Weight loss, physical and psychological patient reported outcomes (PROs) among obese patients (pts) with early breast cancer (BC)

A. Di Meglio[1], M. El-Mouhebb[1], S. Michiels[1], L.W. Jones[2], E. Martin[1], M. Matias[1], A.E. Lohmann[3], F. Joly[4], L. Vanlemmens[5], S. Everhard[6], A.L. Martin[6], J. Lemonnier[6], P. Arveux[7], P.H. Cottu[8], C. Coutant[7], L. Del Mastro[9], A.H. Partridge[10], F. André[1], J.A. Ligibel[10], I. Vaz-Luis[1]

[1]Institut Gustave Roussy, Villejuif, FR, [2]Memorial Sloan Kettering Cancer Center, New York, US, [3]University of Toronto, Toronto, CA, [4]Centre Francois Baclesse, Caen, FR, [5]Centre Oscar Lambret, Lille, FR, [6]UNICANCER, Paris, FR, [7]Centre Georges-François Leclerc, Dijon, FR, [8]Institut Curie, Paris, FR, [9]Ospedale Policlinico San Martino, Genova, IT, [10]Dana-Farber Cancer Institute, Boston, US

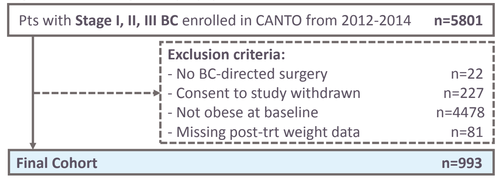
Background

- **Study rationale:** Obese individuals are at risk for several serious and potentially life-threatening conditions, such as hypertension, diabetes, sleep apnea, and coronary heart disease.[a] Obesity is also linked to other physical and psychosocial concerns, including poor physical functioning, reduced capacity for physical activity, increased chronic fatigue, dyspnea, diminished sexual functioning, poor body image, and depression.[b,c] Only few data is available about the relationship between obesity and quality of life in BC survivors, and there is little information about the impact of weight loss on PROs in survivors treated for early BC.
- **Objectives:** To examine the association between weight change after BC diagnosis and PROs among obese 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 pts by end of 2018). Updated information from 5801 pts was accessed (07/2018 data lock) (**Fig. 1**). For this analysis, we used data collected at BC diagnosis (baseline) and during the first post treatment (trt) reassessment, which occurred at a median (interquartile range [IQR]) time of **10.5 months (7.8-12.5 months).**
- **Study variables: 1. Independent variable:** weight change from baseline to post-trt, defined as weight gain (≥+5%), stable weight (±5%), and weight loss (≥-5%). **2. Outcomes of interest: a) Prevalence of poor and severe PROs at baseline and post-trt**, defined by a score <60 on functional scales or ≥40 on symptoms scales of European Organization for Research and Treatment of Cancer Quality of Life questionnaire (EORTC-QLQ) C30/B23, respectively; **b) Change in PROs status from baseline to post-trt**, defined as the proportion of pts transitioning from reporting non-poor functions and non-severe symptoms at baseline to reporting poor functions or severe symptoms post-trt; **c) Prevalence of deterioration of PROs from baseline to post-trt**, defined as reduction/increase ≥10 points on functional/symptoms scales of EORTC-QLQ, respectively. **3.Covariates:** demographic, clinical, tumor and trt characteristics (**Table 1**).
- **Statistical analysis:** Multivariate logistic regression examined associations of weight change with a) prevalence of poor and severe PROs, b) change in PROs status, and c) deterioration of PROs.
- **References:** [a]James WP, 1998; [b]Mond JM, 2009; [c]Chan DSM, 2014.

Fig. 1. CONSORT diagram of pts population



Results

Table 1. Cohort characteristics by weight change from baseline to post-trt; n=993.

Characteristic (% pts)	Gain ≥+5% n=140 (14.1%)	Stable ±5% n=668 (67.3%)	Loss ≥-5% n=185 (18.6%)	p*
Age, mean (SD)	52.4 (10.8)	59.3 (10.5)	58.0 (9.2)	**<.0001**
Charlson score ≥1	28.3	31.5	31.5	.771
Partnered	16.4	25.6	29.9	**.026**
College degree	21.1	21.4	30.2	.167
Active smoker	20.4	9.6	8.2	**.001**
Decreased PA	46.5	40.4	30.6	**.014**
Receipt of CT	60.0	47.0	72.4	**<.0001**
Receipt of ET	75.0	86.1	80.5	**.003**

*Kruskal-Wallis test for continuous and χ^2 test for categorical variables.

- **1. Cohort characteristics:** Obese pts included in this cohort (n=993) represented ~19.3% of the overall CANTO population.
- Mean age was 59.1 years (range 27.0-87.0), mean baseline weight was 89.4 Kg (range, 61.0-153.0) and mean baseline BMI was 34.5 Kg/m^2 (range 30.0-59.0). Charlson comorbidity score was ≥1 among 31.1% and ≥2 among 12.2% pts (max score=7). 79.5% pts had HR+/HER2-, 12.8% HR±/HER2+,and 7.6% HR-/HER2- BC.
- Between BC diagnosis (baseline) and post-trt, 14.1% pts gained weight, 67.3% remained stable, and 18.6% lost weight. **Table 1** displays pts characteristics by weight change category: pts who lost weight tended to be older, partnered, and non-active smokers and fewer among them reported to have decreased PA from baseline to post-trt compared to those who gained weight (CT=chemotherapy, ET=endocrine therapy; at this follow-up time, 53.6% pts had received CT and 83.5% pts were on ET for a median of 4.2 months [IQR 2.9-5.4] overall).

- **2. Prevalence of poor and severe PROs at baseline and post-trt:** Prevalence of poor functions and severe symptoms increased from baseline to post-trt across all domains of EORTC-QLQ C30/B23, with the exception of emotional function (**Fig. 2A**) and was highest in pts who gained weight between baseline and post-trt (**Fig. 2B**).
- In multivariable models, women whose weight remained stable and those who lost weight appeared to be less likely to report poor functions or severe symptoms compared to those who gained weight with respect to all outcomes explored (**Table 2**).
- A loss of 5% of baseline weight (18.6% pts) significantly reduced odds of poor post-trt global health, poor physical and role function, severe pain and dyspnea vs. 5% weight gain (14.1% pts, **Table 2**).
- In addition, in sensitivity analyses, (1) a loss of at least 10% of baseline weight (7.2% pts) was significantly associated with reduced odds of reporting poor post-trt body image (adjusted OR [95%CI]= 0.24 [0.06-0.98]) compared to a 10% increase in weight (3.1% pts), and (2) consistent results were obtained where weight change was modeled as a continuous variable (data not shown).

Table 2. Adjusted* Odds Ratios (95% CI) of poor/severe PROs by 5% Weight Changes (vs. Weight Gain [ref.] - 14.1% of pts); n=993.

Domain/Scale	Stable Weight - 67.3%	Weight Loss - 18.6%
Global Health	0.82 (0.49-1.36)	**0.45 (0.24-0.86)**
Physical Function	**0.45 (0.24-0.83)**	**0.37 (0.17-0.79)**
Emotional Function	0.80 (0.47-1.38)	0.53 (0.27-1.04)
Social Function	0.71 (0.38-1.32)	0.45 (0.19-1.03)
Role Function	0.64 (0.37-1.13)	**0.48 (0.23-0.99)**
Fatigue	0.93 (0.56-1.53)	0.76 (0.41-1.39)
Pain	**0.55 (0.33-0.92)**	**0.34 (0.18-0.65)**
Insomnia	0.75 (0.45-1.25)	0.61 (0.33-1.16)
Dyspnea	**0.45 (0.25-0.80)**	**0.21 (0.09-0.48)**
Body Image	0.66 (0.37-1.15)	0.55 (0.28-1.10)
Side Effects	0.71 (0.34-1.32)	0.67 (0.31-1.44)
Arm Symptoms	0.85 (0.51-1.52)	0.79 (0.42-1.48)

*adjusted for baseline characteristics in Table 1 + baseline BMI, type of BC and axillary surgery, anxiety/depression scores, and baseline level of the outcome

Fig 2A. Prevalence (%) of poor/severe PROs at baseline and after trt

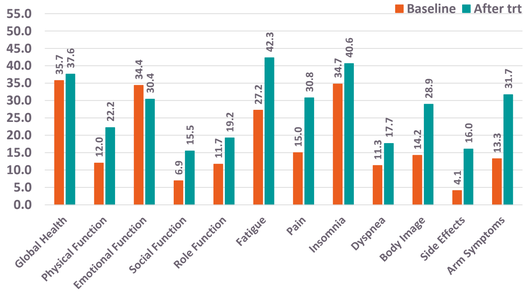
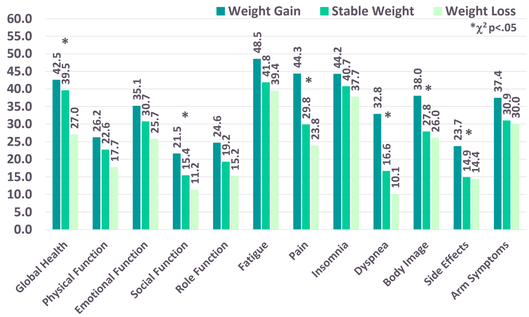
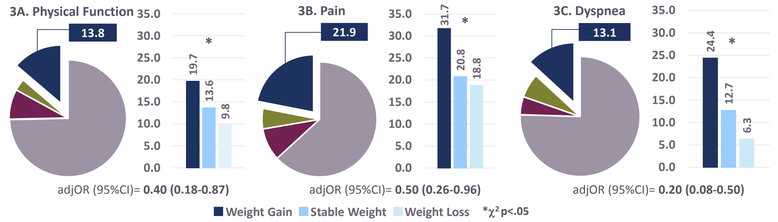


Fig. 2B. Distribution (%) of pts reporting poor or severe PROs after trt by weight change



- **3. Change in PROs status:** 13.8% pts that had not reported poor physical function at baseline did report so after trt. Accordingly, 21.9% and 13.1% pts that had not reported severe pain or dyspnea at baseline did report so after trt, respectively. Pts that lost weight between baseline and post-trt had lowest rates and significantly reduced odds of transitioning from non- to poor/severe status over the same period vs. those gaining weight (**Fig. 3A-C**).

Fig. 3. % of pts transitioning from non-poor to poor physical function (4A), from non-severe to severe pain (4B), and from non-severe to severe dyspnea (4C) between baseline and post-trt, and respective distribution (%) by weight change. OR (95% CI) for weight loss vs. gain (adjusted).



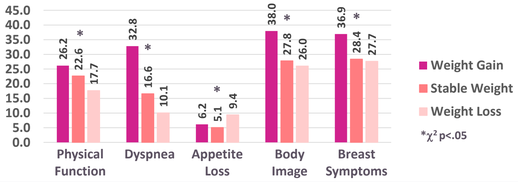
- **4. Deterioration of PROs from baseline to post-trt:** A considerable proportion of pts experienced significant deterioration in PROs from BC diagnosis to post-trt , including 40.6% pts reporting deterioration of physical function, 35.3% of dyspnea, 39.8% of body image, and 56.4% of breast symptoms (**Fig. 4A**). Deterioration rates were highest among women who gained weight (**Fig. 4B**). In multivariable models, women who lost weight had significantly reduced odds of deterioration of physical function, dyspnea and body image vs. those who gained weight (**Table 4**). Odds of reducing appetite were highest among those who lost weight (**Fig. 4** and **Table 4**).

Table 4. Adjusted Odds Ratios (95%CI) of deteriorated PROs by Weight Change (vs. Weight Gain [ref.] - 14.1% of pts); n=993.

Domain/Scale	Stable Weight (67.3%)	Weight Loss (18.6%)
Physical Function	**0.67 (0.42-1.04)**	**0.57 (0.32-0.99)**
Dyspnea	**0.67 (0.42-1.08)**	**0.34 (0.19-0.62)**
Appetite Loss	1.29 (0.64-2.60)	2.04 (0.93-4.49)
Body Image	**0.79 (0.49-1.29)**	**0.53 (0.29-0.97)**
Breast Symptoms	0.82 (0.50-1.36)	0.56 (0.30-1.02)

Fig 4A. Prevalence (%) of deterioration of PROs from baseline to post-trt

Fig 4B. Distribution (%) of pts reporting deteriorated post-trt PROs by weight change



Conclusions

- In this large cohort of obese BC survivors, **severe physical and psychological distress was very common and substantially increased** from BC diagnosis to the post-trt period, **with >1 in 3 pts reporting poor functional status or severe symptoms** in several domains.
- Weight loss between BC diagnosis and the first year afterwards was associated with the lowest rates of poor or severe PROs. **A loss as low as 5% of baseline weight**, corresponding to an average of ~4.5 Kg in this cohort, significantly **reduced the risk of reporting poor post-trt global health, poor physical and role function, severe pain and dyspnea**, and **a loss of at least 10%** reduced the risk of reporting **poor body image**. Vs. gaining weight, losing weight significantly **reduced the odds of** poor or severe post-trt PROs among pts with normal baseline status and those of **post-trt PROs deterioration**.
- A comprehensive approach to the care of obese BC survivors should address the burden of morbidity caused by obesity and by further post-trt weight gain. Weight loss may prevent physical and psychological deterioration occurring during the trt phase and over the first follow-up year, therefore **purposeful weight loss interventions** in the obese BC survivors population should be strongly encouraged.

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