74.9 ± 16.7; $p = 0.12$), peak MAP (sedentary vs. exercise group: 94.8 ± 12.5 vs. 93.2 ± 15.5; $p = 0.63$), and resting 1-min SBP (sedentary vs. exercise group: 114.7 ± 16.7 vs. 111.6 ± 16.1; $p = 0.43$), as shown in Table 4.

Heart rate responses in sedentary and exercise groups

After exercise training, we found significant differences between the two groups in resting heart rate (sedentary vs. exercise group: 83.2 ± 17.8 vs. 73.5 ± 11.1; $p < 0.05$), peak heart rate (sedentary vs. exercise group: 93.7 ± 19 vs.110.6 ± 17.5; $p < 0.05$), 1-min heart rate recovery (sedentary vs. exercise group: 12.4 ± 8.5 vs. 26.4 ± 15.7; $p < 0.05$), 3-min heart rate

Table 2 Head and neck cancer patient's characteristics of primary cancer types and cancer metastasis

	Sedentary group ($N = 38$)	Exercise group ($N = 34$)
Cancer type		
Adenoid cystic	0	1
Buccal	1	0
Cheek mucosa	2	0
Esophagus	1	1
Hypo pharyngeal	5	7
Lip	1	1
Laryngeal	1	0
Nasopharyngeal	17	20
Oropharyngeal	4	1
Oral cavity	1	1
Parotid	0	1
Palate gingiva	1	0
Palate		
Hard palate	1	1
Soft palate	0	1
Salivary gland ductal	1	0
Tonsil	1	0
Tongue	5	3
Cancer metastasis		
Hard palate	1	0
Intracranial invasion	0	0
Liver	0	1
Lung	0	1
Lymph node		
Distal	1	0
Neck	24	22
Lymphadenopathy	0	1
Pyriform sinus	1	0
Posterior pharyngeal wall	1	0
Retropharyngeal node	1	0
Upper gum	1	0

recovery (sedentary vs. exercise group: 13.9 ± 7.3 vs. 36.9 ± 17.5; $p < 0.05$), we found no significant differences between the two groups in resting 1 min (sedentary vs. exercise group: 81.2 ± 19 vs. 84.2 ± 14.3; $p = 0.46$), resting 3 min (sedentary vs. exercise group: 79.8 ± 18.1 vs. 73.6 ± 12.4.; $p = 0.1$), as shown in Table 4.

Table 3 Basic characteristics and body composition in sedentary and exercise group at pre/posttraining

	Sedentary group ($N = 38$)		Exercise group ($N = 34$)	
	Pretraining	Posttraining	Pretraining	Posttraining
Body weight (kg)	59.1 ± 11.3	58.1 ± 11.4*	60.6 ± 10.1	60 ± 9.9
Height (m)	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1
BMI (kg/m^2)	22.3 ± 3.8	21.9 ± 4*	22.4 ± 2.9	22.1 ± 2.9
Body fat (%)	24.1 ± 6.3	23.6 ± 7.9	23.6 ± 6.3	23.1 ± 5.3
Visceral fat	8.2 ± 5.5	7.8 ± 5.7	7.9 ± 4.7	7.4 ± 4.5*
Skeletal muscle rate	31.8 ± 4.6	32.3 ± 4	32.1 ± 3.8	33.6 ± 4.1*

*$p < 0.05$ pretraining versus posttraining

Table 4 The BP, HR, SpO2, and RPP in sedentary and exercise group at pre/posttraining

	Sedentary group ($N = 38$)		Exercise group ($N = 34$)	
	Pretraining	Posttraining	Pretraining	Posttraining
Rest				
SBP	120.7 ± 18.3	116 ± 15.6	114.4 ± 18.7	104.2 ± 11.1*#
DBP	74.3 ± 12.7	75.8 ± 10.3	70.9 ± 13.3	61.9 ± 8.9*#
Peak				
SBP	129.1 ± 21.1	124.1 ± 17.7	132.4 ± 28.7	129.9 ± 27.3
DBP	82.1 ± 11.4	80.2 ± 11.8	79.2 ± 13.7	74.9 ± 16.7
1-min recovery				
SBP	119.9 ± 17.5	114.7 ± 16.7	122.6 ± 22.5	111.6 ± 16.1*
DBP	78.7 ± 11.7	77.8 ± 11.4	77.6 ± 12.3	67.4 ± 9.8*#
3-min recovery				
SBP	116.3 ± 16.9	113.1 ± 15.2	119.9 ± 25.7	101.3 ± 15.8*#
DBP	78.4 ± 13.7	78.5 ± 10	76.5 ± 14.6	61.2 ± 12.7*#
Rest MAP	89.8 ± 13.8	89.2 ± 11.1	85.4 ± 13.8	76 ± 8.5*#
Peak MAP	97.8 ± 12.9	94.8 ± 12.5	96.9 ± 17.4	93.2 ± 15.5#
1-min MAP	92.4 ± 12.3	90.1 ± 12	92.6 ± 14.4	82.2 ± 10*#
3-min MAP	91.1 ± 13.2	90 ± 10	91 ± 17.6	74.6 ± 13.1*#
Rest HR	77.9 ± 16.5	83.2 ± 17.8*	83.3 ± 12.4	73.5 ± 11.1*#
Peak HR	88 ± 19.6	93.7 ± 19*	93.9 ± 18.1	110.6 ± 17.5*#
Rest 1-min HR	77.7 ± 17.2	81.2 ± 19	82.8 ± 13.6	84.2 ± 14
Rest 3-min HR	77.6 ± 16.8	79.8 ± 18.1	81.8 ± 11.7	73.6 ± 12.4*
Rest 1-min HRR	10.3 ± 8.2	12.4 ± 8.5	11 ± 8.5	26.4 ± 15.7*#
Rest 3-min HRR	10.4 ± 8.1	13.9 ± 7.3	12.1 ± 11	36.9 ± 17.5*#
Rest SpO2	97.8 ± 1.1	97.3 ± 1.6	97.3 ± 1.8	97.8 ± 1.6
Peak SpO2	97.5 ± 2.8	97.6 ± 1.6	98 ± 1.1	97.6 ± 1.2
Rest 1-min SpO2	98.2 ± 1.4	98.2 ± 1.1	97.9 ± 1.7	98.1 ± 1.3
Rest 3-min SpO2	97.9 ± 1.6	98.2 ± 1.1	98.1 ± 1.4	97.5 ± 1.5
Rest RPP	9491 ± 2951.2	9637.8 ± 2353.1	9549.1 ± 2196.2	7661.4 ± 1460.2*#
Peak RPP	11,352.3 ± 3285.4	11,686.9 ± 3163.4	12,494.4 ± 4011.8	14,459.1 ± 2600.9*#
Rest 1-min RPP	9304. ± 2600.9	9299.4 ± 2464.7	10,213.1 ± 2741.4	9451.4 ± 2413.6
Rest 3-min RPP	9029.6 ± 2506	9008 ± 2281.1	9863.8 ± 2790.6	7515.4 ± 1947.9*#

*$p < 0.05$ pretraining versus posttraining; # $p < 0.05$ versus sedentary group

SBP, systolic blood pressure; *DBP*, diastolic blood pressure; *MAP*, mean arterial pressure; *HR*, heart rate; *HRR*, heart rate recovery; *SpO2*, oxygen saturation; *RPP*, rate-pressure product

Oxygen saturation and rate-pressure product (RPP) in sedentary and exercise groups

After exercise intervention, we found no significant differences between the two groups in resting SpO_2 (sedentary vs. exercise group: 97 ± 1.6 vs. 98 ± 1.6; $p = 0.21$), peak SpO_2 (sedentary vs. exercise group: 98 ± 1.6 vs. 98 ± 1.2; $p = 0.95$), resting 1-min SpO_2 (sedentary vs. exercise group: 98 ± 1.1 vs. 98 ± 1.3; $p = 0.73$), and resting 3-min SpO_2 (sedentary vs. exercise group: 98 ± 1.1 vs. 98 ± 1.5; $p = 0.27$), as shown in Table 4. In addition, we also found significant differences between the two groups in resting RPP (sedentary vs. exercise group: 9637.8 ± 2353.1 vs. 7661.4 ± 1460.2; $p < 0.05$), peak RPP (sedentary vs. exercise group: 11656.9 ± 3163.4 vs.14459.1 ± 4314.7; $p < 0.05$), 3-min RPP (sedentary vs. exercise group: 9008 ± 228.1 vs. 7515.4 ± 1947.9; $p < 0.05$), we found no significant differences between the two groups in 1-min RPP (sedentary vs. exercise group: 9299.7 ± 2464.7 vs. 9451.4 ± 2413.6; $p = 0.79$), as shown in Table 4.

Rate of perceived exertion (RPE) and walking distance

In Table 5, we found significant differences between the two groups in resting RPE (sedentary vs. exercise group: 11 ± 0.9 vs. 10.6 ± 1; $p < 0.05$), peak RPE (sedentary vs. exercise group: 12 ± 1.2 vs. 11 ± 0.5; $p < 0.05$), resting 1-min RPE (sedentary vs. exercise group: 11.4 ± 0.8 vs. 11 ± 0.7; $p < 0.05$), and resting 3-min RPE (sedentary vs. exercise group: 11 ± 0.8 vs. 10.6 ± 0.8;

Table 5 The RPE and walking distance in sedentary and exercise group at pre/posttraining

	Sedentary group ($N = 38$)		Exercise group ($N = 34$)	
	Pretraining	Posttraining	Pretraining	Posttraining
Rest RPE	11.1 ± 0.9	11.2 ± 0.9	11.1 ± 0.8	10.6 ± 1*#
Peak RPE	11.4 ± 1.1	11.9 ± 1.2	11.4 ± 1	11.1 ± 0.5*#
Rest 1-min RPE	10.9 ± 0.7	11.4 ± 0.8*	11.1 ± 0.8	10.6 ± 0.7*#
Rest 3-min RPE	10.9 ± 0.7	11.2 ± 0.7	11 ± 0.6	10.6 ± 0.8*#
Distance (meter)	392.2 ± 119.2	353.4 ± 84.9*	410.1 ± 74.7	543.8 ± 54*#

*$p < 0.05$ pre training versus post training # $p < 0.05$ versus sedentary group

RPE, rate of perceived exertion

$p < 0.05$) after exercise training. In addition, in sedentary group, we found the rest 1-min RPE was significantly reduced after 8 weeks (10.9 ± 0.7 vs.11.4 ± 0.8; $p < 0.05$). Moreover, we also found significant differences between the two groups in walking distance (sedentary vs. exercise group: 353.4 ± 84.9 vs.543.8 ± 54; $p < 0.05$). Importantly, in sedentary group, we found the distance of working test was significantly reduced after 8 weeks (392.2 ± 119.2 vs.353.4 ± 84.9; $p < 0.05$). The distance of working test was significantly increased after 8 weeks in exercise group (410.1 ± 74.7 vs.543.8 ± 54; $p < 0.05$).

Discussion

Previous studies have shown that breast cancer patients doing exercise training before chemotherapy treatment experience reduced side effects related to cardiac dysfunction. However, there have been limited studies focused on the exercise responses and body composition in H&N cancer patients receiving chemotherapy. In addition, exercise has been used as an approach for cancer rehabilitation; however, investigations have not been confirmed whether exercise intervention could prevent chemotherapy-impaired normal exercise responses and body composition. In this present study, we suggested that H&N cancer patients improve their cardiovascular physiological responses such as BP, HR, HR recovery, and exercise capacity after 8 weeks of exercise training.

Blood pressure refers to the pressure of the blood in the circulatory system, and it is often measured since it is closely related to the force and rate of the heartbeat and the diameter and elasticity of the arterial walls. A higher blood pressure had been connected with one increased risk of cardiovascular dysfunction [28]. We know that chemotherapy drugs induce cardiovascular disease. Previous study have suggested that exercise training can reduce the incidence of cardiovascular disease by 30% and the incidence of mortality by 52% [22]. In addition, exercise training can reduce the activity of the sympathetic nervous system, thus increasing parasympathetic activity that achieves regulation of blood pressure [19]. In this present study, we reported that exercise training reduced SBP in exercise group but not in control after 6-minute walk test.

The use of chemotherapy in cancer patients is the most common cause of hypertension, because chemotherapy inhibits the signal of vascular endothelial growth factor, thus causing reduced nitric oxide synthesis, reduced vasoconstriction, and sodium ion excretion in vitro, and in turn causing hypertension [7]. We found that resting BP was decreased; the peak BP during was increased, and the BP recovery was improved after exercise training in H&N patients receiving chemotherapy. Moreover, heart rate response during exercise reflects the adaptation of cardiovascular system [21]. Chemotherapy drugs which induce abnormality in the baroreceptors are connected with upregulated sympathetic activity as well as a repression of parasympathetic activity, causing in elevated heart rate in cancer patients [25]. In this present study, we found that after 8 weeks of exercise intervention, the sedentary group resting heart rate was higher than that of the exercise group and was significantly reduced in the exercise group.

Most treatments for cancer patients involve chemotherapy and radiotherapy, and it is known that chemotherapy is likely to cause damage to the patient's body and systemic side effects caused by a decline in the physiological function of patients, which may affect their daily life activities and reduce their quality of life. In this present study, a decreased body weight was found in the control group but not in the exercise group. This finding is important since previous studies suggested that a decreased body weight could predict poor prognosis for h H&N cancer patients [1, 13]. In addition, our findings also suggested that 8 weeks of exercise training have beneficial effects on cardiovascular physiological responses such as BP, HR, HR recovery, and RPE in H&N cancer patients receiving chemotherapy. Results from 6-minute walk test suggested that exercise training increased exercise capacity in exercise group. These results suggest that exercise can help to prevent abnormal exercise responses and exercise capacity reduction which are caused by chemotherapy in H&N cancer patients. Some limitations should be discussed of this study. At first, we only included subjects from one hospital. Second, comparing with other studies, the number of subjects is related small. A multi-center study or a multi-country study will be our further direction in our future study.

Author contributions Kun-Ling Tsai had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Ching-Hsia Hung, Chung-Lan Kao. Acquisition, analysis, or interpretation of data: Wei-Ming Tsai and Shih-Hung Chan. Drafting of the article: Kun-Ling Tsai and Chia-Jui Yen. Critical revision of the article for important intellectual content: Hui-Ching Cheng, Wan Ting Jheng, Yan-Jhen Lu. Obtained funding: Kun-Ling Tsai, Chia-Jui Yen, and Ching-Hsia Hung. Statistical analysis: Chia-Jui Yen, Ching-Hsia Hung, Chung-Lan Kao. Study supervision: Kun-Ling Tsai and Chia-Jui Yen.

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Compliance with ethical standards

Ethics approval and consent to participate The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of National Cheng Kung University Hospital Institutional Review Board, Tainan, Taiwan (B-ER-105-102). Written informed consent was obtained from individual or guardian participants.

Consent for publication Not applicable.

Conflict of interests The authors declare that they have no conflicts of interest.

References

1. Albergotti WG, Davis KS, Abberbock S, Bauman JE, Ohr J, Clump DA, Heron DE, Duvvuri U, Kim S, Johnson JT, Ferris RL (2016) Association of pretreatment body mass index and survival in human papillomavirus positive oropharyngeal squamous cell carcinoma. Oral Oncol 60:55–60
2. Angsutararux P, Luanpitpong S, Issaragrisil S (2015) Chemotherapy-induced cardiotoxicity: overview of the roles of oxidative stress. Oxid Med Cell Longev 2015:795602
3. Baldwin ER, Baldwin TD, Lancaster JS, McNeely ML, Collins DF (2012) Neuromuscular electrical stimulation and exercise for reducing trapezius muscle dysfunction in survivors of head and neck cancer: a case-series report. Physiother Can 64:317–324
4. Chiang CJ, Lo WC, Yang YW, You SL, Chen CJ, Lai MS (2016) Incidence and survival of adult cancer patients in Taiwan, 2002-2012. J Formos Med Assoc 115:1076–1088
5. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP (2011) American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc 43:1334–1359
6. Gehring K, Kloek CJ, Aaronson NK, Janssen KW, Jones LW, Sitskoorn MM, Stuiver MM (2018) Feasibility of a home-based exercise intervention with remote guidance for patients with stable grade II and III gliomas: a pilot randomized controlled trial. Clin Rehabil 32:352–366
7. Gressett SM, Shah SR (2009) Intricacies of bevacizumab-induced toxicities and their management. Ann Pharmacother 43:490–501
8. Iwamoto J (2017) Calcium and bone metabolism across women's life stages. Exercise and sport to increase bone strength in accordance with female lifecycle. Clin Calcium 27:715–721
9. (1996) Physical activity and cardiovascular health. NIH Consensus Development Panel on Physical Activity and Cardiovascular Health. Jama 276:241–246
10. Kesaniemi YK, Danforth E Jr, Jensen MD, Kopelman PG, Lefebvre P, Reeder BA (2001) Dose-response issues concerning physical activity and health: an evidence-based symposium. Med Sci Sports Exerc 33:S351–S358
11. Kim K, Gu MO, Jung JH, Hahm JR, Kim SK, Kim JH, Woo SH (2018) Efficacy of a home-based exercise program after thyroidectomy for thyroid cancer patients. Thyroid 28:236–245
12. Laboratories ATSCoPSfCPF (2002) ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 166:111–117
13. Li ZQ, Zou L, Liu TR, Yang AK (2015) Prognostic value of body mass index before treatment for laryngeal squamous cell carcinoma. Cancer Biol Med 12:394–400
14. Madeddu C, Deidda M, Piras A, Cadeddu C, Demurtas L, Puzzoni M, Piscopo G, Scartozzi M, Mercuro G (2016) Pathophysiology of cardiotoxicity induced by nonanthracycline chemotherapy. J Cardiovasc Med (Hagerstown) 17(Suppl 1):S12–S18
15. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O (2012) Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev:CD008465
16. Mohamady HM, Elsisi HF, Aneis YM (2017) Impact of moderate intensity aerobic exercise on chemotherapy-induced anemia in elderly women with breast cancer: a randomized controlled clinical trial. J Adv Res 8:7–12
17. Navidi M, Phillips AW, Griffin SM, Duffield KE, Greystoke A, Sumpter K, RCF S (2018) Cardiopulmonary fitness before and after neoadjuvant chemotherapy in patients with oesophagogastric cancer. Br J Surg 105:900–906
18. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC et al (1995) Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. Jama 273:402–407
19. Ren CZ, Yang YH, Sun JC, Wu ZT, Zhang RW, Shen D, Wang YK (2016) Exercise training improves the altered renin-angiotensin system in the rostral ventrolateral medulla of hypertensive rats. Oxid Med Cell Longev 2016:7413963
20. Reynolds T (1992) “User-friendly” cancer statistics review features new format. J Natl Cancer Inst 84:1470–1471
21. Romero SA, Minson CT, Halliwill JR (2017) The cardiovascular system after exercise. J Appl Physiol (1985) 122:925–932
22. Sakamoto S, Yokoyama N, Tamori Y, Akutsu K, Hashimoto H, Takeshita S (2009) Patients with peripheral artery disease who complete 12-week supervised exercise training program show reduced cardiovascular mortality and morbidity. Circ J 73:167–173
23. Sallis R (2015) Exercise is medicine: a call to action for physicians to assess and prescribe exercise. Phys Sportsmed 43:22–26
24. Schakman O, Kalista S, Barbe C, Loumaye A, Thissen JP (2013) Glucocorticoid-induced skeletal muscle atrophy. Int J Biochem Cell Biol 45:2163–2172
25. Souza VB, Silva EN, Ribeiro ML, Martins Wde A (2015) Hypertension in patients with cancer. Arq Bras Cardiol 104:246–252
26. van Vulpen JK, Peeters PH, Velthuis MJ, van der Wall E, May AM (2016) Effects of physical exercise during adjuvant breast cancer

treatment on physical and psychosocial dimensions of cancer-related fatigue: a meta-analysis. Maturitas 85:104–111
27. Wall BA, Galvao DA, Fatehee N, Taaffe DR, Spry N, Joseph D, Newton RU (2014) Maximal exercise testing of men with prostate cancer being treated with androgen deprivation therapy. Med Sci Sports Exerc 46:2210–2215
28. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS, Mc GTS (2004) Guidelines for management of hypertension: report of the fourth working party of the British hypertension society, 2004-BHS IV. J Hum Hypertens 18:139–185
29. Wonders KY, Reigle BS (2009) Trastuzumab and doxorubicin-related cardiotoxicity and the cardioprotective role of exercise. Integr Cancer Ther 8:17–21

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