Deterioration of Physical Activity Level and Metabolic Risk Factors After Early-Stage Breast Cancer Diagnosis

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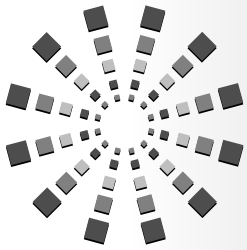

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KEY WORDS
Body composition
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Sedentary behavior

Background: In breast cancer patients, a lack of physical activity (PA) is 1 causative factor of weight gain during adjuvant treatment. It may increase the risk of treatment adverse effects, comorbidities, and deleterious long-term outcomes. **Objective:** We aimed to describe the evolution of PA level and sedentary behavior in breast cancer patients between diagnosis and adjuvant chemotherapy onset following surgery and identify predictive factors associated with these changes early after breast cancer diagnosis. **Methods:** Baseline data of 60 patients enrolled in a pilot randomized controlled trial of PA are presented. PA levels were estimated at adjuvant chemotherapy onset after surgery and retrospectively for the period at diagnosis. Height, weight, waist circumference, and bioelectrical impedance were measured at chemotherapy onset. Linear regression analysis evaluated factors associated with relative changes of PA level and sedentary behavior. **Results:** Moderate PA decreased and sedentary behavior increased between diagnosis and chemotherapy onset. A grade III breast cancer was associated with a greater decrease in PA level.

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Conversely, keeping a professional occupation and adherence to nutritional guidelines were associated with maintained PA level. The majority (88%) of patients had excessive adiposity at chemotherapy onset. **Conclusions:** There was a significant deterioration of PA level between diagnosis and chemotherapy onset, and deleterious adiposity was present in most patients. **Implications for Practice:** This study further emphasizes the need to motivate breast cancer patients toward engaging in a healthy lifestyle early after diagnosis and adhering to PA programs, which should be included in their clinical management.

With more than 1 600 000 cases diagnosed annually, breast cancer is the most common cancer in women worldwide.[1] After a diagnosis of breast cancer, lifestyle-related factors, such as weight gain, obesity, and overweight,[2] as well as sedentary behavior,[3] have been shown in observational studies to be associated with poorer long-term outcomes in breast cancer patients. In the largest American cohort study of breast cancer patients, moderate to vigorous physical activity (PA), defined as an intensity greater than 3 metabolic equivalents, considerably decreased, between the second and the eighth month after diagnosis, with an average reduction of more than 3 h/wk. During the same period, there was a 2-fold increase in the proportion of patients with no moderate PA.[4] Numerous prospective cohort studies have shown that a lack of PA is 1 causative factor of weight gain[3] and of worsening body composition during breast cancer treatment.[5] The lack of PA, weight gain, and poor body composition can affect the ability of patients to carry out daily activities and increase the risk of developing long-term comorbidities such as cardiovascular diseases, diabetes, hypertension, and other metabolic disorders.[6] A decrease in moderate PA after breast cancer diagnosis is also associated with a 4-fold greater risk of death.[7]

Patients are likely to reduce their PA by decreasing their occupational activities[8] and often with the aim of promoting recovery after surgery, or following advice from practitioners to rest to manage their fatigue.[9] Being employed (compared with being retired) and smoking appear to predict a decrease in moderate PA after completion of treatment.[10] Furthermore, age, body weight, lifestyle, level of education, and breast cancer stage have been shown to predict functional limitations 12 months after breast cancer diagnosis (ie, difficulties in completing tasks of everyday life).[10–12]

Conversely, moderate PA practiced during and after adjuvant treatment of breast cancer can improve physical fitness, quality of life, self-image, and treatment adherence as well as reduce fatigue, as shown in randomized controlled trials.[13–15] Large cohort studies have suggested that it may also reduce the risk of mortality regardless of body mass index (BMI).[15] More generally, adherence to nutritional guidelines has been associated with a 35% lower risk of mortality in breast cancer survivors.[16] Despite accumulating evidence supporting the beneficial role of PA after breast cancer diagnosis, PA programs are not yet routinely integrated in clinical management, and the energy expenditure due to moderate to vigorous PA in patients remains lower than that in healthy women.[17]

Changes in PA and sedentary behavior after breast cancer diagnosis and before the start of chemotherapy have not been described in the literature. The first aim of the present study was therefore to assess the evolution of PA level and sedentary behavior from the time of breast cancer diagnosis to the onset of adjuvant chemotherapy following surgery. The second aim was to identify predictive factors associated with relative changes of PA level and sedentary behavior early after breast cancer diagnosis. We hypothesized that the same factors found in the literature to be associated with a decrease in PA or functional limitations after breast cancer treatment[10,11] also influence the evolution of PA level between breast cancer diagnosis and chemotherapy onset.

■ Methods

Study Setting

This study is a secondary analysis of baseline data collected in the ongoing randomized controlled trial PASAPAS (NCT01331772, www.ClinicalTrials.gov).[10,11] This trial was designed to assess the feasibility of a supervised PA intervention in 60 breast cancer patients starting adjuvant chemotherapy. The sample size was defined for the primary objective of the trial. All participants signed an informed consent.

Study Participants

The study population consists of women aged between 18 and 75 years, all patients at a comprehensive cancer center for a first nonmetastatic and noninflammatory localized breast cancer and candidate for adjuvant chemotherapy after surgery. All were living within a 60-km perimeter of the cancer center. They had to be volunteers and available to participate in the PASAPAS protocol (6-month PA and/or nutritional intervention and 6-month follow-up). Patients were not eligible if they had medical contraindications to PA, such as serious or unstable conditions relating to cardiovascular, respiratory, or other chronic diseases including uncontrolled diabetes, malnutrition, eating disorders, bone metastases, and severe osteoporosis.

Data Collection

Data for the present study were collected by a single and trained research assistant on the first day of adjuvant chemotherapy (T_1). They comprised both baseline measurements taken at chemotherapy onset (T_1), including patients' PA level data, anthropometrics,

and body composition, and PA level data assessed retrospectively concerning the week prior to diagnosis (T_{diag}). All clinical data were retrieved from patients' medical records. All other data were collected by a dietitian.

■ Socio-Economic, Individual Risk Factors, and Clinical Parameters

Socioeconomic and epidemiologic risk factors were collected at T_1 using an interviewer-administered questionnaire. Socioeconomic data included age, family status, level of education, professional status, and the distance from residence to cancer center. Individual risk factors included menopausal status and the lifestyle-related factors smoking status and duration, alcohol consumption over the last 6 months, and dietary intake (assessed using a 3-day food diary). Clinical factors, including Scarff Bloom Richardson (SBR) grade, stage (pTpN), and HER2 receptor status, were retrieved from patients' medical records.

■ Physical Activity Level

Data to assess participants' PA level were collected using the PAQAP,[19] a validated and reproducible PA questionnaire. The questionnaire was administered twice during the interview, once for PA assessment at baseline (T_1) corresponding to PA performed over the week prior chemotherapy onset, and a second to retrospectively assess usual PA based on that performed the week before diagnosis (T_{diag}). The interviewee indicated a mean time spent in usual activities listed in different categories: occupational activities, leisure time activities, household activities, basic activities of daily living, and transportation. The data collected by the PAQAP questionnaire for T_1 and for T_{diag} recall were analyzed to define patients' time spent in moderate PA (≥3 metabolic equivalents) expressed in minutes per week or minutes per day, which appears to be baseline threshold in terms of long-term outcomes.[16] Also analyzed was the time spent doing activities sitting or lying down (other than sleeping), which included sitting time in screen activities (television and computer), for occupation, leisure, and activities of daily living (such as taking meals), which permitted the differentiation between avoidable and unavoidable sedentary behavior. The use of PAQAP also allowed the estimation of maximal oxygen uptake (estimated VO_{2max} in milliliters per minute per kilogram) and mean habitual daily energy expenditure (in kilojoules per day).

■ Anthropometrics and Body Composition

Baseline (T_1) anthropometrics included height (using a fathom accurate to 0.1 cm) and body weight (using a mechanical scale recalibrated at each measurement: SECA, 761 7019004, 2011; Seca GmbH & Co, Hamburg, Germany; accurate to 0.5 kg). Body mass index (in kilograms per meter squared) was calculated; patients with a BMI from 25 to 29.9 kg/m^2 were considered as overweight, and those with a BMI equal to or greater than 30 kg/m^2 were considered as obese, in accordance with the World Health Organization reference values. The research assistant measured waist circumference (in centimeters) to the nearest 0.1 cm using a measuring tape; a waist circumference equal to or greater than 80 cm indicates risk factors of metabolic disease.[20] Body weight for T_{diag} was self-reported by patients. Body mass index at T_{diag} was calculated using baseline height.

Body composition at baseline (T_1) was estimated using a bioelectrical impedance analysis (QuadScan 4000 v3.11; Bodystat, Ltd, Isle of Man, UK) to assess percentage body fat (%BF) and fat-free mass (FFM; in kilograms).[21] Patients were asked to lie down for 10 minutes prior to body composition assessment. They were classified using a scale of %BF according to age and sex.[22]

■ Assessment of Guidelines Adherence

A score to measure patients' adherence to dietary and PA guidelines over the last 6 months before chemotherapy onset was created according to the guidelines of the French "Programme National Nutrition Santé"[23] and to international guidelines of the World Cancer Research Fund.[2,24] This score, ranging from 0 to 9, was computed from the data collected in the 3-day food diary and the PA interview at T_1. Healthy food (eg, fruit and vegetables) consumption and PA were given a positive score, and unhealthy food (eg, alcohol and salt) consumption either no point or a negative score. The maximal score of 9 corresponded to the following consumptions: 1 point for water ≥1 000 mL/d (vs 0 point if <1 000 mL/d), 1.5 points for salt ≤6 g/d (vs 1 point if >6 and ≤8 g/d, 0.5 points if >8 and ≤10 g/d, 0 point if >10 and ≤12 g/d, −0.5 points if >12 g/d), 2 points for fruit and vegetables ≥7.5 portions/d (vs 1 point if ≥5 and <7.5 portions/d, 0.5 points if ≥3.5 and <5 portions/d, and 0 points if <3.5 portions/d), 1 point for red meat ≤500 g/wk (vs 0 point if >500 g/wk), 1 point for cereal products ≥3 and <6 portions/d (vs 0.5 points if ≥6 portions/d, 0.5 point if ≥1 and <3 portions/d, and 0 point if <1 portion/d), 1 point for alcohol consumption <1.4 g/d (equivalent to 1 glass per week) (vs 0.8 points if ≥1.4 and <20 g/d, and 0 point if ≥20 g/d), 1.5 points for moderate PA for ≥60 min/d (vs 1 point if ≥30 and <60 min/d, and 0 point if <30 min/d).

Analysis Plan

Categorical data were described by their frequency, percentage, and frequency of missing values (not included in the calculation of percentages). Quantitative data were described by either mean and standard deviation (SD) for normally distributed variables or median and minimum-maximum values for skewed variables. The Wilcoxon signed rank test was used to compare repeated assessments made at T_{diag} and T_1. The McNemar test was used to compare matched proportions between both periods. The Spearman correlation coefficient was used to calculate the correlations between 2 continuous variables.

The relative percentage changes in moderate PA and screen time (ie, the most representative of deleterious sedentary behavior) between T_{diag} and T_1 were computed as T_1 value minus T_{diag}

value, divided by T_{diag} value and multiplied by 100. Multiple linear regression analyses were performed to investigate the possible associations of socioeconomic, clinical, and lifestyle data on the relative changes in moderate PA and screen time. Given the small sample size that was defined for the primary goal of the trial, the most parsimonious regression models were built to avoid overfitting.[25] A limited number of predictor variables were selected that could potentially be associated with the relative changes in PA level and sedentary behavior based on the existing literature. In the light of the literature reviewed in the Introduction section,[10–12] variables considered in the models were age, SBR grade, menopausal status, education level, occupational activity, smoking status, guidelines score, body weight at diagnosis, and time spent in moderate PA at diagnosis. Bootstrap was used as an alternative approach to produce better approximations for the true small sample properties and to increase the reliability of hypothesis tests. Bootstrap standard errors were computed from 1000 replications. Finally, any problems due to multicolinearity between variables were tested using the variance inflation factor; only low to moderate but no high correlation between the predictor variables was identified.

The time spent by patients in moderate PA was compared with international guidelines of 150 min/wk to assess the PA level in the study population.[26] Screen and sitting times were compared with the mean time spent in screen activities (3.35 h/d)[27] and time spent in activities sitting and lying down (4.03 h/d)[28] among the healthy French population. The daily energy expenditure of patients was compared with the standard values for women of 60 kg in weight and 50 years of age living a sedentary lifestyle (7536 kJ/d).[29] Values of %BF and FFM were compared with those of women from the same age group in the general European population.[30] In order to characterize the study population within the French context, the prevalence of overweight and obesity in this study was compared with that of healthy women in the same age group within the general French population.[31]

Statistical comparisons to national or international recommendations or standards were performed using 1-sample *t* tests for mean values and 1-sample median tests for median values.

The significance level was 5%. All statistical analyses were performed with the SAS software (version 9.3; SAS Institute, Cary, NC).

■ Results

The analysis included 60 women of mean age 52.1 (SD, 10.9) years, newly diagnosed with breast cancer and randomized in the controlled trial PASAPAS between June 2011 and June 2013. Half of the women (50%) were postmenopausal, and 89% had a breast cancer with SBR grade II to III (Table 1). More than half (52%) had completed at least some secondary education. The majority of patients were on sick leave (58%) at chemotherapy onset, and the majority lived with someone at home (82%). They lived at a median distance of 10 km (min–max, 1–55 km) from the cancer center. Half of the patients (50%) were current or former smokers at chemotherapy onset with a mean cigarette consumption of 11.7 (SD, 10.7) pack-years.

Table 1 • Selected Characteristics of the Study Population (n = 60)

Variables	
Age, y	
Mean (SD)	52.1 (10.9)
Median (min–max)	52.7 (26.2–71.5)
Tumor stage, n (%)	
pT1a	2 (3.3)
pT1b	12 (20.0)
pT1c	15 (25.0)
pT2	28 (46.7)
pT3	1 (1.7)
pTx	1 (1.7)
pT1mi	1 (1.7)
Node stage, n (%)	
pN0	30 (50.0)
pN1	25 (41.7)
pN2	2 (3.3)
pN3	2 (3.3)
pNx	1 (1.7)
SBR grade, n (%)	
I	6 (10.5)
II	26 (45.6)
III	25 (43.9)
HER2 status, n (%)	
Negative (0+, 1+ or 2+)	51 (85.0)
Positive (3+)	9 (15.0)
Menopausal status, n (%)	
Premenopausal	23 (38.3)
Postmenopausal	30 (50.0)
Perimenopausal	2 (3.3)
Unknown	5 (8.3)
Type of surgery, n (%)	
Mastectomy	21 (35.0)
Tumorectomy	37 (61.7)
Tumorectomy then mastectomy	2 (3.3)
Time from surgery to chemotherapy, d	
Mean (SD)	48.9 (15.9)
Median (min–max)	44.5 (20.0–113.0)
Family status: living with someone, n (%)	49 (81.7)
Education completed, n (%)	
No diploma or under high school	21 (35.0)
High school	8 (13.3)
Some college/technical training	16 (26.7)
Undergraduate, graduate, or postgraduate	15 (25.0)
Occupational status, n (%)	
Retired	12 (20.0)
Unemployed/housewife	7 (11.7)
Professional activity at chemotherapy onset	6 (10.0)
On sick leave since diagnosis	35 (58.3)
Smoking status, n (%)	
Current smoker	10 (16.7)
Former smoker	20 (33.3)
Non smoker	30 (50.0)
Distance from domicile to center, km	
Mean (SD)	15.4 (15.6)
Median (min–max)	10.3 (1.3–55.0)

Abbreviations: HER2, human epidermal growth factor receptor 2; pNx, lymph node not evaluable; pN0, lymph node negative; pTx, tumor stage not evaluable; pT1, tumor stage 1 (<= 2 cm); pT1mi, microinvasion (<= 1 mm); SBR, Scarff Bloom Richardson.

Table 2 • Physical Activity Level and Sedentary Behavior of Breast Cancer Patients (n = 60) at Diagnosis (T_{diag}) and at Chemotherapy Onset (T_1)

Variables	T_{diag} Median	T_{diag} Min-Max	T_1 Median	T_1 Min-Max	Δ	P^a
Estimated VO_{2max} mL/min/kg	27.8	17.9–37.2	26.5	17.5–34.5	−1.3	<.0001
Daily energy expenditure, kJ/d	7895	6495–10343	7251	6070–9150	−644	<.0001
Time spent in PA ≥3 METs, min/wk	1038.6	75.0–3203.2	858.3	161.5–1693.9	−177.3	<.0001
Sitting and lying time, h/d	9.8	5.8–15.2	10.3	6.0–14.5	+0.5	.44
Screen time activities	2.8	0.0–5.8	3.5	0.0–8.9	+0.7	<.0001
Leisure sitting time other than screen time	2.7	0.7–7.6	4.1	0.8–8.9	+1.4	<.0001
Occupational sitting time	1.2	0.0–6.8	0.1	0.0–5.2	−1.1	<.0001
Daily living sitting time	1.7	0.7–4.1	1.7	0.8–3.8	0	.89

Abbreviations: METs, metabolic equivalents; PA, physical activity; VO_{2max}, oxygen uptake.
[a]Based on Wilcoxon signed rank post hoc analysis.

Chemotherapy onset (T_1) occurred on average 49.9 (SD, 15.9) days after surgery and 96.7 (SD, 33.7) days after diagnosis (T_{diag}).

PA Level Characteristics at the Time of Diagnosis

At the time of diagnosis (T_{diag}), women spent a median time of 1038.6 min/wk (ie, 148.5 min/d) in moderate PA, and almost all (98%) met the international guidelines of 150 min/wk.

The median time spent on screen activities (2.8 h/d, ranging from 0.0–5.8) was below the French population mean time of 3.35 h/d ($P < .0001$). However, the total time spent in activities sitting and lying down was over the national mean ($P < .0001$). PA and sedentary activities at T_{diag} are shown in Table 2.

Anthropometrics and Body Composition

Self-reported anthropometrics at T_{diag} and measured anthropometrics and body composition at T_1 are shown in Table 3. Overall, body weight did not vary significantly between self-reported weight at T_{diag} and measured weight at T_1 ($P = .87$). At T_{diag}, 18 women (30%) were overweight, and 7 (12%) were obese according to their BMI. This proportion is similar to that of female of the same age in the French population (ie, 43% overweight and obese). At T_1, 16 patients (27%) were overweight, and 11 (18%) were obese according to their BMI. With regard to waist circumference, 63% of patients had a visceral adiposity (≥80 cm) representing a metabolic risk. According to the bioelectrical impedance data, the majority of patients (88%) had a high body fat for their age (%BF ≥standard value, $P < .0001$), and for 75%, this value was greater than the European population median ($P < .0001$). At T_1, the patients were not significantly different in terms of FFM from the European population ($P = .17$). Among the study population, despite a normal BMI at T_1, 25 women (42%) were considered at high metabolic risk because of their excessive overall body fat.

Adherence to General Guidelines at Chemotherapy Onset

Median score of adherence to guidelines was 6.5 out of 9 (maximal possible score), ranging from 2.8 to 8.5. The majority of patients did 60 min/d of moderate PA (82%) and followed recommendations for water (80%) and red meat consumption (72%). Inversely, only 25% and 13% of patients followed recommendations for fruit and vegetable consumption and for cereal consumption, respectively. More than half of patients (52%) were considered as nondrinkers of alcoholic beverages. The mean alcohol consumption for 3% of patients was 3.5 (SD, 5.2) g/d, much higher than the national recommendation of 1 glass per day for women, during the 6 months preceding chemotherapy onset.

Change in PA Level From Diagnosis to Chemotherapy Onset

All PA variables of study participants worsened significantly between T_{diag} and T_1. As seen in Table 2, median estimated VO_{2max} and median daily energy expenditure decreased by 1.3 mL/min/kg and 644 kJ/d, respectively ($P < .0001$ for both). Sixteen patients (26%) had a daily energy expenditure greater than standard at T_{diag}, which had decreased below standard by T_1 ($P = .0003$). The median time spent in moderate PA significantly decreased by 25.3 min/d ($P < .0001$). The same proportion of

Table 3 • Anthropometrics and Body Composition of Breast Cancer Patients (n = 60) at Diagnosis (T_{diag}) and at Chemotherapy Onset (T_1)

Variables	T_{diag} Mean	T_{diag} SD	T_1 Mean	T_1 SD	P^a
Anthropometrics					
Height, m			1.61	0.006	
Body weight,[b] kg	65.4	14.6	65.6	16.1	.87
BMI, kg/m^2	25.2	5.3	25.3	5.9	.79
Waist circumference, cm			87.3	14.8	
Body composition					
%BF			35.2	7.2	
FFM, kg			41.5	7.0	

Abbreviations: %BF, percent body fat; BMI, body mass index; FFM, fat-free mass.
[a]Based on Wilcoxon signed rank post hoc analysis.
[b]Declared for T_{diag} corresponding to prediagnosis period.

Table 4 • Results of the Linear Regression Models of the Relative Changes in Moderate Physical Activity and Screen Time Activity From Diagnosis (T_{diag}) to Chemotherapy Onset (T_1)

	% Relative Change in Moderate PA			% Relative Change in Screen-Time Activity		
	Coefficient[a]	Bootstrap SE	*P*	Coefficient[a]	Bootstrap SE	*P*
Intercept	−14.8	37.9	.69	257.4	62.3	.000
Age (continuous scale)	0.3	0.6	.64	−1.8	0.95	.048[b]
SBR grade						
I, II	Reference			Reference		
III	−21.1	8.7	.016[b]	28.3	14.7	.055
Menopausal status						
Premenopausal	Reference			Reference		
Postmenopausal or perimenopausal	−21.9	13.6	.106	−4.2	22.7	.85
Level of education						
Secondary or high school education (1 = yes)	−8.3	8.9	.35	11.1	13.2	.40
Occupational activity kept after diagnosis (1 = yes)	43.6	17.5	.013[b]	−70.4	21.07	.001[c]
Smoking status						
Former smoker	29.5	11.3	.009[c]	−0.9	14.1	.95
Current smoker	8.5	12.2	.48	−10.6	15.6	.49
Never smoked	Reference			Reference		
Guidelines score (continuous scale)	7.09	3.5	.045[b]	−10.3	4.9	.036[b]
Body weight before diagnosis (continuous scale)	−0.18	0.3	.51	−0.5	0.4	.24
Time spent in moderate PA before diagnosis (continuous scale)	−0.03	0.01	<.0001[c]	−0.02	0.01	.013[b]
No. of observations used	52			51		
Adjusted R^2	0.50			0.49		

Abbreviations: PA, physical activity; SBR, Scarff Bloom Richardson.
[a]A positive coefficient means that the dependent variable increases when the independent variable increases (eg, the % of relative change in moderate PA from diagnosis to chemotherapy onset increases with a greater guidelines score). A negative coefficient means that the dependent variable increases when the independent variable decreases, or conversely that the dependent variable decreases when the independent variable increases.
[b]$P < .05$.
[c]$P < .01$.

patients at T_1 followed the international PA guidelines (150 min/wk) as at T_{diag}.

The relative decrease in moderate PA was greater for patients who had a high PA level (greater than guidelines of 150 min/wk) at T_{diag} compared with those with lower PA level ($P < .0001$) (Table 4). Women with an SBR grade III breast cancer also displayed a higher relative decrease in moderate PA than did patients with an SBR grade I or II ($P = .016$).

We observed a smaller relative decrease in moderate PA among former smokers than patients who had never smoked ($P = .009$). Women who had maintained an occupational activity and whose nutritional habits were in line with nutritional guidelines at diagnosis had also a smaller relative decrease in moderate PA ($P = .013$ and $P = .045$, respectively). Age, menopausal status, level of education, and body weight at diagnosis did not significantly influence the relative change in moderate PA.

Change in Sedentary Behavior From Diagnosis to Chemotherapy Onset

The total sitting and lying-down time did not change from T_{diag} to T_1 ($P = .44$) (Table 2). However, breaking down the different situations of sedentary activities revealed that while unavoidable daily living sitting time did not change significantly ($P = .89$), median occupational sitting time decreased by 1.1 h/d ($P < .0001$), and median leisure sitting time (other than screen time) and median screen time increased by 1.4 and 0.7 h/d, respectively ($P < .0001$ for both). Fourteen patients (23%) spending less than the national mean time on screen activities (3.35 h/d) at T_{diag} had increased it to over the national mean at T_1 ($P = .0008$).

The relative increase in screen activities was greater in younger patients ($P = .048$), in those not following nutritional guidelines ($P = .036$), in those with no occupational activity at T_1 ($P = .001$), or in those with a low PA level at T_{diag} ($P = .013$). The SBR grade, menopausal status, education, smoking status, and body weight at diagnosis did not influence the relative change in screen activities.

■ Discussion

To our knowledge, this study is the first to describe the decrease in moderate PA and the increase in sedentary behavior early after breast cancer diagnosis (ie, between diagnosis and adjuvant chemotherapy onset) and to investigate predictive factors of these changes. In our study, a majority of patients displayed metabolic risk factors, principally excessive adipose tissue. The deleterious change in PA level adds a risk of weight gain during and after treatment[3,5] and consequently a risk of treatment adverse effects, comorbidities, and deleterious long-term outcomes.[6,7,9,11,26,32]

In our study, almost all the patients were found to have a PA level that met international guidelines for PA. The study group consisted of volunteer patients who had been offered the opportunity to enter the randomized controlled trial PASAPAS by their oncologist. This suggests a potential selection bias as already physically active patients might be more likely to volunteer. Despite this, we observed a decrease in PA level between diagnosis and chemotherapy onset, illustrated by the high proportion of patients decreasing their energy expenditure to below population standards at T_1. The general decline of PA level could be explained by the patients feeling the need to rest during the healing period after surgery. It could also be due to the current general advice to rest in order to manage fatigue[9] or to the limitation of physical performance and restriction of participation found more often in breast cancer patients compared with women with no cancer history.[33]

Among factors associated with PA changes, we identified that patients diagnosed with grade III breast cancer were more likely to decrease their moderate PA compared with women with grades I and II. This is the first time such an effect of grade has been reported during this time window. Our result is consistent with Kwan et al,[4] showing a largest decline in PA of patients with stage III compared with stage I–II breast cancer between 2 and 8 months after diagnosis. The decrease in moderate PA may be due to the association of stage III breast cancer and upper-body functional limitations.[12] We also identified a greater decrease in PA in patients self-reporting a high PA level at diagnosis compared with those with a low PA level, which confirms Kwan and colleagues' results. Moreover, recent studies have shown that women with breast cancer do not reach their initial PA level until 1 to 3 years after diagnosis.[4,34,35] It suggests that active patients should be strongly encouraged to keep their active lifestyle after diagnosis.[4]

Patients who maintained their occupational activity after diagnosis better maintained their moderate PA and avoided increasing their sedentary behavior between diagnosis and chemotherapy onset. This is inconsistent with results of Devoogdt et al,[10] who showed that being employed was associated with a decrease in PA between pre-surgery and 12 months post-surgery. We can assume that patients who maintain an occupational activity may be more active through their work and transportations. Patients following nutritional guidelines at diagnosis also better maintained their moderate PA and sedentary behavior, as expected. Interestingly, former smokers had a lower decrease in moderate PA than nonsmokers. The literature has shown that former smokers have similar activity levels as never smokers for leisure PA, walking, and cycling, but are more likely to engage in sports than never or current smokers.[36] These observations suggest that a healthier lifestyle, such as smoking cessation, may be associated with a better awareness and understanding by patients of the importance of staying active after a breast cancer diagnosis. Therefore, lifestyle factors and nonadherence to guidelines at diagnosis might be important to consider in breast cancer patients to identify women at risk of reducing their PA level and worsening their long-term outcomes.[16]

In the present study, age, menopausal status, level of education, and body weight at diagnosis were not associated with a decrease in moderate PA between diagnosis and chemotherapy onset. In contrast, overweight and obesity have been associated with a greater decrease in moderate PA between the second and the eighth months after diagnosis.[4] In our study population, these factors would need to be monitored for a longer period as they have been associated with a reduction in survival, independently to clinical, lifestyle, and socioeconomic factors.[11]

A great proportion of our study population were overweight (45%) according to their BMI. Another great proportion (42%) were so-called normal-weight obese[37] (or metabolically obese) according to body composition, and almost all our study population had deleterious body fat at chemotherapy onset. This deleterious body composition can lead to difficulties performing daily activities and so might amplify the change in PA level and lead to difficulties maintaining quality of life through treatment.[6] This situation also adds risks of comorbidities, such as insulin resistance, cardiovascular disease, diabetes, hypertension, and other metabolic disorders.[38] Furthermore, unfavorable changes in body composition can appear during chemotherapy, such as a gain of body fat and loss of fat free mass.[39] These further changes should be avoided.

In parallel to the decrease in moderate PA, data showed that patients increased the time spent in screen activities, such as watching television or on the computer. This can be qualified as a deleterious sedentary behavior with energy expenditure close to rest.[40] Sedentary behavior has been shown to increase anger, fatigue, depression, and mood disorders after treatment of breast cancer[32] and to increase metabolic dysfunction, negatively influence vascular health, and decrease bone mineral density in the general population.[41] Patients did also increase sitting time for leisure activities such as socializing. While sedentary behavior should be avoided, particularly screen-based sedentary behavior, leisure activities that can facilitate social support, even if that be sitting activities, might be encouraged to improve quality of life of patients.[42]

Certain limitations of this study must be considered when interpreting these findings. First, it was based on secondary analyses of some of the baseline data of a randomized controlled trial. There were several methodological limitations, such as causal inference and limitations in statistical power due to limited sample size. This sample size was defined as being sufficient for the primary objective of the randomized controlled trial to explore the feasibility of implementing a supervised PA program. Second, the data obtained may not be generalized to the French population of breast cancer patients because the selection criteria for the study included having no contraindication to PA due to the primary goal of the trial (ie, their PA level was probably higher than that of all breast cancer patients) and because the trial was performed locally for patients living in the large urban area surrounding the cancer center. Finally, PA assessments by an interviewed-based questionnaire, both for T_1 and recall for T_{diag} being done on the same day, may include recall bias and can provoke over- or underestimation of the time spent in reported activities and even more for the period T_{diag} identified a posteriori. It appears, however, that recall of historical PA can be reasonably estimated by a questionnaire over a period of more than a year.[43,44] We therefore hypothesized that the use of the PAQAP questionnaire may avoid such a bias because it allows a high degree of detail as well as feedback on the total time reported by the participant with a 5% precision (over 168 hours, ie, 7 days).[19] A strength of this study is the absence

of any source of interexaminer variability owing to standardized measurement procedures and 1 single operator.

■ Conclusion and Practice Implications

The evolution of the PA level in women between breast cancer diagnosis and the onset of adjuvant chemotherapy has been poorly explored in the literature. Here we have shown that during this period, despite its shortness, patients greatly decrease their moderate PA and largely increase their deleterious sedentary behavior. We also found that almost all the patients had deleterious body fat. The lack of moderate PA, high sedentary behavior, and high adiposity after a breast cancer diagnosis has previously been associated with short- and long-term poor prognosis and comorbidities.[15,32,38,41] Such factors may lead, during adjuvant treatment, to patients adopting an even more unfavorable lifestyle, thus increasing the risk of weight gain and of related adverse effects.

As the vicious circle of the sedentary lifestyle process explains, the more the physiological capacity is altered, inherent to a lack of PA, the more an individual experiences difficulties with PA and thereby loses the desire to be active, thus ceasing engagement in further activity and locking himself/herself into a sedentary lifestyle.[45] This situation may lead to a loss of self-confidence, a larger decrease in PA, and then to other adverse effects such as fatigue, a rapid deterioration in physical fitness, and an increase in functional limitations.[45,46] Functional limitations at the time of diagnosis have been associated with comorbid conditions leading to an increased risk in non–breast cancer death.[11] This underlines possible complications to the nevertheless important challenges that must be faced in maintaining PA levels early after breast cancer diagnosis.

We found that several lifestyle, sociodemographic, and nutritional variables were associated with deleterious change in moderate PA and sedentary behavior. Our findings stress the need for particular nutritional interventions and should guide nurses and clinicians toward implementing PA interventions concomitant to breast cancer treatment to help their patients maintain or adopt moderate PA. Not only can such a program help patients prevent weight gain during treatment,[14,47] but it can also act indirectly to the decrease in spontaneous deleterious sedentary behavior.[47] It has been shown with a high level of evidence that an active lifestyle after diagnosis of breast cancer increases physical fitness and quality of life, as well as reduces fatigue without significant adverse events.[13] It also helps maintain or decrease body fatness,[13,38] which could itself influence sexual hormones, insulin metabolism, and inflammation and reduce the risk of recurrence, of second primary cancer, and of mortality after a breast cancer diagnosis.[15,48] In the ongoing feasibility randomized controlled trial PASAPAS, the 6-month supervised PA program starting from the first day of chemotherapy aims at maintaining PA level and weight during adjuvant treatments for breast cancer. Better still, the program aims to motivate and help patients recover their usual PA level and to rebalance body composition. Given the growing percentage of the population affected by breast cancer worldwide and the important benefits of PA on numerous outcomes, it is now necessary to study the impact of PA and changes in sedentary lifestyle on disease-free and overall survival in a multicenter randomized controlled trial.

We suggest the need for oncologists and nurses to become more involved in this form of nutritional secondary prevention, in particular by giving valid and adapted information to patients with breast cancer. Early in the disease course, nurses could motivate patients to adopt or maintain a healthy lifestyle. This study adds greater emphasis to the need to help patients adopt an active lifestyle as soon as possible after breast cancer diagnosis, through following PA guidelines and engaging in PA programs as part of routine supportive care in cancer treatment.

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