Functional Capacity Predictors in Breast Cancer Women: a Cross-sectional Study

Ana João Silva Costa (anajocosta@gmail.com)
Centro de Reabilitação do Norte https://orcid.org/0000-0002-3460-8968
Margarida Rodrigues
Centro de Reabilitação do Norte
Ismael Carneiro
Centro de Reabilitação do Norte
Inês Machado Vaz
Centro Hospitalar de Trás-Os-Montes e Alto Douro
Miguel P. Almeida
Centro de Reabilitação do Norte
Ana Joaquim
Centro Hospitalar de Vila Nova de Gaia: Centro Hospitalar de Vila Nova de Gaia Espinho EPE
Pedro Antunes
University of Beira Interior: Universidade da Beira Interior
Alberto Alves
University Institute of Maia: Instituto Universitario da Maia
Sofia Viamonte
Centro de Reabilitação do Norte

Original Article

Keywords: Activities of Daily Living, Breast Cancer, Disability, Rehabilitation, Respiratory Muscles

Posted Date: February 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-200888/v1

Abstract

Purpose: Functional capacity (FC) declining has been poorly evaluated and characterized in women with breast cancer (BC). It is expected that FC declining may have an impact on survival, and also compromise quality of life and independence. This study aimed to evaluate the FC of women with BC and identify predictors of obtained results.

Methods: A cross-sectional study including women with BC consecutively referred for a physical medicine and rehabilitation consult between October and December 2019. Glittre-ADL Test (TGlittre), maximal respiratory pressure tests [maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP)] and Modified Fatigue Impact Scale were used in order to assess FC, respiratory muscle strength and fatigue, respectively. Age, professional status, smoking habits, comorbidities, body mass index, duration and status of disease, previous and ongoing treatments were also registered.

Results: A total of 42 women with non-metastatic BC were enrolled with a disease duration of 11.50 months (71), mostly in stage II (53.60%) and under hormone therapy (38.10%). TGlittre performance time was 3.13 minutes (8.72). TGlittre performance time correlated with MIP ($r = -0.373$; $p < 0.01$) and MEP ($r = -0.414$; $p = 0.007$) values and age ($r = 0.711$; $p < 0.010$). Patients with CV and endocrine comorbidities had higher TGlittre time values ($p < 0.01$ and $p = 0.019$, respectively). Age was the only statistically significant predictor ($p=0.041$) of TGlittre variation.

Conclusions: Women with BC presented decreased FC with mean values of TGlittre duration higher than those described in the literature in healthy subjects.

Introduction:

Currently, breast cancer (BC) is the most frequent cancer around the world and it is responsible for 18% of all cancer in women. [1] It is also the primary cause of mortality due to cancer in female, with an estimated 5-year survival of 80% in developed countries. [2] In recent years, the median survival of patients with BC has improved and the prognosis is relatively good when diagnosed early and treated in a timely manner. [3]

The multiple treatment options available, which include surgery, chemotherapy, hormone therapy and radiotherapy, have contributed to increasing survival. [4] However, these treatments are associated with several complications such as lymphedema, pain syndromes, lesion in the peripheral nerves and physical impairment including neuromuscular and musculoskeletal dysfunction. [5–8] In addition, a significant proportion of women with BC suffer mental dysfunction with anxiety, depression and sleeping problems. [9]

Functional status is a multidimensional concept, which includes functional capacity (FC), defined by the maximum potential to perform activities. [10] Thus, compromised functional status, due to all these complications, leads to physical inactivity, causing even greater loss in muscle strength and fatigue.

Moreover, functional impairment may cause a vicious circle leading to generalized weakness, reduction of social participation and impaired quality of life. [11]

Even though FC is expected to decline during treatment in women with BC, these changes have been poorly evaluated and characterized in literature. Which factors contribute to a greater decline in FC among women with BC are also unclear. [12] Therefore, the present study aimed to characterize FC and identify its predictors in women with BC. This study can provide new insights given the association of functional capacity with not only with the capacity of patients in performing activities of daily living (ADL) but also with health-related quality of life.

Materials And Methods:

Subjects and study design

This was a cross-sectional study including women with early BC consecutively referred for a Physical Medicine and Rehabilitation consult in a Rehabilitation Centre, under a protocol with an Oncology Department in Portugal, who agreed to participate in an exercise program, between October and December 2019. Women with menopause and osteoporosis, heart failure class II to IV of New York Heart Association (NYHA), severe anemia, moderate symptomatic anemia, unstable hypertension, uncontrolled diabetes mellitus, or with any other absolute contraindication to exercise were excluded. We included women with 18 or more years, with previously or currently treated BC. Medical records were also inspected for the collection of the following information: age, professional status, comorbidities, smoking habits, Body Mass Index (BMI), years of evolution and BC stage - TNM staging system according American Joint Committee on Cancer (AJCC) 7th edition [13], as well as previous and current treatments. Clinical data were collected by consulting the clinical file. All patients gave their informed consent prior to their inclusion in the study.

Procedures

All the assessments were conducted on the same day by a physician, including the assessment of functional capacity, the respiratory muscle strength and fatigue. All the procedures were explained previously.

Functional capacity

TGlittre was used to evaluate functional limitation and to assess the capacity of patients to performing activities of daily living. It consists of a standardized circuit of 10 meters which must be performed five times, in the shortest possible time, while carrying a backpack weighing 2.5Kg, with de following sequence[14]:

1. From a sitting position, the patient stands and walks along a flat course; crossing a two-step staircase at the midpoint (17 cm height + 27 cm width) and then walks again;

2. At the end, there are two shelves with three objects weighing 1Kg each, positioned on the top shelf (at the shoulder height) to be moved down, one by one, to the lower shelf (at waist height) and subsequently to the floor; then the objects must be placed again on the bottom shelf, and finally moved to the top shelf;
3. The patient walks back, sits again, and immediately starts the next lap, following the same circuit, until five laps are concluded.

Heart rate and peripheral oxygen saturation were recorded using a pulse oximeter, and perceived dyspnea was assessed by the Modified Borg Scale [15], at the beginning and end of the test. The total time to complete the test was also registered.

Even though there are no age-matched reference values of TGlittre in women with BC, Reis CM *et al* [16] developed a reference equation for the time to complete TGlittre based on age and height in apparently healthy individuals. In order to compare our results, the predicted TGlittre time was calculated considering the formula $3.049 + (0.015 \times age_{years}) + (-0.006 \times height_{cm})$. [16]

Respiratory Muscle Strength

The measurement of maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) was performed with a manovacuometer (MicroRPM®, Carefusion, Basingstoke, UK), according to the *American Thoracic Society/European Respiratory Society* guidelines. [17] The maneuvers were performed 3 times and the best value was considered. The lower limit of normality of MIP and MEP was calculated considering the age and sex, according to the formulas $62 - (0.50 \times age_{years})$ and $95 - (0.57 \times age_{years})$, respectively. [18]

Fatigue

The level of fatigue was assessed using the Modified Fatigue Impact Scale (MFIS) - Portuguese version. [19] MFIS is subdivided into physical (10 items) and cognitive (11 items) subscales and assesses the impact of fatigue on daily functioning during the last four weeks. Each item is rated on a five-point scale, ranging from 0 to 4. [20] A total score equal or higher than 38 was considered as the cut-off of fatigue [21].

Statistics

Continuous variables are expressed as means and standard deviations (SD) or medians with interquartile ranges for variables with skewed distributions. Categorical variables are presented as frequencies and percentages. Normal distribution was checked using Shapiro-Wilk test or skewness and kurtosis.

Differences in categorical and continuous variables were tested with the use of Kruskal-Wallis or Mann-Whitney tests. Spearman's coefficient (ρ) was used to assess the strength and direction of the linear relationships between pairs of continuous variables.

The predictor variables of TGlittre variability were determined using a multiple linear regression model. All reported *p*-values are two-tailed, with a *p*-value of 0.05 indicating statistical significance. Statistical analyses were performed using *Software Statistical Package for the Social Sciences* (SPSS) Version 23 (© IBM, Armonk, NY)

Results:

A total of 42 women were included, with an average age of 59.62 ± 9.99 years. The majority (76.19%) of patients had other comorbidities, mostly cardiovascular (CV) and endocrine. Demographic and clinical characteristics are summarized in Table I.

Table I – *Sociodemographic and clinical characteristics of the sample.*

Sociodemographic variables	
Age (years)	**Mean ± SD**
	59.62 ± 9.99
Professional Status	**n (%)**
Currently working	4 (9.52)
Medically discharged	**15 (35.71)**
Retired	7 (16.67)
Unemployed	4 (9.52)
Missings	12 (28.57)
Clinical variables	
BMI[1] (Kg/m^2)	
Mean ± SD	25.91 ± 5.48
Smoking history n (%)	
Current smoker	5 (11.90)
Never smoked	**35 (83.33)**
Previous smoker	2 (4.76)

[1] n = 22

BMI: body mass index; SD: standard deviation; Kg/m^2: kilograms per square meter;

a – Included hypertension, valvular disease, interatrial communication, arrhythmia, peripheral venous insufficiency; b – Included type 2 diabetes mellitus, dyslipidemia, thyroid and parathyroid glands disease; c –Included peptic ulcer, gastritis, esophagitis, gastroesophageal reflux disease, irritable bowel syndrome; d – Included osteoarthritis, rheumatic diseases, upper limb tendinopathy, bone fracture sequelae; e – Included urogynecologic, skin and otorhinolaryngology disorders; f – Included anxiety, depression; g – Included asthma.

Sociodemographic variables	
Comorbidities n (%)	
Cardiovascular[a]	13 (30.95)
Endocrine[b]	**18 (42.86)**
Gastric[c]	4 (9.52)
Musculoskeletal[d]	6 (14.29)
Psiquiatric[f]	11 (26.19)
Respiratory[g]	3 (7.14)
Others[e]	7 (16.67)
[1] n = 22	
BMI: body mass index; SD: standard deviation; Kg/m^2: kilograms per square meter;	
a – Included hypertension, valvular disease, interatrial communication, arrhythmia, peripheral venous insufficiency; b – Included type 2 diabetes mellitus, dyslipidemia, thyroid and parathyroid glands disease; c –Included peptic ulcer, gastritis, esophagitis, gastroesophageal reflux disease, irritable bowel syndrome; d – Included osteoarthritis, rheumatic diseases, upper limb tendinopathy, bone fracture sequelae; e – Included urogynecologic, skin and otorhinolaryngology disorders; f – Included anxiety, depression; g – Included asthma.	

The median time elapsed from the primary diagnosis of BC was 11.50 months (71). Women with BC were mostly (53.60%) in stage II of the disease and under hormone therapy (38.10%) (table II).

Table II – *Breast Cancer Characteristics.*

Duration of disease (months)	**11.50 (71)**
Stage of disease[a] n (%)	
IA	9 (21.42)
IIA	**11 (26.19)**
IIB	**11 (26.19)**
IIIA	7 (16.66)
IIIB	2 (4.76)
IIIC	1 (2.38)
Missing	1 (2.38)
Previous treatment n (%)	
Chemoterapy	**36 (85.71)**
HT	14 (33.33)
Anti-HER2 therapy[b]	2 (4.76)
Radiotherapy	**36 (85.71)**
Surgery	29 (69.01)
Current treatment n (%)	
None	7 (16.67)
Chemoterapy	14 (33.33)
HT	**16 (38.10)**
Anti-HER2 therapy[b]	2 (4.76)
Radiotherapy	1 (2.38)
Radiotherapy + HT	1 (2.38)
Chemotherapy + HT	1 (2.38)
HT: hormone therapy	
a – TNM staging system according AJCC 7th Edition; b – Included trastuzumab or/ and pertuzumab.	

The median time to perform TGlittre was 188.00 seconds (523.00), corresponding to 3.13 minutes (8.71). The shortest time to perform the test was 2.03 minutes and the longest time was 10.75 minutes. Applying the TGlittre reference equation [16], 73.81% of the population spent more time to complete the test than the predicted value, according age and height. About 14% (n = 6) and 24% (n = 10) of patients had MIP /

MEP values below lower limit of normal according to age and sex, respectively. Fifteen women (35.71%) had a total score of MFIS ≥ 38, considered the cut-off of fatigue [21]. Table III presents the functional evaluation results.

Table III – *Descriptive analysis of Glittre ADL-test, Maximal respiratory pressure tests and Modified Fatigue Impact Scale.*

TGlittre time (seconds)	**188.00 (523.00)**
ΔSpO2	**0 (0)**
ΔDyspnea perception	**1.07 ± 1.12**
ΔHR	**28.74 ± 13.27**
Maximal respiratory pressure tests	
MIP (cm H_2O)	63.57 ± 22.64
MEP (cm H_2O)	84.40 ± 25.59
MFIS	
Total Score	32.05 ± 18.55
Cognitive subscale	15.52 ± 11.48
Physical subscale	16.52 ± 8.47

TGlittre: Glittre ADL-test; Δ HR: variation between initial and final heart rate; Δ SpO2: variation between initial and final pulse oxygen saturation; Δ dyspnea perception: variation between initial and final dyspnea perception assessed by the Modified Borg Scale; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; cm H_2O: centimeters of water; MFIS: Modified Fatigue Impact Scale

As shown in table IV, TGlittre performance time correlated with the values of MIP (ρ = -0.373; p < 0.01), MEP (ρ = -0.414; p = 0.007) and age (ρ = 0.711; p < 0.010). Patients with CV pathology had higher TGlittre time comparatively with subjects without that comorbidities – 218.00 (43.50) vs 179 (47.25), (p < 0.01), as well as patients with endocrine pathology – 214.5 (46.00) vs 178.00 (47.00), (p = 0.019). There was no statistically significant difference in the meantime spent in TGlittre among the varied modalities of treatments (table V).

Table IV - *Correlation matrix of selected variables with TGlittre.*

	TGlittre	
	ρ	p-**value**
Age (years)	0.711	**< 0.001**
BMI (Kg/m^2)	0.255	0.252
Disease duration (months)	0.153	0.340
MIP (cm H_2O)	-0.373	**0.016**
MEP (cm H_2O)	-0.414	**0.007**
MFIS total score	0.224	0.158
MFIS physical subscale	0.277	0.080
MFIS cognitive subscale	0.205	0.198
TGlittre: Glittre ADL-test; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; cm H_2O: centimeters of water; MFIS: Modified Fatigue Impact Scale; BMI: body mass index; Kg/m^2: kilograms per square meter; ρ = Spearman correlation coefficient		

Table V - *Comparison of categorical clinical variables and TGlittre time.*

	p-value
Stage of disease	0.441
Previous treatment	0.491
Current treatment	0.608
Comorbidities	0.160
Cardiovascular	**< 0.001**
Endocrine	**0.019**
Gastric	0.596
Musculoskeletal	0.438
Others	0.647
Psiquiatric	0.286
Respiratory	0.981
Smoking history	0.171

Applying a multiple linear regression model including the significant variables, age was the only predictor of variation in TGlittre time (p = 0.041), as exposed in table VI. This model explained 27% (adjusted R^2 = 0.270) of TGlittre time variation (p = 0.006).

Table VI – *Multiple linear regression of predictor variables of TGlittre time (seconds) variability (n = 40)*

	Unstandardized Coefficients		Standardized Coefficients	t	p-value
Model	**B**	**Std. Error**	**Beta**		
(Constant)	53.663	102.018		0.526	0.602
Age (years)	3.210	1.514	0.403	2.121	**0.041**
MIP (cm H_2O)	-0.243	0.621	-0.065	-0.391	0.698
MEP (cm H_2O)	-0.199	0.550	-0.062	-0.363	0.719
Cardiovascular comorbidity	32.768	27.420	0.194	1.195	0.240
Endocrine comorbidity	3.339	25.220	0.021	0.132	0.895
MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; cm H_2O: centimeters of water; Std: standard					

Discussion:

Our study revealed a decreasing of FC in women with BC, with a mean time to perform TGlittre of 3.13 minutes. Currently, there are few studies that evaluated the FC among cancer patients. [12, 22, 23] Among the large number of tests available to evaluate FC, there is no gold standard instrument to assess it in women with BC.

Cancer treatment is associated with numerous adverse side effects, including pain, fatigue, cachexia, reduced strength and lung capacity, diminished range of motion, among others. A significant percentage of women will keep some of these symptoms for months after the end of treatments and will experience treatment-related late effects that may influence not only their quality of life, but also morbidity and mortality. [4, 6, 7, 24]

A reduction of lower limbs muscle strength and endurance, associated with compromised walking ability, have been reported in women with BC. [12, 25] In addition, Kokkonen *et al.* [12] reported poor balance, especially dynamic balance, in 78,1% of women with advanced BC. Impaired muscle strength associated to peripheral neuropathy, induced by neurotoxic chemotherapy agents, can compromise balance and disturb walking, leading to a further decline in FC. [12].

TGlittre was initially developed and validated to assess FC and the ability to perform ADL in patients with chronic obstructive pulmonary disease (COPD). [14] However, the evidence is limited about the performance in patients with other diseases such as cancer. Reis CM *et al.* [16] proposed a reference equation for TGlittre based on anthropometric and demographic variables in apparently healthy subjects. Although the reliability of the equation in women with BC cannot be established, when we applied it in our population, we found that 73.81% of women had higher values than the predicted ones, suggesting the FC compromise among our sample. In another work, Reis CM *et al.* [26] reported the shortest time to complete TGlittre of 2.03 minutes and a mean time of 2.62 minutes in healthy subjects. Similarly, Skumlien *et al* [14], found that the shortest time to perform TGlittre by healthy subjects was 2 minutes. However, it is known that FC decreases with age, and in the study of Côrrea *et al*. [27] with 10 healthy subjects with a mean age of 64 years, the mean time to complete TGlittre was 3.3 minutes. In our study, BC women were younger (59.62 ± 9.99 years) and needed 3.13 minutes to perform TGlittre, suggesting that other factors may play an important role in FC.

Kokkonen *et al* used six-minute walk test (6MWT) to determine functional impairment in women with advanced BC and found that FC was significantly lower compared with healthy subjects. [12] Comparing TGlittre and 6MWT, the last one includes only walking, which may imply a different metabolic profile compared with daily activities. In a study with heart failure patients, Almeida MP *et al*. [28] showed that TGlittre elicited higher ventilatory and cardiovascular responses than 6MWT. On the other hand, TGlittre simulates several daily activities, such as walking, sitting-standing, climbing up and down stairs and moving objects in different heights. It seems to be more representative of ADL and could reflect more faithfully real-life situations and the limitations experienced in a daily basis. Despite an overall correlation of TGlittre with 6MWD in COPD, Skumlien *et al* [14] found a substantial variability, especially in more debilitated patients, showing that TGlittre provided additional information about functional status, particularly in more disabled patients. To our knowledge, this is one of the first studies that evaluate FC in women with BC using TGlittre. We only found a published abstract by Cakmak *et al* [23], which had similar results. They evaluated fifteen BC survivors without any metastasis or active disease, that took a mean time of 3.1 minutes to complete TGlittre.

In our study, age was the only predictor of variation in TGlittre time. As previously described, FC tends to decrease with aging, due to a gradual reduction of muscle strength and oxygen uptake. [29] Women with cardiovascular and endocrine comorbidities spend more time to complete TGlittre. A fundamental condition for many ADL is the ability to perform mainly aerobic, i.e. oxygen-using, work. Such activities require the integrated work of the heart, lungs, and circulatory system to carry oxygen to the metabolically active muscles. [30] The presence of cardiovascular and some endocrine comorbidities, represented in our study by hypertension, diabetes mellitus, dyslipidemia, valvular disease, interatrial communication, arrhythmia and peripheral venous insufficiency, may compromise this mechanism and lead to the limitation of FC. Nonetheless, age was the only predictor of TGlittre variation, regardless of the presence of these comorbidities.

It is important to mention that women with BC may had the difficulty of using the backpack, due to pain caused by the catheter implantation, scars and/ or lymphedema in the upper limb caused by previous surgery. TGlittre was not initially developed to this population, and it would be interesting to report and quantify the impact of these limitations in future studies, in order to adapt it to these population characteristics.

Also, our work revealed that expiratory and inspiratory muscle strength were decreased in 24% and 14% of the patients, respectively. The analysis showed that TGlittre time was inversely correlated with MIP and MEP, suggesting generalized muscle weakness and deconditioning. This respiratory muscle impairment is considered one of the underlying mechanisms of exercise intolerance. [31]

We found that 35.7% of women reported fatigue, which did not correlate with TGlittre time. Fatigue is one of the symptoms most frequently reported by women with BC, with a high variability in prevalence. Besides, it is a multifactorial and subjective symptom, involving biological and psychological aspects, and the physiopathology is not completely understood. [3, 32–34] In another cross-sectional study, with 215 BC women, 72.09% were fatigued, while physically active women showed lower symptoms of fatigue and higher scores for quality of life scales, compared with sedentary ones. [3] Although fatigue did not correlate with TGlittre time, other studies show that feeling tired has a direct impact on functionality and compromises quality of life. [32, 33] The absence of correlation between fatigue and FC reinforces the importance of evaluating FC, which may be compromised even in the absence of self-reported fatigue.

There are limitations in this study. Firstly, it included only patients with criteria to be referred for a physical medicine and rehabilitation consult, and who wanted to participate in an exercise program, which may induce selection biases. It is possible that more vulnerable women or less motivated women may not be referred to our center, and it could overestimate FC and underestimate fatigue of this population.

Secondly, the tests used were not validated for breast cancer patients. The lack of sex and age-matched reference values of TGlittre for this population may compromise the clinical results interpretation. Since it is a relatively new test, more studies are needed to determine the reference values according age groups in healthy people. Additionally, MFIS was originally developed to assess fatigue in patients with chronic diseases, and it is not specific for this population.

Some rehabilitation needs of women with BC are still poorly recognized. Currently, exercise is recognized as a key element in cancer treatment to reduce symptoms and improve physical functioning, mood and quality of life. [35] In order to promote and validate physical and functional improvements during the recovery process, an adequate FC evaluation to assess the physical abilities of BC women could facilitate and optimize the development of exercise-based rehabilitation programs. Despite time-consuming, TGlittre may be a valid test to assess FC in this group of patients.

Conclusion:

Women with BC presented a decreased FC, with mean values of TGlittre duration higher than those described in the literature in healthy subjects. Due to the sedentary lifestyle that characterizes this population, the presence of comorbidities and the multisystemic attainment of BC and different treatments used, we consider that it is essential to evaluate the FC and factors associated with its decline, allowing the optimization of intervention in a rehabilitation program.

Declarations:

Conflicts of interest:

the authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding resource:

none.

Code availability:

N/A

Availability of data and material:

research data are not shared.

Ethics approval:

N/A

Consent to participate:

All patients gave their informed consent prior to their inclusion in the study.

Consent for publication:

All authors consent to the publication of the manuscript

Author´s contributions:

Sofia Viamonte, Inês Machado Vaz, Ana João Costa and Margarida Rodrigues have planned and designed the study. Sofia Viamonte, Ana Joaquim and Pedro Antunes identified and recruted the patients. Material preparation and data collection were performed by Ana João Costa, Margarida Rodrigues, Ismael Carneiro and Miguel P. Almeida. Data analysis was performed by Margarida Rodrigues and Alberto Alves. The manuscript was written by Ana João Costa and all authors read and approved the manuscript.

References:

1. Akram M, Iqbal M, Daniyal M, Khan AU (2017) Awareness and current knowledge of breast cancer 50(1): p. 33
2. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, et al (2008) Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol 9(8): p. 730-56
3. Canario AC, Cabral PU, De Paiva LC, Florencio GL, Spyrides MH, Gonçalves AK (2016) Physical activity, fatigue and quality of life in breast cancer patients. Rev Assoc Med Bras 62(1): p. 38-44
4. Cheville AL, Troxel AB, Basford JR, Kornblith AB (2008) Prevalence and treatment patterns of physical impairments in patients with metastatic breast cancer. J Clin Oncol 26(16): p. 2621-9
5. Bevilacqua JL, Kattan MW, Changhong Y, Koifman S, Mattos IE, Koifman RJ, et al (2012) Nomograms for predicting the risk of arm lymphedema after axillary dissection in breast cancer. Ann Surg Oncol 19(8): p. 2580-9
6. Rietman JS, Dijkstra PU, Debreczeni R, Geertzen JH, Robinson DP, De Vries J (2004) Impairments, disabilities and health related quality of life after treatment for breast cancer: a follow-up study 2.7 years after surgery. Disabil Rehabil 26(2): p. 78-84
7. Merchant CR, Chapman T, Kilbreath SL, Refshauge KM, Krupa K (2008) Decreased muscle strength following management of breast cancer. Disabil Rehabil 30(15): p. 1098-105
8. Glaessel A, Kirchberger I, Stucki G, Cieza A (2011) Does the Comprehensive International Classification of Functioning, Disability and Health (ICF) Core Set for Breast Cancer capture the problems in functioning treated by physiotherapists in women with breast cancer? Physiotherapy 97(1): p. 33-46
9. Fialka-Moser V, Crevenna R, Korpan M, Quittan M (2003) Cancer rehabilitation: particularly with aspects on physical impairments. J Rehabil Med 35(4): p. 153-62
10. Leidy N (1994) Using functional status to assess treatment outcomes. Chest 106(6):1645-6
11. Kocks JW, Asijeec GM, Tsiligiannia IG, Kerstjensb HA, Van der Molen T (2011) Functional status measurement in COPD: a review of available methods and their feasibility in primary care. Prim Care Respir J. 20(3): p. 269-75
12. Kokkonen K, Saarto T, Mäkinen T, Pohjola L, Kautio H, Järvenpää S, et al (2017) The functional capacity and quality of life of women with advanced breast cancer. Breast Cancer 24(1):128-136
13. Edge SB, Compton CC (2010) The American Joint Committee on Cancer: the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. Ann Surg Oncol 17,1471–1474
14. Skumlien S, Hagelund T, Bjørtuft O, Ryg MS (2006) A field test of functional status as performance of activities of daily living in COPD patients. Respir Med 100(2): p. 316-2313
15. Borg GA (1982) Psychophysical bases of perceived exertion. Med Sci Sports Exerc 14(5): p. 377-81
16. Reis CM, Karloh M, Fonseca FR, Biscaro RRM, et al (2018) Functional capacity measurement: reference equations for the Glittre Activities of Daily Living test. J Bras Oneumol 44(5): 370-377

17. American Thoracic Society/European Respiratory (2002) ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med 166(4): 518-624
18. Evans JA, Whitelaw WA (2009) The Assessment of Maximal Respiratory Mouth pressures In Adults. Respir Care 54 (10): 1348-59
19. LR Gomes (2011) Validação da versão portuguesa da Escala de Impacto da Fadiga Modificada e da Escala de Severidade da Fadiga na Esclerose Múltipla. Repositório Universidade do Minho
20. Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF (1994) Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. Clin Infect Dis 18 Suppl 1: p. S79-83
21. Flachenecker P, Ku¨mpfel T, Kallmann B, Gottschalk M, Grauer O, Rieckmann P et al (2002) Fatigue in multiple sclerosis: a comparison of different rating scales and correlation to clinical parameters. Mult Scler 8: 523-26
22. Ramachandran S, Sudhakar S, Thaslim F, Kirthika SV, Padmanabhan K, Samuel AJ (2018) Beware! reduced functional capacity and quality of life with increased fatigue level among the breast cancer survivors undergoing chemotherapy in India. Indian J Palliat Care 24:117-8
23. Cakmak A, Sonbahar-Ulu H, Firat M, Vardar-Yagli N, Saglam M, Calik-Kutukcu E, et al (2019) Pulmonary funcion, respiratory muscle strength and activities of daily life in breast cancer survivors. European Respiratory Journal 54 (suppl 63) PA1162
24. Schmitz K, Speck R, Rye S, Disipio T, Hayes SC (2012) Prevalence of breast cancer treatment sequelae over six years of follow-up: the pulling through study. Cancer 118(8):S2217-S25
25. Cheville AL, Kornblith AB, Basford JR (2011) An examination of the causes for the underutilization of rehabilitation services among people with advanced cancer. Am J Phys Med Rehabil 90:S27-37
26. Reis CM, Silva TC, Karloh M, Araujo CLP, Gulart AA, Mayer AF (2015) Performance of healthy adult subjects in Glitre ADL-test. Fisioter Pesq 22(1):41-47
27. Corrêa KS, Karloh M, Martins LQ, Santos K, Mayer AF (2011) O teste de AVD-Glittre é capaz de diferenciar a capacidade funcional de indivíduos com DPOC da de saudáveis? Ver Bras Fisioter 15 (6):467-73
28. Almeida MP, Montanha T, Marques M, Silva PM et al (2020) Glittre Activities Daily Living Test: Physiological responses in patients with heart failure. Eur J Prev Cardiol 0(00) 1–4
29. Iwama Am, Andrade GN, Shima P, Tani SE, Godoy I, Dourado VZ (2009) The six-minute walk test and body weight-walk distance product in healthy brazilian subjects. Braz J Med Biol Res 42 (11):1080-5
30. Fleg JL, Pina IL, Balady GJ, Chaitman BR, Fletcher B, Lavie C, et al (2000) Assessment of Functional Capacity in Clinical and Research Applications. An Advisory From the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association. AHA Journals 102:1591-1597
31. O'Donnell DE, Webb KA, Langer D, Elbehairy AF, Neder JA, Dudgeon DJ (2016) Respiratory Factors Contributing to Exercise Intolerance in Breast Cancer Survivors: A Case-Control Study. J Pain Symptom Manage 52(1): 54–63.

32. Silva BC, Albuquerque V, Leite J (2010) QOL in Patients Carriers of Breast Neoplasia undergoing chemotherapy treatments. Brazialian Journal of Oncology 56 (2): 227-23633.
33. Bag L, Ferreira EL (2010) Women with cancer and their relationship with physical activity. Rev. Bras. Coen. And Mov 18(4):11-17.
34. Alexander S, Minton O, Andrews P, Stone P (2009) A comparison of the characteristics of disease-free breast cancer survivors with or without cancer related fatigue syndrome. Eur J Cancer 5(3):384-392
35. Tusscher MR, Groen WG, Geleijn E, Sonke GS, et al. (2019) Physical problems, functional limitations, and preferences for physical therapist-guided exercise programs amog Dutch patients with metastatic breast cancer: a mixed methods study. Supportive Care in Cancer Aug;27(8):3061-3070