

ORIGINAL RESEARCH

# Criterion Validity and Responsiveness of the Steep Ramp Test to Evaluate Aerobic Capacity in Survivors of Cancer Participating in a Supervised Exercise Rehabilitation Program



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## Abstract

**Objective:** To evaluate the criterion validity and responsiveness of the steep ramp test (SRT) compared with the cardiopulmonary exercise test (CPET) in evaluating aerobic capacity in survivors of cancer participating in a rehabilitation program.

**Design:** A prospective cohort study in which survivors of cancer performed an SRT and CPET before (T=0) and after (T=1) a 10-week exercise rehabilitation program. Peak work rate achieved during the SRT (SRT-WR<sub>peak</sub>) was compared with peak oxygen consumption measured during the CPET (CPET-V<sub>O<sub>2</sub>peak</sub>), which is the criterion standard for aerobic capacity. Correlation coefficients were calculated between SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> at T=0 to examine criterion validity and between changes in SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> from T=0 to T=1 to determine responsiveness. Receiver operating characteristic analysis was performed to examine the ability of the SRT to detect a true improvement (6%) in CPET-V<sub>O<sub>2</sub>peak</sub>.

**Setting:** University medical center.

**Participants:** Survivors of cancer (N=106).

**Interventions:** Exercise rehabilitation.

**Main Outcome Measures:** Correlation coefficients between CPET-V<sub>O<sub>2</sub>peak</sub> and SRT-WR<sub>peak</sub> and between changes in CPET-V<sub>O<sub>2</sub>peak</sub> and SRT-WR<sub>peak</sub>.

**Results:** An *r* of 0.86 (N=106) was found for the relation between SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> at T=0. An *r* of 0.51 was observed for the relation between changes in SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> (n=59). Receiver operating characteristic analysis showed an area under the curve of 0.74 for the SRT to detect a true improvement in CPET-V<sub>O<sub>2</sub>peak</sub>, with an optimal cutoff value of +0.26 W/kg (sensitivity 70.7%, specificity 66.7%).

**Conclusions:** Because SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> were strongly correlated, the SRT seems a valid tool to estimate aerobic capacity in survivors of cancer. The responsiveness to measure changes in aerobic capacity appears moderate. Nevertheless, the SRT seems able to detect improvement in aerobic capacity, with a cutoff value of 0.26 W/kg.

Archives of Physical Medicine and Rehabilitation 2021;102:2150–6

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Trial Registration No.: ISRCTN10373531.

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<https://doi.org/10.1016/j.apmr.2021.04.016>

Cancer incidence and survival rates are increasing owing to the aging population and improved diagnosis and treatment modalities. This leads to a growing population of survivors of cancer, who live longer with the consequences of cancer and its treatment.<sup>1</sup> Current American College of Sports Medicine guidelines emphasize the strong level of evidence for the positive effects of exercise on physical functioning, fatigue, anxiety, depression, and health-related quality of life in survivors of cancer.<sup>2</sup> An important indicator of physical functioning is aerobic capacity, which is defined as the maximum amount of oxygen that can be taken in, transported, and used by the muscles during prolonged exercise.<sup>3</sup> Aerobic capacity is dependent on the integrative function of the pulmonary, cardiovascular, and metabolic systems and is considered a good reflection of overall health.<sup>4</sup> Moreover, aerobic capacity is found to be inversely related to all-cause and cancer-related mortality.<sup>5,6</sup> Therefore, it is worrying that patients treated for cancer experience a longstanding decline in aerobic capacity of 5%-22%.<sup>7,8</sup> Accurate measurement of aerobic capacity is important not only for the identification of exercise limitations but also for adequate individualized prescription of training intensity and for monitoring of training progress.<sup>9,10</sup>

The criterion standard to examine aerobic capacity is to determine maximum oxygen consumption ( $\text{VO}_2\text{max}$ ) during a maximal incremental exercise test with respiratory gas analysis, usually referred to as the cardiopulmonary exercise test (CPET).<sup>11</sup> A true  $\text{VO}_2\text{max}$  is achieved when oxygen consumption ( $\text{VO}_2$ ) levels off, despite the continuation of exercise with an increasing work rate.<sup>3</sup> In clinical practice, however, this plateau is rarely seen in nonathletic individuals or those with disease. Therefore, the highest  $\text{VO}_2$  attained during a maximal, symptom-limited CPET (CPET- $\text{VO}_2\text{peak}$ ) is considered the best available index of aerobic capacity.<sup>12</sup>

Nevertheless, performing a CPET is not always feasible because the procedures are time consuming and require advanced equipment, trained staff, and medical supervision.<sup>10</sup> Therefore, accurate, nonsophisticated performance-based tests to evaluate aerobic capacity are needed. The steep ramp test (SRT) is a short maximal exercise test performed on a cycle ergometer,<sup>a</sup> with an increasing work rate of 25 W every 10 seconds until voluntary exhaustion. de Backer et al<sup>13</sup> studied the validity of the SRT to estimate aerobic capacity in 37 survivors of cancer attending an exercise program and found a strong correlation ( $r=0.82$ ) between the peak work rate achieved at the steep ramp test (SRT-WRpeak) and CPET- $\text{VO}_2\text{peak}$ . Similar correlations were found in patients with diabetes, healthy children, and children with cystic fibrosis.<sup>14-16</sup> To our knowledge, the responsiveness of the SRT to changes in aerobic capacity has not yet been studied, although this is considered to be an important measurement property for

performance tests used to monitor training progression and to make necessary program adjustments.

Therefore, the objective of this study was to evaluate the criterion validity and responsiveness of the SRT compared with the CPET in evaluating aerobic capacity in survivors of cancer attending a 10-week supervised exercise rehabilitation program. The following a priori hypotheses were formulated. First, based on the results of previous studies,<sup>13</sup> the correlation coefficient between CPET- $\text{VO}_2\text{peak}$  and SRT-WRpeak was expected to be positive and strong ( $>0.70$ ). Second, based on a larger degree of measurement error that comes along with repeated testing, a moderate correlation (0.50-0.70) was expected between the change in CPET- $\text{VO}_2\text{peak}$  and SRT-WRpeak over time.<sup>17,18</sup> Third, and for the same reason, the ability of the SRT to discriminate between participants who did or did not improve in aerobic capacity was expected to be moderate. As such, the area under the curve (AUC) of the receiver operating characteristic (ROC) curve was expected to be in the range of 0.60-0.80.

## Methods

### Participants

Participants were consecutively recruited from the multidisciplinary oncology rehabilitation program at the Department of Physical Therapy of the Maastricht University Medical Center+ between November 2018 and March 2020. This program for survivors of cancer was developed according to national guidelines for oncology rehabilitation.<sup>19</sup> Patients were eligible for the program when they completed active medical treatment and were suffering from physical and psychosocial complaints, as identified by the sports physician, occupational therapist, and psychologist. Contraindications for participation in the rehabilitation program were the inability to perform basic activities of daily living (eg, walking) and the presence of disabling comorbidities that seriously hamper physical exercise (eg, severe heart failure, chronic obstructive pulmonary diseases, neurologic or cognitive disorders). The program consisted of a 10-week physical exercise training program, supplemented with treatment by a psychologist and/or occupational therapist when needed. Patients were included in the study when they met the criteria for participation in the rehabilitation program, completed a CPET and SRT before the start of the exercise program, and gave written informed consent for the use of their usual care data. Participants were excluded for analysis when they were unable to cycle until voluntary exhaustion during 1 or both exercise tests. Data collection procedures were in compliance with the Declaration of Helsinki and were approved by the medical ethics committee of the Maastricht University Medical Center+ (registration no. 2018-0648). This study was reported according to the Consensus-Based Standards for the Selection of Health Measurement Instruments guidelines.

### Exercise program

Participants completed a 10-week supervised exercise program to improve aerobic capacity and muscle strength as part of the multidisciplinary oncology rehabilitation program. The program consisted of 2 training sessions per week, which both started with 1 hour of combined endurance and resistance training, followed by 30 minutes of rest and, subsequently, 30 minutes of varying

#### List of abbreviations:

AUC	area under the curve
CI	confidence interval
CPET	cardiopulmonary exercise test
CPET- $\text{VO}_2\text{peak}$	peak oxygen consumption attained at the cardiopulmonary exercise test
RERpeak	peak respiratory exchange ratio
ROC	receiver operating characteristic
SRT	steep ramp test
SRT-WRpeak	peak work rate achieved at the steep ramp test
$\text{VO}_2$	oxygen consumption
$\text{VO}_2\text{max}$	maximum oxygen consumption.

sports activities in the sports hall or swimming pool. Training intensity of the first part of the program was personalized. To determine the intensity of the resistance training, a submaximal repetition maximum test was performed on each exercise machine to calculate the true 1-repetition maximum. Participants performed 4 strength exercises each session, targeting large muscle groups of the upper body, lower body, and core. Resistance training consisted of 3 sets of 8-12 repetitions, at a training intensity of 60% of the participant's 1-repetition maximum. Endurance training in the first training session of the week consisted of 20 minutes walking on a treadmill, with a walking speed of 80% of their speed that was achieved during a baseline 6-minute walking test. In the other training session, participants performed 2 sets of 10 minutes of interval training on a cycle ergometer, 1 set before and 1 after the resistance training program. Intervals were performed for 60 seconds and 30 seconds at 30% and 65% of the participant's SRT-WR<sub>peak</sub>, respectively.<sup>13</sup> A moderate to high exercise intensity was pursued for all training components, corresponding with a 0-10 Borg rating of perceived exertion of 4-6. Training load was adjusted weekly to achieve this.

## Test procedures

Participants performed a CPET and SRT before the start of the exercise program (T=0) and after 10 weeks of exercise training (T=1). CPET was performed to check for cardiopulmonary comorbidities and contraindications to exercise training and to assess aerobic capacity. The SRT was performed for the interval training prescription, as described by de Backer et al.<sup>13</sup> The CPET and SRT were planned separately, with a between-visit time of 2-7 days. Planning of the CPET and the SRT had to be adapted to the rehabilitation trajectory of the patient, because both tests were part of usual care for all patients participating in the oncology rehabilitation program. Therefore, test order was SRT-CPET at T=0 and CPET-SRT at T=1. Seat height was adjusted to the participant's leg length and the same seat height was used for tests at both T=0 and T=1. Participants were blinded for test outcomes during all tests. The CPET and SRT were performed independently and researchers were blinded for previous test outcomes.

### Steep ramp test

The SRT was performed on an electronically braked cycle ergometer. Participants started with a 3-minute warming-up phase with a work rate of 25 W. After this, the work rate was increased by 25 W per 10 seconds in a ramp-like manner. Participants were instructed to keep cycling until exhaustion, with a pedaling frequency of at least 60 rpm. Peak exercise was defined as the point where the pedal frequency dropped below 60 rpm despite strong verbal encouragement. Voluntary exhaustion was considered to be achieved when participants showed clinical signs of intense effort (eg, unsteady biking, sweating, clear unwillingness to continue exercising). SRT-WR<sub>peak</sub> was expressed in watts per kilogram of body weight and was determined as the highest achieved work rate at peak exercise.

### Cardiopulmonary exercise test

Anthropometric measurements were conducted before the CPET. After brief pretest instructions, baseline cardiopulmonary values were collected during a 2-minute rest period while seated at a cycle ergometer. After the rest period, the participant completed a 3-minute warm-up phase of unloaded cycling. Subsequently, the work rate started to increase by an incremental ramp protocol

adjusted to the patient's self-reported physical activity level, aimed at reaching a maximal effort within 8-12 minutes. Participants were instructed to keep cycling until exhaustion, with a pedaling frequency of at least 60 rpm. The protocol continued until the patient stopped cycling or pedaling frequency fell below 60 rpm, despite strong verbal encouragement. Continuous breath-by-breath analysis was obtained during the test using a Vyntus CPX ergospirometry system<sup>b</sup> calibrated for respiratory gas analysis measurements and volume measurements. Peak exercise was defined as the point where the pedaling frequency dropped below 60 rpm. Respiratory gas analysis values at peak exercise were calculated as the average value over the last 30 seconds before test termination. Similar to the SRT, voluntary exhaustion was considered to be achieved when participants showed clinical signs of intense effort.

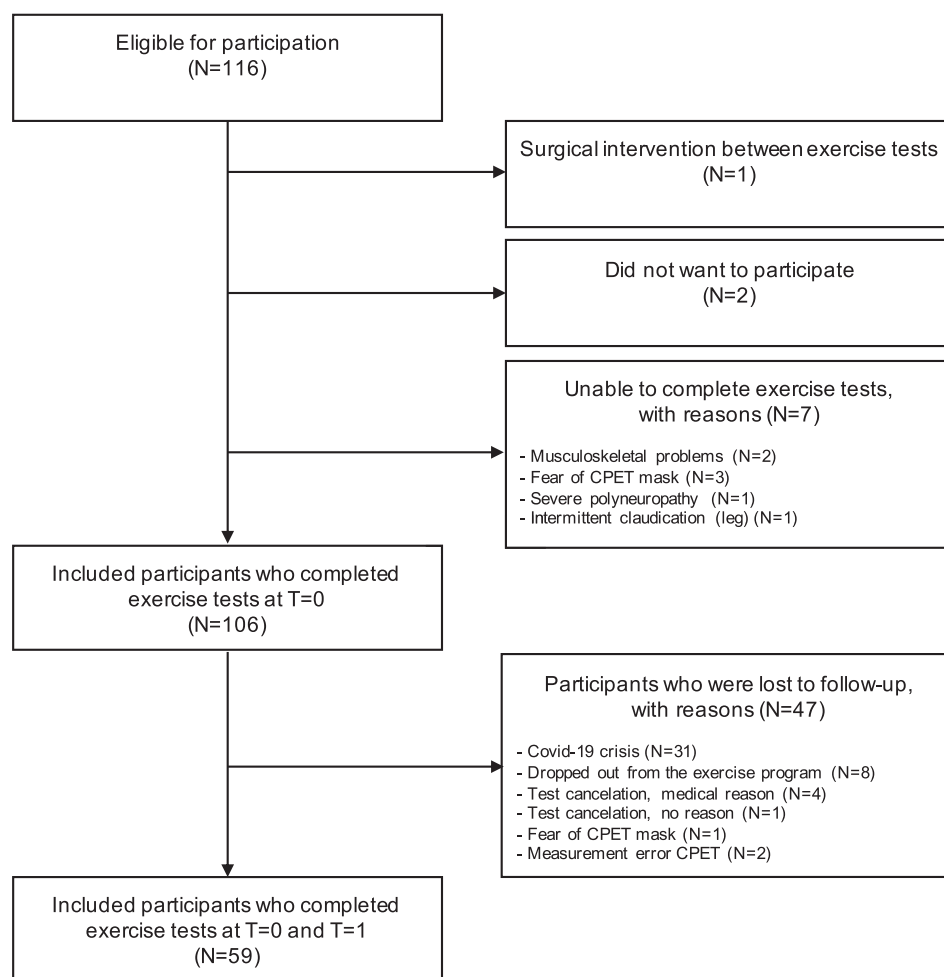
## Statistical analysis

Statistical analyses were performed using SPSS version 23.0.<sup>c</sup> Continuous variables were checked for normality using histograms and Q-Q plots. Patient characteristics and exercise test outcomes are presented as mean  $\pm$  SD or as median and interquartile ranges for continuous variables, as appropriate, whereas data on categorical variables are expressed as frequencies and percentages. Criterion validity of the SRT was evaluated for all participants at T=0 using Pearson or Spearman correlation coefficient, as appropriate, with corresponding 95% confidence intervals (CIs) to quantify the relationship between SRT-WR<sub>peak</sub> and CPET-VO<sub>2peak</sub>. To evaluate the responsiveness of the SRT, the correlation coefficient with corresponding 95% CI was calculated between the absolute change in SRT-WR<sub>peak</sub> and CPET-VO<sub>2peak</sub> from T=0 to T=1 for participants who completed the exercise tests at both time points. ROC curves were plotted between the dichotomized change in CPET-VO<sub>2peak</sub> (improvement vs no improvement) and the absolute change in SRT-WR<sub>peak</sub>. The minimal detectable change for improvement in CPET-VO<sub>2peak</sub> was defined as a relative increase of  $\geq 6\%$ .<sup>20</sup> The AUC of the ROC curve with corresponding 95% CI was calculated to evaluate the ability of the SRT to detect a true improvement in CPET-VO<sub>2peak</sub> of  $\geq 6\%$  over time. The Youden index (sensitivity+specificity-1) was calculated for all points of the ROC curve. The highest value was selected as a potential cutoff point to indicate the minimal detectable change in CPET-VO<sub>2peak</sub>. When the sensitivity for this cutoff point was  $<70.0\%$ , a second cutoff value was chosen at the highest Youden index where the sensitivity was  $\geq 70.0\%$ , because sufficient sensitivity is required to detect training progression. Sensitivity, specificity, and predictive values (%) were calculated for the cutoff value(s).

## Results

### Participant characteristics

Of the 116 patients who were eligible to participate, 106 (91.4%) were included in the analysis. Seven patients (6.0%) dropped out because they were unable to complete 1 or both of the exercise tests until voluntary exhaustion at T=0. One patient was excluded because of a surgical intervention between the CPET and SRT at T=0. Test results at T=1 were available for 59 participants (55.7%). For 31 of the 47 participants (66.0%) who were lost to



**Fig 1** Flowchart of participant inclusion.

follow-up, the rehabilitation program and tests at T=1 were postponed or canceled because of the coronavirus disease 2019 pandemic, during which all outpatient activities were canceled for 4 months. This period was too long for the purpose of this study; therefore, no catch-up measurements were undertaken for these participants. See [figure 1](#) for a flowchart of participant inclusion. The final sample consisted of 78 women (73.6%) and 28 men (26.4%). Mean age was  $56.6 \pm 11.0$  years and breast cancer was the most prevalent diagnosis (48.1%). Further baseline characteristics are summarized in [table 1](#) for all participants (N=106) and for those who completed both exercise tests at T=0 and T=1 (n=59).

### Exercise test outcomes

SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> are presented in [table 2](#) for all participants at T=0 (N=106) and for the participants who completed tests at both T=0 and T=1 (n=59), with corresponding change scores. Mean  $\pm$  SD was  $3.0 \pm 0.9$  W/kg for SRT-WR<sub>peak</sub> and  $19.5 \pm 5.2$  mL/kg/min for CPET-V<sub>O<sub>2</sub>peak</sub> at T=0. Median (interquartile range) between-visit time for the SRT and CPET was 5 (2) days at T=0 and 7 (5) days at T=1. Participants who completed tests at both T=0 and T=1 showed a mean change of  $0.4 \pm 0.3$  W/kg (+12.9%) on the SRT-WR<sub>peak</sub> and a mean change of  $2.0 \pm 2.3$  mL/kg/min (+10.0%) on the CPET-V<sub>O<sub>2</sub>peak</sub> after completion of the exercise program. Forty-one participants showed a

relative increase of  $\geq 6\%$  in CPET-V<sub>O<sub>2</sub>peak</sub> and thus a true improvement in aerobic capacity (69.5%).

### Validity and responsiveness

A Pearson *r* of 0.86 (95% CI, 0.80-0.90) was found for the relation between SRT-WR<sub>peak</sub> and CPET-V<sub>O<sub>2</sub>peak</sub> at T=0 ([fig 2](#)). A Pearson *r* of 0.51 (95% CI, 0.29-0.68) was found for the relation between individual change scores in SRT-WR<sub>peak</sub> and the CPET-V<sub>O<sub>2</sub>peak</sub> from T=0 to T=1 ([fig 3](#)). ROC analysis showed an AUC of 0.74 (95% CI, 0.60-0.87) of the SRT to discriminate between participants who did or did not improve in aerobic capacity (increase in CPET-V<sub>O<sub>2</sub>peak</sub>  $\geq 6\%$ ) after the rehabilitation program ([fig 4](#)). The maximal value of the Youden index was found at 0.38 W/kg, which therefore was chosen as a potential cutoff value. Using this cutoff value resulted in a sensitivity of 56.1%, a specificity of 83.3%, a positive predictive value of 88.5%, and a negative predictive value of 45.5%. A second value was chosen, aiming for a sensitivity  $\geq 70.0\%$ . The highest Youden index for a sensitivity  $\geq 70.0\%$  was found at 0.26 W/kg, which therefore was chosen as the optimal cut-off point of the SRT to detect a true improvement in aerobic capacity. When using this cutoff value in the sample, 35 participants (58.3%) improved aerobic capacity according to the SRT. This resulted in a sensitivity of 70.7%, a

**Table 1** Baseline characteristics of the participants

Characteristic	Participants Who Completed Tests at T=0 (N=106)	Participants Who Completed Tests at T=0 and T=1 (n=59)
Sex (n)		
Male	28 (26.4)	16 (27.1)
Female	78 (73.6)	43 (72.9)
Age (y)	56.6±11.0	54.6±11.0
Body height (cm)	169.6±7.9	170.3±8.1
Body mass (kg)	79.0±13.8	79.1±12.1
Body mass index (kg/m <sup>2</sup> )	27.5±4.8	27.4±4.7
Cancer type (n)		
Breast cancer	51 (48.1)	30 (50.8)
Colorectal cancer	9 (8.5)	3 (5.1)
Lung cancer	7 (6.6)	3 (5.1)
Lymphomas	6 (5.7)	4 (6.8)
Prostate cancer	4 (3.8)	2 (3.4)
Other	29 (27.4)	17 (28.8)
Metastasis (n)		
No metastasis	77 (72.6)	45 (76.3)
Lymphatic metastasis	17 (16.0)	9 (15.3)
Hepatic metastasis	5 (4.7)	2 (3.4)
Skeletal metastasis	4 (3.8)	1 (1.7)
Other	3 (2.8)	2 (3.4)
Treatment (n)		
Surgery	80 (75.5)	47 (79.7)
Chemotherapy	62 (58.5)	33 (55.9)
Radiotherapy	55 (51.9)	26 (44.1)
Hormone therapy	32 (30.2)	20 (33.9)
Immunotherapy	11 (10.4)	7 (11.9)
Stem cell transplantation	4 (3.8)	2 (3.4)

NOTE. Values are presented as n (%) for categorical variables and as mean ± SD for continuous variables.

specificity of 66.7%, a positive predictive value of 82.9%, and a negative predictive value of 50.5% (table 3).

## Discussion

The objective of this study was to examine the criterion validity and responsiveness of the SRT to evaluate aerobic capacity in survivors of cancer. Three a priori hypotheses were formulated. Pearson's correlation analysis showed a strong relationship ( $r=0.86$ ) between SRT-WRpeak and CPET-VO<sub>2</sub>peak at T=0. This

indicates that the SRT has good validity to measure aerobic capacity, confirming the first hypothesis. These findings are similar to the results of de Backer et al,<sup>13</sup> who found an  $r$  of 0.82 between SRT-WRpeak and CPET-VO<sub>2</sub>peak. The SRT seemed to be a valid measurement tool in previous studies with other populations as well.<sup>14-16</sup> These findings are promising because the SRT is a practical test and is less expensive and time consuming than the CPET and can be performed without medical supervision. However, the CPET in survivors of cancer is used not only as a test to measure aerobic capacity but also for the assessment of exercise-limiting factors and exercise-induced cardiovascular risk.<sup>19</sup> Because this information cannot be obtained during the SRT, it is not recommended to use the SRT as an alternative for the CPET in survivors of cancer with increased cardiovascular risks, such as pre-existing cardiovascular disease, treatment with cardiotoxic chemotherapy, and left-sided chest radiation.<sup>8</sup> Yet, the SRT can be used to provide insight in the aerobic capacity of survivors of cancer and to personalize physical exercise training program prescription.

A moderate correlation was found between change in SRT-WRpeak and CPET-VO<sub>2</sub>peak ( $r=0.51$ ), which is in agreement with the second hypothesis. This indicates that the SRT has a moderate responsiveness and might not be the most accurate tool to measure change in aerobic capacity. The current study was the first to examine the responsiveness for aerobic capacity of the SRT. However, a prediction model that was developed by Backer et al<sup>13</sup> and extended and externally validated by Stuiver et al<sup>21</sup> to predict aerobic capacity in individual patients with cancer based on the SRT showed acceptable results at group level but was insufficiently accurate to estimate CPET-VO<sub>2</sub>peak in individual patients. This is in accordance with the current findings of a moderate responsiveness because responsiveness is a measurement property of agreement between individual changes over time.<sup>18</sup>

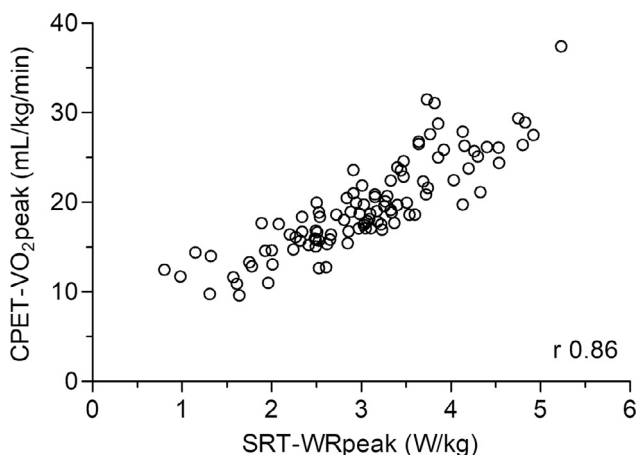
The third and last hypothesis was aimed at testing the ability of the SRT to discriminate between participants who did or did not improve in CPET-VO<sub>2</sub>peak. An AUC of 0.60-0.80 was expected and results confirmed this. Results showed an AUC of 0.74, which implicates that the SRT is sufficiently responsive to indicate a true improvement in aerobic capacity over time.<sup>22</sup> The maximal value of the Youden index was found at 0.38 W/kg; however, using this cutoff value would result in a low sensitivity (56.1%). Because positive feedback is a strong motivator during rehabilitation, the number of false negatives of a performance test should be minimized. Therefore, a sensitivity of 70.0% was pursued, which resulted in an optimal cutoff point of an improvement in SRT performance of 0.26 W/kg to detect a true improvement in CPET-VO<sub>2</sub>peak ( $\geq 6\%$ ).

For both the SRT and CPET, a maximal effort was considered to be reached when participants showed clinical signs of

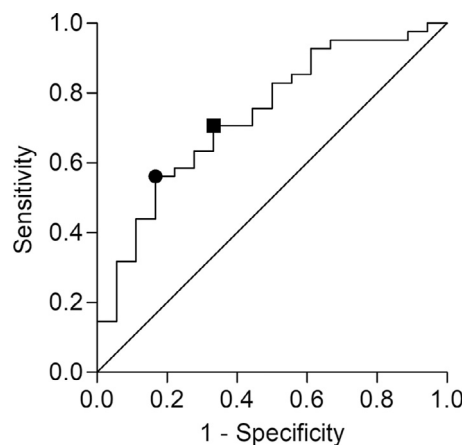
**Table 2** Exercise test outcomes

Test	Participants Who Completed Tests at T=0 (N=106)		Participants Who Completed Tests at T=0 and T=1 (n=59)			
	T=0	T=1	T=0	T=1	Change	% Change
<b>SRT-WRpeak (W/kg)</b>	3.0±0.9	3.1±0.9	3.1±0.9	3.5±1.0	0.4±0.3	12.9
SRT test duration (min:s)	01:30±00:25	01:33±00:25	01:33±00:25	01:48±00:26		
<b>CPET-VO<sub>2</sub>peak (mL/kg/min)</b>	19.5±5.2	20.1±5.3	20.1±5.3	22.1±6.3	2.0±2.3	10.0
CPET test duration (min:s)	09:43±01:35	09:49±01:31	09:49±01:31	11:01±02:07		

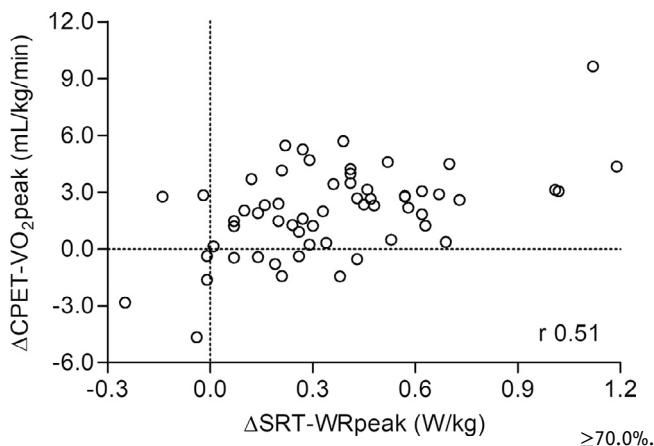
NOTE. Values are presented as mean ± SD. SRT duration and CPET duration are the duration of loaded cycling during these tests and are expressed in minutes and seconds.



**Fig 2** Scatterplot for the relationship between SRT-WRpeak and CPET-VO<sub>2</sub>peak with the corresponding Pearson correlation coefficient (*r*).



**Fig 4** ROC curve for the ability of the SRT to detect a true improvement in CPET-VO<sub>2</sub>peak. Potential cutoff values are displayed in the graph. ●, a cutoff value of 0.38 W/kg, which has a sensitivity lower than 70.0%; ■, the optimal cutoff value of 0.26 W/kg.



**Fig 3** Scatterplot for the relationship between change over time ( $\Delta$ ) in SRT-WRpeak and CPET-VO<sub>2</sub>peak with the corresponding Pearson correlation coefficient (*r*).

voluntary exhaustion, which is a subjective criterion. An objective criterion that is often used to confirm a maximal effort at the CPET is a respiratory exchange rate at peak exercise ( $RER_{peak} \geq 1.10$ ).<sup>23</sup> After analyzing the study data, we noticed that not all patients performed a maximal effort at the CPET, according to the  $RER_{peak}$  criterion. These findings are in agreement with several other studies in survivors of cancer, which also show that a  $RER_{peak} \geq 1.10$  is often not reached in this population.<sup>24,25</sup> To elucidate whether this influenced our results concerning the validity and responsiveness of the SRT, we performed a post hoc analysis. As such, a subgroup of patients who met the  $RER_{peak}$  criterion and a subgroup of patients who did not met this objective criterion were created.

Mean  $\pm$  SD  $RER_{peak}$  was  $1.16 \pm 0.09$  in the total sample ( $N=106$ ) at  $T=0$ . Post hoc analysis showed that 77 participants (72.6%) reached an  $RER_{peak} \geq 1.10$  at  $T=0$ . Participants who did not achieve an  $RER_{peak} \geq 1.10$  at  $T=0$  ( $n=29$ , 27.4%) reached an  $RER_{peak}$  ranging from 0.96-1.09. Mean  $\pm$  SD  $RER_{peak}$  was  $1.17 \pm 0.10$  at  $T=0$  and  $1.18 \pm 0.10$  at  $T=1$  in the group of participants ( $n=59$ ) who completed CPETs at  $T=0$  and  $T=1$ . The post

**Table 3** Sensitivity, specificity, and predictive values of the SRT to detect improvement in aerobic capacity

SRT Cutoff Value (W/kg)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
0.38*	56.1	83.3	88.5	45.5
0.26†	70.7	66.7	82.9	50.0

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

\* The cutoff value with the highest Youden index.

† The cutoff value with the highest Youden index with a sensitivity

hoc analysis demonstrated that 42 of these participants (71.2%) reached an  $RER_{peak} \geq 1.10$  during both CPETs. Because objective criteria for a maximal effort do not exist for the SRT, the heart rate at peak exercise during the SRT was compared between the SRTs at  $T=0$  and  $T=1$ . Participants who completed the SRT at  $T=0$  and  $T=1$  reached mean peak heart rates of respectively  $137 \pm 23$  bpm and  $140 \pm 22$  bpm. These results demonstrate only minor differences between  $T=0$  and  $T=1$  in  $RER_{peak}$  and peak heart rate at the SRT and CPET, respectively. Therefore, it can be assumed that participants showed equal levels of effort during the SRT and CPET tests at  $T=0$  and  $T=1$ .

Subsequently, validity and responsiveness analyses were repeated in the subgroup of participants who met the criteria of an  $RER_{peak} \geq 1.10$  at the CPETs. For validity, this post hoc analysis showed an  $r$  of 0.84 for the relation between SRT-WRpeak and CPET-VO<sub>2</sub>peak at  $T=0$ . For responsiveness, an  $r$  of 0.50 was found for the relation between individual change scores of SRT-WRpeak and CPET-VO<sub>2</sub>peak. ROC analysis showed an AUC of 0.74. These results are similar to the original study results, in which all participants who showed voluntary exhaustion were included, even if they failed to reach an  $RER_{peak} \geq 1.10$ . As such, it appeared that the delivered effort, based on the objective  $RER_{peak}$  criterion, did not affect the study results.

## Study limitations

One study limitation was the fact that the test order was not randomized. Randomization could not be performed because the CPET and SRT were part of usual care and had to be adapted to the rehabilitation trajectory of the patient. Consequently, day-to-day performance variation could have influenced the results of the validity and responsiveness of the SRT.

## Conclusions

Results suggest that the SRT is a valid tool to estimate aerobic capacity in survivors of cancer. Moderate correlations between change scores indicate that the SRT has a limited responsiveness to measure changes in aerobic capacity. Nevertheless, ROC analysis indicates that the SRT is able to determine whether aerobic capacity has truly improved, with cut-off point of 0.26 W/kg.

## Suppliers

- a. Lode Corival, Lode BV.
- b. Vyntus CPX, CareFusion Netherlands.
- c. SPSS Statistics for Windows, version 23.0, IBM Corp.

## Keywords

Cancer survivors; Exercise test; Exercise therapy; Rehabilitation; Validation study

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## References

1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 2016;66:271–89.
2. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. *Med Sci Sports Exerc* 2019;51:2375–90.
3. Hill AV, Lupton H. Muscular exercise, lactic acid, and the supply and utilization of oxygen. *QJM* 1923;16:135–71.
4. Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation* 2016;134:e653–99.
5. Mandsager K, Harb S, Cremer P, Phelan D, Nissen SE, Jaber W. Association of cardiorespiratory fitness with long-term mortality among adults undergoing exercise treadmill testing. *JAMA Netw Open* 2018;1:e183605.
6. Vainshelboim B, Muller J, Lima RM, et al. Cardiorespiratory fitness, physical activity and cancer mortality in men. *Prev Med* 2017;100:89–94.
7. Hurria A, Jones L, Muss HB. Cancer treatment as an accelerated aging process: assessment, biomarkers, and interventions. *Am Soc Clin Oncol Educ Book* 2016;35:e516–22.
8. Jones LW, Courneya KS, Mackey JR, et al. Cardiopulmonary function and age-related decline across the breast cancer survivorship continuum. *J Clin Oncol* 2012;30:2530–7.
9. Winters-Stone KM, Neil SE, Campbell KL. Attention to principles of exercise training: a review of exercise studies for survivors of cancers other than breast. *Br J Sports Med* 2014;48:987–95.
10. Jones LW, Eves ND, Haykowsky M, Joy AA, Douglas PS. Cardiorespiratory exercise testing in clinical oncology research: systematic review and practice recommendations. *Lancet Oncol* 2008;9:757–65.
11. Ross RM. ATS/ACCP statement on cardiopulmonary exercise testing [author reply]. *Am J Respir Crit Care Med* 2003;167:1451.
12. Day JR, Rossiter HB, Coats EM, Skasick A, Whipp BJ. The maximally attainable  $\text{VO}_2$  during exercise in humans: the peak vs maximum issue. *J Appl Physiol* (1985) 2003;95:1901–7.
13. de Backer IC, Schep G, Hoogveen A, Vreugdenhil G, Kester AD, van Breda E. Exercise testing and training in a cancer rehabilitation program: the advantage of the steep ramp test. *Arch Phys Med Rehabil* 2007;88:610–6.
14. Rozenberg R, Busmann JB, Lesaffre E, Stam HJ, Praet SF. A steep ramp test is valid for estimating maximal power and oxygen uptake during a standard ramp test in type 2 diabetes. *Scand J Med Sci Sports* 2015;25:595–602.
15. Bongers BC, de Vries SI, Helders PJ, Takken T. The steep ramp test in healthy children and adolescents: reliability and validity. *Med Sci Sports Exerc* 2013;45:366–71.
16. Bongers BC, Werkman MS, Arets HG, Takken T, Hulzebos HJ. A possible alternative exercise test for youths with cystic fibrosis: the steep ramp test. *Med Sci Sports Exerc* 2015;47:485–92.
17. Hopkins WG. Measures of reliability in sports medicine and science. *Sports Med* 2000;30:1–15.
18. De Vet HC, Bouter LM, Bezemer PD, Beurskens AJ. Reproducibility and responsiveness of evaluative outcome measures: theoretical considerations illustrated by an empirical example. *Int J Technol Assess Health Care* 2001;17:479–87.
19. van den Berg JP, Velthuis MJ, Gijzen BC, Lindeman E, van der Pol MA, Hillen HF. Integraal Kankercentrum Nederland. Richtlijn ‘Oncologische revalidatie’ [Guideline “Cancer rehabilitation”]. *Ned Tijdschr Geneesk*. 2011;155:A4104.
20. Keteyian SJ, Brawner CA, Ehrman JK, et al. Reproducibility of peak oxygen uptake and other cardiopulmonary exercise parameters: implications for clinical trials and clinical practice. *Chest* 2010;138:950–5.
21. Stuijver MM, Kampshoff CS, Persoon S, et al. Validation and refinement of prediction models to estimate exercise capacity in cancer survivors using the steep ramp test. *Arch Phys Med Rehabil* 2017;98:2167–73.
22. De Vet HC, Terwee CB, Mokkink LB, Knol DL. *Measurement in medicine: a practical guide*. Cambridge, United Kingdom: Cambridge University Press; 2011.
23. Steins Bisschop CN, Velthuis MJ, Wittink H, et al. Cardiopulmonary exercise testing in cancer rehabilitation: a systematic review. *Sports Med* 2012;42:367–79.
24. Santa Mina D, Au D, Papadopoulos E, et al. Aerobic capacity attainment and reasons for cardiopulmonary exercise test termination in people with cancer: a descriptive, retrospective analysis from a single laboratory. *Support Care Cancer* 2020;28:4285–94.
25. Canada JM, Trankle CR, Carbone S, et al. Determinants of cardiorespiratory fitness following thoracic radiotherapy in lung or breast cancer survivors. *Am J Cardiol* 2020;125:988–96.