Master's thesis

NTNU
Norwegian University of Science and Technology

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Validity of the Ekblom-Bak Ergometer Cycle Test in Adult Cancer Survivors Undergoing Rehabilitation

Master's thesis in Physical Activity and Health (Movement Science)
Supervisor: Marius Steiro Fimland
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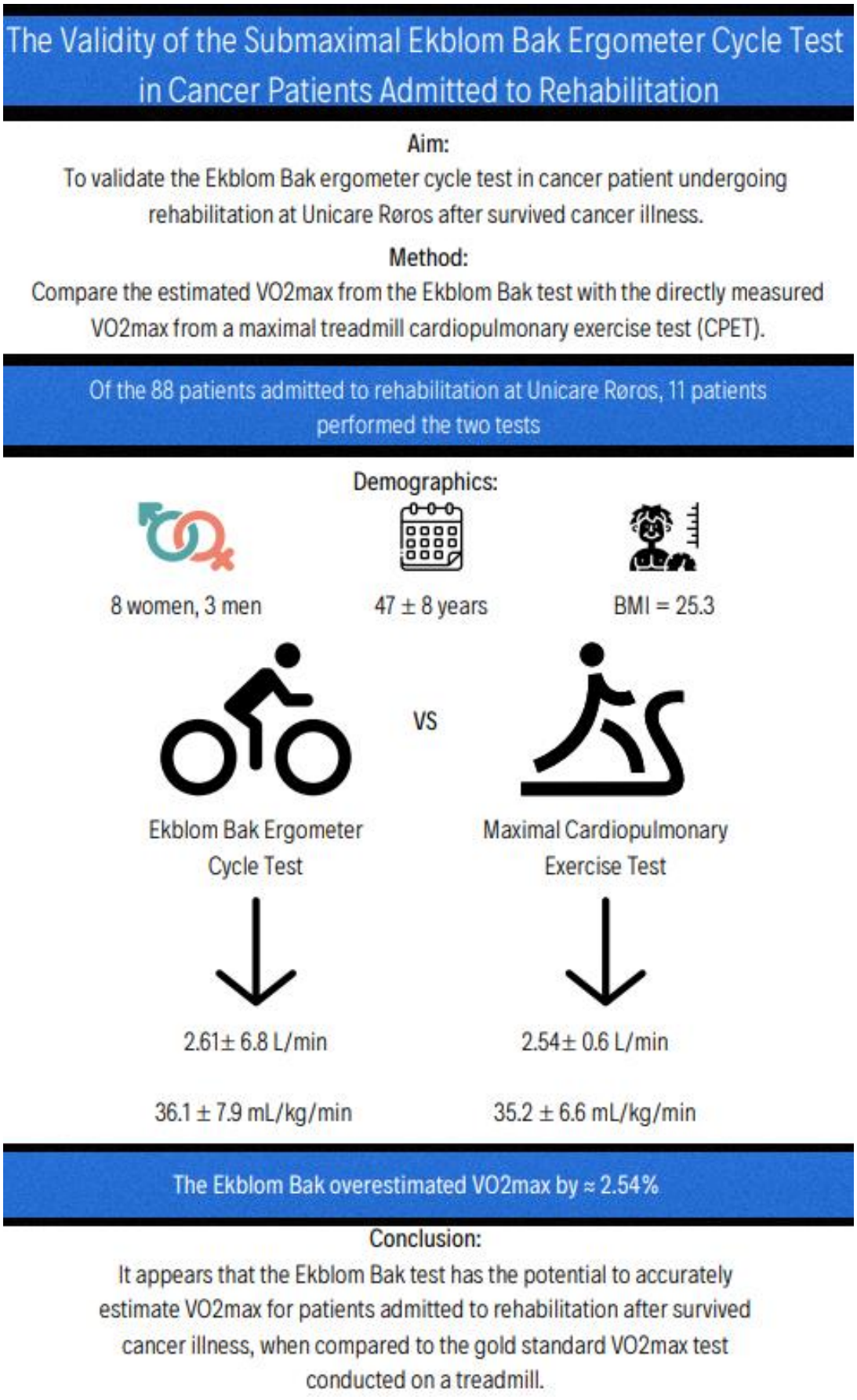
Infographic



Abstract

Objective: To assess the validity of the Ekblom-Bak Ergometer Cycle test in cancer survivors undergoing rehabilitation after having survived cancer illness. The validation was done by comparing the estimated VO_2max from the Ekblom-Bak test with the directly measured VO_2max from a maximal treadmill cardiopulmonary exercise test (CPET).

Method: The two exercise tests were performed on patients undergoing rehabilitation for cancer. They were performed in the same order during their three-week extended stay. In the analysis, the paired sample t-test was performed to compare the mean between the two tests, and the Pearson correlation analysis was performed to establish the correlation. The Bland Altman plots were performed, with limits of agreement (LoA), to determine the bias and agreement between the two tests.

Results: In the final analysis, 11 participants were included. The estimated values from the Ekblom-Bak ergometer cycle test overestimated VO_2max by 2.56% (absolute) and 2.52% (relative) compared to the CPET. The correlation between the two tests was $r = 0.963$ ($p<0.001$, absolute) and $r = 0.926$ ($p<0.001$, relative). For the agreement between the two tests, the absolute VO_2max was: bias: 0.07 L/min (LoA: -0.34 - 0.48 L/min), and the relative was: bias: 0.9 mL/kg/min (LoA: -5.08 - 6.88 mL/kg/min).

Conclusion: The findings in the present study suggest that the Ekblom-Bak test has the potential to accurately estimate VO_2max compared to the gold standard VO_2max in cancer survivors admitted to rehabilitation.

Keywords: Cancer, Rehabilitation, Cardiorespiratory Fitness, Ekblom-Bak Test, Validation Study

Abstrakt

Hensikt: Studiets mål var å validere den submaksimale Ekblom-Bak testen for pasienter på rehabilitering etter overlevd kreft. Dette ble gjort ved å sammenligne det estimerte maksimale oksygenopptaket (VO_2maks) fra Ekblom-Bak testen med det faktisk målte maksimale oksygenopptaket fra en maksimal kardiopulmonal belastningstest (CPET).

Metode: De to testene ble utført på pasienter under rehabilitering etter kreft. De to testene ble gjennomført i samme rekkefølge i løpet av pasientenes tre uker lange opphold. I analysene ble en paired sample t-test utført for å sammenligne forskjell i gjennomsnittet fra de to testene, og Pearsons korrelasjonsanalyse ble gjennomført for å se på korrelasjonen mellom testene. Bland Altman plottene ble gjennomført med limits of agreement (LoA) for å se på skjevheten og likheten mellom testene.

Resultat: 11 deltakere ble inkludert i analysen. De estimerte verdiene fra Ekblom-Bak testen overestimerte VO_2maks med 2.56% (absolutt) og 2.52% (relativ) i sammenligningen med den faktisk målte VO_2maks (CPET). Korrelasjonen mellom de to testene var $r = 0.963$ ($p<0.001$, absolutt) og $r = 0.926$ ($p<0.001$, relativ). I likheten mellom de to testene, var skjevheten for den absolutte verdien: 0.07 L/min (LoA: -0.34 - 0.48 L/min) og for den relative: 0.9 mL/kg/min (LoA: -5.08 - 6.88 mL/kg/min).

Konklusjon: Resultatet fra dette studiet tilsier at Ekblom-Bak testen potensielt kan gjennomføre en valid estimering av VO_2maks sammenlignet med gullstandardtesten for VO_2maks i kreftoverlevende på rehabilitering.

Nøkkelord: Kreft, Rehabilitering, Kondisjon, Ekblom-Bak Test, Valideringsstudie

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Introduction

Cancer is a diverse and complex set of diseases that can begin in roughly any organs and tissue in the body, causing abnormal cells to grow uncontrollably. This uncontrollable growth may lead to cancer spreading to other parts and organs in the body. Cancer is the second leading cause of death globally and stands accountable for 10 million deaths in 2020 (World Health Organization, n.d.). Although cancer is a leading cause of death worldwide and the percentage of individuals who get cancer increases, the number of people getting completely healthy increases simultaneously (Larsen et al., 2021). With this increase in both cases of cancer and cases of survival, the need for rehabilitation, depending on the severity of the disease, is increasing concurrently. It is shown that rehabilitation after cancer can improve the patient's ability to live with their symptoms (Smith et al., 2020). It is also shown that cardiovascular diseases are a competing cause of mortality and morbidity in cancer survivors (Wittekind & Gilchrist, 2021; Williamson et al., 2021) and that improved cardiorespiratory fitness (CRF) can increase survival rate in patients with cardiovascular disease and cancer (Williamson et al., 2021). Therefore, evaluating the cardiorespiratory fitness of cancer survivors admitted to rehabilitation can be a valuable tool for developing effective rehabilitation programs.

CRF is a predictor of both physical performance and functional capacity. It has also been shown to be a strong and independent predictor of disease-specific and all-cause mortality (Strasser & Burtscher, 2018). Therefore, CRF is considered one of the strongest predictors of future life and longevity in healthy people (Strasser & Burtscher, 2018; Gremeaux et al., 2012). The gold standard for measuring CRF is maximal oxygen uptake (VO_2max), which is found through performing cardiopulmonary exercise testing (CPET) (Tran, 2018). A CPET is often performed on a treadmill with increasing workload until exhaustion or until the rate of oxygen utilization plateaus. This plateau is at the end of the CPET and is considered the best evidence of a VO_2max (Albouaini et al., 2007). However, this procedure is time-consuming, requires a trained practitioner to operate the test and analyse the data, and demands fewer available facilities with expensive lab equipment (National Guideline Centre (UK), 2016; Kieu et al., 2020). Another downside of the CPET is that it requires participants to perform until exhaustion. In rehabilitation for cancer, it is considered safe for cancer survivors to exercise and perform until exhaustion (Campbell et al., 2019). However, it is not guaranteed that all patients can perform until maximal exhaustion. This may relate to concerns like cancer-related fatigue, psychological impairments like depression and anxiety, and physical

dysfunction like atrophy, strength loss, and cardiac and pulmonary dysfunction after a severe disease and treatment (Mustian et al., 2012). Therefore, an option can be to perform submaximal tests, which are easier to perform for the patients, as well as reduced expenses and time spent performing the tests.

Submaximal testing allows the participants to do less demanding activities, which helps overcome the many limitations of maximal exercise testing (Noonan & Dean, 2000). Submaximal tests often avoid the needs previously mentioned for maximal testing regarding the laboratories, equipment, time, and cost. It also allows patients to perform tests in a more comfortable resistance (Abut et al., 2016). The most significant disadvantage of submaximal testing compared to maximal effort tests is the relation to predictive accuracy. It requires a regression model to predict or estimate the actual value in maximal tests (Abut et al., 2016). Many submaximal tests are developed for patients to perform when maximal testing is not feasible due to a lack of time, resources, or contraindications for patients to perform maximal tests. One of the most commonly used submaximal tests is an ergometer cycle test called the Åstrand test (Ratter et al., 2014). Nevertheless, in 2012, a new submaximal ergometer cycle test was developed called the Ekblom-Bak ergometer cycle test (EB-test). The EB-test showed a significantly improved accuracy in estimating VO_2max compared to the similar Åstrand test (Ekblom-Bak et al., 2014: Väisänen et al., 2020). The EB-test was later revised in a healthy adult population and showed a further strong and valid correlation in the estimation of VO_2max in a wide variety of fitness levels (19-76 mL/kg/min) and age (20-86 years).

The EB-test is a time-efficient, easily administered, and low-cost test, that could appear to be a test with low risk for patients to perform in a rehabilitation setting if the gold standard maximal CPET test is not attainable (Ekblom-Bak et al., 2014; Björkman et al., 2016). However, there is limited research on the EB-test in patient groups and cancer survivors admitted to rehabilitation. Currently, only one study has tried to test the validity of a patient population, and this study was performed on breast-cancer patients while under treatment with chemotherapy (Mijwel et al., 2016). The study found that the EB-test overestimated the VO_2peak and found that the EB-test could not accurately predict the VO_2peak in the population. Henceforth, there is interest in investigating cancer survivors undergoing rehabilitation for mapping and treatment of late effects. Therefore, the objective of the present study is to evaluate the validity of the Ekblom-Bak ergometer cycle test in cancer survivors admitted to rehabilitation by comparing the estimated VO_2max data from the submaximal Ekblom-Bak cycle test with the VO_2max data from the gold standard CPET treadmill test.

Methods

Participants

The participants were recruited from patients attending rehabilitation for cancer at Unicare Røros in Norway. At Unicare Røros, the rehabilitation program emphasizes mapping and treatment of the late effects of the disease. During the start of the patient's stay at the centre, they were orally informed about the project by the leader of the cancer team and asked to attend a plenary information meeting during their second week at the centre—the patients who were interested in the project attended voluntarily. The patients were given written and oral information about the project in the plenary meeting. Every patient provided informed written consent before performing tests in the project. This study employed a convenience sampling method, which involved including all patients undergoing rehabilitation for cancer who were willing to participate in the research. The inclusion criteria for the study required the patients to have survived their cancer illness and completed their treatment. They would also have to be cleared for participation by the doctor at the centre, ensuring that every participant willing to participate had no contraindications for maximal exercise testing.

Further, all data was collected as required by the Declaration of Helsinki, and the rules for confidentiality and privacy were met. The Regional Committees for Medical and Health Research Ethics (REK) Southeast C treated the project application with application number 492103. The project falls outside the scope of the Health Research Act, cf. § 2 and § 4 letter a). Approval from REK is not required to carry out the project.

Test information

The patients were informed that a maximal CPET and a submaximal EB-test would occur. Before they were to complete the tests, they were given pre-test instructions. These instructions included that they should not have performed any vigorous physical activity within 24 hours before the tests and that they should not consume a significant amount of food within two hours before the tests, as well as nicotine and any fluid other than water. The rehabilitation plans of the participants were alternated and modified to accommodate these instructions. These alterations included changing the time to eat meals and some modifications in the exercise program the day before the tests. Instructions on Borg's rating of perceived exertion from 6-20 were given before the EB-tests, as the participants were to categorize their subjective feelings during the test (Borg, 1982).

Maximal test (Cardiopulmonary exercise test)

The VO_2max test was performed on a treadmill (Woodway PPS 55 Med, Waukesha, WI, USA). Before the test started, the participants were fitted with a mask covering the mouth and nose (Hans Rudolph, Germany), and it was made sure this mask was the right size relative to the participant's face to prevent gas leakage. This mask was fitted with a Digital Volume Transducer (DVT) that was connected to the Vyntus CPX (Vyaire Medical, Hoechberg, Germany). This device measures and analyses the gas exchange between oxygen and carbon dioxide with each breath while the participant performs the test. Before the test, the DVT and Vyntus CPX had to be calibrated to ensure the correct gas levels. This automatic procedure requires a calibration gas (5.00 ± 0.01% CO2 and 16.00 ± 0.01% O2 (Vyaire Medical, Hoechberg, Germany)) and the already circulating air in the room to ensure a legitimate calibration.

The test was performed with a pre-defined protocol programmed in the Sentrysuite test software (Vyaire Medical, Hoechberg, Germany) called the Ramp protocol. In this pre-programmed protocol, the test is performed at a self-selected pace for the entirety of the test. This pace is selected for the test subject with help from the training personnel at the rehabilitation centre in collaboration with the responsible person who is managing the test. The protocol had a warm-up phase included, which lasted for 4 minutes, consisting of a speed of 2 km/h (kilometres per hour) slower than the pace selected for the actual test, and with a 0 percent incline. When the warm-up phase was completed, the test began. The test was performed at the pre-defined pace for the entirety of the test and had an increase in incline for each minute by 2 percent. While this increase occurred every minute, it reached a maximal incline percentage of 20, 10 minutes into the test. If the participant could perform longer than these 10 minutes and only reached a submaximal work rate, the protocol could be manually adjusted to ensure that the participant reached maximal effort. The protocol from the Sentrysuite test software can be found in Appendix 1. As these tests were conducted on a population with little to no experience on a treadmill, they were given permission to hold on to fitted handles on the treadmill if they felt uncomfortable or lost balance.

Submaximal test (Ekblom-Bak ergometer cycle test)

The EB-test was performed on an electronically braked cycle ergometer (Monark 928E, Vansbro, Sweden), and the participants were fitted with a chest-worn heart rate monitor (Polar H10, Kempele, Finland). Before the test began, the participants were asked if they had

performed any vigorous physical activity or had eaten any substantial meal within two hours before the test, even though the participants were given pre-test instructions and the rehabilitation plan was changed to accommodate the test. The test administrator helped fit the heart rate monitor, adjust the ergometer cycle, and inform the participants about Borg's RPE scale. The participants were then further given instructions regarding the approximately eight minutes extended test. Before the test began, the test manager made sure the ergometer cycle was calibrated. Then the participants were instructed to cycle for four minutes straight, with a pedalling rate of 60 repetitions per minute (RPM), at a pre-defined work rate of 30 watts (W) which applied to all participants.

Further, the participants would then go directly into a new four-minute period with a higher workload decided by the test administrator. The higher workload was decided by information on training status and training background provided by the participant, as well as body size, gender, and information on the disease. The test administrator would then use this information to decide a workload that would take the participants to an RPE ≈ 14. The participants would then cycle the first minute on this workload before being asked by the administrator to assess where they were on the RPE scale. If the RPE was < 10, the load was increased by 60 W, and the four-minute working period would restart. If the RPE were between 10 and 11, the workload would be increased with 30 W, and the four-minute period would restart. If the RPE were reported to be between 12-16, the test would be continued and finished. Then lastly, if the RPE were 17 or higher, the test would be terminated and be completed after a 20-minute resting period or at another time. During the last minute, meaning between minute three and four on each of the two workloads, the heart rate was noted on four occasions (at 3.15, 3.30, 3.45, and 4.00 minutes), and a mean heart rate was calculated. The protocol in its entirety can be found in Appendix 2.

For the calculations of the estimation of VO_2max, the EB-test uses an equation consisting of a difference in heart rate relative to the increase in watts, defined as power output (PO). The PO is found in a table where the pre-defined factor matches the watts the participants have performed during the test. The equation also depends on the factors of gender and age of the participant. For the calculations of the VO_2max, an Excel (Microsoft Excel, 2019) sheet provided by The Swedish School of Sport and Health Sciences was used. This Excel sheet was both easily accessible and easy to use and had the formula for the calculation already integrated into the sheet. These calculations can also be performed without the Excel sheet,

for men the equation looks like this; $\dot{V}O2peak = 2.04900 - 0.00858\ (age) - 0.90742\ (\Delta HR/\Delta PO) + 0.00178\ (\Delta PO) - 0.00290\ (HR\ at\ standard\ work\ rate)$, and for women; $\dot{V}O2peak = 1.84390 - 0.00673\ (age) - 0.62578\ (\Delta HR/\Delta PO) + 0.00175\ (\Delta PO) - 0.00471\ (HR\ at\ standard\ work\ rate)$ (Björkman et al., 2016).

Statistical analysis

All necessary statistical analyses were performed in IBM SPSS Statistics 27 (SPSS Inc, Chicago, IL, USA). In the statistical analyses, the statistically significant level was set to $p<0.05$. The descriptive data are presented as mean ± SD (standard deviation). Due to the small sample size, histograms and QQ plots were used to check for normal distribution. To check the difference between the two tests, with a confidence interval of 95%, a paired sample t-test was performed. Pearson's correlation coefficient (r) was calculated for the correlation between the two tests. The correlation coefficient was seen as weak if it was under 0.10 and was classified as modest between 0.1 - 0.3, moderate between 0.3 - 0.5, strong between 0.5 - 0.8, and very strong between 0.8 - 1.0.

For the coefficient of variation, the standard deviation (SD) of the difference between the estimated and measured VO_2max was divided by the mean of the measured VO_2max. This describes the relative variation of the data and determines how much the difference between the two varied in relation to the mean of VO_2max. A linear regression was calculated to find the standard error of estimate (SEE), to quantify the variability around the regression line. A Bland Altman plot was created with limits of agreement (LoA) to evaluate the agreement or disagreement between the two tests. In the Bland Altman plot, the y-axis represents the difference between the two tests, while the x-axis represents the mean of the two tests. To calculate the LoA, the upper and lower limit was calculated by the formula: Mean difference between measured and estimated VO_2max ± 1.96 times the standard deviation of the difference between measured and estimated VO_2max. The LoA represents the range of 95%, in which the values are expected to fall. The plot is useful in identifying systematic bias or outliers and assessing the agreement.

Results

The final analysis included a sample of 11 participants, all of whom had survived cancer illness in recent years and were now admitted to rehabilitation, having achieved cancer remission. Of these participants, 8 were female, and 3 of them male. The cancer diagnoses among these 11 participants included one case each of myeloma, lymphatic cancer, colorectal cancer, brain tumor and testicular cancer, and six cases of breast cancer. The recruitment and exclusion process for the sample is depicted in Figure 1. The mean age of the participants was 47 years, with a mean Body Mass Index (BMI) of 25.3. Table 1 provides a summary of the demographic and descriptive characteristics of the population.

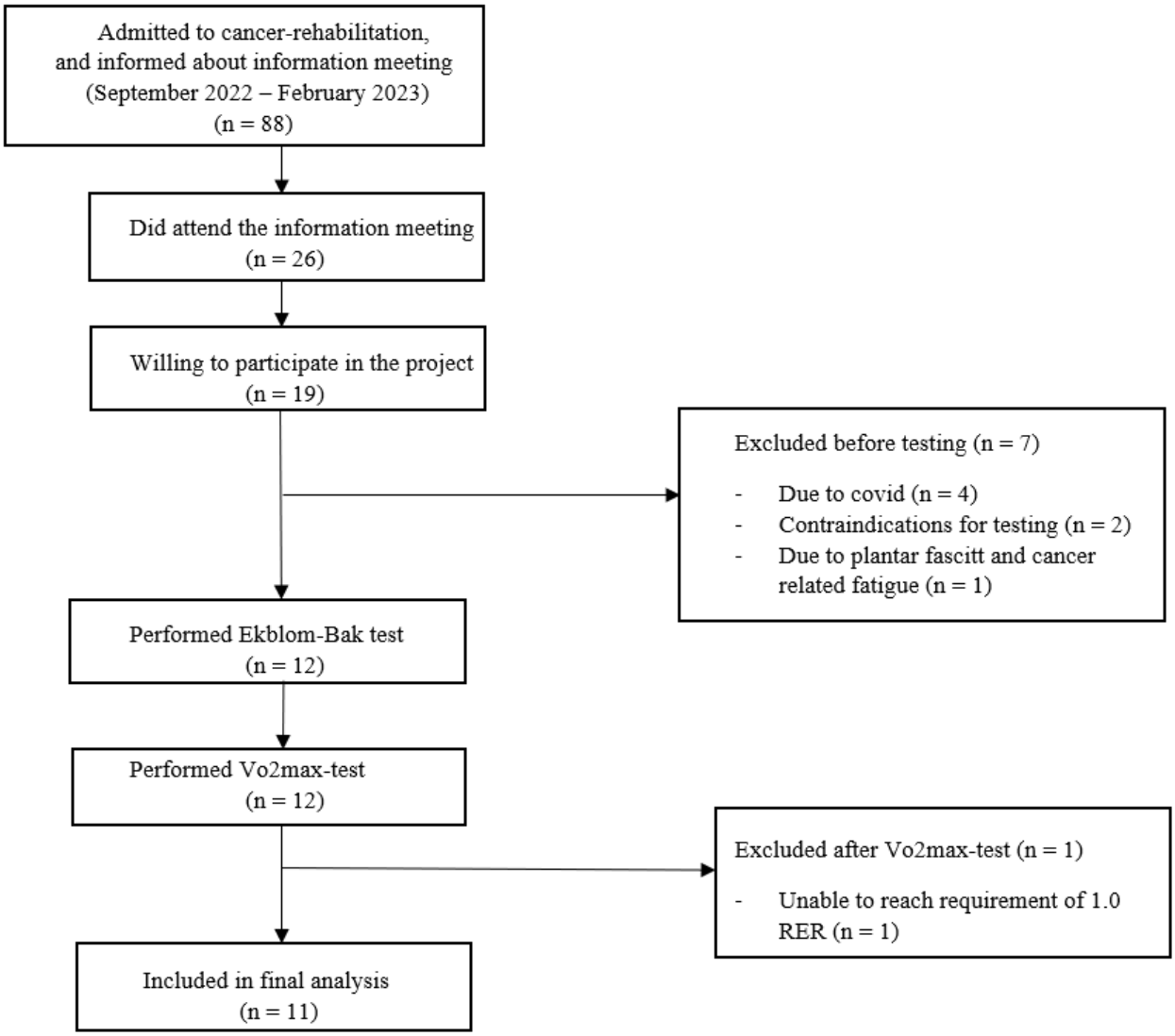

Figure 1: Flow of participants in the study. RER = Respiratory Exchange Ratio

Table 1: The characteristics of the sample that is included in the final analysis (mean ± standard deviation).

	All (n = 11)	***Women (n = 8)***	***Men (n = 3)***
Age (years)	*47.2 ± 8.4*	*47.3 ± 8. 9*	*47.0 ± 8.9*
Height (cm)	*170.5 ± 5.8*	*168.9 ± 5.8*	*174.7 ± 4.0*
Weight (kg)	*73.1 ± 11.7*	*71 ± 10.8*	*78.5 ± 14.4*
BMI	*25.3 ± 5.0*	*25.1 ± 5.3*	*25.8 ± 5.1*

BMI = Body Mass Index; cm = Centimetres; kg = Kilograms

In the submaximal EB-test, the higher work rate varied from 90-120 Watts, while the subjective scores from the Borg scale varied from 12 to 15. In this study, the EB-test was found to overestimate VO_2max by 2.56% ($p = 0.302$) for all participants in absolute VO_2max value and by 2.52% ($p = 0.351$) in relative VO_2max. The coefficient of variation (CV) was high for both absolute and relative values at 21.7% and 18.8%, respectively, indicating variability and low precision in the findings. The standard error of estimate (SEE) was calculated to be 0.16 for absolute values and 2.63 for relative values, indicating good predictive accuracy.

Table 2: Presentation of the result from the maximal cardiopulmonary test and the Ekblom-Bak cycle test

	All (n = 11)	**Women (n = 8)**	**Men (n = 3)**
Ekblom-Bak			
Absolute L/min; (mean ± SD)	2.61 ± 6.8	2.35 ± 0.4	3.3 ± 0.85
Relative mL/kg/min; (mean ±SD)	36.1 ± 7.9	34 ± 8.16	41.7 ± 3.59
CPET			
Absolute L/min; (mean ± SD)	2.54 ± 0.55	2.35 ± 0.3	3.1 ± 0.81
Relative mL/kg/min; (mean ±SD)	35.2 ± 6.6	33.9 ± 7.17	38.5 ± 4
Between test difference			
Absolute (L/min); mean [95% CI]	0.07 [-0.1, 0.2]	0.00 [-0.17, 0.17]	0.25 [0.12, 0.38]
Relative (mL/kg/min); mean [95% CI]	0.9 [-1.1, 2.9]	0.04 [-2.6, 2.7]	3.2 [0.8, 5.6]
Correlation coefficient			
Absolute; (r)	0.963	0.877	0.999
Relative; (r)	0.926	0.924	0.974
Coefficient of variation			
Absolute; (%)	21.65 %	12.74 %	26.69 %
Relative; (%)	18.76 %	21.11 %	10.41 %
Standard error of estimate			
Absolute; L/min	0.16	0.21	0.05
Relative; mL/kg/min	2.63	2.97	1.27

SD = Standard Deviation; CI= Confidence Interval; L = Litres; mL = Millilitres; kg = Kilograms; min = Minute; r = Correlation Coefficient; % = Percentage

The agreement between the measured VO_2max from the CPET and estimated VO_2max from the EB-test for the absolute VO_2max value in all participants was: bias: 0.07 L/min (LoA: -0.34 - 0.48 L/min) and the agreement for the relative VO_2max was: bias: 0.9 mL/kg/min (LoA: -5.08 - 6.88 mL/kg/min). Figure 2 shows a Bland Altman analysis with degrees of freedom for all participants. A describes the agreement concerning the absolute VO_2max between the two tests, and B describes the agreement concerning the relative VO_2max between the two tests.

The correlation between the two tests was found to be very strong, with coefficients of 0.963 ($p<0.001$) and 0.926 ($p<0.001$) for absolute and relative VO_2max, respectively. Figure 3 visually depicts the correlation between the two sets of values, where A illustrates the correlation between the absolute values, while B presents the correlation between the relative VO_2max values.

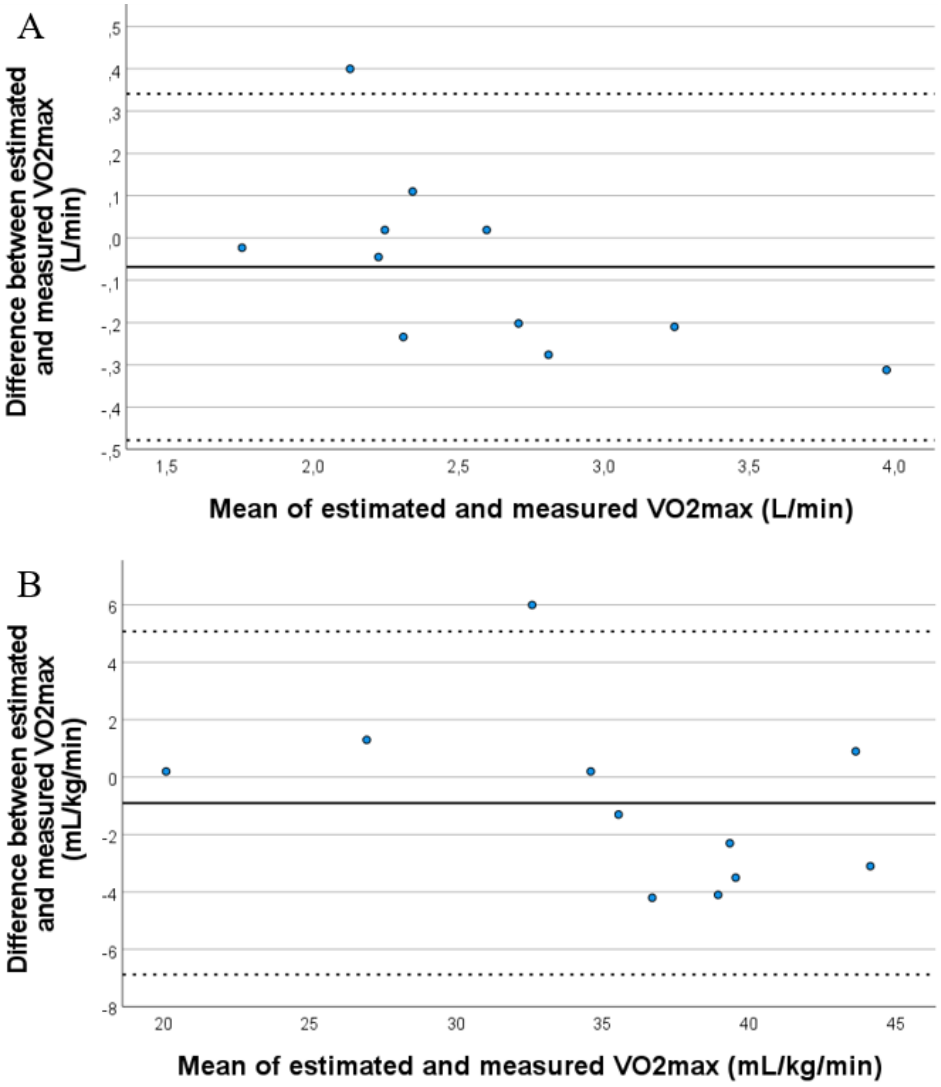

Figure 2: A Bland-Altman plot to represent the agreement between two methods of measurement. The absolute difference between EB-test and CPET is displayed in (A), and the relative difference is displayed in (B). The graph includes horizontal lines which represents the mean bias (black line), as well as upper and lower limits of agreement (LoA) (black dotted line).

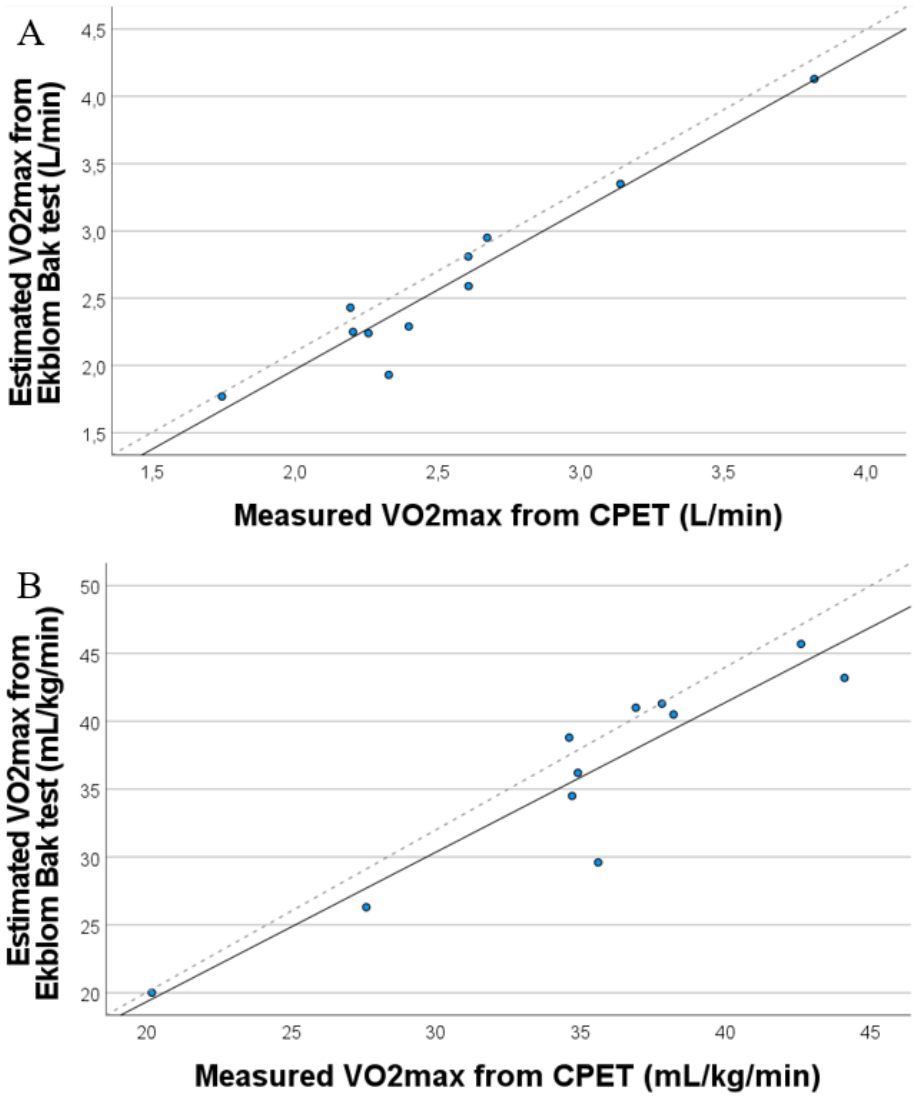

Figure 3: Correlation analysis between the estimated VO_2max from the EB-test in Y-axis, and the measured VO_2max from the CPET in the X-axis (black line). Included a representation of the absolute positive correlation (dotted line).

Discussion

The present study aimed to validate the submaximal Ekblom-Bak ergometer cycle test in cancer survivors admitted to rehabilitation. This was done by comparing the estimated VO_2max from the Ekblom-Bak ergometer cycle test with the VO_2max from the gold standard CPET performed on a treadmill. The results showed that the EB-test overestimated VO_2max by 2.56% (2.61 vs. 2.54 L/min) for the absolute VO_2max and by 2.52% (36.1 vs. 35.2 mL/kg/min) in the relative VO_2max, which is a mean in-between difference between the two tests of 0.07 L/min and 0.9 mL/kg/min. The agreement between the two tests was good and had a significant, very strong correlation of 0.963 ($p<0.001$) for the absolute VO_2max and 0.926 ($p<0.001$) for the relative VO_2max in the entire population. The Bland-Altman analysis indicated that, overall, the EB-test yielded a reliable measure of agreement between the two

tests. However, one value was found to be outside the limits of agreement. The coefficient of variation indicated high variability and low precision in the findings for absolute and relative VO_2max, with 21.7% and 18.8% for absolute and relative, respectively. The standard error of estimate indicated a good predictive accuracy as the values were 0.16 for absolute and 2.63 relative VO_2max, respectively.

The result of the study indicates that the Ekblom-Bak ergometer cycle test has the potential to predict VO_2max in a population of cancer survivors. These results are consistent with previous studies that have examined the validity of the EB-test in healthy populations. For example, a study performed by Björkman et al. (2016), which aimed to develop the Ekblom-Bak equation further, found that the EB-test could validly estimate the VO_2max in a healthy population with an age gap between 20-86 years of age and a wide range of fitness levels, spanning from 19 to 76 mL/kg/min. The study found a similar in-between difference of -0.01 L/min, with a correlation of 0.90 and a SEE of 0.28 L/min, compared to the present study`s in-between difference of 0.07 L/min, correlation of 0.963 and SEE of 0.16 L/min. Similarly, another study by Björkman et al. (2018) found the EB-test to be reasonably valid in adolescents aged between 10 to 15 years of age. The study reported similar results, with an in-between difference of 0.09 L/min, a correlation of 0.86, and a SEE of 0.28 L/min.

Further, a study by Väisänen et al. (2020) aimed to validate the EB-test for an elderly population. The age varied from 65-75 years of age, and it was found that the EB-test predicted a valid estimation of the VO_2max in elderly women but not in all men. The study found a similar in-between difference of 0.02 L/min in all women, with a correlation of 0.88, compared to the in between difference of 0.09 L/min and correlation of 0.963 in the present study. The study also found an in-between difference of 0.05 in all men but with a weaker correlation of 0.44. In addition, a study was performed by Schultz et al. (2020) to test the validity of the EB-test in a population aged between 25 to 73 years of age. The study found that the EB-test significantly underestimated the VO_2max for absolute and relative values, contradicting the present study. In the study by Schultz et al., the absolute VO_2max was found to be underestimated by 0.48 L/min, with a correlation coefficient of 0.97. The relative VO_2max was also underestimated by 6.17 mL/kg/min, with a correlation coefficient of 0.98. These differences between the actual and estimated values were larger than the present study's results, which showed a small overestimation of 0.09 L/min and 2.63 mL/kg/min for the absolute and relative VO_2max, respectively.

Regarding the Coefficient of Variation, other studies have reported a smaller CV than the present study`s CV of 21.7%. The study by Bjørkman et al. (2016) mentioned a lower CV of 8.7%, and Väisänen et al. (2020) reported a CV of 11.1% and 11.6% for women and men, respectively. This variability between the studies may be due to differences in the populations. Therefore, the CV should therefore be interpreted cautiously as it may be less robust due to the small sample size of 11 participants in the present study. Further, it is important to consider that the high CV may be because of individual factors such as differences in fitness level, treatment history, and type of cancer participants have survived. This may argue that the test is not suitable for precise individual assessment.

In the present study, the fittest and most well-functioning patients seemed willing to participate as their cardiorespiratory fitness level was high. The previously mentioned studies by Bjørkman et al., Väisänen et al., and Schultz et al., conducting research on healthy populations found 3.18 L/min, 31.4 mL/kg/min, and 30.7 mL/kg/min as the mean VO_2max in all participants, respectively. Other reference data, like the HUNT studies in Norway, found that the mean VO_2max in a healthy population was 47.2 mL/kg/min and 38.4 mL/kg/min for men and women aged 40-49 years old, respectively (Loe et al., 2013). The mean VO_2max in this study was 2.54 L/min and 35.2 mL/kg/min, arguing that the participants in the present study had reasonably good cardiorespiratory fitness.

To the author's knowledge, only one study has been performed on a patient population, particularly cancer patients. The study performed by Mijwel et al. (2016) investigated the estimation of VO_2peak in patients with breast cancer while undergoing chemotherapy and found a mean VO_2peak of 1.90 L/min, which is notably smaller than in the present study. Those tests were performed on 8 women and found that the EB-test overestimated VO_2peak by 0.79 ($r = 0.21$) L/min, a 42% overestimation that contradicts this present study. The study also found a CV of 21%, similar to this study, which the similar number of participants can explain. In comparison to the study conducted by Mijwel et al. on a similar group of cancer patients and the data from the healthy populations, the current study's findings suggest that despite their illness and strenuous treatments, the participants had a relatively high level of cardiorespiratory fitness, as evidenced by their mean VO_2max. The mean VO_2max in this study was as high, or even higher than in some of the previously mentioned studies, indicating that the participants had an impressive level of fitness considering the challenges they had faced.

The differences between this study's findings and the findings of Mijwel et al., (2016) can be explained by the fact that the participants in this study had survived their cancer illness and had finished the more strenuous treatments during the last couple of years. On the other hand, the participants in the study by Mijwel et al. were undergoing chemotherapy during the testing, which could have significant implications on the physiological responses to the test conducted, as chemotherapy can lead to a decrease in physical function and loss of muscle mass (Browall et al., 2018; Peel et al., 2014), as well as significantly impaired cardiopulmonary function in women with breast cancer (Klassen et al., 2014). As a result, these physiological responses could potentially impact the results of the test conducted on the population of Mijwel et al., compared to the present study`s results.

In the present study, an electronically braked ergometer cycle (Monark 928E) was used to perform the Ekbom Bak test, instead of a mechanically braked ergometer cycle (Monark 828E) that was used in developing the test by Ekblom-Bak et al., (2014), as well as in the study by Väisänen et al., and both studies by Björkman et al., who found the Ekblom-Bak ergometer cycle test to be valid. A limitation of this electronically braked cycle is that it measures the workload in Watt (W) and not Kilopond as it has been done in the previous studies mentioned. Despite the potential variation in the work rate between Kilopond's and W, the Swedish School of Sport and health science has devised a calculation for converting Kilopond's to W, which can help standardize and compare the results obtained from the test. According to these conversions, the workload of 0.5 Kilopond's is approximately 32W at a cadence of 60 RPM on the cycle. This created a problem in the electronically braked ergometer cycle as it only can increase the workload by 5W at a time, creating a small deficit in workload as compared to the Kilopond. An example is that the highest workload in this study was performed at 120W and not 127W, which would have been equal to 2.0 Kilopond's. This is a slight difference, but it could have affected the result. It is possible to think that the result may be overestimated because the formula used to calculate the VO_2max anticipates that the work is performed at, for example, 127W, while it is performed at 120W. This leads to potentially lower heart rate responses than anticipated for the given workload and, thus, an overestimation of VO_2max due to the formula-derived workload being higher than the performed workload.

In addition, the estimation of the Ekblom-Bak ergometer cycle test is only validated with the mechanically braked cycle. It is uncertain if the electronically braked cycle and the resistance it provides are similar to the mechanically braked cycle the test is validated for. Different

ergometer cycles may give different work rate responses at the same resistance (Ekblom-Bak et al., 2014). An example of this can be the significant underestimation found in the study by Schulz et al. (2020). This study conducted the tests on a recumbent cycle ergometer (Lode, Corival, Groningen, The Netherlands), which is not a Monark ergometer cycle. This raises uncertainty regarding the validity of the studies not using the mechanically braked Monark 828E.

The present study has some limitations, and one of them is the small sample size. In a validation study like this, a small sample size of only 11 participants may affect the generalizability of the findings. This small sample size reduces the study's statistical power, thus, making it difficult to detect significant differences or associations in the data. This also leads to the risk of bias and errors that can impact the validity of the findings. In the presented study, recruiting participants was difficult, as the study was performed in a rehabilitation centre. During the patient's stay in this rehabilitation centre, they go through a cramped schedule, with little room for spare time and breaks. During a typical day at the centre, they have multiple exercise classes, rehabilitation sessions, one-to-one conversations, and other informational classes. There seemed to be low interest in the study due to not wanting to miss these planned rehabilitation classes and exercises, as well as being too tired to participate. Another problem regarding the tight schedule was the pre-test protocol, where they could not perform any vigorous physical activity within 24 hours before the test, as well as they should not have consumed a significant amount of food as well as nicotine and any fluid other than water within two hours before the tests. As the participants did not want to miss any planned exercises in the rehabilitation program, there would, in some cases, not have been 24 hours of no exercise before the EB-test. In addition, the spare time found to complete the EB-test was often tighter than the requirement of 2 hours after meals, although no closer than 1 hour and 30 minutes. This may have influenced the results, as it is not entirely in allegiance with the pre-test protocol.

Another limitation of this study is that it is possible that only the more well-trained patients at the rehabilitation centre were willing to participate. Observations of patients at the centre, as well the shown fitness level of the participants included, suggest that those who chose to participate in study tended to be more motivated as well as in better physical shape. Additionally, the study required participants to perform a strenuous maximal VO_2max test as part of the inclusion criteria, which may have deterred less motivated or less functioning patients from participating. Therefore, it is plausible that the participants in this study were

the fittest and most well-functioning patients at the rehabilitation centre. This may lead to selection bias, as the test is only validated for patients with higher values of cardiovascular fitness. This potential selection bias towards fitter cancer survivors may limit our ability to generalize the findings of our study and fully understand the potential of the Ekblom-Bak ergometer cycle test in the broader cancer population. Despite these limitations, the findings may still be relevant for cancer survivors with higher cardiovascular fitness levels and may have some clinical implications for this patient group. The EB-test can be useful for assessing their cardiovascular fitness at the beginning of their rehabilitation to guide and tailor their exercise prescriptions. Although, it may not be generalizable to the broader cancer-population. As mentioned, the study suffered from a small sample size, and a more prominent inclusion of patients could have increased the statistical power of the findings, especially in the male population, as there were only three male participants.

The findings of this study have some practical implications for the rehabilitation of cancer survivors. First, the results suggest that the EB-test is a promising tool for assessing cardiorespiratory fitness in cancer survivors. The test is easily administered, requires less time than the gold standard VO_2max test, and can be completed without the need for specialized equipment or personnel. This may have important practical implications for healthcare settings that serve cancer survivors, as it may allow for more frequent monitoring of cardiorespiratory fitness during rehabilitation. Additionally, the study suggests that the EB-test is safe and feasible for use in cancer survivors, which may help to improve patient safety during exercise testing and rehabilitation programs. Overall, the findings suggest that the EB-test may be a useful tool during rehabilitation for cancer survivors, and further research with larger sample sizes may be needed to fully understand the potential of this test.

Conclusion

In conclusion, the Ekblom-Bak ergometer cycle test has the potential to accurately estimate VO_2max compared to the gold standard VO_2max test conducted on a treadmill on a population of cancer survivors admitted to rehabilitation. The EB-test offers several advantages, including its ease of administration, low cost, and less time-intensive nature, particularly when compared to the gold standard test. These results suggest that the EB-test may represent a feasible and viable alternative to the maximal CPET in cancer survivors admitted to rehabilitation, especially for individual's incapable of performing until maximal exertion.

This study represents only a novel inquiry into the applicability of the EB-test in cancer survivors undergoing rehabilitation. Given the lack of research examining the Ekblom-Bak ergometer cycle test in this population, there is a need for further investigation to achieve a more robust and representative sample with more significant variation in fitness levels. Therefore, future research efforts should expand the inquiry scope to include a more extensive and more diverse population of cancer survivors in rehabilitation.

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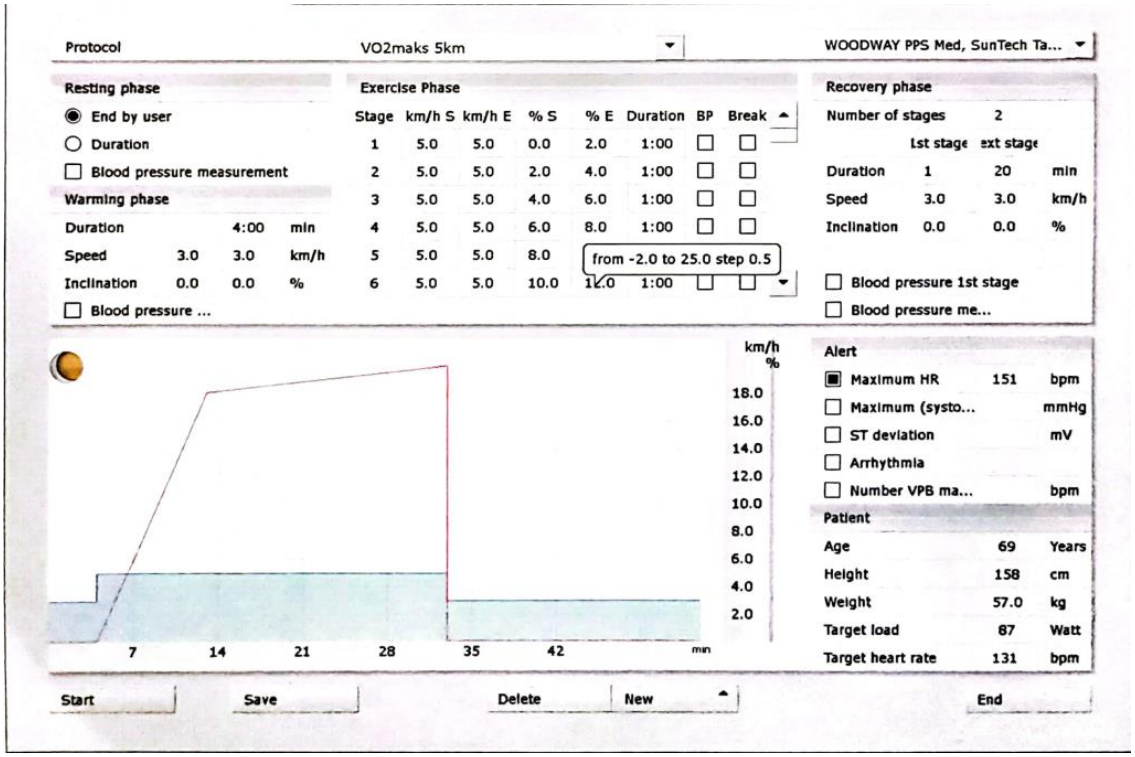
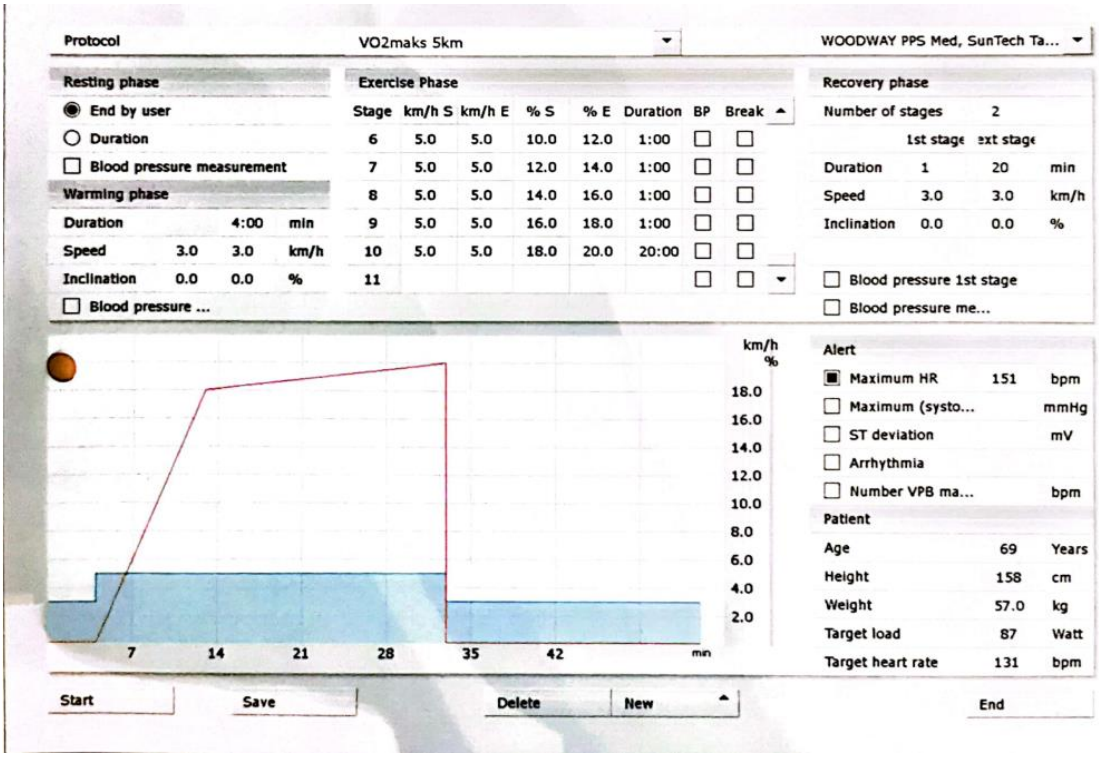
Appendices

Appendix 1: VO_2max-protocol





Appendix 2: Ekblom-Bak Ergometer cycle test protocol.

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The EKBLOM-BAK test
- a submaximal cycle ergometry test for estimation of VO_2max

The test is based on change in heart rate between a low standard workrate (same workrate for all subjects performing the test), followed by an individually chosen higher workrate (4 min each). The pedalling rate is 60 rpm, and average heart rate is measured during the last minute on each workrate, respectively.

1. Calibrate the ergometry cycle according to standard procedures.

2. Ensure that the individual being tested has followed conventional pre-test conditions (comment on this in the end of this manual).

3. Adjust seat and handlebar, and introduce Borg's RPE-scale.

4. Before the test, estimate a suitable higher work rate to allow the individual to reach a heart rate in the range 120-150 bpm (for individuals < 50 years) and 110-140 bpm (for individuals ≥ 50 years), respectively, aiming at a rated perceived exertion of ≈ 14 according to the Borg RPE-scale. The table below gives a rough guide to reach these pre-requisites with regard to sex and activity level.

	Woman	Man
Inactive	59 or 64 W	88 or 95 W
Low	88 or 95 W	118 or 127 W
Moderate	118 or 127 W	147 or 159 W
High	147 or 159 W	177 or 191 W

The watts depends on whether the work rate is measured by the flywheel or the pedals

5. Start standard work rate pedalling for 4 min at 60 rpm and the standard resistance. Check each minute that both pedalling speed and resistance are kept constant.

6. Measure average heart rate during the 4th min by taking notes of the heart rate at four occasions (3.15, 3.30, 3.45, and 4.00) and average these.

7. Increase resistance to the higher individual work rate (point 4 above). Check each minute that both pedalling speed and resistance are kept constant.

8. Ask for RPE during the 2nd min at the higher rate.

9. If RPE is
   < 10, increase resistance with 1 kp and redo point 8.
   10-11, increase with 0.5 kp and redo point 8.
   12 – 16, maintain rate and go to point 10.
   17 or higher, stop the test and let the subject rest for 20 min before performing a new test at a lower rate. However, it is preferable to cease testing and perform the test on another occasion.

10. Measure average heart rate during the 4th min at the higher rate by taking notes of the heart rate at four occasions (3.15, 3.30, 3.45, and 4.00) and average these.

11. After completed test, ask for RPE for the 4 min at the higher rate.

Procedure for estimating VO_2max

Electronically
An application for estimating VO_2max with the EKBLOM-BAK test is available at www.gih.se/ekblombaktest.

Manually
Input the relevant variables* into the following equation:

Men
$VO_2max = Exp((2.04900 - 0.00858*Age) – (0.90742*\Delta HR/\Delta PO) + (0.00178*\Delta PO) – (0.00290*HR \text{ at standard work rate}))$

Women
$VO_2max = Exp((1.84390 - 0.00673*Age) – (0.62578*\Delta HR/\Delta PO) + (0.00175*\Delta PO) – (0.00471*HR \text{ at standard work rate}))$

* ΔHF/ΔPO with 2 decimals; Sex 0=Woman, 1=Man; Age in years.

Higher work rate (watts)#	Factor for higher work rate
59 or 64	32
88 or 95	64
118 or 127	95
147 or 159	127
177 or 191	159
206 or 222	191
235 or 254	222

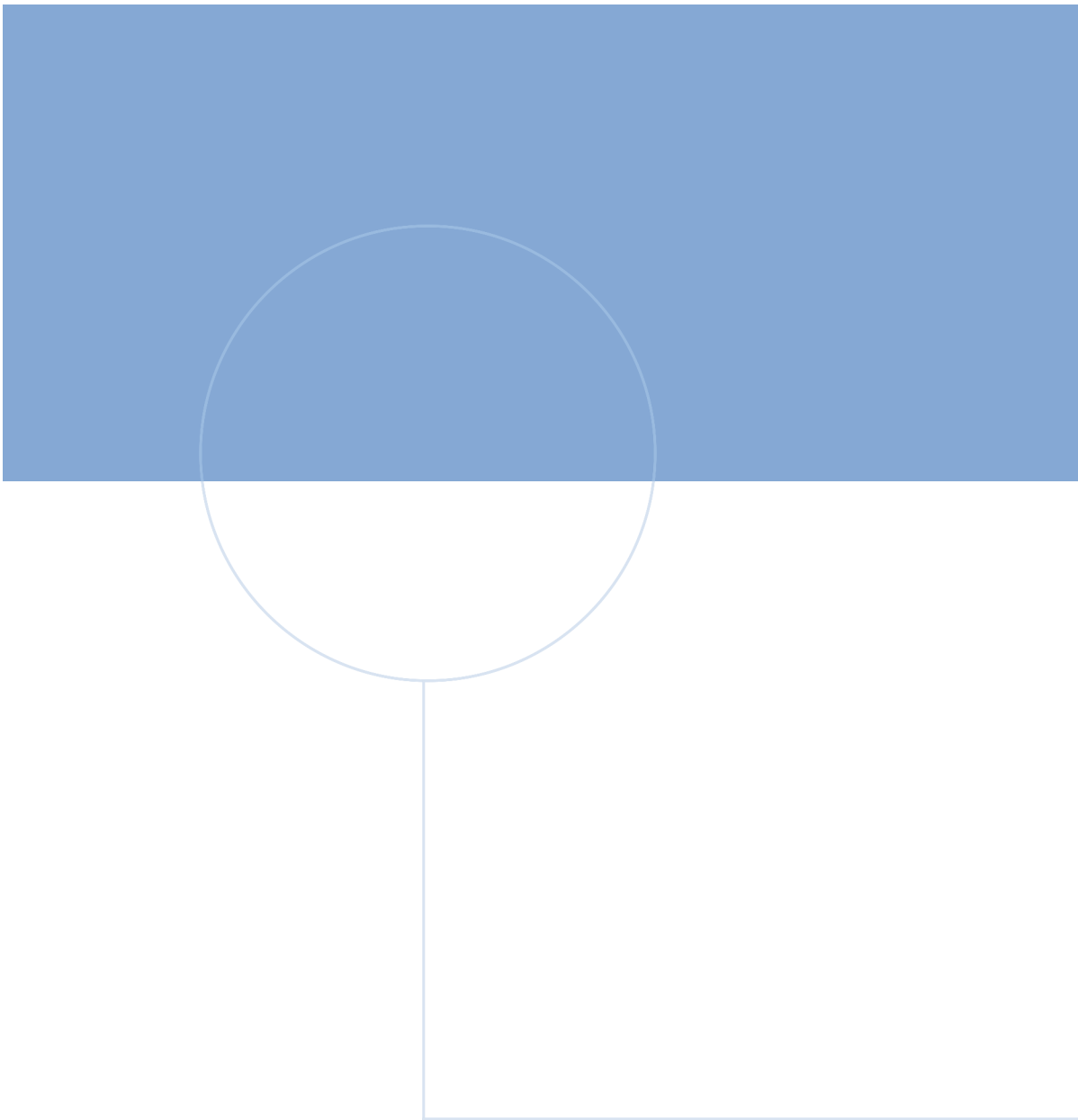
Notate Bene
The test has not been validated for electronically braked ergometers.

The test is only valid within the VO_2max range 19-62 $ml \cdot min^{-1} \cdot kg^{-1}$ for women and 24-76 $ml \cdot min^{-1} \cdot kg^{-1}$ for men, and age range 21-86 years for women and 20-84 years for men.

Conventional pre-test conditions include restrictions such as
- A heavy meal no later than 3 hours before the test.
- Smoking no later than 2 hours before the test.
- No vigorous activity on the day before and on the same day as the test.
- Avoiding running, cycling or stressing to the test.

If these pre-test conditions are not complied to, or if the individual being tested is taking medications that could influence the heart rate response, it is likely that the heart rate response and the estimation of VO_2max could be influenced.

The test was developed using a mechanically braked Monark cycle ergometer (Model 828E). It is important to consider that other types of cycle ergometers may give different work rate responses when adding the same resistance at higher work rates, and consequently a variation in the pulse response.
Available on www.gih.se/ekblombaktest is a list over equipment needed for the test and the Borg RPE scale.



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