

Overweight, obesity and weight gain after breast cancer (BC): a prospective clinical study

A. Di Meglio¹, M. El-Mouhebb¹, S. Michiels¹, L.W. Jones², M. Annonay¹, A. Zingarello¹, M. Matias¹, S. Everhard³, A.L. Martin³, P. Arveux⁴, O. Tredan⁵, P. Soulie⁶, P.H. Cottu⁷, A.H. Partridge⁸, L. Del Mastro⁹, J.A. Ligibel⁸, F. André¹, I. Vaz-Luis¹

¹Institut Gustave Roussy, Villejuif, FR, ²Memorial Sloan Kettering Cancer Center, New York, US, ³UNICANCER, Paris, FR, ⁴Centre Georges-François Leclerc, Dijon, FR, ⁵Centre Léon Bérard, Lyon, FR, ⁶Centre Paul Papin, Angers, FR, ⁷Institut Curie, Paris, FR, ⁸Dana-Farber Cancer Institute, Boston, US, ⁹Ospedale Policlinico San Martino, Genova, IT

Background

Study rationale: The epidemic of overweight and obesity is a relevant public health issue in the general population worldwide. Evidence exists that obesity and weight gain are common in women diagnosed with BC and that excess weight and unfavorable energy balance are linked to poor quality of life and worse BC-specific outcomes.^a Fewer data are available that describe weight changes and evaluate robust associations with weight gain following BC in a European population.

Objectives: To investigate prevalence and longitudinal patterns of overweight/obesity and weight changes in the post-BC diagnosis period and identify clinical factors that are associated with weight gain among a large population of French BC survivors.

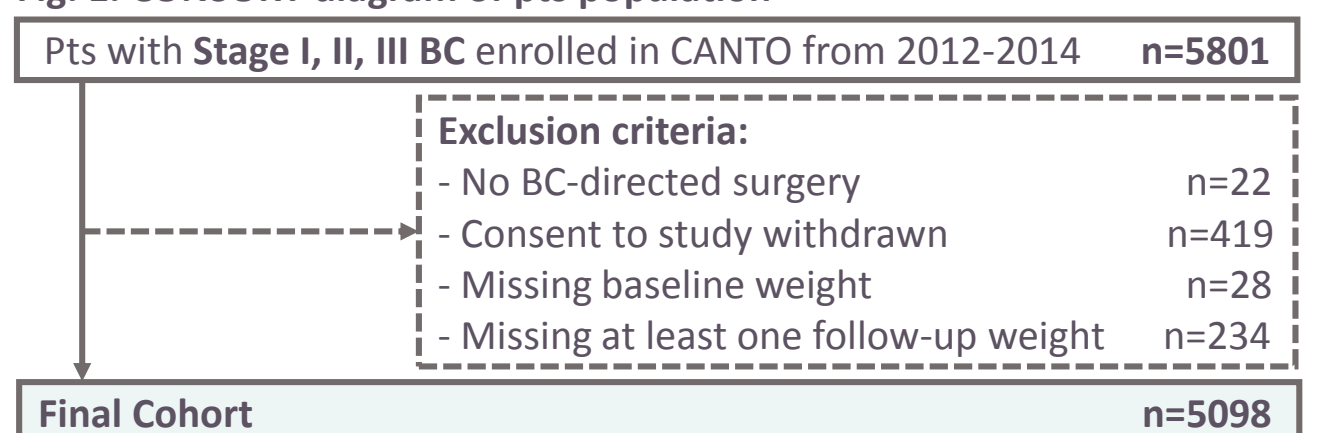
Patients and Methods

Data source: We used data from an ongoing prospective multicenter clinical study of women with early BC treated across 26 French cancer centers (CANcer TOxicities [CANTO]; NCT01993498; expected end of accrual of 12000 patients [pts] by end of 2018). For this analysis, updated information from 5801 pts was accessed (07/2018 data lock) (Fig. 1). Pts were assessed at BC diagnosis (baseline) and at a median (IQR) time of: **T1= 10.5 months (8.0-12.4)** and **T2= 22.3 months (20.1-24.8)**.

Study variables: **1. Exposure variables:** Dedicated nurses collected clinical (including Body Mass Index [BMI; Kg/m²]) and BC treatment data, and assessed health behaviors (including physical activity [PA] as per Global Physical Activity Questionnaire [GPAQ]-16) and psychosocial factors (including anxiety and depression as per the Hospital Anxiety and Depression Scale [HADS]). Standard WHO categories were used for BMI (ie, 25.0-29.9, Overweight; and ≥30.0, Obese) and PA (insufficiently active= never meets/reduces exposure below 10 MET-h/week between baseline and T1/T2; sufficiently active= maintains/achieves at least 10 MET-h/week between baseline and T1/T2). **2. Outcomes of interest:** Overtime risk of overweight or obesity, weight gain ≥5% of baseline weight (considered as clinically meaningful)^b, and cancer recurrence rates.

Statistical analysis: Group-Based Trajectory Modeling^c assessed overtime risk of overweight/obesity and associated factors. Multivariate logistic regression examined factors associated with odds of significant weight gain at T1 and T2 and associations between baseline BMI and cancer recurrence. In sensitivity analyses, we also modeled weight change as a continuous variable using multivariate generalized linear models.

References: ^aLigibel JA, 2012; ^bSaquib N, 2007; ^cNagin DS, 2005 and 2010.



Results

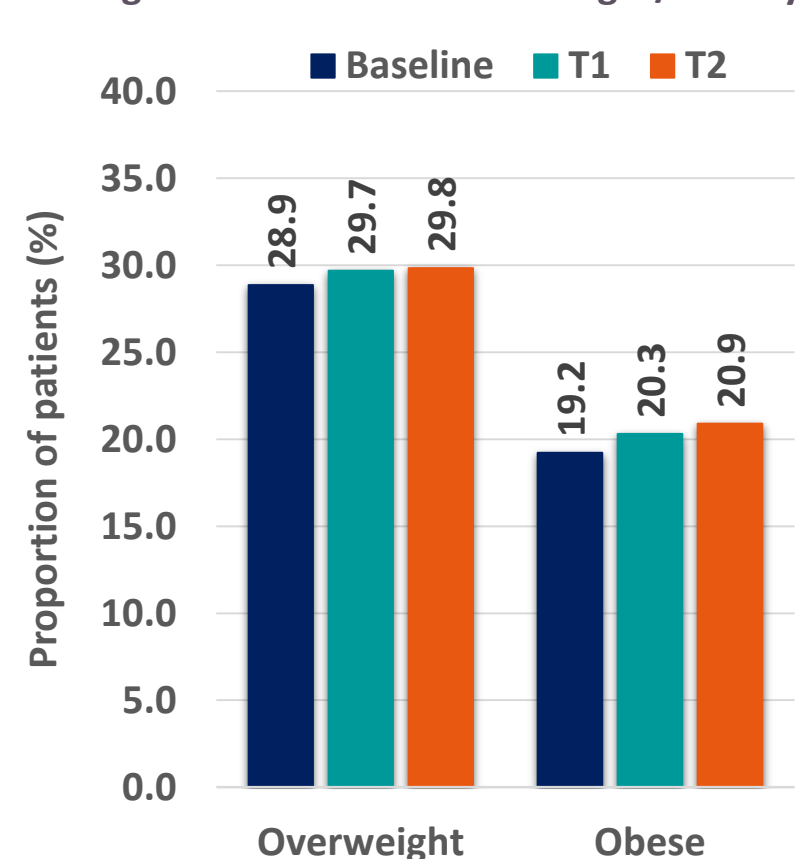
1. Cohort characteristics: Baseline pts characteristics are summarized in Table 1. Prevalence of overweight/obesity at baseline was 48.1% (Fig. 2) and increased to 50.0% at T1 and to 50.7% at T2. A minority of pts was underweight (2.3%, 2.6%, and 2.0% at each time point, respectively).

Table 1. Baseline characteristics of the overall cohort (% pts, n= 5098).

Characteristic	% pts	Characteristic	% pts		
Age at diagnosis	<50 years	30.4	Education level	Primary school	15.2
	≥50 and <65 years	43.4		High school	47.2
	≥65 years	26.2		College or higher	37.6
Menopausal status	Premenopausal	38.0	Marital status	Partnered	77.5
	Postmenopausal	62.0		Single	22.5
Anxiety	Mean score (SD)	9.0 (4.2)	Smoking status	Active/Former smoker	38.4
Depression	Mean score (SD)	4.2 (3.6)		Never smoker	61.6
PA exposure baseline to T1	Insufficiently active	37.4	PA exposure baseline to T2	Insufficiently active	36.4
	Sufficiently active	62.6		Sufficiently active	63.6
BC subtype	Hormone receptor + HER2 +	87.2	BC stage	I	49.8
		14.8		II/III	50.2
BC surgery	Mastectomy	26.6	Receipt of CT	Yes	54.0
	Partial surgery	73.4		No	46.0
Receipt of ET	Yes	80.8	Type of ET	Tamoxifen ^o	35.5
	No	19.2		Aromatase Inhibitor ^o	64.5

CT= Chemotherapy; ET= Endocrine therapy; ^o± aLHRH

Fig. 2. Prevalence of overweight/obesity



2. Definition of risk groups for overweight/obesity: Multivariate Group-Based Trajectory Modeling showed that 49.0% of pts, the **high risk group (1)**, had a very high overtime risk of being overweight/obese: % of risk was 91.0% at baseline, 97.8% at T1, and 97.7% at T2. This group includes most women who were already overweight/obese at baseline, and who remained so over time (Fig. 3). Among the remaining 51.0% of women, the **low risk group (2)**, risk of overweight/obesity increased from 2.9% at baseline to 4.1% at T1, to 7.7% at T2.

Analysis of characteristics defining membership to risk groups: Several baseline characteristics were associated with higher likelihood of belonging to the high vs low risk group of overweight/obesity (Table 2). After entering exposure to PA into the model as a continuous time-dependent covariate, we observed a significant interaction between scores of PA and shape of the trajectory of risk, both in the high (p=.0001) and low (p=.001) risk groups (Fig 3).

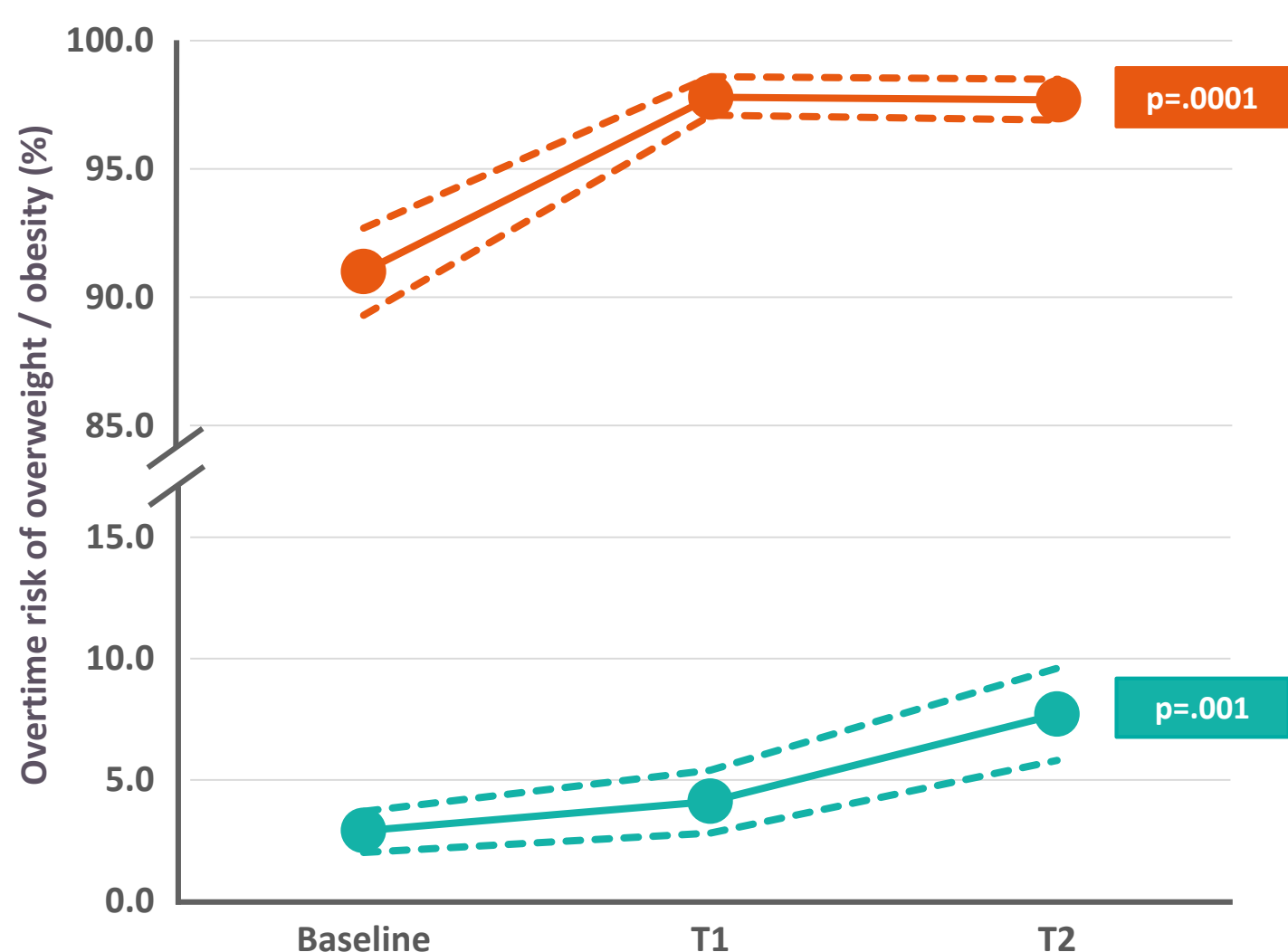


Fig 3. Overtime risk of overweight/obesity

- (1) High risk group for overweight/obesity= 49.0% of pts
- (2) Low risk group for overweight/obesity= 51.0% of pts

Continuous lines= estimate for the risk
Dotted lines= 95% Confidence limits for the estimates

p values indicate significance of the interaction between physical activity [entered as continuous time-dependent covariate] and trajectory shape

Table 2. Characteristics associated with membership to high vs. low risk of being overweight/obese. Odds ratios (OR [95% CI]) adjusted for all listed factors + smoke, receipt of CT and ET.

Age (continuous, for each 5-year increase)	1.10 (1.05-1.16)
Pre vs postmenopausal	0.75 (0.64-0.92)
Primary school vs high school/college	2.25 (1.86-2.72)
Breast Cancer stage I vs II/III	0.63 (0.54-0.74)
Mastectomy vs partial surgery	0.80 (0.69-0.94)

3. Weight gain after BC: Overall, mean weight was **68.2 Kg (range 38.0-153.0)**. **16.9% and 24.0% of pts gained ≥5% of baseline weight by T1 and T2, respectively.** Factors associated with increased odds of weight gain are reported in Table 2 (similar results from sensitivity analyses, data not shown).

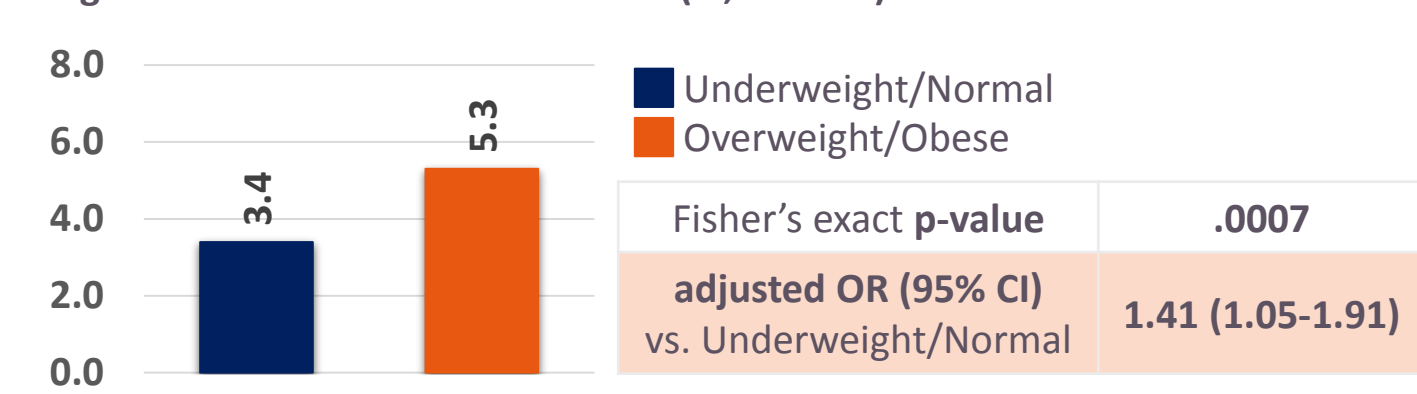
Table 2. Characteristics associated with weight gain at T1 and T2. *Adjusted for characteristics in Table 1 + baseline BMI, alcohol, axillary surgery, and radiotherapy. **Also adjusted for weight gain at T1. ^categorized as defined in methods. Bolded results are statistically significant (p<.05).

Characteristic	Variable	Level	T1 (n=4879)			T2 (n=4687)		
			% pts gaining weight	Mean n. Kg gained	OR* (95% CI)	% pts gaining weight	Mean n. Kg gained	OR** (95% CI)
Total	-	-	16.9	+6.1	-	24.0	+6.6	-
Age at diagnosis		<50 years	24.8	+6.5	2.48 (1.65-3.73)	35.5	+7.1	1.98 (1.28-3.06)
		≥50 and <65 years	16.6	+5.8	2.04 (1.50-2.75)	23.6	+6.3	1.95 (1.45-2.64)
		≥65 years	8.2	+5.7	Ref.	11.3	+5.9	Ref.
Depression, HADS		For each 1-point increase	-	-	1.03 (1.01-1.06)	-	-	1.03 (1.01-1.07)
		BC surgery	Mastectomy	19.4	+6.1	1.06 (0.84-1.34)	28.3	+6.8
		Partial surgery	16.0	+6.1	Ref.	22.4	+6.5	Ref.
		Receipt of CT		Yes	20.7	+6.3	1.30 (1.03-1.65)	29.0
No	12.4			+5.7	Ref.	18.1	+6.2	Ref.
Receipt of ET		Yes	16.5	+6.1	1.19 (0.78-1.82)	23.8	+6.6	1.29 (0.99-1.67)
		No	18.7	+6.0	Ref.	24.7	+6.5	Ref.
PA exposure [^]		Insufficiently active	16.4	+6.2	0.98 (0.81-1.18)	25.5	+6.9	1.24 (1.01-1.52)
		Sufficiently active	16.7	+6.0	Ref.	22.0	+6.3	Ref.
Weight gain at T1		For each 1-Kg gained	-	-	-	-	-	1.56 (1.50-1.62)
		For each 6-Kg gained	-	-	-	-	-	14.41 (11.39-18.07)

4. Overweight, obesity and cancer recurrence: At ~2 years post initial BC diagnosis, 221/5098 recurrence events were observed, including local (n=30), nodal (n=28), distant (n=131) BC recurrences, and second cancers (n=85) (total n not adding up to 221 due to pts experiencing ≥1 type of cancer recurrence).

Pts who were overweight or obese at the time of BC diagnosis had higher odds of any recurrence as compared to those who were underweight/normal (Fig. 4; OR from logistic regression is adjusted for age, menopausal status, BC stage, subtype, and grade, type of BC and axillary surgery, and receipt of CT and ET).

Fig 4. Cancer recurrence rates at T2 (%; n=5098)



Conclusions

In this large prospective epidemiological study, **almost half of French BC survivors were already overweight or obese at the time of BC diagnosis**, and had an increasingly higher risk of remaining so over time.

Up to 1 in 4 pts gained substantial weight by year-2 after BC diagnosis, gaining up to 7.1 Kg. Women who were younger, those with higher baseline depression scores, those who were insufficiently physically active, and those who had already gained weight by year-1 had significantly increased odds of weight gain by year-2. Receipt of CT was strongly associated with weight gain, whereas a trend was present among pts receiving ET for ≥1 year.

Despite being overall low, **recurrence rates 2 years post BC diagnosis were significantly higher among overweight/obese vs. underweight/normal pts.** This study contextualizes the problematic of overweight, obesity, and weight gain after BC in the setting of survivorship care in Europe, pointing at an area in urgent need of improvements. Our data will inform dedicated and pragmatic weight control and weight loss interventions targeting BC survivors.

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