original reports abstract

Impact of Breast Cancer Treatment on Employment: Results of a Multicenter Prospective Cohort Study (CANTO)

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PURPOSE Adverse effects of breast cancer treatment can negatively affect survivors' work ability. Previous reports lacked detailed clinical data or health-related patient-reported outcomes (PROs) and did not prospectively assess the combined impact of treatment and related sequelae on employment.

METHODS We used a French prospective clinical cohort of patients with stage I-III breast cancer including 1,874 women who were working and ≥ 5 years younger than legal retirement age (≤ 57 years) at breast cancer diagnosis. Our outcome was nonreturn to work (non-RTW) 2 years after diagnosis. Independent variables included treatment characteristics as well as toxicities (Common Toxicity Criteria Adverse Events [CTCAE] v4) and PROs (European Organization for Research and Treatment of Cancer [EORTC] Quality of life Questionnaires, Breast cancer module [QLQ-BR23] and Fatigue module [QLQ-FA12], Hospital Anxiety and Depression Scale) collected 1 year after diagnosis. Logistic regression models assessed correlates of non-RTW, adjusting for age, stage, comorbidities, and socioeconomic covariates.

RESULTS Two years after diagnosis, 21% of patients had not returned to work. Odds of non-RTW were significantly increased among patients treated with combinations of chemotherapy and trastuzumab (odds ratio [OR] *v* chemotherapy-hormonotherapy: for chemotherapy-trastuzumab, 2.01; 95% CI, 1.18 to 3.44; for chemotherapy-trastuzumab-hormonotherapy, 1.62; 95% CI, 1.10 to 2.41). Other significant associations with non-RTW included grade ≥ 3 CTCAE toxicities (OR *v* no, 1.59; 95% CI, 1.15 to 2.18), arm morbidity (OR *v* no, 1.59; 95% CI, 1.19 to 2.13), anxiety (OR *v* no, 1.47; 95% CI, 1.02 to 2.11), and depression (OR *v* no, 2.29; 95% CI, 1.34 to 3.91).

CONCLUSION Receipt of systemic therapy combinations including trastuzumab was associated with increased odds of non-RTW. Likelihood of unemployment was also higher among patients who reported severe physical and psychological symptoms. This comprehensive study identifies potentially vulnerable patients and warrants supportive interventional strategies to facilitate their RTW.

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INTRODUCTION

More than 85% of patients with breast cancer (BC) live > 5 years after diagnosis in Western countries,[1] with a current prevalence reaching > 3 million 5-year survivors in North America and Europe.[2] A meta-analysis of 36 North American and European studies suggested that BC survivors were at higher risk of unemployment compared with individuals without a history of cancer.[3] One-third of patients with BC are < 55 years old at time of diagnosis,[4] with several years within the workforce ahead before retirement, in an era where the legal retirement age is globally increasing.[5] Employment issues among BC survivors are therefore a major challenge.

Return to work (RTW) after BC is a complex process that is strongly influenced by medical factors such as treatment and its related adverse events.[5-8] Previous studies suggested that work ability could be impaired by chemotherapy,[9-12] mastectomy,[10,11,13] or axillary node dissection.[12,14] In addition, a late onset of adverse effects of BC treatment is possible for a substantial proportion of patients, and many of them experience fatigue, cognitive impairment, psychological distress, and arm dysfunction for a long time after treatment completion.[15-18] All these effects can affect employment. Indeed, studies suggested associations of work ability with BC treatment–related adverse events such as shoulder impairment[19] and fatigue.[20,21] In addition, psychological distress after cancer experience was also shown to adversely affect job reintegration.[20,21]

Nevertheless, most of the existent evidence comes from cross-sectional studies based on small samples or from retrospective registries or administrative data

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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with limited information on treatment.[22] For instance, many studies lack detailed clinical information on prediagnosis comorbidities.[9,12,20,23] Furthermore, most studies do not evaluate different types of toxicities simultaneously and do not use validated patient-reported outcome (PRO) measures to assess physical and psychological domains. In addition, the therapy landscape for patients with early BC has changed over time, particularly during the last decade. The majority of patients now receive multimodality therapy, including new chemotherapy and endocrine therapy agents and targeted therapies such as trastuzumab.[24,25] Therefore, a clear and comprehensive assessment of the burden of contemporary BC treatment and its related toxicities on employment is lacking.[22] Understanding the independent impact of BC treatment and its adverse effects on employment is urgently needed to better inform patients, health care providers, employers, and policy makers. The aim of this study was to identify treatment-related correlates of RTW 2 years after diagnosis, using data of a large multicenter cohort of patients with BC, including detailed information on treatment and women's health status before and after treatment.

METHODS

Data Source

We used data of a prospective clinical cohort of patients diagnosed with stage I-III primary BC and no prior history of cancer other than basal cell skin cancer or in situ cervical carcinoma within the past 5 years (CANTO [Cancer Toxicities]; NCT01993498). Inflammatory BC was excluded. The cohort aimed to assess treatment-related toxicities and their psychosocial impact. Data were collected in 26 French cancer care centers. Treatment and tumor classification were extracted from medical files. Patients' medical history, prediagnosis comorbidities, and a set of physical treatment-related toxicities were collected during face-to-face health examinations by trained clinical research nurses. PROs were collected by means of validated self-reported paper questionnaires assessing physical and psychological outcomes. Socioeconomic data were gathered through an ad hoc self-reported paper questionnaire gathering items from diverse French population-based surveys.[26,27] These data were collected prospectively at 3 time points: at diagnosis (baseline); at the first post-treatment visit (T1), 3 to 6 months after the end of primary treatment; and at the second post-treatment visit (T2), which occurred on average 2 years after diagnosis (median, 23 months, interquartile range, 21-25 months; Fig 1). End of primary treatment was defined as the end of primary surgery, chemotherapy, or radiotherapy, whichever came last. Anti–human epidermal growth factor receptor (HER2) therapy and hormonal therapy could be ongoing, if indicated. The study was approved by the French regulatory authorities. All patients enrolled in the study were age ≥ 18 years and provided written informed consent.[28]

Study Cohort

The study included the data of 5,801 patients enrolled in the CANTO cohort between March 21, 2012 and January 7, 2015 (first data lock). We restricted our analysis to women age < 57 years old at time of diagnosis (N = 2,883) for women to be at least 5 years away from the French legal retirement age (62 years old) at baseline. Women with no information on work situation at baseline (n = 124), not employed at baseline (n = 401), and not treated with curative intent (patients with no surgery, n = 2) were excluded, as well as patients with evidence of local or distant recurrence or patients who died before the end of the study (n = 72). Of the 2,284 eligible patients, 124 were lost to clinical follow-up, and 286 did not report information on RTW at T2 (n = 410, 18% of eligible patients). Response rate to RTW assessment questions was associated with age, receipt of hormone therapy, and occupational class but did not differ in terms of stage, number of prediagnosis comorbidities, type of surgery or axillary dissection, or receipt of radiotherapy or chemotherapy (Appendix Table A1, online only). The final study sample included 1,874 respondents (Fig 2).

Variables

Our outcome of interest was non-RTW (binary variable grouping part-time and full-time workers). Information on RTW was collected at T2.

Socioeconomic covariates measured at diagnosis included age (< 40, 40-49, ≥ 50 years), having a partner (yes/no), and number of economically dependent children living in the household (0, 1, > 1). As a proxy of socioeconomic status, we used income of the household (< 2,000€, 2,000-4,000€, > 4,000€) and women's occupational class according to the 6-category version of the French classification,[29] which is roughly equivalent to the US classification: professionals and managers, technicians and associate professionals, clerks, manual workers, farmers, and self-employed. Because of small numbers, farmers were grouped with self-employed. Part-time and full-time employment before diagnosis were distinguished. Work-life imbalance (whether the woman gave priority to professional or personal life) at diagnosis was also assessed.

Clinical variables included stage (based on American Joint Committee on Cancer 7th edition)[30] and prediagnosis comorbid medical conditions. The latter were evaluated using the Charlson comorbidity index[31] (0/≥ 1) and a binary variable assessing the presence of ≥ 3 additional comorbid medical conditions not captured by the Charlson index but that can have a substantial burden on a woman's life and affect RTW (among the following medical areas: neurologic, cardiovascular, respiratory, GI, renal, hepatobiliary, endocrine, musculoskeletal, urogenital, hematologic, dermatological, psychiatric).

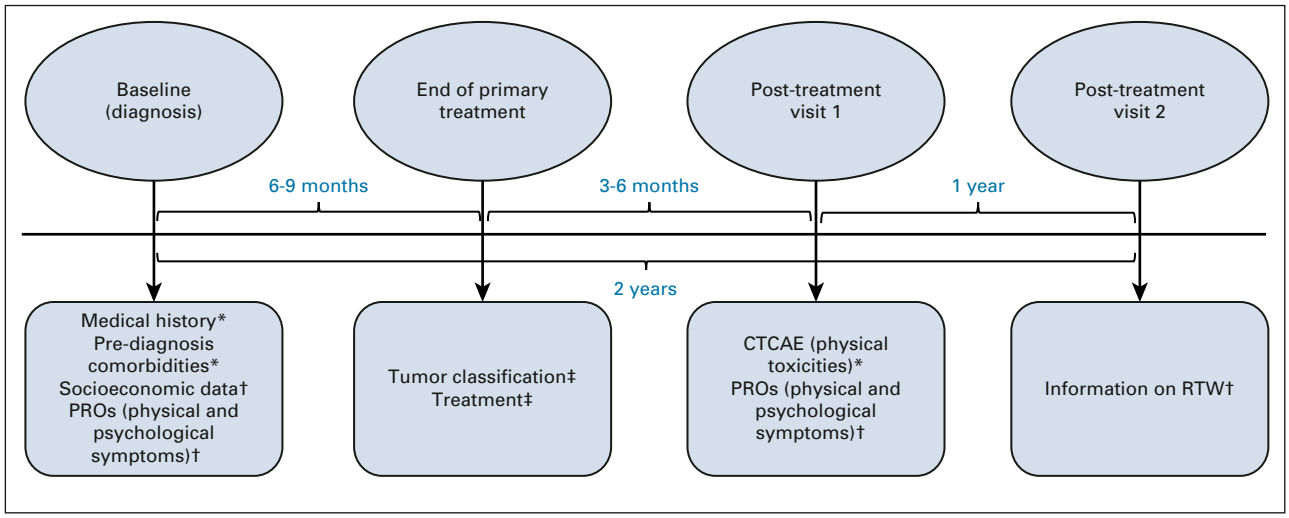

FIG 1. Design of the data collected and used in the analysis. (*) Data collected during a face-to-face health examination by a trained clinical research nurse. (†) Data collected by means of self-reported paper questionnaires. (‡) Data extracted from medical files. CTCAE, Common Toxicity Criteria Adverse Events; PRO, patient-reported outcome; RTW, return to work.

Treatment variables included receipt of radiotherapy (yes/no), surgery, and systemic treatments. Types of surgery (conservative, mastectomy, axillary node dissection, sentinel node dissection) and types of systemic treatment (chemotherapy, hormone therapy [HT], trastuzumab) were combined as described in Table 1, to account for different therapeutic strategies.

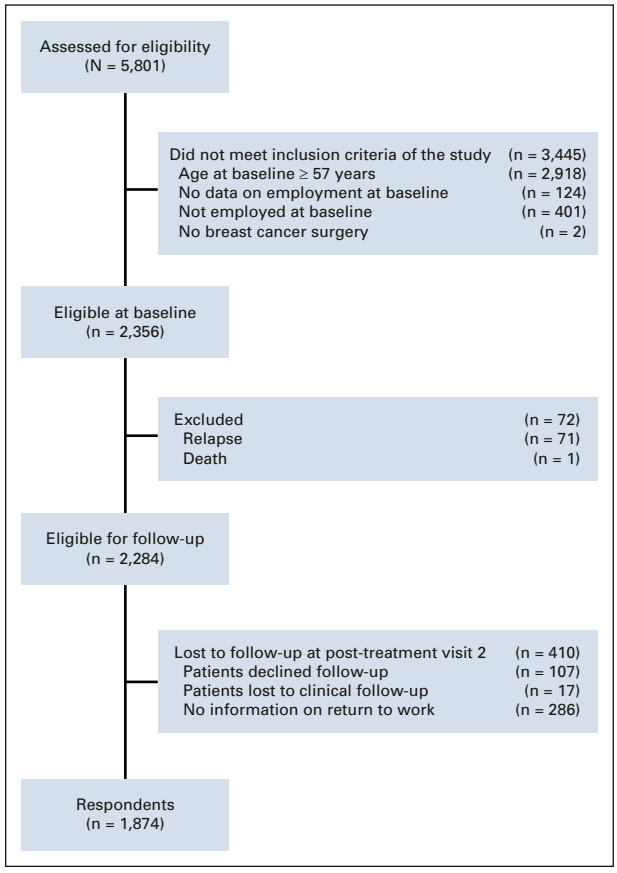

FIG 2. Flowchart of patient population.

Toxicities and PROs were collected at baseline and at T1. A set of physical toxicities was collected by a clinical research nurse during a face-to-face examination using the Common Toxicity Criteria Adverse Events Scale (CTCAE), version 4,[32] and coded as severe when any grade ≥ 3 toxicity was reported. The number of severe CTCAE toxicities (reported in the following areas: cardiovascular, gynecologic, rheumatological, GI, dermatological, pulmonary, neurologic) was computed and then dichotomized (0, ≥ 1). Additional physical toxicities were assessed using 3 clinically relevant symptom subscales of the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire, breast cancer module (QLQ-BR23)[33,34] (namely: systemic therapy side effects, arm and breast morbidity). These 3 subscales were categorized as severe (yes/no) when a patient scored ≥ 40 on the respective scale.[35,36] Severe physical, emotional, and cognitive fatigue were defined using the EORTC quality of life questionnaire, fatigue module (QLQ-FA12) (score ≥ 50 on the respective scale).[37] Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS).[38] Both subscales were categorized into 3 categories (noncase [0-7], doubtful [8-10], case [11-21]). All these variables had ≤ 5% missing values except the Charlson comorbidity index, which had 7% missing values (Appendix Table A2, online only).

Statistical Analyses

Binary logistic regression analyses were performed to identify correlates of non-RTW. We first adjusted for treatment variables as well as clinical and socioeconomic covariates collected at diagnosis (model 1) and then additionally adjusted for CTCAE toxicities and PROs collected

TABLE 1. Factors Associated With Non-RTW at the Second Post-Treatment Visit 2 Years After Diagnosis: Multivariable Logistic Regressions

		Model 1		Model 2	
Factor	**%**	**OR**	**95% CI**	**OR**	**95% CI**
Socioeconomic covariates at diagnosis[a]					
Age, years					
18-39	13.2	1.00		1	
40-49	46.2	1.03	0.71 to 1.51	1.01	0.68 to 1.50
50-56	40.6	1.60	1.08 to 2.39	1.61	1.06 to 2.45
Having a partner					
No	15.9	1.00		1	
Yes	84.1	1.15	0.80 to 1.67	1.17	0.79 to 1.74
No. of children					
0	28.9	1.00		1	
1	26.6	0.94	0.68 to 1.31	0.88	0.63 to 1.24
> 1	44.5	0.91	0.66 to 1.24	0.88	0.63 to 1.22
Occupational class					
Professionals and managers	24.6	1.00		1.00	
Technicians and associate professionals	24.0	1.00	0.68 to 1.47	0.95	0.64 to 1.42
Clerks	39.4	1.49	1.04 to 2.13	1.42	0.97 to 2.07
Self-employed (farmers, craftsmen, and shopkeepers)	5.3	1.14	0.63 to 2.08	1.09	0.58 to 2.05
Manual workers	6.7	2.34	1.42 to 3.87	2.17	1.28 to 3.69
Income of the household					
> 4,000€ per month	32.9	1.00		1.00	
2,000-4,000€ per month	48.7	1.35	0.99 to 1.85	1.26	0.90 to 1.75
< 2,000€ per month	18.4	1.94	1.27 to 2.96	1.65	1.06 to 2.59
Working hours					
Full-time employment	75.3	1.00		1.00	
Part-time employment	24.7	1.50	1.12 to 2.00	1.51	1.12 to 2.04
Work-life imbalance					
Equal importance to personal and professional life	47.4	1.00		1.00	
Personal life is more important	39.8	1.28	0.99 to 1.65	1.29	0.98 to 1.68
Professional life is more important	9.9	1.14	0.75 to 1.73	1.06	0.68 to 1.65
Clinical covariates					
Stage					
Stage I	44.8	1.00		1.00	
Stage II	44.0	1.28	0.94 to 1.76	1.41	1.01 to 1.97
Stage III	11.3	1.86	1.17 to 2.94	1.99	1.22 to 3.23
Charlson comorbidity index[a]					
0	85.9	1.00		1.00	
≥ 1	14.1	1.54	1.12 to 2.13	1.52	1.08 to 2.14
Additional comorbid conditions[a]					
< 3	79.4	1.00		1.00	
≥ 3	20.6	1.64	1.24 to 2.16	1.39	1.03 to 1.87

(continued on following page)

TABLE 1. Factors Associated With Non-RTW at the Second Post-Treatment Visit 2 Years After Diagnosis: Multivariable Logistic Regressions (continued)

Factor	%	Model 1		Model 2	
		OR	95% CI	OR	95% CI
Treatment					
Radiotherapy					
No	8.4	1.00		1.00	
Yes	91.6	0.79	0.49 to 1.26	0.77	0.47 to 1.26
Combinations of local treatments					
Conservative surgery + sentinel node dissection	47.7	1.00		1.00	
Conservative surgery + axillary dissection	22.2	1.13	0.78 to 1.63	1.06	0.72 to 1.56
Mastectomy + sentinel node dissection	6.3	1.15	0.65 to 2.05	1.16	0.64 to 2.13
Mastectomy + axillary dissection	23.8	1.72	1.19 to 2.48	1.65	1.12 to 2.44
Combinations of systemic treatments					
Chemotherapy + hormone therapy	41.2	1.00		1.00	
Hormone therapy alone	30.9	0.96	0.68 to 1.36	1.03	0.71 to 1.49
Chemotherapy alone	9.3	1.58	1.05 to 2.37	1.49	0.96 to 2.29
Chemotherapy + trastuzumab	4.7	2.15	1.29 to 3.57	2.01	1.18 to 3.44
Chemotherapy + trastuzumab + hormone therapy	10.4	1.66	1.14 to 2.42	1.62	1.10 to 2.41
None	3.5	1.32	0.66 to 2.65	1.42	0.67 to 2.97
Toxicities and PROs[b]					
≥ 1 CTCAE severe physical toxicity[c]					
No	84.5	—		1.00	
At least one	15.5	—		1.59	1.15 to 2.18
Severe breast morbidity					
No	75.3	—		1.00	
Yes	24.7	—		0.97	0.70 to 1.33
Severe arm morbidity					
No	73.0	—		1.00	
Yes	27.0	—		1.59	1.19 to 2.13
Severe systemic therapy adverse effects					
No	90.9	—		1.00	
Yes	9.1	—		1.43	0.95 to 2.14
Severe physical fatigue					
No	77.2	—		1.00	
Yes	22.8	—		1.31	0.94 to 1.83
Severe cognitive fatigue					
No	84.3	—		1.00	
Yes	15.7	—		1.02	0.70 to 1.49
Severe emotional fatigue					
No	82.2	—		1.00	
Yes	17.8	—		1.46	1.00 to 2.13
Anxiety					
Noncase	53.3	—		1.00	
Doubtful case	26.3	—		1.71	1.26 to 2.32
Case	20.4	—		1.47	1.02 to 2.11

(continued on following page)

TABLE 1. Factors Associated With Non-RTW at the Second Post-Treatment Visit 2 Years After Diagnosis: Multivariable Logistic Regressions (continued)

Factor	%	Model 1		Model 2	
		OR	95% CI	OR	95% CI
Depression					
Noncase	83.4	—		1.00	
Doubtful case	11.1	—		1.05	0.70 to 1.59
Case	5.5	—		2.29	1.34 to 3.91

NOTE. France, CANTO cohort, 2018; imputed data set. Model 1: ORs are adjusted for socioeconomic covariates, clinical covariates, and treatment. Model 2: ORs are adjusted for all the variables listed in the table.

Abbreviations: CTCAE, Common Toxicity Criteria Adverse Events; €, Euros; RTW, return to work; PROs, patient-reported outcomes; OR, odds ratio.

[a]Variables collected at diagnosis.

[b]Variables collected at the first post-treatment visit (3-6 months after end of primary treatment).

[c]CTCAE grade ≥ 3 cardiovascular, gynecologic, rheumatological, GI, dermatological, pulmonary, or neurologic toxicity.

at T1 (model 2). We assessed pairwise correlation between the symptom-related covariates using χ^2 test and Cramer's V and tested interactions between correlated variables. Multiple imputations were performed with the fully conditional specification method. We ran sensitivity analyses using QLQ-FA12 subscale scores as continuous variables in the absence of a validated threshold to dichotomize the continuum of scores. We also analyzed the impact of change in severe toxicities between baseline (diagnosis) and T1 for EORTC and HADS subscales.

Odds ratio (ORs) and 95% CIs were estimated. All tests were 2-sided at the 0.05 significance level. The R statistical package (version 3.2.3; R foundation, Vienna Austria) was used.

RESULTS

Cohort Characteristics

The mean age at diagnosis was 47 years. At diagnosis, 24.6% were professionals or managers and 39.4% were clerks (Table 1). A total of 30.0% of women reported comorbidities, measured by the Charlson or the additional comorbidity index. Overall, 30.1% of patients underwent mastectomy; 65.6%, 82.5%, and 15.1% of patients received chemotherapy, HT, and trastuzumab, respectively. The most prevalent combinations of local and systemic treatments were conservative surgery and sentinel node dissection (47.7%) and chemotherapy combined with HT (41.2%).

At the first post-treatment visit (T1), 15.5% of patients reported at least one severe physical CTCAE toxicity. Severe physical, cognitive, and emotional fatigue were reported by 22.8% 15.7%, and 17.8% of patients, respectively. In addition, 20.4% were anxious and 5.5% were depressed.

Two years after diagnosis (T2), 399 (21.3%) patients had not returned to work. Among them, 73.9% were on sick leave, 8.5% were unemployed and seeking work, 5.5% received disability benefit, 6.5% were retired, and 5.6% were in another situation. Among women who worked full time at diagnosis, 23.6% had become part-time employees.

Correlates of Non-RTW

In univariate analyses (Appendix Table A2), patients who had received combinations of treatment with trastuzumab, those who had undergone mastectomy and axillary node dissection, and those who reported severe physical or psychological symptoms were less likely to be working ($P < .001$). In the first regression model focused on treatment characteristics (model 1, Table 1), odds of non-RTW were significantly increased for patients who were ≥ 50 years, those who had undergone mastectomy and axillary node dissection, and those who had received combinations of chemotherapy and trastuzumab. Odds of non-RTW were also significantly elevated among women with stage III BC, who reported prediagnosis comorbidities, worked part time at diagnosis, and had lower occupational classes or income (Table 1).

In a separate model that included CTCAE toxicities and PROs collected at T1 (model 2, Table 1), the same associations emerged as compared with model 1, although ORs were reduced among patients with ≥ 3 additional comorbid conditions and a low occupational class or income. By contrast, the ORs remained stable among patients who had undergone mastectomy and axillary dissection or patients who were treated with combinations of chemotherapy and trastuzumab (with or without HT). Physical and psychological symptoms associated with non-RTW were severe physical toxicity as per CTCAE, severe arm morbidity, anxiety, and depression. A trend toward higher odds of non-RTW was observed among patients with severe physical or emotional fatigue and severe systemic therapy adverse effects. Sensitivity analyses using different ways of coding PROs, as described in the methods, gave

consistent results (data not shown). Models including the type of chemotherapy regimen (anthracycline-taxane based *v* other) yielded identical results, and no effect of the chemotherapy regimen on RTW was observed (Appendix Table A3, online only).

DISCUSSION

More than 70% of working-age women are in the labor force in Western countries.[39] Employment after diagnosis and treatment of BC is therefore a major public health challenge.

Our study clarified the independent effect of BC treatment and its impact on employment. BC treatment is now standardized by national and international guidelines. We studied the effect of standard combinations of treatments that reflect the current different therapeutic strategies used in the treatment of nonmetastatic BC. Among local treatments, we found that only the most aggressive strategies (combination of mastectomy and node dissection) had a negative long-term impact on employment. The fact that we looked at these strategies together may explain the inconsistency of the effects previously found in the literature for mastectomy alone or axillary dissection alone.[8] Regarding systemic treatments, chemotherapy alone was associated with non-RTW in model 1, but not in model 2, when accounting for treatment toxicities. Previous studies on RTW after BC usually included treatment or toxicities, but a few included both (notably fatigue). Over the 4 studies including both fatigue and treatment in multivariable models,[21,40-42] most of them did not find that chemotherapy was significantly associated with RTW in patients with BC.[21,41,42] Our results suggest an independent effect of trastuzumab on RTW, with significantly increased odds of non-RTW for all combinations that include trastuzumab and chemotherapy (with or without HT), although, on average, patients had stopped trastuzumab 10 months before RTW was assessed (only 1 woman was still treated at T2). Combination of trastuzumab and chemotherapy is the standard of care for patients with biologically aggressive HER2-positive early BC. To our knowledge, only 2 studies on RTW after BC included trastuzumab, with no suggestion of impact of this treatment on employment, but they were based on limited samples.[9,43] Clinical studies report that trastuzumab is well tolerated by patients, with very few grade ≥ 3 toxicities, but potential persistent fatigue.[44] It is possible that patients who receive trastuzumab for HER2-positive BC have subtle clinical late effects, but they may also be more likely to perceive themselves as sick for a longer time, being overwhelmed with fear of relapse and accumulation of treatments.

Part of the influence of treatment on RTW is due to treatment adverse effects. Although health status at diagnosis is a confounding factor in this association, many studies fail to account for prediagnosis comorbidities.[20,43,45-47] Our results underline the importance of these comorbidities, which were strongly associated with RTW and were reported by 30% of the patients, even in our cohort of relatively young patients. Therefore, our results have the ability to suggest the importance of both physical and psychological symptoms at first post-treatment visit on RTW after careful control for prediagnosis comorbidities.

We investigated multiple physical and psychological symptoms. Our study, consistent with prior research, suggested that physical treatment adverse effects such as arm morbidity impact RTW through reduced work capacity.[19] We also investigated the role of fatigue, which has been shown to have an effect on RTW of BC survivors.[20,21] In previous studies, fatigue was measured through questionnaires assessing global fatigue, combining the different aspects of fatigue (eg, physical, emotional).[11,20,21,42,43] This is the first report, to our knowledge, separately assessing the impact of different domains of fatigue on RTW with a validated questionnaire (EORTC QLQ-FA12). Using a more granular indicator, we showed that, when taking into account multiple physical and psychological symptoms, none of the subdomains of fatigue was correlated with RTW. Still, our results show a trend for a negative impact of emotional and physical fatigue on employment after BC.

Psychological factors were also associated with RTW. These factors may be induced by cancer diagnosis, cancer symptoms, or cancer treatments; they also may preexist or be increased by cancer. Consistent with the literature, we found that anxiety and/or depression were associated with RTW.[19-21] The literature is fragmented and rarely includes physical and psychological symptoms simultaneously, whereas our analysis included multiple symptoms showing that several physical toxicities as well as several psychological symptoms were strongly and negatively correlated with RTW. Thus, our results suggest the multidimensional aspect of RTW and the importance of accounting for various health domains.

Our results are based on a large prospective study of patients recruited in 26 different centers across France. Our study presents several strengths, namely its large sample size, its longitudinal design, and the quality of the data collected. The data included detailed information on treatment and health status before diagnosis and at first post-treatment visit. The study included physical treatment-related toxicities, collected during a face-to-face examination and through validated quality-of-life questionnaires specific to BC, and also psychological symptoms, which often were not included in previous studies.[9-14,46,48,49] The longitudinal design allowed us to collect those symptoms 1 year before our measure of RTW and thus to minimize bias occurring in cross-sectional design when simultaneously assessing the variable of interest and the outcome. Working conditions shown to be related to RTW, such as employer accommodation and support[48,50] or attitudes about work since diagnosis,[51] were not assessed. Yet, occupational category or part-time employment were taken

into consideration. As in any longitudinal study, our data suffer from attrition, with approximately 18% of patients lost to follow-up. This could have affected the rate of non-RTW (21%), yet it was close to the rate found in a French national population-based survey (25%).[26] As usually observed in the literature, patients with a higher socioeconomic position were more likely to respond. The final sample was still large and allowed us to model the influence of different therapeutic strategies and of multiple physical and psychological symptoms on RTW. To our knowledge, this report is the first to include both physical and psychological symptoms and to control for prediagnosis comorbidities and socioeconomic status on such an important sample.[42]

Given the importance of employment for rehabilitation, it is essential to provide patients with BC with programs to support them in job reintegration. However, even though returning to the workplace allows many patients to maintain a sense of normalcy or control,[52] a substantial proportion of them need to take time to recover, especially if they experience long-lasting psychological symptoms. Consistent with 2 systematic reviews investigating the effect of interventions on RTW among cancer survivors, our results highlight the need to propose multidisciplinary interventions that not only focus on vocational issues but also involve physical and psychosocial components, for helping patients with BC to reintegrate the workforce.[53,54] In particular, this comprehensive study identified potentially vulnerable patients and thus warrants additional research focusing on these patients who lag behind and on supportive interventional strategies to facilitate their RTW.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Impact of Breast Cancer Treatment on Employment: Results of a Multicenter Prospective Cohort Study (CANTO)

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APPENDIX

TABLE A1. Characteristics of Respondents and Nonrespondents (N = 2,284)

	Respondents (n = 1,874)		Lost to Clinical Follow-Up at T2 (n = 124)		No Information on RTW at T2 (n = 286)		
Characteristic	**No.**	**%**	**No.**	**%**	**No.**	**%**	***P***
Age, years							.04
18-39	248	13.2	9	7.3	45	15.7	
40-49	866	46.2	54	43.5	142	49.7	
50-56	760	40.6	61	49.2	99	34.6	
Occupational class							.01
Self-employed (farmers, craftsmen, and shopkeepers)	99	5.4	9	7.7	22	7.9	
Clerks	713	39.1	56	47.9	136	49.1	
Manual workers	122	6.7	9	7.7	15	5.4	
Technicians and associate professionals	441	24.2	20	17.1	49	17.7	
Professionals and managers	449	24.6	23	19.7	55	19.9	
Missing	50	—	—	—	—	—	
Stage							.39
Stage I	839	44.8	52	43.7	131	45.8	
Stage II	824	44.0	54	45.4	134	46.9	
Stage III	211	11.3	13	10.9	21	7.3	
Charlson comorbidity index							.59
0	1,506	86.0	96	85.7	232	87.5	
1	128	7.3	11	9.8	15	5.7	
≥ 2	117	6.7	5	4.5	18	6.8	
Missing	123	—	—	—	—	—	
Radiotherapy							.25
Yes	1,716	91.6	104	87.4	264	92.3	
No	158	8.4	15	12.6	22	7.7	
Stage							.39
Stage I	839	44.8	52	43.7	131	45.8	
Stage II	824	44.0	54	45.4	134	46.9	
Stage III	211	11.3	13	10.9	21	7.3	
Surgery							.71
Conservative	1,310	69.9	83	68.6	206	72.0	
Mastectomy	564	30.1	38	31.4	80	28.0	
Lymph node surgery							.22
Sentinel node dissection	1,011	53.9	67	55.4	170	59.4	
Axillary dissection	863	46.1	54	44.6	116	40.6	
Radiotherapy							.25
Yes	1,716	91.6	104	87.4	264	92.3	
No	158	8.4	15	12.6	22	7.7	
Chemotherapy							.14
Yes	1,230	65.6	68	57.1	181	63.3	
No	644	34.4	51	42.9	105	36.7	

(continued on following page)

TABLE A1. Characteristics of Respondents and Nonrespondents (N = 2,284) (continued)

Characteristic	Respondents (n = 1,874)		Lost to Clinical Follow-Up at T2 (n = 124)		No Information on RTW at T2 (n = 286)		*P*
	No.	%	No.	%	No.	%	
Hormone therapy							.02
Yes	1,546	82.5	95	81.2	216	75.5	
No	328	17.5	22	18.8	70	24.5	
Trastuzumab							.82
Yes	283	15.1	16	13.7	40	14.0	
No	1,591	84.9	101	86.3	246	86.0	

NOTE. France, CANTO cohort, 2018; not imputed data set.
Abbreviations: RTW, return to work; T2, post-treatment visit 2 (2 years after diagnosis).

TABLE A2. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Univariate Analysis (n = 1,874)

	Total		No RTW		
Factor	**No.**	**%**	**No.**	**%**	***P***
Socioeconomic covariates at diagnosis[a]					
Age, years					
18-39	248	13.2	52	21.0	[b]
40-49	866	46.2	160	18.5	
50-56	760	40.6	187	24.6	
Missing	0	—	0	—	
Having a partner					
No	292	15.6	64	21.9	.88
Yes	1,566	83.6	334	21.3	
Missing	16	—	1	—	
No. of children					
0	489	28.1	118	24.1	.16
1	461	26.5	99	21.5	
> 1	790	45.4	155	19.6	
Missing	134	—	27	—	
Occupational class					
Professionals and managers	457	24.4	65	14.2	[c]
Technicians and associate professionals	445	23.7	76	17.1	
Clerks, service and sales workers	730	39.0	187	25.6	
Farmers, craftsmen, and shopkeepers	99	5.3	19	19.2	
Manual workers	125	6.7	47	37.6	
Missing	18	—	5	—	
Income of the household					
> 4,000€ per month	322	18.1	95	29.5	[c]
2,000-4,000€ per month	865	48.7	191	22.1	
< 2,000€ per month	590	33.2	88	14.9	
Missing	97	—	25	—	
Working hours					
Full-time employment	1,301	75.6	241	18.5	[c]
Part-time employment	421	24.4	111	26.4	
Missing	152	—	47	—	
Work-life imbalance					
Equal importance to personal and professional life	888	48.8	724	50.5	.79
Personal life is more important	746	41.0	564	39.4	
Professional life is more important	185	10.2	145	10.1	
Missing	55	—	42	—	
Clinical covariates					
Stage					
Stage I	839	44.8	142	16.9	[c]
Stage II	824	44.0	190	23.1	
Stage III	211	11.3	67	31.8	
Missing	0	—	0	—	

(continued on following page)

TABLE A2. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Univariate Analysis (n = 1,874) (continued)

	Total		No RTW		
Factor	**No.**	**%**	**No.**	**%**	***P***
Charlson comorbidity index[a]					
0	1,506	86.0	299	19.9	[c]
≥ 1	245	14.0	72	29.4	
Missing	123	—	28	—	
Additional comorbid conditions[a]					
< 3	1,472	78.5	287	19.5	[c]
≥ 3	382	20.4	108	28.3	
Missing	20	—	4	—	
Treatment					
Radiotherapy					
No	158	8.4	39	24.7	.32
Yes	1,716	91.6	360	21.0	
Missing	0	—	0	—	
Types of surgery and node dissection					
Conservative surgery + sentinel node dissection	893	47.7	147	16.5	[c]
Conservative surgery + axillary dissection	417	22.3	92	22.1	
Mastectomy + sentinel node dissection	118	6.3	25	21.2	
Mastectomy + axillary dissection	446	23.8	135	30.3	
Missing	0	—	0	—	
Systemic treatment					
Chemotherapy + hormone therapy	772	41.2	163	21.1	[c]
None	65	3.5	13	20.0	
Hormone therapy alone	579	30.9	92	15.9	
Chemotherapy alone	175	9.3	45	25.7	
Chemotherapy + trastuzumab	88	4.7	30	34.1	
Chemotherapy + trastuzumab + hormone therapy	195	10.4	56	28.7	
Missing	0	—	0	—	
Toxicities and PROs[d]					
No. of severe toxicities[e]					
0	1,562	83.4	300	19.2	[c]
≥ 1	287	15.3	93	32.4	
Missing	25	—	6	—	
Breast morbidity					
No	1,339	71.5	247	18.4	[c]
Yes	431	23.0	129	29.9	
Missing	104	—	23	—	
Arm morbidity					
No	1,298	69.3	214	16.5	[c]
Yes	475	25.3	163	34.3	
Missing	101	—	22	—	

(continued on following page)

TABLE A2. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Univariate Analysis (n = 1,874) (continued)

	Total		No RTW		
Factor	**No.**	**%**	**No.**	**%**	***P***
Systemic therapy adverse effects					
No	1,615	86.2	308	19.1	[c]
Yes	158	8.4	68	43.0	
Missing	101	—	23	—	
Severe physical fatigue					
No	1,373	73.3	231	16.8	[c]
Yes	399	21.3	146	36.6	
Missing	102	—	22	—	
Severe cognitive fatigue					
No	1,496	79.8	277	18.5	[c]
Yes	275	14.7	100	36.4	
Missing	103	—	22	—	
Severe emotional fatigue					
No	1,459	77.9	252	17.3	[c]
Yes	309	16.5	123	39.8	
Missing	106	—	24	—	
Anxiety					
None	951	50.7	136	14.3	[c]
Possible case	467	24.9	127	27.2	
Probable case	360	19.2	115	31.9	
Missing	96	—	21	—	
Depression					
None	1,484	79.2	266	17.9	[c]
Possible case	196	10.5	59	30.1	
Probable case	98	5.2	53	54.1	
Missing	96	—	21	—	

NOTE. France, CANTO cohort, 2018; not imputed data set.

Abbreviations: CTCAE, Common Toxicity Criteria Adverse Events; PRO, patient-reported outcome; RTW, return to work.

[a]Variables collected at diagnosis.

[b]$P < .01$ by χ^2 test.

[c]$P < .00$ by χ^2 test.

[d]Variables collected at the first post-treatment visit (3-6 months after end of primary treatment).

[e]CTCAE grade ≥ 3 cardiovascular, gynecologic, rheumatological, GI, dermatological, pulmonary, or neurologic toxicity.

TABLE A3. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Multivariable Logistic Regressions

		Model 1		Model 2	
Factors	**%**	**OR**	**95% CI**	**OR**	**95% CI**
Socioeconomic covariates at diagnosis[a]					
Age, years					
18-39	13.2	1.00		1.00	
40-49	46.2	1.03	0.70 to 1.50	1.00	0.67 to 1.49
50-56	40.6	1.59	1.07 to 2.36	1.60	1.05 to 2.43
Having a partner					
No	15.9	1.00		1.00	
Yes	84.1	1.15	0.80 to 1.67	1.17	0.79 to 1.74
No. of children					
0	28.9	1.00		1.00	
1	26.6	0.94	0.68 to 1.31	0.88	0.63 to 1.24
> 1	44.5	0.91	0.66 to 1.24	0.88	0.63 to 1.22
Occupational class					
Professionals and managers	24.6	1.00		1.00	
Technicians and associate professionals	24.0	1.00	0.68 to 1.47	0.95	0.64 to 1.42
Clerks	39.4	1.48	1.04 to 2.13	1.41	0.97 to 2.06
Self-employed (farmers, craftsmen, and shopkeepers)	5.3	1.14	0.62 to 2.07	1.08	0.57 to 2.04
Manual workers	6.7	2.34	1.42 to 3.88	2.17	1.28 to 3.68
Income of the household					
> 4,000€ per month	32.9	1.00		1.00	
2,000-4,000€ per month	48.7	1.36	0.99 to 1.86	1.26	0.91 to 1.75
< 2,000€ per month	18.4	1.94	1.27 to 2.96	1.65	1.06 to 2.59
Working hours					
Full-time employment	75.3	1.00		1.00	
Part-time employment	24.7	1.50	1.12 to 1.99	1.51	1.12 to 2.04
Work-life imbalance					
Equal importance to personal and professional life	47.4	1.00		1.00	
Personal life is more important	39.8	1.28	0.99 to 1.65	1.29	0.99 to 1.69
Professional life is more important	9.9	1.14	0.75 to 1.74	1.07	0.68 to 1.66
Clinical covariates					
Stage					
Stage I	44.8	1.00		1.00	
Stage II	44.0	1.29	0.94 to 1.77	1.41	1.01 to 1.97
Stage III	11.3	1.87	1.18 to 2.97	2.00	1.23 to 3.25
Charlson comorbidity index[a]					
0	85.9	1.00		1.00	
≥ 1	14.1	1.55	1.12 to 2.14	1.52	1.08 to 2.14
Additional comorbid conditions[a]					
< 3	79.4	1.00		1.00	
≥ 3	20.6	1.62	1.23 to 2.14	1.38	1.02 to 1.86

(continued on following page)

TABLE A3. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Multivariable Logistic Regressions (continued)

		Model 1		Model 2	
Factors	**%**	**OR**	**95% CI**	**OR**	**95% CI**
Treatment					
Radiotherapy					
No	8.4	1.00		1.00	
Yes	91.6	0.79	0.49 to 1.26	0.77	0.47 to 1.26
Combinations of local treatments					
Conservative surgery + sentinel node dissection	47.7	1.00		1.00	
Conservative surgery + axillary dissection	22.2	1.13	0.78 to 1.62	1.05	0.72 to 1.55
Mastectomy + sentinel node dissection	6.3	1.14	0.64 to 2.03	1.15	0.63 to 2.11
Mastectomy + axillary dissection	23.8	1.70	1.18 to 2.46	1.64	1.11 to 2.41
Trastuzumab					
No	84.9	1.00		1.00	
Yes	15.1	1.56	1.13 to 2.14	1.53	1.10 to 2.15
Hormone therapy					
No	17.5	1.00		1.00	
Yes	82.5	0.69	0.51 to 0.93	0.72	0.52 to 0.99
Type of chemotherapy					
No chemotherapy	34.4	1.00		1.00	
Anthracycline-taxane based	61.3	1.06	0.76 to 1.49	0.98	0.69 to 1.41
Other type of regimen	4.3	1.19	0.65 to 2.16	1.05	0.56 to 1.96
Toxicities and PROs[b]					
≥ 1 CTCAE severe physical toxicity[c]					
No	84.5	—		1.00	
At least one	15.5	—		1.59	1.16 to 2.18
Severe breast morbidity					
No	75.3	—		1.00	
Yes	24.7	—		0.97	0.70 to 1.33
Severe arm morbidity					
No	73.0	—		1.00	
Yes	27.0	—		1.59	1.19 to 2.13
Severe systemic therapy adverse effects					
No	90.9	—		1.00	
Yes	9.1	—		1.43	0.96 to 2.15
Severe physical fatigue					
No	77.2	—		1.00	
Yes	22.8	—		1.31	0.94 to 1.83
Severe cognitive fatigue					
No	84.3	—		1.00	
Yes	15.7	—		1.03	0.71 to 1.49
Severe emotional fatigue					
No	82.2	—		1.00	
Yes	17.8	—		1.45	0.99 to 2.13

(continued on following page)

TABLE A3. Factors Associated with Non-RTW at the Second Post-Treatment Visit, 2 Years After Diagnosis: Multivariable Logistic Regressions (continued)

		Model 1		Model 2	
Factors	**%**	**OR**	**95% CI**	**OR**	**95% CI**
Anxiety					
Noncase	53.3	—		1.00	
Doubtful case	26.3	—		1.71	1.26 to 2.31
Case	20.4	—		1.47	1.02 to 2.11
Depression					
Noncase	83.4	—		1.00	
Doubtful case	11.1	—		1.05	0.70 to 1.58
Case	5.5	—		2.28	1.34 to 3.90

NOTE: France, CANTO cohort, 2018; imputed data set.

Abbreviations: CTCAE, Common Toxicity Criteria Adverse Events; PRO, patient-reported outcome; RTW, return to work.

[a]Variables collected at diagnosis.

[b]Variables collected at treatment the first post-treatment visit (3-6 months after end of primary treatment).

[c]CTCAE grade ≥ 3 cardiovascular, gynecologic, rheumatological, GI, dermatological, pulmonary, or neurologic toxicity.