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ORIGINAL RESEARCH

Characterization of Physical Activity Levels in Female Breast Cancer Survivors: Relationship With Lymphedema (AtiLinf)

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The development of lymphedema (LE) is a major concern in breast cancer treatment, and it is crucial to understand the best ways to prevent and treat it. Physical activity has shown to be effective, safe, and feasible in controlling complications arising from treatments, as well as improving function and quality of life in breast cancer survivors. This study aimed to investigate the relationship between physical activity with grip strength and LE development in breast cancer survivors. A cross-sectional analytical study was conducted and women who had survived breast cancer between 1 and 5 years after surgery were selected. Participants completed the International Physical Activity Questionnaire Short Form, the volume of upper limb (UL) was measured by perimetry, handgrip strength was assessed with the JAMAR dynamometer, and the Actigraph accelerometer was placed on the waist. It was found that 50% of the sample was overweight, 28.3% were obese, and 52% of the participants had grip strength below the recommended level. They had an average energy expenditure of 1.2 (0.1) metabolic equivalents, 8.3 (1.8) hours/day of sedentary activity, and spent an average of 61% of their awake time in sedentary activity per day. Significant correlations were found between grip strength on the affected side and the difference in volume between the UL ($r_p = -.303$, $P = .041$) as well as between body mass index (BMI) and the difference in volume between the UL ($r_p = .341$; $P = .020$). Moreover, a significant correlation between BMI and the volume of the affected UL was found ($r_p = .848$, $P = .000$). BMI and grip strength of the affected side were identified as significant predictors of LE, both with P values less than .05. Although physical activity cannot directly prevent LE, it may contribute by helping to control BMI and promote higher levels of grip strength, both of which are important factors in the prediction of LE.

Keywords*:* exercise, oncology, handgrip strength, accelerometry, body mass index

Key Points

- Higher BMI and lower grip strength are significant predictors of lymphedema development in breast cancer survivors.
- Physical activity did not directly correlate with reduced lymphedema risk but may help control BMI and maintain grip strength, indirectly aiding prevention.
- Breast cancer survivors in the study exhibited high levels of sedentary behavior, spending about 61% of their waking hours inactive.

Oncological diseases are considered a global problem with increasing prevalence, and in recent years, there has been a significant increase in the average life expectancy of women who have survived breast cancer.[1–3] In many situations, this means living with chronic complications of treatment, such as pain, loss of upper limb (UL) strength, and lymphedema (LE), among others.[4–8] It is essential to use effective therapeutic strategies to improve the sequels of breast cancer treatment.[9] Promoting an active and healthy lifestyle plays an important role in preventing cancer recurrence and increasing survival. While improving quality of life, it prevents and controls treatment side effects and risk factors, especially the development of cardiovascular disease, which has a high incidence in breast cancer survivors.[4,10–12] Currently, the significance of physical activity (PA) and regular physical exercise (PE) in the prevention and treatment of various diseases, including breast cancer, is widely recognized. These activities have demonstrated their ability to facilitate enhancements in lymphatic drainage, muscle strength, aerobic capacity, fatigue management, anxiety reduction, and self-esteem improvement. Moreover, they effectively diminish other symptoms and complications associated with breast cancer, leading to an overall improvement in the functionality and health-related quality of life for breast cancer survivors.[5,13,14] Handgrip strength is an important measure in this context, since it is a simple and efficient indicator to assess the general strength of the UL, motor function, and objective functional capacity of the UL in women who are breast cancer survivors. In turn, this assessment is essential for prescribing more targeted therapeutic

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interventions, including PE and strengthening program for the functional recovery of breast cancer survivors.[15,16]

Despite this, PE and PA levels tend to decrease during treatment and do not return to prediagnosis levels after the end of treatment, which may be related to the side effects of various oncological therapies.[17] In this study, the primary aim was to assess the PA levels among breast cancer survivors. We also wanted to estimate the frequency, duration, and intensity of PA and investigate whether these PA levels correlated with the volume of the UL and grip strength. In addition, a secondary objective was to explore predictive relationships among the variables under investigation.

Materials and Methods

This study employs an analytical observational design with a cross-sectional approach. The participants selected for this study were women who had survived breast cancer, aged 18 years or older, and had completed the active phase of breast cancer treatment. Additionally, the inclusion criteria specified that the participants should have undergone surgery within a timeframe of 1–5 years. Participants provided their informed consent prior to participation. Women with metastases, bilateral breast surgery, inability to understand Portuguese language, and untreated infection were excluded. The study was approved by the Ethics Committee of Lisbon Health Technology School (80-2022) and the Ethics Committee of the Prof. Dr. Fernando Fonseca Hospital (103/2022). All participants were evaluated at 2 different times. In the first moment, the characterization form was filled out, and height, weight, UL volume, and handgrip strength were measured. UL volume was calculated using the simplified truncated cone formula based on circumference measurement using a metal anthropometric tape. The calculation of the volume of a truncated cone is: $V = h(C1^2 + C1C2 + C2^2) + 12\pi$, where V is the volume of the segment, $C1$ and $C2$ are the lengths of the circles at each end of the segment, and h is the distance between them.[18,19] For handgrip strength, we used JAMAR dynamometer in a seated position, with the shoulder in a neutral position, the elbow flexed at 90° and the wrist between 0° and 30° of extension. An isometric contraction was requested. This procedure was performed 3 times on each UL, alternating with a rest period of 60 seconds between each repetition. All participants were encouraged by positive feedback, and the best of the 3 attempts was counted.[20–22] Subsequently, the recommended grip strength was calculated for each participant according to age, height, and weight using the formula presented by Wang et al.[23] To assess daily PA, an accelerometer (wGT3X-BT, ActiGraph Corporation) was worn on the waist for 7 consecutive days for each individual, with instructions to maintain their usual routine and removing it only for sleeping and water-based activities (ie, swimming, bathing, etc). In addition, each time the device was removed, participants were asked to record the time and reason for removal in a spreadsheet.[24–26] It should be noted that the calculations were carried out based on valid hours/waking hours, that is, the time the accelerometer was placed. After 7 days of use, the second visit took place when the equipment was returned, and the International Physical Activity Questionnaire Short Form was administered by a researcher who was trained for these methods.[27]

Raw acceleration data was collected at 100 Hz and then converted to 60-second epochs using ActiLife software version 6.13.4 (ActiGraph Corporation). Nonwear time calculation was based on the overlap of the Troiano algorithm and the device auto-detection.[28] Afterward, energy expenditure was estimated using the Freedson combination formula, and cut points were taken from Keadle Women's Health, followed by metabolic equivalents' (MET) calculation using the Freedson formula for adults. Bouts were calculated using 10-minute criteria.[29,30]

Statistical Analysis

A global analysis and characterization of the sample included descriptive statistics in which the mean values, SD, and minimum and maximum values were obtained. According to each of the specific objectives and the nature of the variables, the most appropriate statistical tests were selected to verify the relationship between the variables under study and whether such correlations were significant. The significance level used was 95% ($P < .05$). For the correlation analysis between quantitative variables with normal distribution, the Pearson coefficient (r_p) test was used: time in sedentary activity, time in light activity, number of steps, volume of the affected limb, volume of the unaffected limb, difference in volumes between the limbs, body mass index (BMI), grip strength on the affected side, grip strength on the dominant side, and grip strength on the nondominant side. Spearman correlation test (r_s) analyzed qualitative variables or non-normal distributions: MET variables, time in moderate activity, total moderate to vigorous PA (MVPA), and LE level. One-way analysis of variance (Z) and Kruskal–Wallis (H) test compared the mean/distribution of MET values; time in sedentary/light/moderate activity; total MVPA; and number of steps in the group of women without LE, with subclinical LE, and LE. Student t test for 2 independent samples compared the mean values of grip strength between the group that underwent surgery on the dominant side and the group that underwent surgery on the nondominant side. Additionally, multiple linear regression analysis and adjusted logistic regression were conducted to determine whether BMI; grip strength; the number of steps; and time spent in sedentary activity, light PA, and moderate PA can predict the development of LE in the affected limb. It is noteworthy that the assumption of homogeneity of variance was met, and normality was tested using the Kolmogorov–Smirnov test ($n > 30$).

Results

The sample consisted of 46 female participants with a mean age of 56.9 (9.5) years who underwent surgical treatment for breast cancer with a mean postoperative period of 37.5 (14.1) months (Table 1). It is observed that 50% of the sample were overweight and 28.3% were obese, with a mean BMI of 28.2 (4.3) (Table 2).

The analysis of the clinical parameters (Table 2) shows that most of the participants are right-handed and that underwent surgery on the left side. The majority underwent conservative surgery, and the predominant axillary approach was sentinel lymph node biopsy, with axillary lymph node dissection.

Table 1 Characterization of the Sample (n = 46), According to Age, BMI, and Postoperative Time (in Weeks)

	Mean (SD)	Min–max
Age, y	56.9 (9.5)	35–77
BMI, kg/m^2	28.2 (4.3)	19.0–38.9
Postop time, mo	37.5 (14.1)	16–65
Postop time, y	2.6 (1.3)	1–5

Abbreviations: BMI, body mass index; max, maximum; min, minimum; postop, postoperation.

Volume of UL and Grip Strength

Regarding the volume of the UL, the mean difference in volume between the affected and unaffected ULs was 56.1 (100.7) cm^3 (Table 3). It was found that 71.7% of the participants had no LE, 26.1% had subclinical LE, and 2.2% had mild LE (Table 2). As for the evaluation of grip strength, the sample presented an average of 23.0 (6.5) kg on the dominant side and 21.9 (6.6) kg on the nondominant side (Table 3).

Table 2 Characterization of the Sample (n = 46; Number of Cases [%]) According to BMI, Dominant Side, Affected Side, and Type of Therapy (Surgery, Chemotherapy, Radiotherapy, Immunotherapy, and Hormone Therapy)

Clinical variables	Number of cases (%)
BMI	
Normal weight	10 (19.2)
Overweight	23 (44.2)
Grade I obesity	11 (21.2)
Grade II obesity	2 (3.8)
Dominant side	
Right	43 (93.5)
Left	03 (6.5)
Affected side	
Right	15 (32.6)
Left	31 (67.4)
Presence of LE	
Absence of LE	33 (71.7)
Subclinical LE (5%–10%)	12 (26.1)
LE light (10%–20%)	01 (2.2)
Type of surgery	
Mastectomy	21 (45.7)
Conservative surgery	25 (54.3)
Axillary approach	
ALND	13 (28.3)
SNB	33 (71.7)
Chemotherapy	31 (67.4)
Radiotherapy	34 (73.9)
Hormone therapy	42 (91.3)
Immunotherapy	05 (10.9)

Abbreviations: ALND, axillary lymph node dissection; BMI, body mass index; LE, lymphedema; SNB, sentinel lymph node biopsy.

Patterns and Levels of PA

Analyzing the results of the International Physical Activity Questionnaire (Table 4), the majority of participants considered themselves moderately active. In addition, it was found that the participants spent an average of 5.3 (2.5) hours per day sitting during the 7-day week (Table 5).

Regarding the information collected by the accelerometer (Table 5), the participants have an average of 1.2 (0.1) METs, which is close to the rest metabolic expenditure level. Moreover, they spend an average of 8.3 (1.8) hours per day in sedentary activity, that is, they spend an average of 61% of their awake time per day in sedentary activity. It should be noted that the participants accumulate an average of 0.5 (0.6) hour of MVPA per day and make a daily average of 6717 (2805) daily steps.

Correlation Between PA and UL Volume

To analyze the influence of PA levels on UL volume and the development of LE, correlations between variables were assessed. No significant associations were found between MET of task and the difference in UL volumes ($r_s = -.067$; $P = .657$) nor between time spent in sedentary activity ($r_p = -.154$; $P = .308$), light activity ($r_p = .047$; $P = .756$), or moderate activity ($r_s = -.101$; $P = .504$) and the difference in volumes between limbs. Additionally, no significant associations were observed between total MVPA ($r_s = -.101$; $P = .504$) or the number of steps ($r_p = -.115$; $P = .447$) and UL volume. Similarly, there were no significant effects of MET (H = 0.930; $P = .628$); time spent in sedentary activity ($Z = 1.102$; $P = .341$), light activity ($H = 0.213$; $P = .899$), or moderate activity (H = 2.091; $P = .351$); total MVPA (H = 2.091; $P = .351$); and number of steps (Z = 0.554; $P = .579$) on the stage of LE (absence of LE, subclinical LE, and mild LE).

Correlation Between PA and Grip Strength

No significant correlation was found between PA levels and grip strength of the affected side ($r_s = .220$; $P = .141$) nor between time spent in sedentary activity ($r_p = .165$; $P = .274$), light activity ($r_p = .147$; $P = .328$), or moderate activity ($r_s = .166$; $P = .270$), and grip strength of the affected side. A 2-sample independent Student's *t* test was conducted to compare the mean grip strength between the group of women who underwent surgery on the dominant side and those who had surgery on the nondominant side, revealing that grip strength was not affected by the surgical side. Specifically, the grip

Table 3 Characterization of the Sample (n = 46) According to the Volume of the Upper Limb (in Cubic Centimeters) and Grip Strength (in Kilograms)

Clinical variables	Mean (SD)	Min to max
Volume affected side, cm^3	2134.7 (398.6)	1329.9 to 3143.3
Volume unaffected side, cm^3	2078.6 (361.5)	1378.5 to 2974.5
Difference in volumes, cm^3	56.1 (100.6)	−100.8 to 333.0
Dominant side grip strength, kg	23.0 (6.5)	8.0 to 40.0
Nondominant side grip strength, kg	21.9 (6.6)	5.0 to 36.0
Normative value of dominant side grip strength	25.0 (3.3)	18.2 to 32.3
Normative value of nondominant side grip strength	24.0 (3.1)	17.6 to 30.7

Abbreviations: max, maximum; min, minimum.

strength of the group that had surgery on the dominant side was similar to the average grip strength of the group that had surgery on the nondominant side ($t = -.243$; $P = .808$).

Correlation Between Grip Strength and UL Volume

Significant correlations were observed between grip strength of the affected side and the difference in volumes between ULs ($r_p = -.303$; $P = .041$).

Correlation Between BMI and UL Volume

Additionally, a strong positive correlation was found between BMI and the difference in volumes between ULs ($r_p = .341$; $P = .020$) and between BMI and the volume of the affected UL ($r_p = .848$; $P < .001$). This indicates that higher BMI is associated with greater volume in the affected UL and a larger difference in volumes between the affected and unaffected ULs.

Predictive Statistics

A multiple linear regression analysis was conducted to assess whether BMI, grip strength of the affected side, and the number of steps can predict the development of LE in the affected limb. The analysis yielded a statistically significant model, ($F_{2,43} = 5.776$, $P = .006$, $R^2 = .212$). The BMI variable ($\beta = 0.364$, $t = 2.679$, $P = .010$) and the grip strength of the affected side ($\beta = -0.309$, $t = -2.280$, $P = .028$) were both identified as predictors of LE. The equation describing this relationship is: $y = b_0 + b_1 \cdot x_1 + b_2 \cdot x_2$, specifically, (volume difference between limbs, in cm^3) = −88.226 + 8.604 (BMI in kg/m^2) + (−4.502) (grip strength of the affected side in kg).

Additionally, variable categorization was performed, and adjusted logistic regression was applied to determine whether time spent in sedentary activity, light PA, and moderate PA increases the likelihood of belonging to the subclinical or mild LE category. However, no significant results were observed.

Table 4 Characterization of the Sample According to the IPAQ-SF (n = 46)

Clinical variables	Number of cases, %
Low active	34.8 (16)
Moderately active	45.7 (21)
Highly active	19.6 (9)

Abbreviation: IPAQ-SF, International Physical Activity Questionnaire Short Form.

Discussion

The present sample is characterized by high BMI values, which represents a relevant factor since it is known that obese and overweight women have a higher overall mortality rate; a higher breast cancer mortality rate; and an increased risk of developing other complications, recurrence, and metastasis.[31,32]

The low incidence rate of LE in the present sample can be explained by the lower representation of axillary dissection. The presented justification is supported by the fact that the incidence of LE is 4 times higher in surgery with axillary lymph node dissection compared with sentinel lymph node biopsy and by the knowledge that 15% of LE cases occur after 5 years after surgery as well.[33]

It was found that 52% of the participants had a grip strength lower than recommended. The deficit in grip strength in the present sample is consistent with the study by Perez et al,[20] who found a decrease in electromyographic activity in the flexor muscles of the wrist and fingers, extensor carpi ulnaris, and triceps brachii on the surgical side, mainly in cases of breast cancer surgery on the nondominant side.[20,23]

Regarding the information collected by the accelerometer, it is verified that participants spent roughly 228 minutes per week in MVPA, and the American College of Sports Medicine recommends that cancer survivors who have completed the active phase of treatment increase the duration and intensity of their activities, as tolerated and without worsening side effects, until they reach the recommendations for healthy adults (ie, at least 150 minutes of moderate-intensity PA per week or 75 minutes of vigorous activity per week [equivalent to 7.5 MET h/wk] is recommended).[24] That means, on average, they are complying with the given

Table 5 Values of Physical Activity Obtained From Actigraph Accelerometry and Number of Hours in the Sitting Position (IPAQ; n = 46)

Physical activity variables	Mean (SD)	Min–max
Number of hours sitting per day (wk)	5.3 (2.8)	1.0–10.0
Number of hours sitting per day (weekend)	5.2 (2.6)	0.5–12.0
Number of hours sitting per day (7 d)	5.3 (2.5)	0.9–10.6
Accelerometer valid hours	95.4 (13.8)	52.4–121.8
Kcals per day	341.9 (225.5)	58.8–1416.1
MET rate	1.2 (0.1)	1.0–1.7
Sedentary activity, h/wk	58.0 (12.6)	32–91
Light activity, h/wk	33.5 (10.9)	15–66
Total MVPA, h/wk	3.8 (4.2)	0–24
Sedentary activity, %	61.1 (11.3)	36.6–79.9
Light activity, %	34.9 (9.6)	19.3–59.6
MVPA, %	3.9 (3.9)	0.2–22.8
Steps counts (7 d)	47,024.3 (19,639.8)	14,767.0–114,611.0

Abbreviations: IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalents; MVPA, moderate to vigorous physical activity; max, maximum; min, minimum.

recommendations. However, there is a large discrepancy between participants. It is verified high levels of sedentary lifestyle since it is considered by Canadian guidelines that 8 hours per day sedentary, based on device-measured data, is associated with increased mortality risk.[34]

No significant associations were found between MET and difference in UL volumes (r_s = −.067; *P* = .657) or between time spent in sedentary (r_p = −.154, *P* = .308), light (r_p = .047; *P* = .756), or moderate activity (r_s = −.101; *P* = .504), with difference in volumes between members. According to the literature review conducted, it was expected that a relationship would be found between PA levels, and the volume of UL would be affected by surgery, since one of many benefits of PA and exercise is to promote lymphatic flow. The explanation for this relation is that the contraction of muscles causes compression of lymph nodes and valves, stimulating lymphatic flow in lymphatic vessels and thus reducing the risk of developing LE.[35] In addition, it is thought that PA and PE may promote lymphangiogenesis and recruitment of dormant lymphatic vessels, as lymphatic flow during PE is 2 to 3 times greater than at rest, requiring a greater capacity of the lymphatic system.[36] According to this author, PE causes an increase in blood pressure and cardiac output, resulting in increased capillary filtration and interstitial pressure. This facilitates the entry of fluids and proteins into the lymphatic capillaries and consequently increases lymphatic propulsion. In this sense, it is essential to interrupt periods of prolonged immobilization, including sitting time, to avoid venous and lymphatic stasis, as well as the "numbness" of the lymphatic vessels as a result of the lack of stimulation and stress triggered by the facilitating mechanisms of lymphatic return.[36,37]

There was no significant correlation between PA levels (MET rate) and grip strength on the affected side (r_s = .220; *P* = .141) nor between time spent in sedentary activity (r_s = .165; *P* = .274), light-intensity PA (r_s = .147; *P* = .328), MVPA (r_s = .166; *P* = .270), and grip strength on the affected side. Likewise, grip strength on the dominant/nondominant side was not affected by the side of surgery (z = −0.243; *P* = .808). It is known that breast cancer survivors have a decrease in muscle function and grip strength in the operated limb and that surgery on the nondominant limb results in a greater loss of grip strength on the same side compared with surgery on the dominant side.[20] Perez et al[20] justify this phenomenon by claiming that dominance and the operated side influence the scapular kinematics, which changes the UL movements after surgery, especially in operations on the dominant side, which corresponds to the more agile and coordinated side.[20]

However, significant correlations were found between grip strength on the affected side and the difference in volume between the UL (r_s = −.303, *P* = .041), indicating that the lower the grip strength on the affected side, the greater the volume difference. This is a relevant indicator because breast cancer survivors avoid vigorous or excessive UL exercise, including activities of daily living, for fear of developing LE. There are higher rates of inactivity in the group of women with LE and a protective approach due to fear of exacerbation with activity and exercise. However, it is now known that exercise does not increase the risk of exacerbation of LE, and it is recommended that this population engage in higher levels of PA and regular exercise throughout life.[38] In addition, muscle activity during exercise is thought to stimulate lymphatic transport persons.[12,38]

Furthermore, a low positive correlation was found between BMI and the difference in UL volumes (r_s = .341; *P* = .020) and between BMI and the volume of the affected UL (r_s = .848, *P* = .000). It is known that sedentary individuals tend to increase their body mass, which triggers an undesirable progression of the disease, as overweight and obesity are considered risk factors for the development of LE.[39] In addition, obesity causes inflammation and hormonal imbalances, which may affect the function of the lymphatic system, increasing the risk of developing LE.[40]

The multiple linear regression analysis identified a significant model to predict the development of LE in the affected limb, explaining approximately 21.2% of the variation in volume difference between the limbs. BMI and grip strength of the affected side were identified as significant predictors of LE, both with *P* values less than .05. The resulting equation indicates that an increase of 1 unit in BMI is associated with an increase of 8.604 cm^3 in volume difference, while an increase in grip strength is associated with a reduction of 4.502 cm^3 in volume difference. This suggests that a higher BMI increases the risk of LE, while greater grip strength may have a protective effect.

By conducting the present study, it was possible to increase knowledge about the PA habits of breast cancer survivors, who are characterized by high levels of physical inactivity and sedentary lifestyles. It was not possible to establish an association between levels of PA and LE, but the observations suggest that although PA cannot directly prevent LE, it can play an important role in indirectly preventing its development, helping to control BMI and promoting superior levels of grip strength. In this sense, the practice of PA is considered an important adjuvant therapeutic modality, since it attenuates and prevents some adverse effects of breast cancer treatment, which is why its promotion in this population is essential.

Conclusions

No significant associations were found in this study between PA levels and the development of LE or a reduction in UL grip strength. However, the findings, combined with other research, suggest that PA may still play an important role by influencing BMI, which can affect both UL volume and grip strength. BMI was identified as a risk factor for LE, and LE, in turn, has been linked to reduced grip strength. Therefore, while the direct impact of PA on LE and grip strength was not observed, PA could still indirectly help by controlling BMI and improving strength thereby potentially reducing the risk of both LE and strength decline. These results have important implications for risk assessment and prevention of LE, indicating that monitoring BMI and grip strength may be relevant for identifying at-risk individuals and implementing appropriate interventions. Promoting an active lifestyle remains essential in minimizing post-treatment complications in breast cancer survivors.

Limitations and Future Prospects

A replication of the present study with a larger sample size and a greater number of women with LE could make it possible to observe the direct influence of PA levels on the development of LE and on grip strength and to understand whether PA can prevent the occurrence of sequelae resulting from breast cancer treatments. In the present study, it was not possible to objectify the influence of the types of breast and axillary surgery and the different adjuvant therapies on PA levels, LE volume, and grip strength. The main limitations of this study include the small sample size and the lack of a sufficient number of participants with LE, which restricted the ability to detect potential associations. A sample size calculation using a 95% confidence level, a population size of 8954 (incidence women breast cancer, in 2022, in Portugal),[41] and a 5% margin of error indicated an ideal sample size of 369 participants. Additionally, the influence of surgical types and adjuvant therapies could not be fully explored. A key limitation of the study is related to the increasing incidence of LE over time since surgery, which may lead to selection bias. Participants who are earlier in their postsurgery period might exhibit a lower frequency of LE, potentially skewing the results. Additionally, the relationship between LE and infection complicates this issue, as individuals with LE face a heightened risk of infections. Excluding these individuals from the study could have resulted in the loss of relevant cases or introduced other biases, further affecting the study's findings. With increased knowledge on these topics, it will be possible to improve health care delivery by providing the necessary tools for individuals to best self-manage their chronic disease. There is a great need to increase knowledge about modifiable risk factors and preventive strategies to reduce the effects of treatment sequelae in breast cancer survivors.

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