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ORIGINAL ARTICLE

Association between pre-diagnosis BMI, physical activity, pathologic complete response, and chemotherapy completion in women treated with neoadjuvant chemotherapy for breast cancer

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Abstract

Purpose Physical activity and lower BMI have shown benefit for breast cancer survival, but the association between these factors, pathologic complete response (pCR), and chemotherapy completion is not clear. We evaluated whether BMI and physical activity are associated with pCR and chemotherapy completion during neoadjuvant breast cancer treatment.

Methods We conducted a retrospective case–control study of women given neoadjuvant chemotherapy for stage I–III breast cancer between 2010 and 2016. A medical record review provided pCR, chemotherapy completion, and patient characteristics. A telephone survey assessed physical activity 1 year before diagnosis. Unconditional logistic regression models identified factors associated with pCR and chemotherapy completion.

Results In our cohort ($n=243$), the average age was 52.9 years (SD 13.0) and mean BMI was 29.5 kg/m^2 (SD 7.0). Seventy-five (31%) patients had pCR and 168 (69%) had residual disease. Patients with pCR had lower mean BMI than those with residual disease (28.2 (SD) vs. 30.1 (SD), $P=0.04$). Exercise was associated with completion of chemotherapy (OR 7.6, 95% CI 1.4–41.2, $P=0.02$).

Conclusions Pathologic complete response was associated with lower BMI; chemotherapy completion was associated with exercising at CDC-recommended levels prior to breast cancer diagnosis.

Keywords Breast cancer · Physical activity · BMI · Neoadjuvant chemotherapy · Pathologic complete response

Introduction

Neoadjuvant chemotherapy is a treatment option for patients with locally advanced breast cancer in which chemotherapy is given prior to surgery and/or radiation therapy. It has been shown to reduce tumor volume and allow for more women to be able to choose breast-conserving surgery [1]. Pathological examination of resected tissue following neoadjuvant chemotherapy allows for the determination of a pathological complete response (pCR), which is a favorable prognostic factor associated with longer survival than those with residual disease [2].

Many studies have found that obesity at the time of breast cancer diagnosis is associated with poorer outcomes and with an increased risk of breast cancer recurrence and mortality [3–5]. However, the relationship between BMI and pCR rates from neoadjuvant chemotherapy for breast cancer is not as well understood, with data from recent studies reporting mixed results [6–10]. Several studies have also shown that metabolic syndrome is associated with poorer breast cancer outcomes [11, 12]. Insulin resistance specifically has been found to be associated with increased breast cancer mortality [13].

Higher levels of physical activity following breast cancer diagnosis have been associated with reduced breast cancer deaths [14–18]. The relationship between pre-diagnosis physical activity and breast cancer outcomes has been investigated, but with more inconsistent findings [16, 19–24]. To our knowledge, there have not been any studies looking at

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the association between pre-diagnosis physical activity and pCR rates following neoadjuvant chemotherapy.

Completing more doses of chemotherapy throughout the treatment course has been found to be related to improved breast cancer outcomes and survival [25]. There is some evidence that higher levels of physical activity after diagnosis may be associated with increased rates of completing chemotherapy regimens as prescribed [26]. However, there have not been any studies to date that investigated the association between physical activity prior to breast cancer diagnosis and neoadjuvant chemotherapy completion. Given the gap in knowledge regarding how these factors are associated with outcomes from neoadjuvant chemotherapy, we sought to evaluate whether there is a relationship between pre-diagnosis BMI, physical activity, and pCR. We also evaluated additional lifestyle factors including diet and alcohol consumption. Additionally, we investigated these factors associated with neoadjuvant chemotherapy completion rates.

Materials and methods

We conducted a retrospective case–control study to examine the effect of physical activity and BMI prior to diagnosis on pCR rates and chemotherapy completion for women treated with neoadjuvant chemotherapy for early-stage (I–III) breast cancer between the years 2010 and 2016. This study was approved by the Human Investigation Committee at Yale University.

Sample

We identified eligible participants using the Yale Cancer Center Tumor Registry, a database of all patients treated for cancer at Smilow Cancer Hospital at Yale New Haven Hospital (YNHH) and the Yale Cancer Center. Eligible patients were females over the age of 18 treated with neoadjuvant chemotherapy for early-stage invasive breast cancer during the years 2010–2016. Included patients had neoadjuvant chemotherapy followed by surgical resection and had a pathology report that recorded either pCR or residual disease following surgery. Eligible patients needed to have sufficient treatment information recorded in the electronic medical record (EMR) to determine chemotherapy completion. Patients treated on a clinical trial chemotherapy regimen were excluded from the study.

For the telephone survey, participants needed to be able to understand and respond to questions in English, and we excluded patients who had relapsed with metastatic disease or who had died. We sent emails to the medical oncologists of patients deemed eligible for the telephone survey with a 14-day opt out period and attempted to contact patients over the telephone for whom we had physician approval.

Patient characteristics

We conducted a medical record review using data from the Tumor Registry and the EMR at YNHH. Information obtained from the tumor registry included demographic information, age at diagnosis, AJCC tumor staging [27], tumor markers, hormone receptor status, medical oncologist, as well as pCR vs. residual disease. The determination of pCR or residual disease from the tumor registry was verified against the pathology report in the EMR. Data abstracted from the EMR included measured BMI before and after treatment, menopausal status, and medications listed in the EMR for diabetes, hypertension, and hyperlipidemia.

Chemotherapy completion

Chemotherapy treatment information, including the chemotherapy regimen and completion rate, was also obtained from the medical record. We defined the expected number of treatments for each medication and recorded whether the patient met the expected number of treatments. The expected number of treatments was defined by looking at the oncologist' notes in the medical record detailing the treatment plan. We then calculated the percentage of cycles actually completed out of the number expected to determine the percentage of cycles completed. We also recorded if there was a cycle delay longer than 7 days, and the number of days after the scheduled treatment the dose was actually given. Dose adjustments were recorded if the dose was reduced for a given cycle. Participants who had dose adjustments were not considered to have received the full dose of chemotherapy. We categorized participants as receiving the full dose of chemotherapy without delays, receiving the full dose with delays, or not receiving the full dose by either reduced dose or reduced number of cycles. We considered "chemotherapy completion" to be receiving full doses of all prescribed chemotherapy, with or without cycle delays. Reasons noted in the physicians' documentation for dose adjustments or delays were also recorded.

Physical activity measurement

Physical activity, fruit and vegetable intake, and alcohol consumption in the year prior to diagnosis were assessed via telephone survey. Verbal informed consent was obtained over the telephone before proceeding with the survey. Participants were asked if they ate more than five fruit and vegetable servings per day and how many alcoholic beverages they consumed each week on average. To assess physical activity, we used the Modifiable Activity Questionnaire developed by Kriska et al., which asks about the number of hours per week

spent doing recreational activities such as walking, jogging, using the StairMaster, and playing tennis [28]. A $5 coffee shop gift card was offered for completing the survey.

The metabolic equivalent of task-hours per week (MET-h) was determined by multiplying the hours per week spent on each activity by the estimated MET value of that activity [29]. We considered exercisers to be those who completed at least 7.5 MET hours per week, which is the equivalent of the CDC recommendation of 2.5 h/week of moderate-intensity exercise at three METs or greater.

Data analysis

The data were recorded and compiled using the OnCore Enterprise Research data management system version 15.2.6. We compared the characteristics of the entire sample for the medical record review with the participants who completed the telephone survey to ensure that the telephone survey was a representative sample. We first conducted univariate analyses to identify factors associated with pCR and chemotherapy completion, and then performed multivariate analyses to determine if significant associations remained after adjusting for potential cofounders. For the pCR analysis, the patients who had a pCR were considered cases, and those with residual disease were considered controls. For the chemotherapy completion analysis, those patients who received full doses of all prescribed chemotherapy were considered cases, and those who did not receive the complete course of treatment were considered controls. This allowed us to calculate odds ratios for pCR and chemotherapy completion based on a number of factors of interest.

We performed a multivariate logistic regression analysis for pCR to adjust for potential cofounders. The impact of exercise on chemotherapy completion among the survey cohort was also evaluated in a multivariate logistic regression with covariate adjustment for potential confounders. Chemotherapy cycles completed was also treated as a continuous variable to identify factors associated with a higher percentage of cycles completed. All statistical analyses were performed using SAS 9.4 (Cary, NC). Significance level was set as P value < 0.05, two-sided.

Results

We assessed the eligibility of 393 patients who received neoadjuvant chemotherapy for breast cancer at Yale New Haven Hospital between the years 2010 and 2016 (Fig. 1). Ninety-eight patients did not have treatment information recorded in the EMR, because the data was not transferred from paper records. We conducted 243 medical record reviews of eligible patients. Of the 243 patients reviewed, we attempted

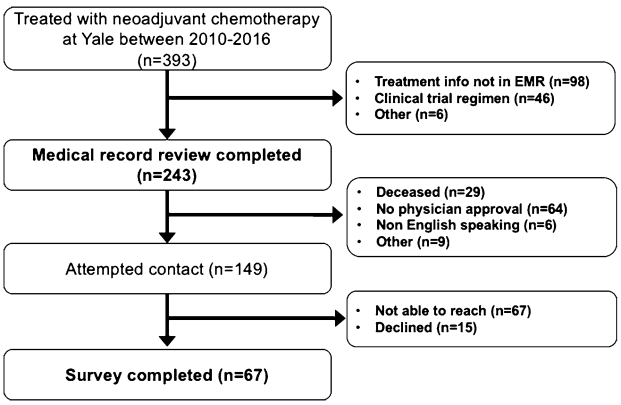

Fig. 1 This flow diagram shows the number of subjects at each stage of recruitment for the study. Ultimately, 243 patients were included in the medical record review, and 67 patients completed the telephone survey. The arrows pointing to the right show the number of subjects at each stage who were not included going forward, and the reasons for exclusion at each stage

to contact 149 over the phone and completed 67 surveys (Fig. 1).

The overall sample of 243 patients had an average age of 52.9 years (SD 13.0) and a mean pre-treatment BMI of 29.5 kg/m^2 (SD 7.0). The patients were 74% non-Hispanic White and 44% were premenopausal. Most of the patients had AJCC stage II cancer at diagnosis (55%), with 17% stage I and 28% stage III. The 67 patients who completed the telephone survey did not significantly differ from the overall sample in terms of demographics or tumor characteristics (Table 1).

All study participants received a standard neoadjuvant chemotherapy regimen that did not include investigational medications. One hundred and eighty-two patients (75%) received taxane-based therapy, and 53 patients received anthracycline-based therapy (22%). Six patients received a regimen containing both anthracycline and taxane (2%), and two patients received CMF therapy (1%).

Factors associated with pCR

Of the sample of 243 patients, 75 (31%) had a pCR and 168 (69%) had residual disease following neoadjuvant chemotherapy. Age at diagnosis, race, premenopausal status, diabetes, and physical activity (exercise > 7.5 MET hours per week) were not significantly associated with pCR status. However, patients who had a pCR had a lower BMI prior to breast cancer diagnosis than those with residual disease (28.2 (SD 5.9) vs. 30.1 (SD 7.4), $P = 0.04$). Patients with hormone receptor-negative and HER-2-positive tumors were most likely to have a pCR (75%). In contrast, patients with hormone receptor-positive and HER-2-negative tumors were least likely to have a pCR (19%). The AJCC stage was also

Table 1 Sample characteristics

	Overall ($n=243$)	Telephone survey ($n=67$)	P value
Age at diagnosis, mean (SD)	52.9 (13.0)	54.8 (12.2)	0.17
Race (n, %)			0.23
White, non-Hispanic	180 (74%)	54 (80%)	
Black, non-Hispanic	38 (16%)	10 (15%)	
Hispanic	18 (7%)	3 (4%)	
Other (unknown)	7 (3%)	0	
Premenopausal (n, %)	108 (44%)	25 (37%)	0.4
AJCC stage at diagnosis (no, %)			0.57
I	42 (17%)	14 (21%)	
II	134 (55%)	36 (54%)	
III	68 (28%)	17 (25%)	
Hormone receptor status (n, %)			0.13
HR −, HER2 −	73 (30%)	18 (27%)	
HR −, HER2 +	20 (8%)	3 (4%)	
HR +, HER2 −	115 (47%)	39 (58%)	
HR +, HER2 +	36 (15%)	7 (10%)	
Pre-treatment BMI, mean(SD)	29.5 (7.0)	29.7 (7.9)	0.76
Post-treatment BMI, mean(SD)	29.2 (6.8)	29.0 (7.5)	0.79
Cycle delays (no, %)	90 (37%)	21 (31%)	0.94
Average # days delayed (n)	12.4	9.7	0.4
Dose adjusted or missed (no, %)	89 (37%)	25 (37%)	0.99
Cycle delay, dose adjusted or missed (no, %)	135 (56%)	37 (55%)	0.94

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related to pCR ($P=0.002$) (Table 2). Stage III was least likely to have a pCR (15%) (Table 2).

In the multivariate analysis, after controlling for age at diagnosis, hormone receptor status and AJCC stage at diagnosis, baseline BMI remained a significant predictor of pCR. The adjusted odds ratio of higher BMI on pCR was 0.95 (95% CI 0.91–0.997, $P=0.04$) (Table 3). Hormone receptor status also remained an independent predictor of pCR in the adjusted analysis.

Factors associated with chemotherapy completion

One hundred and fifty patients (63%) completed all of their prescribed doses of chemotherapy without dose reductions (Table 4). Fifty-six percent of the cohort had either a dose reduction or a delay of 7 days or more (Table 1). The most common medical symptoms requiring delayed administration of doses were myelosuppression (31%), infection (17%), and neuropathy (11%) (Table 5). Neuropathy was also a common reason for adjusting the dose of chemotherapy or for missing the cycle altogether, as it was a reason for 33% of the dose adjustments. Myelosuppression (20%) and fatigue (9%) were also frequently given as reasons that physicians adjusted or skipped doses.

Patients who completed all doses of chemotherapy as prescribed were younger than those who did not, with a mean age of 51.4 years (SD 13.0) for completers and 55.4 years (SD 12.6) for non-completers. Premenopausal women were more likely to complete treatment than postmenopausal women (70% vs 57%, $P=0.004$). Those who were taking medication for diabetes were less likely to be completers (40% vs. 93%, $P=0.01$). BMI, hormone receptor status, and cancer stage did not show an association with chemotherapy completion.

Among the 67 patients who completed telephone survey, those who reported exercising more than 7.5 MET hours per week prior to diagnosis were more likely to complete chemotherapy at the prescribed dose (76% vs 36%, $P=0.002$). After controlling for age at diagnosis, fruit and vegetable intake, drinking more than one alcoholic drink per week, BMI, menopausal status, diabetes medication and diastolic blood pressure, the adjusted odds ratio for exercise on chemotherapy completion was 7.6 (95% CI 1.4–41.2, $P=0.02$) (Table 6). Older age at diagnosis and diastolic blood pressure remained independent predictors of completion in the adjusted model. Drinking alcohol and premenopausal status were significantly associated with completing chemotherapy only in unadjusted analysis. When using the percentage of prescribed cycles completed as primary outcome for these

Table 2 Unadjusted association between patients' characteristics, clinical factors, and pCR

	Residual disease ($n=168$)	PCR ($n=75$)	P value
Age at diagnosis, mean(SD)	53.6 (13.0)	51.6 (12.8)	0.28
Race (n, %)			0.85
White, non-Hispanic	126 (70%)	54 (30%)	
Black, non-Hispanic	24 (63%)	14 (37%)	
Hispanic	13 (72%)	5 (28%)	
Other (unknown)	5 (71%)	2 (29%)	
Premenopausal (n, %)			0.11
Yes	67 (63%)	40 (37%)	
No	101 (74%)	35 (26%)	
AJCC stage at diagnosis (n, %)			0.002
I	23 (56%)	18 (44%)	
II	86 (65%)	47 (35%)	
III	58 (85%)	10 (15%)	
Hormone receptor status (n, %)			< 0.0001
HR −, HER2 −	49 (67%)	24 (33%)	
HR −, HER2 +	5 (25%)	15 (75%)	
HR +, HER2 −	95 (83%)	19 (17%)	
HR +, HER2 +	19 (53%)	17 (47%)	
Pre-treatment BMI, mean(SD)	30.1 (7.4)	28.2 (5.9)	0.04
Post-treatment BMI, mean(SD)	27.7 (7.2)	27.9 (5.6)	0.04
Number of cycles prescribed (mean, SD)	12.8 (4.5)	12.9 (4.6)	0.88
Percentage of cycles completed (mean, SD)	95% (14%)	93% (18%)	0.52
100% complete (n, %)	126 (69%)	57 (31%)	
85–99% complete (n, %)	20 (69%)	9 (31%)	
< 85% complete (n, %)	19 (73%)	7 (27%)	
Regimen completion			0.83
Full dose received without delays	72 (70%)	31 (30%)	
Full dose received with delays	33 (72%)	13 (28%)	
Full dose not received	63 (67%)	31 (33%)	
Medication for DM (n, %)			0.30
Yes	21 (78%)	6 (22%)	
No	147 (68%)	69 (32%)	
Medication for DM, HTN, or HLD (n, %)			0.20
Yes	73 (74%)	26 (26%)	
No	95 (66%)	49 (34%)	
Of those completing phone survey:	R ($n=46$)	pCR ($n=21$)	P value
Exercise > 7.5 MET-h/week (n, %)			0.95
Yes	31 (67%)	14 (67%)	
No			
Fruit and vegetable > 5 servings/day (n, %)			0.27
Yes	22 (76%)	7 (24%)	
No	24 (63%)	14 (37%)	
Alcohol > 1 drink/week, (n, %)			0.30
Yes	26 (74%)	9 (26%)	
No	20 (63%)	12 (38%)	

AJCC American Joint Committee on Cancer, *DM* Diabetes Mellitus, *HTN* Hypertension, *HLD* Hyperlipidemia

Table 3 Adjusted predictors of pCR

Predictors	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Baseline BMI	0.96 (0.92, 1.002)	0.06	0.95 (0.91, 0.997)	0.04
Age at diagnosis, years	0.99 (0.97, 1.009)	0.27	0.98 (0.96, 1.003)	0.09
Hormone receptor status		< 0..0001		< 0.0001
HR −, HER2 +	6.13 (1.99, 18.84)	0.0004	6.95 (2.08, 23.17)	0.0005
HR +, HER2 −	0.41 (0.20, 0.82)	< 0.0001	0.43 (0.21, 0.89)	< 0.0001
HR +,HER2 +	1.83 (0.81, 4.13)	0.45	1.70 (0.72, 3.98)	0.69
HR −, HER2 −	1.00		1.00	
AJCC stage at diagnosis (*n*, %)		< 0.003		0.06
I	4.54 (1.82, 11.29)	0.01	3.12 (1.17, 8.28)	0.06
II	3.17 (1.48, 6.77)	0.18	2.20 (0.98, 4.94)	0.48
III	1.00		1.00	

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67 patients, only older age and taking medication for diabetes were significantly associated with lower percentage of completion.

Chemotherapy completion and pCR

We did not find an association between chemotherapy completion and pCR ($P = 0.51$). Of note, 24% of those who completed the regimen without delays had a pCR, comparing to 39% of those who did not complete the regimen. The average number of treatment cycles prescribed did not differ between the pCR and residual disease group, with an average of 12.8 (SD 4.5) and 12.9 (SD 4.6) cycles prescribed, respectively. Similarly, the percentage of cycles completed did not impact pCR, as 27% of patients who completed < 85% cycles had a pCR, compared to 31% of patients who completed ≥ 85% cycles (Table 2).

Discussion

This study evaluated the association between pre-diagnosis BMI and physical activity on pCR and neoadjuvant chemotherapy completion for breast cancer. We conducted a medical record review of 243 patients who received neoadjuvant chemotherapy for early-stage (I–III) invasive breast cancer. We also conducted a telephone survey to assess physical activity in 67 of these patients. Our results suggest that lower BMI prior to breast cancer diagnosis is associated with pCR from neoadjuvant chemotherapy ($P = 0.04$), and BMI remained an independent predictor of pCR in adjusted analysis. In addition, patients who exercised at recommended levels of 2.5 h/week prior to breast cancer diagnosis were more likely to complete neoadjuvant chemotherapy as prescribed ($P = 0.03$).

Our finding that lower BMI is associated with pCR is supported by other studies showing that lower BMI is related to improved breast cancer outcomes [3–5, 30]. There is also recent data to support that lower BMI is associated with pCR in patients receiving neoadjuvant chemotherapy [6, 10]. For example, in a study of over 1100 patients receiving neoadjuvant chemotherapy for invasive breast cancer, Litton et al. found that overweight and obese patients were significantly less likely to have a pCR than normal weight patients [6]. However, our findings contradict the results of several studies that did not find any association between pre-diagnosis BMI and pCR [7, 8].

One mechanism that may explain the link between BMI and breast cancer is through metabolic factors such as triglycerides, hypertension, and elevated blood glucose. A recent study showed that these metabolic syndrome components worsen during neoadjuvant chemotherapy [31]. Additionally, metabolic syndrome may be associated with a more aggressive tumor biology [12]. Our study did not find that patients taking medications for hypertension, diabetes, or high cholesterol had lower rates of pCR. However, we did find that patients taking medication for diabetes were less likely to complete chemotherapy as prescribed.

We evaluated whether physical activity prior to breast cancer diagnosis may lead to improved outcomes from neoadjuvant chemotherapy, as there is existing evidence that higher levels of physical activity following breast cancer diagnosis has been associated with improved breast cancer survival [14–18]. However, our study did not find an association between physical activity prior to breast cancer diagnosis and pCR from neoadjuvant chemotherapy. This is in agreement with several studies that did not find an association between physical activity prior to breast cancer diagnosis and outcome, although these studies were not specific to neoadjuvant chemotherapy [23, 24]. For example, one study found that women who had

Table 4 Unadjusted association of factors with completion of chemotherapy at the prescribed dosage

	Incomplete ($n=89$)	Complete ($n=150$)	P value
Age at diagnosis, mean (SD)	55.4 (12.6)	51.4 (13.0)	0.02
Race (n, %)			0.76
White, non-Hispanic	68 (38%)	110 (62%)	
Black, non-Hispanic	11 (30%)	26 (70%)	
Hispanic	7 (41%)	10 (59%)	
Other (unknown)	3 (43%)	4 (57%)	
Premenopausal (n, %)			0.004
Yes	32 (30%)	74 (70%)	
No	57 (43%)	76 (57%)	
AJCC stage at diagnosis (n, %)			0.55
I	17 (41%)	24 (59%)	
II	50 (38%)	81 (62%)	
III	21 (32%)	45 (68%)	
Hormone receptor status (n, %)			0.08
HR −, HER2 −	34 (47%)	39 (53%)	
HR −, HER2 +	9 (45%)	11 (55%)	
HR +, HER2 −	38 (34%)	73 (66%)	
HR +, HER2 +	8 (23%)	27 (77%)	
Pre-treatment BMI, mean(SD)	30.2 (8.0)	29.0 (6.4)	0.26
Post-treatment BMI, mean(SD)	29.5 (7.7)	28.9 (6.2)	0.49
Medication for DM, HTN, or HLD (n, %)			0.11
Yes	39 (41%)	56 (59%)	
No	50 (35%)	94 (65%)	
Medication for DM (n, %)			0.01
Yes	15 (60%)	10 (40%)	
No	74 (83%)	140 (93%)	
Of those completing phone survey	Incomplete ($n=25$)	Complete ($n=42$)	
Exercise > 7.5 MET-h/week (n, %)			0.002
Yes	11 (24%)	34 (76%)	
No	14 (63%)	8 (36%)	
Fruit and vegetable > 5 servings/day (n, %)			0.35
Yes	9 (31%)	20 (69%)	
No	16 (42%)	22 (58%)	
Alcohol > 1 drink/week, (n, %)			0.04
Yes	9 (36%)	26 (62%)	
No	16 (64%)	22 (38%)	

AJCC American Joint Committee on Cancer, *DM* diabetes mellitus, *HTN* hypertension, HLD hyperlipidemia

higher levels of pre-diagnosis recreational physical activity had lower all-cause mortality, but not breast cancer-specific mortality [24]. However, there have been a number of studies that did find associations between higher pre-diagnosis physical activity and greater survival after breast cancer [16, 19–22]. The relationship between pre-diagnosis physical activity and breast cancer outcomes may be dependent on factors such as hormone receptor status that we did not have a large enough sample size to investigate. Schmidt et al. found that recreational activity prior to diagnosis was associated with a 34% lower risk of death for women with ER-positive (but not ER-negative) tumors [20].

Completion of chemotherapy regimens has also been associated with improved breast cancer outcomes. Adequate dose intensity of chemotherapy is important for treatment success and has been associated with longer disease-free survival for women treated with adjuvant chemotherapy for breast cancer [25, 32, 33]. Two randomized controlled trials of physical activity during adjuvant chemotherapy found that the exercise group had a significantly lower rate of dose adjustments and a higher number of completed treatments

Table 5 Reasons for chemotherapy regimen modifications

Reasons for doses delayed by 7 or more days	*N*, %
Neuropathy	10 (11%)
Myelosuppression	28 (31%)
Febrile neutropenia	4 (4%)
Pain	5 (6%)
Infection	15 (17%)
Constipation/diarrhea	6 (7%)
Fatigue	2 (2%)
Other medical reasons	19 (21%)
Reasons for doses adjusted or missed	*N*, %
Neuropathy	32 (33%)
Myelosuppression	20 (20%)
Febrile neutropenia	4 (4%)
Pain	4 (4%)
Infection	7 (7%)
Constipation/diarrhea	6 (6%)
Fatigue	9 (9%)
Other medical reasons	16 (16%)

In cases where more than one reason was given for regimen modification, the more severe symptom was counted

[26, 34]. While these studies suggest that physical activity during treatment may improve the chances of completing treatment, our study looked specifically at physical activity prior to breast cancer diagnosis, a metric that has not yet been investigated in terms of chemotherapy completion. In our study, those who reported exercising more than 7.5 MET hours per week prior to diagnosis were more likely to complete chemotherapy at the prescribed dose (76% vs 36%, $P=0.002$).

Another important finding of our study is the high number of patients who had either dose reductions or cycle delays. Fifty-six percent of the cohort had either a dose reduction or delay of 7 days or more. This is in accordance with data published by Denduluri et al. in 2015 [26]. They looked at dose delays, reductions, and missed doses across a wide range of breast cancer chemotherapy types and treatment settings, and found that as many as 40% of patients did not receive the full dose of taxane-based or anthracycline-based therapies. Importantly, the authors of this study state that reduced dose intensity was more common in obese patients and those with limited daily activities, suggesting a possible association between activity and chemotherapy completion, though not measured directly in their study.

The most common reasons for dose reductions or delays in our study were myelosuppression and neuropathy. These were also the top reasons for chemotherapy adjustment noted by Van Waart et al. in a trial of patients undergoing adjuvant chemotherapy for breast cancer [26]. The high number of patients who did not receive the full dose intensity of their breast cancer treatments highlights the importance of finding interventions that can help patients tolerate the full therapeutic dose, including physical activity.

Our study has several limitations. This study was conducted at a single academic medical center, and a high percentage of the patients were white, which may limit the generalizability of the findings. The physical activity data was self-reported and may not be as reliable as more objective means of measuring activity such as with activity trackers. The percentage of chemotherapy cycles completed out of the number prescribed was used as a marker for chemotherapy dose intensity, but we did not collect the doses of medication administered to calculate the exact dose intensity. Additionally, our ability to measure metabolic syndrome markers was limited by the absence of lab results (A1C, triglycerides, LDL) in the EMR for most patients.

We sought to evaluate whether physical activity and BMI were associated with pCR and chemotherapy completion in women treated with neoadjuvant chemotherapy for breast cancer. The results of our study suggest that a higher BMI and diseases of metabolic syndrome were associated with lower rates of pCR, and an association between physical activity and chemotherapy completion. Further research with more objective measures of physical activity as well as markers of metabolic syndrome should investigate the relationship between physical activity,

Table 6 Predictors of chemotherapy completion at the prescribed dose from phone survey ($n=67$)

Predictors	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Exercise ≥ 7.5 met-h/week	5.4 (1.8, 16.3)	0.003	7.6 (1.4, 41.2)	0.02
Age at diagnosis, years	0.9 (0.86, 0.96)	0.0007	0.9 (0.8, 1.0)	0.03
Diastolic blood pressure, mmHg	1.1 (1.01, 1.13)	0.01	1.1 (1.0, 1.2)	0.04
Premenopausal	5.3 (1.5, 17.9)	0.008	1.0 (0.1, 10.9)	0.97
Diabetes medication	0.2 (0.1, 1.1)	0.06	0.9 (0.1, 5.5)	0.90
BMI	1.0 (0.9, 1.0)	0.43	1.1 (1.0, 1.2)	0.24
Fruit and vegetable > 5 daily servings	1.6 (0.6, 4.5)	0.35	0.3 (0.1, 1.7)	0.16
Alcohol > 1 drink/week	2.9 (1.0, 8.1)	0.04	3.5 (0.7, 16.8)	0.12

BMI, and outcomes from neoadjuvant chemotherapy. The results of this study highlight the importance of lifestyle behaviors in improving the likelihood of breast cancer treatment success.

Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Yale University Human Investigation Committee, protocol number 2000021102, initial approval 6/14/2017.

Informed consent Informed consent was obtained from all individual participants included in the study.

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