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Screening for Physical Activity Levels in Non-Metastatic Breast Cancer Patients Undergoing Surgery: An Observational Study

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Abstract

Background: Physical activity (PA) can play a role in lowering the risk of breast cancer (BC), but also in reducing perioperative complications and treatments related side effects, improving the quality of life and decreasing mortality in BC survivors. PA and nutritional screening are not offered to patients after cancer diagnosis as standard of care, even in high quality breast units. **Methods:** From February 2019 to March 2020, we performed a preoperative physical and nutritional screening in 504 consecutive BC patients waiting for surgery. The screening included an IPAQ questionnaire to evaluate the level of physical activity; nutritional screening with measurement of anthropometric parameters (weight, height, waist and hips circumference, BMI, and waist hip ratio) and evaluation of body composition using Bioelectrical Impedance Analysis (BIA). **Results:** The majority of patients in our series resulted physically inactive: clustering the IPAQ scores, 47% of patients proved to be physically inactive (MET score $<$700), 34% moderately active (MET score 700-2520), and only 19% physically active (MET score $>$ 2520). In addition, approximately half of the patients (49.01%) resulted overweight or obese, and more than half (55.2%) had a percentage of fatty tissue over the recommended cut off for adult women. **Conclusions:** Our data confirm that assessment of PA levels should become part of the standard preoperative evaluation of BC patients and behavioral interventions should be offered to them, in order to pre-habilitate for surgery and improve outcomes. IPAQ Questionnaire and body composition analysis could be quick and easy screening tools in order to identify which patients may need more support in being active during and after anticancer treatments.

Keywords

breast Cancer, prehabilitation, physical activity, personalized medicine

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Background

An extensive number of epidemiological studies and guidelines have confirmed the importance of physical activity (PA) both in primary and tertiary prevention of breast cancer (BC).[1-6]

In addition, obesity and weight gain after treatments are important negative prognostic factors for survival among women affected by this disease.[7-10] In a study by Goodwin et al[11] 84.1% of patients with BC gained weight, in particular body fat, in the first year after diagnosis, with an increased risk of recurrence and reduced survival. PA has been associated with weight loss and weight maintenance among healthy individuals[12,13] and recent studies have shown a favorable effect of exercise on body weight among BC survivors.[14,15]

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While the physical and psychosocial benefits of participating in PA programs during and following BC treatments are well understood, less is known about rates and uptake of PA following diagnosis.[16,17] In fact, few studies about PA levels among women recently diagnosed with BC have been conducted so far.[18] Recently, the Health, Eating, Activity, and Lifestyle (HEAL) study reported that women diagnosed with BC were significantly less physically active within1 year from diagnosis than they were during the year before diagnosis.[19]

In this study, we present the results of a systematic preoperative screening of PA and nutritional status in a consecutive series of non-metastatic BC patients waiting for surgery, using the IPAQ questionnaire, nutritional screening with measurement of anthropometric parameters and body composition analysis.

Materials and Methods

From February 28, 2019 to March 6, 2020, all the patients with histologically proven BC treated in the Breast Surgical Unit of the Fondazione Policlinico Agostino Gemelli IRCCS underwent a preoperative assessment as part of the standard of care, including a brief psychoncological interview and a nutritional counseling conducted by a team of psychologists, surgeons, biologists, and dietitians trained in oncology.

For this study we retrospectively analyzed data collected during the physical and nutritional screening performed within a few days from communication of diagnosis: physical activity screening included an IPAQ questionnaire (International Physical Activity Questionnaire) to evaluate the levels of physical activity; the nutritional screening included measurement of anthropometric parameters (weight, height, waist and hips circumference, body mass index, and waist hip ratio) and evaluation of body composition using bioelectrical impedance analysis (BIA). Patients with motor disabilities or psychiatric conditions were excluded from the study, as well as patients with advanced disease, due the potential impact of metastases on nutritional and physical activity levels.

The study protocol was approved by the ethics committee of the hospital (approval number 0009991/22; ID 4734).

International Physical Activity Questionnaire (IPAQ Questionnaire)

Different types of PA performed as part of everyday life were investigated using the IPAQ questionnaire. In particular, patients were asked to report (1) all the vigorous activities performed in the last 7 days for at least 10 minutes at a time; (2) all the moderate activities performed in the last 7 days for at least 10 minutes at a time; (3) all the time spent walking in the last 7 days (at work and at home, walking from place to place, and any other walking done for recreation or sport); (4) time spent sitting on weekdays during the last 7 days (at work, at home, and during leisure time). Activities that implied hard physical effort and made breathing much harder than normal were classified as "vigorous" physical activities, while activities that made breathing somewhat harder than normal were classified as "moderate."

Metabolic equivalents (METs) were used to quantify the duration and intensity of the activity combined. METs were then converted into MET-hours per week, to define the sum of MET levels for each activity multiplied by the duration of the activity performed. Based on a total MET-hours per week score, patients were classified as physically active (MET score >2520), moderately active (MET score 700-2519), or inactive (MET score <700).[20,21]

Anthropometric Measures

Anthropometric measures included height, weight, body mass index, waist circumference, and waist hip ratio (WHR).

Height was measured using a mechanical stadiometer (measuring stations and column scales SECA 711; GmbH & Co. KG, Hamburg, Germany) to the nearest 0.5 cm (without shoes) in standing position, while the patient is facing directly ahead, feet together, arms by the sides, heels, buttocks, and upper back in contact with the stadiometer. Weight was measured using a mechanical scale accurate to the nearest 0.1 kg (measuring stations and column scales SECA 711; GmbH & Co. KG, Hamburg, Germany) without clothes. Body mass index (BMI) was calculated using the following formula: kg/m^2. Circumferences were measured at the smallest circumference of the waist, above the belly button, at widest part of the buttocks (hip). Every measure is approximated to the nearest 0.5 cm using a stretch-resistant tape (Ergonomic circumference measuring tape; SECA 201; GmbH & Co. KG, Hamburg, Germany). Waist-hip ratio was calculated using the following formula: waist circumference (cm)/hip circumference (cm).

Body Composition Analysis

Body composition assessment was performed using segmental multifrequency-bioelectrical impedance analysis (SMF-BIA; DS Medica model Human im touch; Milan, Italy), a safe and easy procedure routinely employed in our clinical practice. BIA consists in low electricity voltage passing through electrode patches applied on hands and feet, to measure body impedance and composition, including fat mass (FM), fat free mass (FFM), and hydration.

The exam was conducted with patients lying supine, with legs apart and arms not touching the body. All evaluations were conducted using 6 surface standard electrode

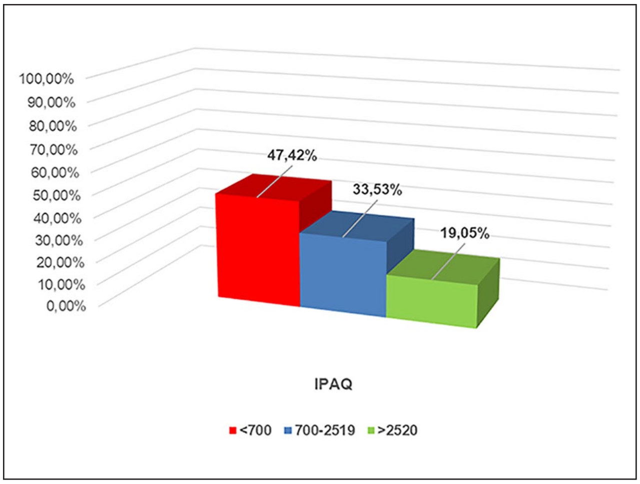

Figure 1. IPAQ Questionnaire results: 239 patients Inactive (<700 MET); 169 patients moderately active (700-2519 MET); 96 patients active (>2520 MET).

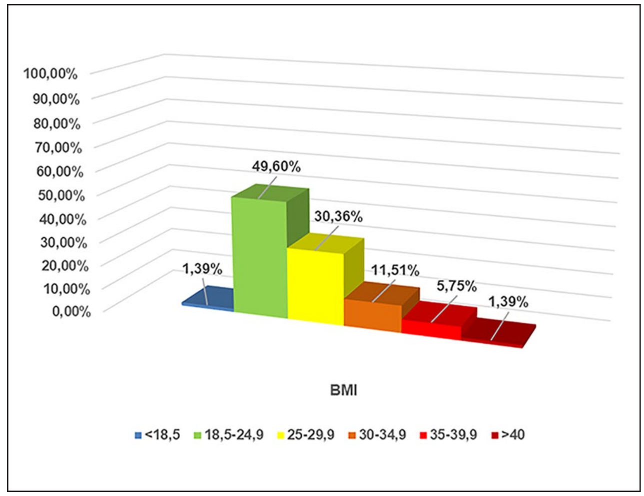

Figure 2. BMI distribution.

(exa-polar) technique on the hands and feet.[22] Physical parameters directly measured in Ohms were resistance (Z), reactance (X_c) at 50 kHz, and 800 µA phase angle (Φ) calculated using the following equation: phase angle = (resistance/reactance) × (180/π). Derived parameters considered were: fat mass (FM), fat free mass (FFM) both in kilograms (kg) and percentage (%). Hydration referred to total body water (TBW) was calculated in liters (L) and percentage (%).

Statistical Analysis

Results from raw data were used to extrapolate main descriptive statistical parameters including mean, standard deviation, and percentage for anthropometric and body composition information. Moreover, data from BMI, WHR, and IPAQ score were used to divide the sample into different groups according to physical and nutritional status. Statistical analysis was conducted through GRETL software and Python scripts.

Results

A 504 consecutive patients were enrolled, aged between 28 and 91 years old [mean age 57.63, standard deviation (SD) 13.29].

Based on the results of the IPAQ questionnaire, the majority of BC patients in our cohort resulted physically inactive (47.42%) or only moderately active (33.53%) while just 19.05% resulted physically active (Figure 1). By splitting the moderately active category in 2 parts, taking the median value (1819 MET) as a new cut off, 135 (79.88%) patients out of 169 resulted below the cut off, while 34 (20.12%) patients were in the upper end of the range (above 1819 MET).

According to BMI, just 1.39% of our patients resulted underweight, 49.60% normal weight, 30.36% overweight, 11.51% obese class I (moderately obese), 5.75% obese class II (severely obese), 1.39% obese class III (very severely obese; Figure 2). Analysis of WHR [(0.88 (mean); 0.10 (IQR)] and waist circumference [(91.06 (mean); 18 (IQR)] placed patients in our cohort either in a moderate or high cardiovascular and metabolic syndrome risk group.[23]

Body composition parameters were also assessed by the bioelectrical impedance analysis. Among the body composition parameters, fat mass (FM) [31.88 % (median); 14.8 IQR)] revealed a cohort over the healthy range, while fat free mass (FFM) [68.13% (median); 14.9 (IQR)] was proven under the lower cut-off recommended (76%-81%) for an adult woman (Figure 3).

Clustering the FM%, 10.5% of our cohort resulted under the lower cut-off recommended (20% FM), 34.3% resulted in an ideal range (20%-30% FM) while 55.2% resulted above average (<30% FM). Clustering the FFM%, 6.9% of our cohort resulted over the cut off recommended (81% FFM), 18.8% resulted in an ideal range (76%-81% FFM) while 74.2% resulted under the lower cut-off recommended (76% FFM; Figure 3).

In addition, BIA was also used to calculate patients' hydration (TBW [34.17 L (mean); 5.11 (SD)] [52.13% (mean); 7.14 (SD)] and phase angle [5.04° (mean); 0.82 (SD)] which resulted in a normal status, even if in the lower part of the scale.[24,25]

Discussion

Physical activity (PA) is an important factor in establishing and maintaining a sense of well-being and enhancing quality of life (QOL), even after a BC diagnosis.[5-9,11-16]The literature shows that the majority of cancer patients undergoing

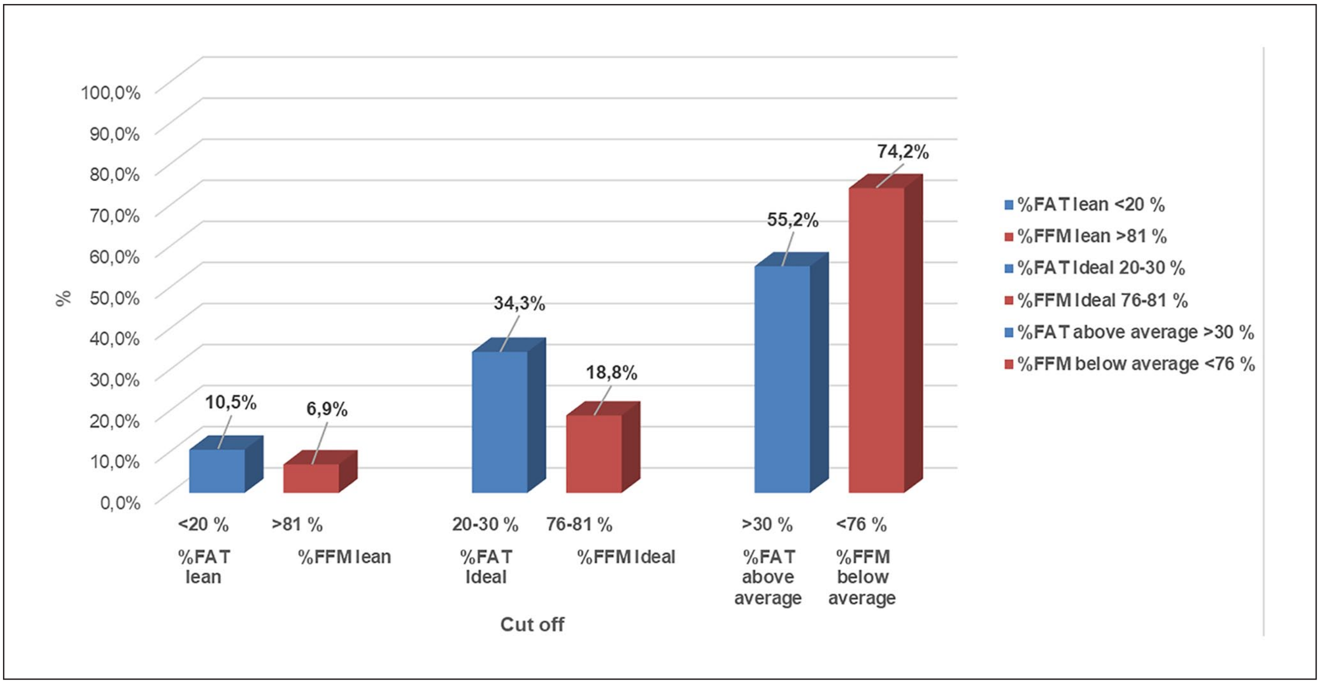

Figure 3. Body composition analysis.

curative surgery do not meet the international recommendations on PA preoperatively.[22]

Emerging evidence suggests that PA improves the ability of a person to cope mentally and physically with hospitalization and surgery, leading to decreased postoperative completion rates, reduced length of hospital stay and time of recovery, and improved quality of life.[26] A recent systematic review found that the implementation of a preoperative exercise program was effective in reducing the number of postoperative complications and the length of hospital stay in patients undergoing lung cancer surgery.[27]

A number of other studies have confirmed that higher levels of preoperative PA are associated with positive postoperative outcomes. In an observational cohort study of patients undergoing BC surgery, it was shown that those who undertook regular PA for at least 2 to 3 hours per week had a higher probability of feeling physically recovered 3 weeks after surgery compared to the physically inactive population.[28,29]

PA after cancer diagnosis also seems to increase survival rates even among those who were inactive before diagnosis.[30] However, the optimal types of exercise and levels of PA frequency and duration in relation to prognosis in BC patients are under investigation.

In addition to increased survival, an association between PA and increased QOL after cancer diagnosis has consistently been shown, regarding both physical and functional well-being, as well as psychological and emotional well-being.[31-33] Nevertheless, studies have shown reduced levels of PA after diagnosis among patients treated for BC,[17,34] while being physically active even at low levels (at least 60 minutes per day) increases the likelihood of good self-rated health and is associated with a lower risk of several common cancer-related symptoms such as pain, depression, and anxiety.[30,35,36]

Overall, a huge proportion of BC survivors do not meet the recommended levels of PA,[10] so that interventions aimed at promoting PA after diagnosis are likely to be among the most effective behavioral interventions in order to reduce mortality and recurrence rates and increase QOL.[37]

Several tools are available to measure physical activity, including self-reported questionnaires, indirect calorimetry, direct observation, heart rate telemetry, and movement sensors.[38] Unfortunately, these methods have well-known limitations[39] and there is no gold-standard criterion.[40,41] Movement sensors such as accelerometers have recently grown in popularity as a measure of PA,[42] thanks to their objective measurements and relatively small size. Nevertheless, due to their costs, accelerometers are not routinely used in large-scale cohort studies, where questionnaires are more frequently used,[43,44] with potential biases and risks for overestimated (from by 36% to 173%) or underestimated (28%) PA levels.[45] In a systematic review, including 23 validation studies, only 6 studies provided comparisons between PA levels derived from the IPAQ-SF questionnaire and data measured by wearable devices.[46]

PA influences a diverse array of metabolic, hormonal, and immunologic pathways, including circulating estrogen levels, insulin-like growth factors (IGFs), low-level chronic inflammation and oxidative stress, immune function, adipokines, DNA damage, and telomerase activity.[47,48] The Pre-Operative Health and Body (PreHAB) Study tested the impact on tissue and serum biomarkers of a pre-operative exercise intervention in 49 randomized women with newly diagnosed BC. Participants randomized to the exercise intervention received social/behavioral support to increase physical activity to 220 minutes of exercise per week, including 40 minutes of strength training and 180 minutes of moderate-intensity, aerobic exercise. Participants were required to take part in two 60 to 90 minutes supervised exercise sessions, led by American College of Sports Medicine—certified exercise trainers, per week and performed the remainder of their exercise as unsupervised aerobic training.

At the end of the intervention period, there was a significant reduction in leptin ($P < .008$), a trend toward a decrease in IGF-1 ($P < .08$) and changes in tumor gene expression but not in Ki-67 measures in active participants compared with controls.[49] Physically active individuals also tend to have higher sunlight exposure and consequently higher levels of vitamin D, which modulates cell proliferation.[50-55]

Moreover, the responsiveness of specific tumor subtypes to the effects of different types and modalities of exercise is also largely unknown.[56-63] Jones et al[64] investigated whether post-diagnosis exercise could differently affect outcomes in women with early stage BC on the basis of tumor clinicopathologic and molecular features. An exercise-associated reduction in BC-related deaths was apparent for tumors <2 cm [HR, 0.50; 95% confidence interval (CI), 0.34-0.72], well/moderately differentiated tumors (HR, 0.63; 95% CI, 0.43-0.91), and ER positive tumors (HR, 0.72; 95% CI, 0.53-0.97), concluding that the ER (Estrogen Receptor) +/PR (Progesterone Receptor)+/ HER2−/low-grade clinical subtypes are those that respond better to exercise. In a retrospective analysis of 2987 early BC patients, Holmes et al[65] found that exercise exposure (≥9 MET hours per week) was associated with a significant 50% reduction in BC related deaths in ER positive tumors compared to a non-significant 9% reduction in ER negative tumors.

Data in our study confirm the importance of an adequate preoperative assessment, that should include nutritional and PA screening and body composition analysis in order to early detect risk factors and leverage lifestyle interventions (eg, nutritional and psychological support, physical training, smoking, and alcohol cessation). Unfortunately, there is still a critical lack of appropriate evaluation of these parameters and patient-centered behavioral counseling is not encompassed in the routine pathways of cancer care.

Conclusions

Despite the key role of PA in reducing perioperative outcomes and improving side effects management after BC diagnosis, a huge proportion of patients are not routinely assessed. Data that emerged from our study confirm the urgent need to include evaluation of PA and nutritional status in the routine preoperative workup of every BC patient, in order to inform surgical care plans. Women may be more amenable to behavioral changes following a BC diagnosis, particularly under the guidance of clinicians and allied health professionals.

In a future perspective, a gold standard for a reliable evaluation of the PA levels in every cancer patient is needed, so that the general advice "exercise works for everything" could turn into a more targeted prescription based on the patient's attitudes and prescriptions for prehabilitation or rehabilitation needed to tolerate surgery and other treatments.

List of Abbreviations

BC	Breast cancer
BIA	Bioelectrical impedance analysis
BMI	Body mass index
ER	Estrogen receptor
FFM	Fat free mass
FM	Fat mass
HER-2	Human epidermal growth factor receptor 2
IGF-1	Insulin grow factor-1
IQR	Interquartile range
IPAQ	International Physical Activity Questionnaire
MET	Metabolic equivalent of task
NA	Not available
PA	Physical activity
PR	Progesterone receptor
QOL	Quality of life
SD	Standard deviation
SMF-BIA	Segmental multifrequency-bioelectrical impedance analysis
TBW	Total body water
TNF	Tumor necrosis factor
WCRF	World Cancer Research Fund
WHO	World Health Organization
WHR	Waist hip ratio

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Author Contributions

SM (Study design, writing, review). MMR (Study design, data collection, statistical analysis, writing), AF (Data collection, writing), CR (Data collection, writing), DG (Data collection, writing), CM (Data collection), ADM (Data collection), MD (Statistical analysis), RM (writing, review)

Availability of Data and Materials

Addition material are available contacting the corresponding author.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Author Stefano Magno declares that he has no conflict of interest. Author Maria Maddalena Rossi declares that she has no conflict of interest. Author Alessio Filippone declares that he has no conflict of interest. Author Cristina Rossi declares that she has no conflict of interest. Author Donatella Guarino declares that she has no conflict of interest. Author Claudia Maggiore declares that she has no conflict of interest. Author Annalisa Di Micco declares that she has no conflict of interest. Author Maddalena Dilucca declares that she has no conflict of interest Author Riccardo Masetti declares that he has no conflict of interest. All authors have read and approved the manuscript. The authors declare that they have no competing interests.

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Ethical Approval and Consent to Participate

All the procedures performed during the study comply with the National and regional guidelines and European Society of Breast Cancer Specialist (EUSOMA) quality criteria updated in 2020 available at https://www.eusoma.org/en/recommendations/breast-centre-requirements/1-148-1- and in accordance with the ethical standards of our Institution available at https://www.policlinicogemelli.it/scienzeinnovazione-ricerca/comitato-etico/. The study protocol was approved by the ethics committee of the hospital (approval number 0009991/22; ID 4734).

Consent for Publication

This study is a retrospective gathering of data from patients' medical records, so the written consent for publication from all participants was not necessary because the screening was part of the normal clinical practice that all patients did. Patients consented to the screenings as part of their medical procedures.

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