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Applying Pre-Participation Exercise Screening to Breast Cancer Survivors: A Cross-Sectional Study

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Abstract

Purpose—Clinical guidelines recommend that breast cancer (BrCa) survivors be prescribed exercise. However, clinicians often do not prescribe exercise citing the presence of multiple health issues found among cancer survivors. No study has examined the proportion of BrCa survivors that can be prescribed a community/home based unsupervised exercise program safely and independently, without further medical investigations or supervision.

Methods—Participants included BrCa survivors who received treatment at a university healthcare system between 2009-2014. We applied previously identified published guidelines for health conditions that may impede BrCa survivors from completing a community/home based exercise program. Logistic regression models were used to quantify the magnitude of the association between demographic and clinical characteristics and the ability to perform community/home based exercise.

Results—Among 667 BrCa survivors, 65% to 75% were classified as able to complete community/home based exercise as recommended by the clinical guidelines. Older age, black race, treatment with chemotherapy, and treatment with radiation were associated with the potential need for further medical evaluation prior to starting exercise.

Conclusions—A large proportion of BrCa survivors can be prescribed community/home based exercise program safely and independently, without further medical investigations or supervision. Future research will be needed to determine how to identify the subset of BrCa survivors that may benefit from medical evaluation prior to starting exercise in a manner that doesn't interrupt clinical oncology workflow. Approximately 35% of BrCa survivors may benefit from medical evaluation prior to starting community/home based exercise.

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Keywords

Physical activity; breast cancer; survivorship

INTRODUCTION

Research that has emerged over the past 20 years demonstrates that exercise may improve various physiologic and psychological sequelae of breast cancer (BrCa) treatment [1–3], which includes cancer-related fatigue, impairments in quality of life, and decrements in cardiorespiratory fitness, muscular strength, and physical functioning [3–7]. In addition, regular participation in physical activity may be associated with a lower risk of BrCa recurrence and death [8–12]. The American College of Sports Medicine (ACSM), American Cancer Society (ACS), and National Comprehensive Cancer Network (NCCN) clinical practice guidelines recommend all cancer survivors to perform: “1) 150-minutes of moderate-intensity aerobic activity or 75-minutes of vigorous-intensity aerobic activity per week; 2) 2–3 weightlifting or muscle strengthening sessions per week; and 3) neuromuscular and flexibility activities on days of exercise” [1, 13, 14]. Exercise possesses pharmacological properties like medicine, and is most efficacious when prescribed with the appropriate volume, intensity, and modality to improve a specific health outcome [3, 15].

Despite clinical recommendations that advise all BrCa survivors to engage in regular physical activity or exercise [1, 13, 14], healthcare providers may be reluctant to prescribe exercise to their patients due, in part, to competing health conditions often found among cancer survivors, such as lymphedema, cardiovascular disease, and cancer-related fatigue [16], which may necessitate tailoring or individualizing the exercise prescription to maximize effectiveness and safety. Consequently, only one-in-five of BrCa survivors report that their healthcare provider has offered recommendations about engaging in healthy lifestyle behaviors, such as participating in regular physical activity [17]. Similar exercise prescribing patterns are observed among colorectal, endometrial, human papillomavirus (HPV)-related head and neck cancer survivors.

The current infrastructure in oncology often results in cancer survivors participating in exercise with minimal guidance and limited or no supervision [18]. BrCa survivors with multiple health conditions may require different volumes, intensities, and modalities of exercise to safely and effectively improve health outcomes. Healthcare providers may benefit from a standardized approach to identify BrCa survivors for whom it may be appropriate to safely refer a community or home-based exercise program that is consistent with the ACSM/ACS/NCCN clinical guidelines. Prior studies have estimated that as few as 20% of colorectal cancer, 15% of endometrial, and 39.3% of head and neck cancer survivors could be prescribed a community/home based exercise program without the potential need for further medical screening [19, 20, 42]. This study aimed to examine the proportion of BrCa survivors that can be prescribed a community/home based unsupervised exercise program safely and independently, without further medical investigations or supervision.

METHODS

Study Sample

Participants were eligible if they were: aged ≥21 years; diagnosed with BrCa (International Classification of Disease, 9th Revision [ICD-9]: 174.*); and received surgery for BrCa in the University of Pennsylvania Health System (UPHS) between the years of 2009 and 2014. Eligible participants have also had a subsequent visit approximately six-months (± three-months) after completion of their cancer-directed therapies (with the exception of hormonal or targeted treatment). We excluded women who were aged ≥90 years; with metastatic disease; or without the requisite health information. Data were abstracted from UPHS electronic medical records. This study was approved by University of Pennsylvania Institutional Review Board.

Primary Dependent Variable

Cancer survivors may be most likely to adopt recommendations about healthy lifestyle behaviors six-months after completing their primary cancer-directed therapies [21]. Six-months is suggested because it is the shortest interval of time that allows for the survivors to recuperate from acute symptoms of cancer treatment and are still receptive to learning, and adopting new healthy lifestyle practices [19, 20].

In order to develop a comprehensive list to define whether survivors would be able to perform community/home based exercise after a cancer diagnosis (Appendix Table 1, [19]), a review of previously published clinical recommendations for exercise was conducted that identified potential health conditions that may suggest the need for further medical evaluation [18]. This list has been applied in colorectal, endometrial, and head and neck cancer survivors previously [19, 20, 42]. The health conditions were classified into ten system-specific categories (Table S1). The identification of one or more relevant health conditions signified the potential need for further medical evaluation. For this analysis, if no relevant health conditions were identified, the ability to perform community/home based unsupervised exercise was assumed.

Data abstraction

Data was abstracted from the UPHS electronic medical records, by research staff with access to the complete medical records, including demographic information (such as age and race), clinical information (such as cancer stage (American Joint Committee on Cancer Staging Manual, Seventh Edition), and cancer-directed therapies). Measures for cancer care were collected at six-months after completing cancer-directed therapies (with the exception of hormonal or targeted treatment) using ICD-9 or procedure codes listed in the electronic medical record.

Covariates

We used the date of cancer diagnosis to calculate age. Race was categorized as black, white, or other. Cancer-related characteristics included cancer stage (Ductal carcinoma in situ (DCIS), I, II, III) [22], type of cancer-directed therapy (radiation and chemotherapy), type of

surgery (lumpectomy vs. mastectomy), reconstructive surgery, and the Charlson comorbidity index [23].

Analysis

Using the abstracted electronic medical record data, a sum of all health conditions was generated and then categorized into BrCa survivors that had zero versus one or more health condition(s). Values of zero signified the ability to perform community/home based exercise. Values above zero signified the potential need for further medical evaluation. Means and standard deviations, and *t*-tests were used to describe and compare continuous variables. Frequencies, proportions, and chi-square tests were used to describe and compare categorical variables. In this cross-sectional study, we sought to identify factors associated with BrCa survivors who have no serious health issues that would prevent safe participation in community/home based exercise (i.e., that are eligible to exercise without further medical investigations or supervision). Univariate logistic regression and multivariable logistic regression models were used to quantify odds ratios (OR) and 95% Confidence Intervals (CIs). For all covariates, we had ≥80% statistical power to detect odds ratios ≥1.6. We also conducted sensitivity analyses that excluded common health conditions among BrCa survivors including hypertension, diabetes, arthritis, morbid obesity (Body Mass Index ≥40 kg/m^2), and hyperlipidemia [24, 25]. Associations were considered statistically significant when at or below an alpha of 0.05. All analyses were performed using SAS® (version 9.4).

RESULTS

A total of 1,520 BrCa survivors were identified as having the requisite six-month follow up data. Among those ineligible: 93 had stage IV (metastatic) BrCa; 449 had missing BMI measures; three were ≥90 years; and 308 were excluded due to missing baseline treatment-related characteristics. Overall, 667 BrCa survivors met all inclusion conditions. BrCa survivors included in the analytic sample were younger (55.7±12.3 vs. 58.0±12.3; P<0.001) and were more likely to be treated with mastectomy (57.9% vs. 38.7%, P<0.001), compared to those who were excluded, respectively. The racial and cancer stage distribution of the excluded women were similar women included in the analysis (results not shown).

Among the 667 survivors who met all inclusion criteria, the mean age at diagnosis was 55.0±12.3 years. Age ranged from 24 to 89 (Table 1). Most women were white (74%); 19% had ductal carcinoma in situ (DCIS); 47.1% had stage I disease; 25% had stage II disease; and 9% stage III disease. Forty-three percent were treated with breast conserving therapy (lumpectomy); 44% were treated with chemotherapy; 39% were treated with radiation; and approximately 30% completed reconstructive surgery.

The prevalence of individual and system-specific health conditions, which may suggest the potential need for further medical evaluation, varied widely (Table 2). Health conditions with the highest prevalence included hypertension (10.6%), morbid obesity (7.5%), thyroid disease (6.7%), anemia (6.0%), and diabetes (4.2%). The median number of health conditions was zero and ranged from 0 to 5 (Figure 1 (a)). Sixty-five percent of the study population had no identified health conditions, 26.1% had one, 6% had two, and 3% had three or more of the selected health conditions.

In the sensitivity analysis, we excluded health conditions common among BrCa survivors including hypertension, diabetes, arthritis, morbid obesity (BMI ≥40 kg/m^2), and hyperlipidemia. In this sensitivity analysis, the median number of health conditions was zero and ranged from 0 to 5 (Figure 1 (b)). Seventy-five percent of the study population had no identified health conditions, 18.7% had one, 3.1% had two, and 2.8% had three or more of the selected health issues.

Older age, black race, treatment with chemotherapy, and treatment with radiation were variables associated with being less likely to be able to participate community/home-based exercise in the univariate logistic regression model (Table 3). Conversely, having a mastectomy or having reconstructive surgery was independently associated with being more likely to be able to perform community/home-based exercise. In multivariate-adjusted logistic regression, older age (OR: 0.98, 95% CI: 0.96-0.99; P =0.015), black race (versus white) (OR: 0.44, 95% CI: 0.30-0.64; P<0.001) treatment with chemotherapy (OR: 0.61, 95% CI: 0.43-0.87; P=0.007) and treatment with radiation (OR: 0.69, 95% CI: 0.49-0.98; P=0.039) were indepedently associated with being less likely to be able to participate community/home-based exercise. Results were similar in the sensitivity analysis that excluded common health issues among from the composite outcome (results not shown).

DISCUSSION

The principal finding of this study is that approximately 65% of BrCa survivors may be able to participate community/home-based exercise at the dose suggested by the ACSM/ACS/NCCN clinical guidelines, six-months after completion of their cancer-directed therapies. This finding complements the previously-described relationship examining the ability to prescribe community/home-based exercise among colorectal, endometrial, and head and neck cancer survivors [19, 20, 42]. Our study also suggests that BrCa survivors who were older, of black race, were treated with chemotherapy or radiation were more likely to potentially need further medical evaluation prior to engaging in community/home-based exercise.

Physical activity has been observed with a lower risk of BrCa recurrence and BrCa specific mortality [4, 8]. In addition, exercise has been shown to improve bone health, cardiovascular fitness [30–33], and reduce cancer-specific side effects such as musculoskeletal symptoms from hormonal breast cancer therapies, lymphedema, and cancer-related fatigue [6, 30, 34].

Despite the ACSM/ACS/NCCN clinical guidelines and above-described benefits of exercise for BrCa survivors, only 25% of providers recommend exercise to their patients [17]. Providers are reluctant to recommend exercise, citing competing health issues and the lack of an infrastructure to refer patients [36]. They also report lack of education, resources, and time to formally explain and recommend exercise during clinical visits [40]. On the other hand, cancer patients may experience a decrease in ability and motivation to exercise [41], uncertainty about what types of exercise are safe, and how to commence or sustain an exercise program [35], as well as lack of time, access, and support for lifestyle changing [40]. The provider’s recommendation is one of the most important motivating force for survivors to change lifestyle behaviors, such as adding exercise to their daily routine. Given

that 65% of breast cancer survivors lack the competing health conditions to not prescribe unsupervised exercise, it is necessary to establish a proper infrastructure and a change in culture for clinicians to encourage breast cancer patients participate in regular exercise as recommended by the ACSM/ACS/NCCN clinical guidelines.

Additionally, although 65% of BrCa survivors may be able to participate community/home-based exercise, it is noteworthy that 35% of BrCa may require additional resources to enable their safe participation in an exercise program. Thirty-five percent of the approximate three-million BrCa survivors currently living in the United States translates to approximately one-million women for whom there may be value for further medical evaluation prior to engaging in community/home-based exercise [37, 38]. Given the substantial number of BrCa survivors (and other types of cancer survivors) who may benefit from referral, there exists an urgent need to train health and fitness professionals with the knowledge, skills, abilities, and sources that are necessary to safely individualize and implement exercise programs that are appropriate for the unique needs of cancer survivors. Oncologists will require proper training to acknowledge the role of physical activity among cancer survivors, to be able to identify those who may benefit from a referral to medically based exercise program, and to prepare them to be able to exercise on their own [40]. Medically based exercise program, such as physical therapy, under some conditions, is covered by third-party health insurance [33]. It is possible to reduce the financial burden and increase cancer survivors' participation through a system in place with facilities and reimbursement for prescribed exercise programs [40]. With the proper infrastructure in place, oncology providers can consider referring their patients to physical therapists, rehabilitation physicians, and other health professionals to promote the safe participation in exercise. Our data can also be leveraged to guide healthcare providers in the identification of the subset of patients, perhaps patients with older age, of black race, treated with chemotherapy and/or radiation therapy, who may benefit from further medical evaluation or supervision prior to engaging in community/home based exercise safely and independently.

There are several limitations that should be acknowledged to add context to our findings. One major limitation is the potential lack of generalizability. This is a cross-sectional study in one university healthcare system. Estimates for the prevalence of common health issues such as hypertension and diabetes were lower in our sample population than estimates found in prior studies using national data matched for age and race [39]. These discrepancies may be attributed to the observation that the included hospitals are large tertiary care centers, and the characteristics of BrCa survivors that are treated in this health system may not reflect characteristics of BrCa survivors treated in the community setting across the United States. Additionally, although all necessary information required for the ACSM/ACS/NCCN guidelines for exercise prescription was available in this population, our analyses were limited to what was found in the electronic medical record. It is therefore possible that common, but non-malignant health issues, which were not the oncologists' priority, were not recorded in the oncology specified electronic medical record. Our exploratory logistic regression models had sufficient statistical power to detect effects as small as 1.6. It is plausible that smaller, yet still clinically important effects may have been missed. Another limitation is that over 50% of our sample size was lost to exclusion criteria. The women in the analytic sample were significantly younger. The younger age of our analytic sample may

make our estimates conservative. Based on these limitations, it is plausible that our results may overestimate the percentage of BrCa survivors for whom oncologists could safely prescribe community/home based exercise.

Conversely, there are several strengths to this study such as a large sample size, which allowed us to have sufficient statistical power to examine demographic and clinical correlates. Our sample included 28% non-white BrCa survivors, which improves the demographic generalizability of our sample to the broader population of BrCa survivors in the United States. Our data were abstracted from the electronic medical record following a systematic search process that has been validated [19, 20, 42].

In conclusion, our findings suggest that 65% to 75% of BrCa survivors may be prescribed community/home-based unsupervised exercise safely and independently, six-months after completing cancer-directed therapies, at the dose suggested by the ACSM/ACS/NCCN clinical guidelines, without need for further medical investigations or supervision. BrCa survivors who were older, of the black race, received chemotherapy, and received radiation, associated with being more likely to benefit from further medical evaluation prior to engaging in community/home-based exercise safely and independently. Oncologists may consider the benefits of exercise especially for breast cancer patients without competing health issues and feel confident in making recommendations to participate in exercise programs. Future studies should focus on investigating the strategies to establish an effective infrastructure in clinical setting to support providerssafely prescribe exercise to the three-million BrCa survivors living in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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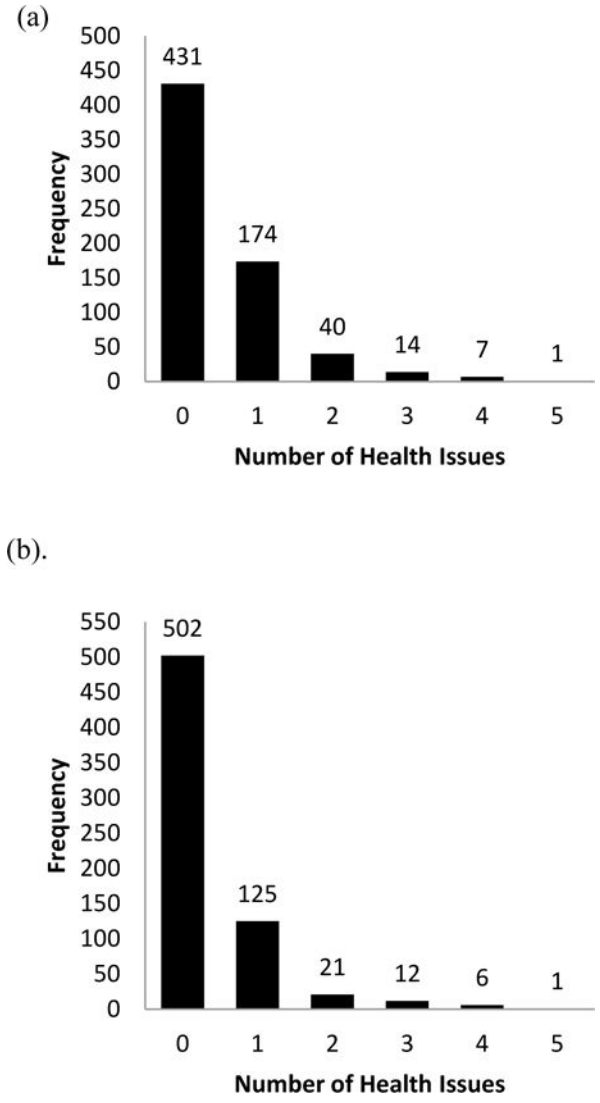

Figure 1.

a. Distribution of health-issues that preclude unsupervised exercise in (a) the primary outcome analysis, and (b) the sensitivity analysis that excluded hypertension, diabetes, arthritis, morbid obesity (BMI ≥40 kg/m2), and hyperlipidemia.

Table 1

Demographic and clinical variables

	Overall (n=667)	
Age at Diagnosis [a]	55.0±12.3	
	N	%
Race		
White	481	72.1
Black	154	23.1
Other	32	4.8
Stage		
DCIS	126	18.9
I	314	47.1
II	167	25.0
III	60	9.0
Surgery		
Lumpectomy	284	42.6
Mastectomy	383	57.4
Chemotherapy		
No	407	61.0
Yes	260	39.0
Radiation		
No	371	55.6
Yes	296	44.4
Reconstructive Surgery		
No	468	70.2
Yes	199	29.8

[a]Variables are mean ± standard deviation

Table 2

Health-issues that preclude to participate in unsupervised exercise program (N=667)

Health Issues	N	%
Hematologic - any of the following	**46**	**6.90**
White Blood Cells <3,000	18	2.70
Low Hemoglobin (<10g/dl)	40	6.00
Musculoskeletal - any of the following	**3**	**0.45**
Fracture of Hip/Back/Legs	3	0.45
Systemic - any of the following	**18**	**2.70**
Fever >100°F	5	0.75
Malaise	13	1.95
Gastrointestinal - any of the following	**12**	**1.80**
Severe Nausea	10	1.50
Fecal or Urinary Incontinence	2	0.30
Cardiovascular - any of the following	**40**	**6.00**
Chest Pain	9	1.35
Pulse >100 or <50 beats.min^{-1}	12	1.80
Irregular Pulse	7	1.05
Ankle Edema	10	1.50
Congestive Heart Failure	3	0.45
Heart Valve Disease	10	1.50
Aortic Stenosis	3	0.45
Ventricular Ectopy	6	0.90
Coronary Angioplasty	2	0.30
Pulmonary - any of the following	**25**	**3.75**
Severe Dyspnea	10	1.50
Coughing or Wheezing	14	2.10
Chest Pain with Deep Breath	6	0.90
Neurologic - any of the following	**4**	**0.60**
Blurred Vision	2	0.30
Neuropathy	2	0.30
Comorbidities - any of the following	**164**	**24.59**
Hypertension	71	10.64
Heart Murmur	2	0.30
Diabetes	28	4.20
Arthritis	2	0.30
Osteoporosis	17	2.55
COPD	4	0.60
Depression	24	3.60
Morbid Obesity	50	7.50
Lymphedema	8	1.20
Hyperlipidemia	18	2.70

Health Issues	N	%
Thyroid Disease	41	6.15
Liver Disease	4	0.60

Table 3

Association between demographic and clinical variables and who can be safely prescribed community/home-based unsupervised exercise program

Variable	Univariate Model		Multivariate Model	
	OR (95% CI)[a]	*P*	OR (95% CI)[a]	*P*
Age - Continuous	0.98 (0.97–0.99)	0.020	0.98 (0.96–0.99)	0.015
Race				
White	1.00 (Ref)		1.00 (Ref)	
Black	0.41 (0.28-.59)	<0.001	0.44 (0.30–0.64)	<0.001
Other	1.13 (0.51–2.49)	0.772	0.90 (0.40–2.03)	0.804
Pathology Stage				
DCIS	1.19 (0.76–1.87)	0.430	–	–
I	1.00 (Ref)		–	–
II	0.79 (0.54–1.17)	0.237	–	–
III	0.72 (0.41–1.27)	0.261	–	–
Chemotherapy				
No	1.00 (Ref)		1.00 (Ref)	
Yes	0.61 (0.44–0.85)	0.003	0.61 (0.43–0.87)	0.007
Radiation				
No	1.00 (Ref)		1.00 (Ref)	
Yes	0.58 (0.42–0.81)	<0.001	0.69 (0.49–0.98)	0.039
Surgery (%)				
Lumpectomy	1.00 (Ref)		–	–
Mastectomy	1.59 (1.12–2.12)	0.008	–	–
Reconstructive Surgery				
No	1.00 (Ref)		–	–
Yes	1.39 (0.97–1.99)	0.066	–	–

[a]Odds Ratio (OR) from Logistic Regression and 95% Confidence Interval (95% CI).