

Monitoring Training Progress During Exercise Training in Cancer Survivors: A Submaximal Exercise Test as an Alternative for a Maximal Exercise Test?

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ABSTRACT. May AM, van Weert E, Korstjens I, Hoekstra-Weebers JE, van der Schans CP, Zonderland ML, Mesters I, van den Borne B, Ros WJ. Monitoring training progress during exercise training in cancer survivors: a submaximal exercise test as an alternative for a maximal exercise test? Arch Phys Med Rehabil 2010;91:351-7.

Objective: To examine the use of a submaximal exercise test in detecting change in fitness level after a physical training program, and to investigate the correlation of outcomes as measured submaximally or maximally.

Design: A prospective study in which exercise testing was performed before and after training intervention.

Setting: Academic and general hospital and rehabilitation center.

Participants: Cancer survivors (N=147) (all cancer types, medical treatment completed ≥ 3 mo ago) attended a 12-week supervised exercise program.

Interventions: A 12-week training program including aerobic training, strength training, and group sport.

Main Outcome Measures: Outcome measures were changes in peak oxygen uptake (VO_{2peak}) and peak power output (both determined during exhaustive exercise testing) and submaximal heart rate (determined during submaximal testing at a fixed workload).

Results: The VO_{2peak} and peak power output increased and the submaximal heart rate decreased significantly from baseline to postintervention ($P < .001$). Changes in submaximal heart rate were only weakly correlated with changes in VO_{2peak} and peak power output. Comparing the participants performing submaximal testing with a heart rate less than 140 beats per minute (bpm) versus the participants achieving a heart rate of 140bpm or higher showed that changes in submaximal heart rate in the group cycling with moderate to high intensity (ie,

heart rate ≥ 140 bpm) were clearly related to changes in VO_{2peak} and peak power output.

Conclusions: For the monitoring of training progress in daily clinical practice, changes in heart rate at a fixed submaximal workload that requires a heart rate greater than 140bpm may serve as an alternative to an exhaustive exercise test.

Key Words: Exercise test; Heart rate; Oxygen consumption; Rehabilitation; Survivors.

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ALTHOUGH THE PROGNOSIS for cancer patients has improved, a substantial number of patients continue to report physical and psychologic complaints after completing primary treatment.¹ Exercise training has become increasingly recognized as beneficial to cancer survivors and seems to be associated with less severe side effects during and after cancer treatment.¹⁻⁵ Reviews of the effectiveness of exercise interventions after cancer treatment demonstrate a beneficial effect on physical fitness and also on overall quality of life and physical functioning.^{3,6} Consequently, interest in validated fitness evaluation tools for the purpose of monitoring the physical fitness level and training progress of cancer survivors participating in exercise training has been growing.

The criterion standard for assessing physical fitness is VO_{2peak} .^{7,8} The VO_{2peak} is assessed by means of respiratory gas analysis during graded exercise testing up to exhaustion. However, in daily clinical practice, such an exercise test has several disadvantages. It may be unpleasant for cancer survivors and requires experienced personnel and medical supervision, as well as the use of expensive equipment. For monitoring training progress throughout the training program, exercise

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List of Abbreviations

bpm	beats per minute
HR _{high group}	participants who performed baseline submaximal exercise testing with a mean heart rate of 140bpm or higher
HR _{low group}	participants who performed baseline submaximal exercise testing with a mean heart rate lower than 140 bpm
HR _{peak}	heart rate at peak
HR _{rest}	heart rate at rest
HR _{tr}	training heart rate
1RM	1 repetition maximum
rpm	revolutions per minute
VO_{2peak}	peak oxygen uptake

testing is necessary. Frequently performing an exhaustive exercise test places a serious burden on cancer survivors. Hence, for monitoring purposes, a validated submaximal exercise test, which is easily performed, inexpensive, well accepted by cancer survivors, and capable of tracking the improvements in $\text{VO}_{2\text{peak}}$, would have greater applicability in daily clinical practice.^{9,10}

Research in the field of cardiac and pulmonary rehabilitation has shown moderate to high correlations between submaximal and maximal exercise capacity, and it was concluded that submaximal testing is a useful substitute to maximal exercise testing.¹¹⁻¹⁴ To date, no submaximal test has been validated in cancer survivors. It is conceivable that cancer survivors might react differently to submaximal exercise testing because they often experience fatigue of which the physiologic basis is still poorly understood.¹⁵ Also, the effect of cardiovascular complications secondary to known cardiotoxic and pulmotoxic effects of many chemotherapeutic agents and the effects of radiation to the mediastinum on submaximal exercise outcome is not yet known.

The aim of the present study was to validate a submaximal exercise test in cancer survivors to be used for monitoring purposes. For this purpose, an exhaustive exercise test was used to evaluate the effect of a 12-week supervised physical training program in cancer survivors. In addition, all participants performed a 10-minute submaximal cycle ergometer test at a fixed power output with submaximal heart rate as the outcome measure. This allowed us to validate the use of a submaximal exercise test in oncology patients. Our present objectives were (1) to validate the use of the submaximal exercise test in detecting change in fitness level after our 12-week physical training program, and (2) to investigate whether the change in heart rate at a fixed submaximal workload was related to the change in $\text{VO}_{2\text{peak}}$ and peak power output from preintervention to postintervention. We expected the change in this physiologic parameter measured at a fixed submaximal workload to be negatively and linearly associated with the change in peak exercise capacity; that is, the greater the decrease in submaximal heart rate, the greater the increase in $\text{VO}_{2\text{peak}}$ and peak power output.

METHODS

The present prospective study uses data of a randomized multicenter trial that was conducted in 4 Dutch centers: 2 university medical centers, 1 general hospital, and 1 rehabilitation center. The medical ethics committee from the University Medical Center Utrecht and the local research ethics committees approved the study that was performed according to the Helsinki Declaration of 1975, as revised in 1983.

Participants

Inclusion criteria were age of at least 18 years; last cancer treatment completed at least 3 months before study entry; estimated life expectancy to be at least 1 year judged by the patient's physician; and referred for rehabilitation by a medical specialist or general practitioner based on the presence of at least 3 of the following 6 criteria: physical complaints, reduced physical capacity, psychologic problems, increased levels of fatigue, sleep disturbances, and problems coping with reduced physical and psychosocial functioning. Cancer survivors were excluded if they had cognitive disturbances, serious psychopathology or emotional instability that might impede participation in the rehabilitation program (these criteria were judged by a psychologist or social worker), or if they needed intensive medical treatment or rehabilitation. Patients who took medica-

tion that might affect their heart rate were also excluded. All participants provided written informed consent.

Intervention

The present intervention has been described in more detail elsewhere.^{16,17}

Physical training. Sessions (twice weekly, 2h per session) consisted of a personalized exercise program based on baseline graded exercise testing. Each session consisted of aerobic exercise (bicycle ergometer, 30min per session) and strength training (30min) followed by group sports (60min). The physical training was supervised by 2 physical therapists and was progressed according to a standardized protocol.

Aerobic bicycle training. Intensity was determined using the Karvonen formula¹⁸ that used the HR_{peak} obtained from baseline exhaustive exercise testing and the HR_{rest} to calculate the HR_{tr} . Exercise training was at an HR_{tr} of ($\text{HR}_{\text{rest}} + 40\%$ to 50% of [$\text{HR}_{\text{peak}} - \text{HR}_{\text{rest}}$]) during the first 4 weeks and was gradually increased to ($\text{HR}_{\text{rest}} + 70\%$ to 80% of [$\text{HR}_{\text{peak}} - \text{HR}_{\text{rest}}$]) in week 12.

Strength training. 1RM was determined for each upper- and lower-extremity exercise used in this study. Resistance training intensity started at 30% of the 1RM with a frequency of 10 to 20 repetitions over 3 series during the first week and was increased until 50% to 60% of baseline 1RM in week 12. Resistance exercise was performed using machines targeting large muscle groups—for example, leg press (focusing on quadriceps femoris, glutei, gastrocnemius), vertical row (longissimus, biceps brachii, rhomboideus), and bench press (pectoralis major, triceps brachii).

Group sports. Sports such as badminton, soccer, swimming, and balancing games were performed with the aim being to promote enjoyment of sports and overcome any lack of confidence cancer survivors may have felt about exercising.

Outcomes

Sociodemographic and medical data were collected at baseline. Medical data were confirmed by the referring physicians.

Physical fitness was assessed at baseline (T0) and postintervention (T1; ie, at least 2–7d after completing the last exercise training session). T0 and T1 tests were consistently performed by the same assessor who was not involved in the intervention. Participants were asked to refrain from food and beverages (except water) during the 2 hours before exercise testing.

Exhaustive exercise test. Participants cycled at 60rpm with no workload for 1 minute to adapt to the cycle ergometer.^a The exercise test started with a workload of 20W, and the load was increased every minute by 10, 15, or 20W until voluntary exhaustion. The increase in load was estimated using formulas provided by Wasserman et al.¹⁹ Subjects were encouraged during the test. The test ended when the patient was limited by volitional exhaustion, clinical symptoms (such as a significant arrhythmia), or when the participant was unable to maintain a cycling rate of 60rpm. In addition, physiologic criteria, like respiratory quotient greater than 1.1 and achieving or exceeding predicted heart rate, were used to check objectively whether the patients worked to exhaustion. Heart rate was recorded continuously during the whole test using Polar S610i.^b Blood pressure was measured before and after the exhaustive exercise test. Participants also rated their dyspnea and rate of perceived exertion on a 15-point (6–20) Borg scale before and after the test. Expired gases, measured on a breath-by-breath basis, were analyzed using Oxycon Delta,^c Oxycon Champion,^c Metamax MMX,^d or K4b^{2,e} in the 4 centers, respectively. The differences in measured oxygen uptake and

carbon dioxide output between analysis systems in the different centers were small (-3.4% to 2.4% difference from overall mean at 150W) and fell within the range of day-to-day variability²⁰ (data not shown). The $\text{VO}_{2\text{peak}}$ was calculated as the mean of oxygen consumption values collected during the final 30 seconds of exercise. Peak power output was defined as workload at exhaustion.

Submaximal exercise test. The submaximal exercise test was also performed on a cycle ergometer. Subjects completed the submaximal test within 2 to 7 days after the exhaustive exercise test. Before the test, subjects remained at quiet rest in a supine position for 10 minutes with no distractions. Then, participants cycled at 60rpm for 10 minutes at a fixed power output, namely 50% of peak power output determined during baseline graded exercise testing. Using that workload, all cancer survivors were expected to be able to finish the test without being exhausted and without developing an adverse event. The test phase was preceded by a 1-minute warmup and followed by a 3-minute cooldown, both at 25% of peak power output. The test was performed in a quiet environment, and subjects were asked not to talk during cycling. Participants rated their dyspnea and rate of perceived exertion on a 15-point (6–20) Borg scale before and after the test. Heart rate was recorded continuously during the test using Polar S610i. Mean heart rate, the primary endpoint, was defined as the mean of all recorded heart rates from minute 3 to 10. A decreased mean heart rate from baseline to postintervention during cycling at the same fixed workload indicated improved aerobic fitness.

Data Analysis

Analyses (R software, version 2.3.1)^f were performed according to the intention-to-treat principle. Only 2-sided significance tests were used ($\alpha < .05$).

In order to retain power and to prevent bias from missing values in a selected group of respondents, missing values of outcome variables were imputed by the mean of the predicted distribution given the hierarchical structure and specific characteristics of the person (age, sex, weight, group allocation) by using Bayesian statistics. Subjects with missing baseline values were not taken into account (exhaustive graded exercise testing: $n=3$ due to untreated hypertension, lymphedema in both legs, and claustrophobia caused by the mask covering nose and mouth; submaximal exercise testing: $n=3$ due to logistics). The reasons for these missing values were unrelated to noncompliance, withdrawal, or losses to follow-up and were not affected by the treatment these participants were assigned to. Therefore, postrandomization exclusion was appropriate.²¹

Changes in outcome variables from baseline to postintervention were analyzed using linear mixed-effects models.

With a view to examine the relationship between change in submaximal heart rate and change in $\text{VO}_{2\text{peak}}$ and peak power output, Spearman rank correlation coefficients were calculated. Correlations were also determined for 2 subgroups: namely, for participants who performed baseline submaximal exercise testing with a mean heart rate measured between 3 and 10 minutes of either below or above 140bpm (HR_{low} group and HR_{high} group, respectively). The reason for this distinction was that a heart rate below 140bpm is regulated by both the parasympathetic nervous vagus and the sympathetic nervi accelerantes, whereas a heart rate above 140bpm is regulated solely by the nervi accelerantes, after which a linear relationship is assumed between heart rate and oxygen uptake.^{22,23} Fisher's r -to- z transformation followed by Cohen's formula were performed to determine whether correlations differ between the HR_{low}

Table 1: Baseline Characteristics of Study Subjects (N=147)

Characteristics	Value
Age (y)	48.8±10.9
Sex	
Female	123 (83.7)
Male	24 (16.3)
Body mass index ($\text{kg}\cdot\text{m}^{-2}$)	27.5±6.2
Type of cancer	
Breast	82 (55.8)
Hematologic	23 (16.6)
Gynecologic	17 (11.6)
Urogenital	9 (5.5)
Colon	3 (2.0)
Lung	4 (2.7)
Other	9 (6.2)
Type of treatment	
Surgery	126 (85.7)
Chemotherapy	100 (68.0)
Radiotherapy	84 (57.1)
Time posttreatment (y)	1.3±1.7

NOTE. Data presented as mean \pm SD for continuous variables and frequency (%) for categorical variables.

group and HR_{high} group. Independent samples t tests were used to compare the subjects' characteristics and the percentage of HR_{peak} reached during baseline submaximal testing between these 2 groups.

RESULTS

A total of 147 cancer survivors were included in the study. Table 1 shows the baseline characteristics of the study participants. Fifteen participants discontinued the intervention because of medical reasons or personal reasons ($n=11$ and $n=4$, respectively). Participants completed a mean \pm SD of 20 ± 4.9 of 24 training sessions.

Effects on Maximal and Submaximal Exercise Capacity

The $\text{VO}_{2\text{peak}}$ and peak power output improved significantly from preintervention to postintervention (table 2). In 86.4% of all tests, the level of exhaustion was reached. Heart rate during submaximal exercise testing at a fixed workload decreased significantly from baseline to postintervention (see table 2). No adverse events occurred during either the submaximal or the exhaustive exercise testing.

Association Between Changes in Submaximal and Maximal Exercise Outcomes

Table 2 shows that change in submaximal heart rate is weakly correlated with change in peak power output from baseline to postintervention and tended to be weakly correlated with change in $\text{VO}_{2\text{peak}}$ ($P=.08$).

Subgroup Analyses

It has been suggested that a submaximal test is predictive of maximal aerobic capacity when a heart rate of at least 140bpm is reached.²² Therefore, we also performed the analyses separately for the HR_{low} group (heart rate $<140\text{bpm}$) and the HR_{high} group (heart rate $\geq 140\text{bpm}$). Table 3 shows that participants of the HR_{low} group and HR_{high} group did not differ in sex, type of cancer, type of treatment, time posttreatment, body mass index, and baseline $\text{VO}_{2\text{peak}}$ and peak power output ($P>.05$). Also, baseline fatigue levels were not different

Table 2: Exercise Performance at Baseline and Postintervention, and Correlation of Change in Heart Rate at a Fixed Submaximal Workload With Change in Maximal Exercise Capacity

Variables	Baseline	Postintervention	Change Score (Postintervention – BL) (95% CI)	Correlation [§] (P)
VO ₂ peak (mL·min ⁻¹) [†]	1844.8±559.2	2003.2±582.9	165.0 (131.8 to 198.2)*	-.15 (.08)
VO ₂ peak (mL·kg ⁻¹ ·min ⁻¹) [†]	23.7±7.0	25.8±7.5	2.1 (1.7 to 2.6)*	-.12 (0.1)
W _{peak} (watt) [†]	156.9±47.3	173.0±48.7	16.2 (13.7 to 18.7)*	-.18 (.04)
Submaximal HR (bpm) [‡]	125.4±16.6	120.5±14.9	-4.9 (-6.3 to -3.5)*	1.0

NOTE. Values are mean ± SD or as otherwise indicated.

Abbreviations: BL, baseline; CI, confidence interval; HR, heart rate; W_{peak}, peak power output.

*P<.001 for change from baseline to postintervention using linear mixed-effects model (n=141).

[†]Assessed during exhaustive graded exercise testing.

[‡]Assessed during submaximal exercise testing.

[§]Spearman correlation coefficients were calculated for change of each other outcome with change of submaximal heart rate.

between the 2 groups (data not shown). Subjects of the HR_{high} group were younger compared with the subjects of the HR_{low} group (P=.004).

Table 3 also specifies that the HR_{high} group cycled at a higher percentage of their HR_{peak} compared with the HR_{low} group during baseline submaximal exercise testing. Workload of the submaximal exercise test tended to be higher in the HR_{high} group. The change in heart rate from preintervention to postintervention was larger in the HR_{high} group (P<.001; Cohen's effect sizes²⁴ were .26 and 1.47 for the HR_{low} group and HR_{high} group, respectively, and .43 for the total group). Rated perceived exertion after each submaximal exercise test,

as well as change of rated perceived exertion from baseline to postintervention, was not significantly different between participants of the HR_{low} group and HR_{high} group (data not shown).

Correlational analyses revealed that in the HR_{high} group, changes in submaximal heart rate were clearly related to changes in VO₂peak and peak power output (r=-.51 and -.69, respectively) and borderline with relative VO₂peak (r=-.35), whereas the correlations in the HR_{low} group were not significant (table 4). Indeed, the correlation coefficient in the HR_{high} group was significantly different from the coefficient in the HR_{low} group (P=0.04).

Table 3: Characteristics for the Group Cycling With a Heart Rate Below 140bpm (HR_{low} Group) and Above 140bpm (HR_{high} Group) During Submaximal Exercise Testing at Baseline

Characteristics	HR _{low} Group*	HR _{high} Group*	P [†]
Age (y)	50.0±10.6	43.3±0.7	.004
Sex			
Female	94 (82.5)	23 (85.2)	.7
Male	20 (17.5)	4 (14.8)	
Body mass index (kg·m ⁻²)	27.3±5.8	27.5±6.1	.9
Type of cancer			.2
Breast	68 (59.6)	13 (48.1)	
Hematologic	12 (10.5)	8 (29.6)	
Gynecologic	13 (11.4)	4 (14.8)	
Urogenital	8 (2.6)	0	
Colon	3 (7.0)	1 (3.7)	
Lung	3 (6.1)	0	
Other	7 (2.6)	1 (3.7)	
Type of treatment			
Surgery	98 (86.0)	24 (88.9)	.7
Chemotherapy	78 (68.4)	20 (74.1)	.6
Radiotherapy	70 (61.4)	13 (48.1)	.2
Time posttreatment (y)	1.3±1.7	1.3±1.6	.9
Baseline maximal exercise testing			
VO ₂ peak (mL·min ⁻¹)	1820.7±580.7	1946.8±541.1	.3
VO ₂ peak (mL·kg ⁻¹ ·min ⁻¹)	23.3±6.9	25.3±7.5	.2
W _{peak} (watt)	153.4±46.4	171.7±48.8	.07
Baseline submaximal exercise testing			
Percentage HR _{peak} [‡]	75.9±6.7	82.2±6.4	<.001
Workload (watt)	76.3±33.8	85.4±25.4	.06

NOTE. Data presented as mean ± SD for continuous variables and frequency (%) for categorical variables.

Abbreviation: W_{peak}, peak power output.

*HR_{low} group—participants cycling with a heart rate below 140bpm at baseline (n=114); HR_{high} group—participants cycling with a heart rate ≥140bpm at baseline (n=27).

[†]P value for between-group differences using linear mixed-effects model.

[‡]HR_{peak} was assessed during preintervention exhaustive graded exercise testing.

Table 4: Subgroup Analyses for the Group Cycling With a Heart Rate Below 140bpm (HR_{low} Group) and Above 140bpm (HR_{high} Group) During Submaximal Exercise Testing at Baseline: Exercise Performance at Baseline and Postintervention and Correlation of Change in Heart Rate at a Fixed Submaximal Workload With Change in Maximal Exercise Capacity

Variables	Baseline	Postintervention	Change Score (95% CI)	Correlation (P)
HR _{low} group [†]				
VO _{2peak} (mL·min ⁻¹) [‡]	1820.7±580.7	1977.5±604.7	165.0 (131.8 to 198.2)*	-.10 (0.3)
VO _{2peak} (mL·kg ⁻¹ ·min ⁻¹) [‡]	23.3±6.9	25.4±7.4	2.1 (1.6 to 2.6)*	-.10 (0.3)
W _{peak} (watt) [‡]	153.4±46.4	169.5±48.0	16.2 (13.7 to 18.7)*	-.05 (0.6)
Submaximal HR (bpm) [§]	119.9±13.3	116.5±13.1	-3.5 (-4.9 to -2.0)*	1.0
HR _{high} group [†]				
VO _{2peak} (mL·min ⁻¹) [‡]	1946.8±541.1	2111.7±499.4	165.0 (86.5 to 243.5)*	-.51 (.006)
VO _{2peak} (mL·kg ⁻¹ ·min ⁻¹) [‡]	25.3±7.5	27.6±7.6	2.4 (1.4 to 3.3)*	-.35 (.08)
W _{peak} (watt) [‡]	171.7±48.8	188.1±49.5	16.5 (11.6 to 21.4)*	-.69 (<.001)
Submaximal HR (bpm) [§]	148.6±5.6	137.8±8.7	-10.8 (-14.2 to -7.4)*	1.0

NOTE. Values are mean ± SD or as otherwise indicated.

Abbreviations: CI, confidence interval; W_{peak}, peak power output.

*P<.0001 for change from baseline to postintervention using linear mixed-effects model (n=141).

[†]HR_{low} group—participants cycling with a heart rate below 140bpm at baseline (n=114); HR_{high} group—participants cycling with a heart rate ≥140bpm at baseline (n=27).

[‡]Assessed during exhaustive graded exercise testing.

[§]Assessed during submaximal exercise testing.

^{||}Spearman correlation coefficients were calculated for change of each other outcome with change of submaximal heart rate.

DISCUSSION

In the present study, the effect of a physical training program in cancer survivors was evaluated by means of an exhaustive exercise test and a submaximal test at a fixed workload. Using this design, we were able to investigate the sensitivity to change of the submaximal exercise test by comparing the change in submaximal heart rate with the change in VO_{2peak}, the criterion standard for assessing exercise capacity. We showed that VO_{2peak} and peak power output significantly increased from baseline to postintervention in the present study population. The heart rate response to a fixed submaximal power output was consistent with these findings. In addition, our results revealed that only changes in submaximal heart rate while cycling at a heart rate above 140bpm were associated with changes in VO_{2peak} and peak power output, indicating that during submaximal testing, an exertion of moderate to high intensity is necessary.

The strengths of the present study were the large sample size, the supervised and standardized intervention, low dropout rates, and the validated measure of fitness. A limitation of the present study was the small number of participants in the HR_{high} group (n=27) and that this group consisted of younger subjects compared with the HR_{low} group. Future research should include more cancer survivors cycling at a fixed workload that elicits a heart rate greater than 140bpm to confirm the relationship between changes of submaximal and maximal exercise testing outcomes. All participants in the present study completed the exhaustive exercise test, which suggests that all would have been capable of completing a submaximal test with moderate to high intensity.

The improvements of VO_{2peak} and peak power output reported in the present study are in accordance with the findings of others.^{3,16,25} De Backer et al²⁵ also used a submaximal and an exhaustive exercise test for the evaluation of an 18-week physical training program. Contrary to our results, the authors reported that the heart rate at 50%, 60%, and 70% of peak power output did not decrease in their participants from preintervention to postintervention, whereas VO_{2peak} and peak power output improved significantly. A possible explanation of these opposite findings might be the submaximal testing protocol they used: the test started at 50% of peak power output and was increased by

10% every 3 minutes, sampling the heart rate during the last 15 seconds of each stage. A duration of 3 minutes might be too short in this deconditioned population to achieve a true steady state that is needed for a valid monitoring of a heart rate response to submaximal exercise. In the present study, the participants cycled during 10 minutes at a fixed workload. This duration is in line with recommendations of Astrand and Rodahl,²² who reported that a period of about 4 to 5 minutes is necessary to reach a steady state.

Our finding that only changes in submaximal heart rate while cycling with a heart rate above 140bpm were associated with changes in VO_{2peak} and peak power output might be explained by the findings of Davies,²⁶ who observed that higher intensity work resulted in intraindividual variations in heart rate of 2%, while intraindividual variations at lower intensities were higher and ranged from 3% to 8% when using the Astrand-Ryhming test,²⁷ which is a comparable submaximal cycle ergometer test. Moreover, in healthy subjects Astrand and Rodahl²² recommended a heart rate up to or above 140bpm to generate the best estimate of aerobic capacity. At lower heart rates, fear, excitement, and emotional stress may cause a marked elevation of heart rate at a submaximal work rate without either VO_{2peak} or performance capacity being affected. Thus, the submaximal test seems to be more accurate when using higher workloads.²⁸

Surprisingly, in the HR_{high} group, the relative heart rate was higher compared with the HR_{low} group, indicating that the exercise intensity was greater for the HR_{high} group. During exhaustive graded exercise testing, the obtained level of peak power output is determined by aerobic as well as anaerobic capacity (production of lactate). The latter decreases with increasing age.²² Because subjects in the HR_{high} group were younger compared with the subjects of the HR_{low} group, the contribution of the anaerobic system was possibly larger in the HR_{high} group. As a consequence in this group, cycling at 50% peak power output suggests cycling at a higher percentage VO_{2peak} and, therefore, a higher percentage HR_{peak} than in the HR_{low} group.

Do the present results imply that our submaximal test could replace the exhaustive exercise test? The answer is no, as far as it concerns the assessment of VO_{2peak}, a measurement that is only accurately determined by an exhaustive exercise test using

gas exchange measurements.²² Moreover, as is also proposed by others,²⁵ in cancer survivors, an exhaustive exercise test using gas exchange measurements should be used as a diagnostic tool before the start of the training program to detect cardiac or pulmonary limitations. Cancer survivors are at risk for developing cardiovascular complications secondary to known cardiotoxic and pulmotoxic effects of many chemotherapeutic agents and the effects of radiation to the mediastinum.²⁹ However, our submaximal exercise test proved to be suitable for the evaluation of changes in fitness over the course of a training program. The present study showed that submaximal testing at a moderate to high intensity was feasible, as no complaints were reported. Compared with an exercise test until exhaustion, a submaximal test has several advantages. The test is simple to administer and avoids the expenses, patient discomfort, and increased risk of maximal exercise testing. Taking these advantages and the demonstrated sensitivity to change after physical training into account, we think this test may be an appropriate tool to evaluate the fitness changes that occur in cancer survivors over the course of an exercise training program. However, our findings suggest that the testing procedure used in this study should be modified to accomplish this. We chose a workload of 50% of peak power output to avoid the risk of overstraining our deconditioned population. This intensity was too low to elicit a heart rate response greater than 140 bpm in all participants. Instead of a workload of 50% of peak power output, the procedure described by Astrand and Rodahl²² can be used to select the appropriate workload for reaching a heart rate above 140 bpm. Using this procedure implies that no exhaustive exercise test is needed ahead of the submaximal exercise test. However, in a population of cancer survivors, an exhaustive exercise test is still recommended at the start of an exercise program for the above-mentioned reasons.

CONCLUSIONS

Our supervised, structured exercise program had positive effects on cancer survivors' maximal and submaximal exercise capacity. Changes of submaximal and maximal exercise capacity were only weakly related to each other, possibly because of the insufficient physiologic demand of the submaximal exercise test. When the intensity of the submaximal exercise test was sufficiently high, changes in submaximal heart rate were clearly correlated with changes in VO_2 peak and peak power output. For the monitoring of training progress in a daily clinical practice, changes in heart rate at a fixed submaximal workload requiring a heart rate greater than 140bpm may serve as an alternative to an exhaustive exercise test.

References

1. Mustian KM, Griggs JJ, Morrow GR, et al. Exercise and side effects among 749 patients during and after treatment for cancer: a University of Rochester Cancer Center Community Clinical Oncology Program Study. *Support Care Cancer* 2006; 14:732-41.
2. Fialka-Moser V, Crevenna R, Korpan M, Quittan M. Cancer rehabilitation: particularly with aspects on physical impairments. *J Rehabil Med* 2003;35:153-62.
3. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *Can Med Assoc J* 2006;175:34-41.

4. Stevinson C, Fox KR. Role of exercise for cancer rehabilitation in UK hospitals: a survey of oncology nurses. *Eur J Cancer Care (Engl)* 2005;14:63-9.
5. Stevinson C, Fox KR. Feasibility of an exercise rehabilitation programme for cancer patients. *Eur J Cancer Care (Engl)* 2006; 15:386-96.
6. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2005;14:1588-95.
7. McArdle WD, Katch FI, Katch VL. *Exercise physiology, energy, nutrition and performance*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001.
8. Shephard RJ, Allen C, Benade AJ, et al. The maximum oxygen intake. An international reference standard of cardiorespiratory fitness. *Bull World Health Organ* 1968;38:757-64.
9. Noonan V, Dean E. Submaximal exercise testing: clinical application and interpretation. *Phys Ther* 2000;80:782-807.
10. Takken T. The steep ramp test: questions about sensitivity and reliability. *Arch Phys Med Rehabil* 2008;89:1625.
11. Riley M, McParland J, Stanford CF, Nicholls DP. Oxygen consumption during corridor walk testing in chronic cardiac failure. *Eur Heart J* 1992;13:789-93.
12. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J* 1985;132:919-23.
13. Cahalin LP, Mathier MA, Semigran MJ, Dec GW, DiSalvo TG. The six-minute walk test predicts peak oxygen uptake and survival in patients with advanced heart failure. *Chest* 1996; 110:325-32.
14. Nixon PA, Joswiak ML, Fricker FJ. A six-minute walk test for assessing exercise tolerance in severely ill children. *J Pediatr* 1996;129:362-6.
15. Ryan JL, Carroll JK, Ryan EP, Mustian KM, Fiscella K, Morrow GR. Mechanisms of cancer-related fatigue. *Oncologist* 2007;12 (Suppl 1):22-34.
16. May AM, van Weert E, Korstjens I, et al. Improved physical fitness of cancer survivors: a randomised controlled trial comparing physical training with physical and cognitive-behavioural training. *Acta Oncol* 2008;47:825-34.
17. van Weert E, Hoekstra-Weebers JE, May AM, Korstjens I, Ros WJ, van der Schans CP. The development of an evidence-based physical self-management rehabilitation programme for cancer survivors. *Patient Educ Couns* 2008;71:169-90.
18. Karvonen J, Vuorimaa T. Heart rate and exercise intensity during sports activities. Practical application. *Sports Med* 1988;5:303-11.
19. Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ. *Principles of exercise testing and interpretation*. 3rd ed. Baltimore: Lippincott Williams & Wilkins; 1999.
20. Kuipers H, Verstappen FT, Keizer HA, Geurten P, van Kranenburg G. Variability of aerobic performance in the laboratory and its physiologic correlates. *Int J Sports Med* 1985;6:197-201.
21. Fergusson D, Aaron SD, Guyatt G, Hebert P. Post-randomisation exclusions: the intention to treat principle and excluding patients from analysis. *BMJ* 2002;325:652-4.
22. Astrand P, Rodahl K. Evaluation of physical performance on the basis of tests. *Textbook of work physiology. Physiological bases of exercise*. 3rd ed. Singapore: McGraw-Hill International Editions Medical Science Series; 1986. p 354-90.
23. Bernardis JA, Bouman LN. *Fysiologie van de mens*. 5th ed. Houten: Bohn Stafleu Van Loghum; 1988.
24. Cohen J. *Statistical power analysis for the behavioral sciences*. 2nd ed. Hillsdale: Lawrence Erlbaum Associates; 1988.
25. De Backer I, Schep G, Hoogeveen A, Vreugdenhil G, Kester AD, van Breda E. Exercise testing and training in a cancer rehabilita-

- tion program: the advantage of the steep ramp test. *Arch Phys Med Rehabil* 2007;88:610-6.
26. Davies CT. Limitations to the prediction of maximum oxygen intake from cardiac frequency measurements. *J Appl Physiol* 1968;24:700-6.
 27. Astrand PO, Ryhming I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work. *J Appl Physiol* 1954;7:218-21.
 28. Astrand I, Astrand PO, Hallback I, Kilbom A. Reduction in maximal oxygen uptake with age. *J Appl Physiol* 1973;35:649-54.
 29. Yeh ET, Tong AT, Lenihan DJ, et al. Cardiovascular complications of cancer therapy: diagnosis, pathogenesis, and management. *Circulation* 2004;109:3122-31.
- Suppliers**
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 - f. The R Project for Statistical Computing, <http://www.r-project.org>.