Physical Activity (PA) and patterns of Quality of Life (QOL) after adjuvant chemotherapy (CT) for breast cancer (BC)

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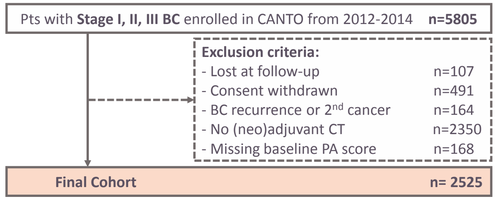
Background

- **Study rationale:** Side effects of BC and of CT may have a persistent negative impact on QoL of cancer survivors. PA was associated with improved BC-specific survival outcomes[a], overall QoL, and ability to function and perform daily activities[b]. The WHO recommends to achieve at least 10 Metabolic Equivalent of Task (MET)-hours/week of PA for healthy adults, and these levels were validated for cancer survivors by the American College of Sports Medicine[c]. Nevertheless, a significant portion of BC survivors remain insufficiently physically active.
- **Objectives:** To describe longitudinal patterns of QoL, define long-term trajectories of risk of having poor QoL, and explore their associations with PA among BC survivors treated with (neo)adjuvant CT.

Patients and Methods

- **Data source:** Prospective longitudinal cohort of patients (pts) with early BC treated since 2012 across 26 French cancer centers (CANcer TOxicities [CANTO]; NCT01993498). Pts that received (neo)adjuvant CT were selected for the present study (**Fig. 1**).
- **Variables of interest. 1.Independent variable:** PA exposure as per Global Physical Activity Questionnaire (GPAQ)-16. **2.Outcome variable:** QoL as per European Organization for Research and Treatment of Cancer QoL questionnaire (EORTC-QLQ) C30. **3.Covariates:** demographic, clinical, tumor and treatment characteristics (**Table 1**).
- **Schedule of longitudinal reassessments:** In this cohort, reassessments occurred at BC diagnosis (baseline) and at a median time [interquartile range, IQR]) of **12 months (11-13)** and **24 months (22-26)** post baseline.
- **Statistical analysis:** Longitudinal mixed-effect models analyzed overtime changes in QoL scores according to baseline level of exposure to PA (as per WHO recommendations: ≥10 vs. <10 MET-hours/week). Multivariate group-based trajectory modeling[d] assessed overtime risk of poor QoL (defined by a score <60 on functional scales [poor function] or ≥40 on symptoms scales [severe symptom] of EORTC-QLQ C30)[e]. Multivariate logistic regression examined factors associated with membership to specific risk trajectories. All models were adjusted for baseline characteristics and for PA as a time dependent covariate.
- **References:** [a]Ballard-Barbash R, 2012; [b]Mishra SI, 2012; [c]Demark-Wahnefried W, 2018; [d]Nagin DS, 2005; [e]Giesinger JM, 2016.

Fig. 1. CONSORT diagram of pts population



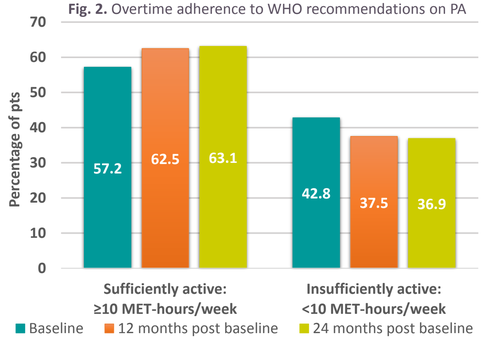
Results

- Selected baseline cohort characteristics are summarized in **Table 1**. Exposure of pts to PA over time by WHO recommendations is depicted in **Fig 2**.

Table 1. Baseline characteristic in the overall cohort (% pts; n=2525).

Age, mean (range), years	52 (22-85)	**Comorbidities** Charlson score ≥1	18.7
Health behaviors		**Social status**	
Body Mass Index ≥ 25	46.2	Married/With a partner	80.3
Active/Former smoker	41.6	Unemployed/On sick leave	65.2
Alcohol servings/day ≥1	12.8	Household income <2000 €	26.4
Tumor characteristics		**Treatment characteristics**	
Stage I	29.2	Total mastectomy	36.1
Grade 3	49.3	Axillary dissection	58.3
Hormone Receptor +	78.8	Anthracyclines + Taxanes	85.6
HER2 +	25.5	Radiation therapy	93.0
		Endocrine therapy	75.8

Fig. 2. Overtime adherence to WHO recommendations on PA

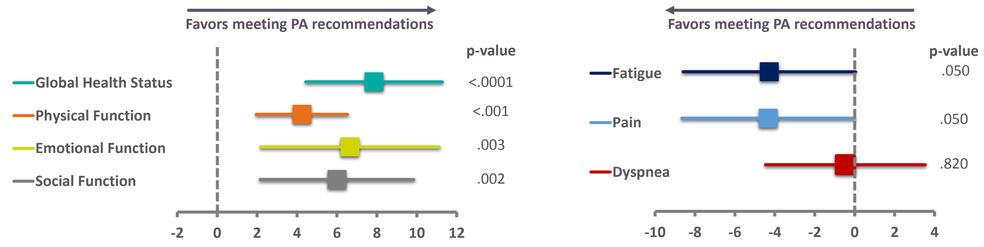


- Absolute mean QoL scores and mean changes over time by level of exposure to PA are displayed in **Table 2** and **Fig. 3**, respectively.

Table 2. Mean scores over time according to exposure to sufficient vs. insufficient levels of PA. Bolded values indicate statistically significant differences between sufficiently and insufficiently active pts (Wilcoxon rank sum test p<.05).

EORTC-QLQ C30	Baseline		12 months post baseline		24 months post baseline	
Domain	Sufficiently active	Insufficiently active	Sufficiently active	Insufficiently active	Sufficiently active	Insufficiently active
Global Health Status	**69.4**	**65.4**	**67.7**	**65.5**	**67.5**	**64.3**
Physical Function	**92.3**	**87.9**	**84.0**	**78.6**	**86.1**	**79.4**
Emotional Function	**64.7**	**62.2**	70.6	70.0	71.0	69.3
Social Function	**90.2**	**87.6**	78.3	78.3	**86.5**	**82.4**
Fatigue	**28.0**	**30.9**	**35.1**	**40.9**	**34.4**	**38.8**
Pain	**16.7**	**19.7**	**27.9**	**32.1**	**28.4**	**32.1**
Dyspnea	12.2	13.1	**20.0**	**24.1**	**19.7**	**23.5**

Fig. 3. Comparison of changes from baseline in QoL scores (sufficiently vs. not sufficiently active pts as per WHO recommendations) by repeated-measures mixed-effect model adjusted for baseline PA, time, baseline PA*time, and characteristics in Table 1 + menopausal and education status



- Pts seem to cluster in distinct trajectories of risk of poor QoL (**Fig. 4A, 4B, 4C**; continuous lines= estimated trajectory, dotted lines= 95% confidence limits of the estimates; p for interaction between PA [time-dependent, continuous] and trajectory shape). We report factors associated with membership to high risk of poor global health status in **Table 3** (similar associations for other domains, not shown) and % pts meeting PA recommendations by risk group in **Table 4**.

Fig. 4A. Risk of poor Global Health Status

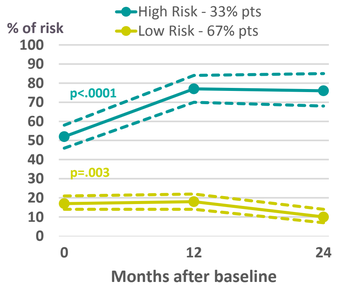


Fig. 4B. Risk of poor Physical Function

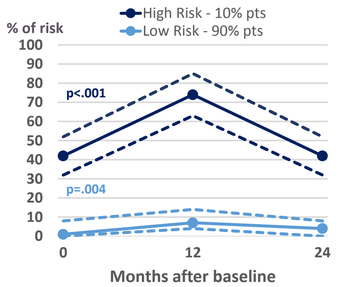


Fig. 4C. Risk of poor Emotional Function

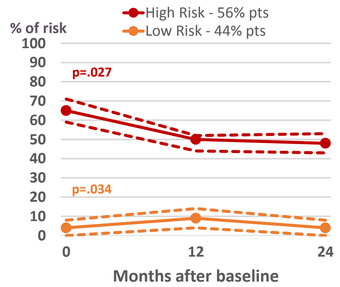


Table 3. Characteristics associated with membership to high risk vs. low risk trajectory of poor Global Health Status: OR (95% CI) adjusted for baseline characteristics in Table 1.

Charlson score ≥ 1 vs. 0	1.4 (1.1-1.9)
Household Income < 2000 € vs. ≥	1.6 (1.2-2.0)
Active/Former smoker vs. never	1.3 (1.1-1.6)
Total mastectomy vs. partial	1.2 (1.1-1.6)

Table 4. % pts meeting WHO PA recommendations and median (IQR) n. of MET-hours/week by trajectory of risk (follow color schema). *denotes significant by group differences (p<.001)

Global Health Status			Physical Function			Emotional Function		
Month 0	Month 12*	Month 24*	Month 0*	Month 12*	Month 24*	Month 0	Month 12	Month 24
56.3%	**57.8%**	**57.2%**	**42.9%**	**43.0%**	**40.3%**	**57.0%**	**62.0%**	**61.7%**
13 (0-40)	**14 (0-34)**	**12 (0-34)**	**4 (0-28)**	**8 (0-28)**	**4 (0-24)**	**14 (0-42)**	**16 (2-39)**	**15 (4-40)**
57.6%	**64.6%**	**65.8%**	**58.5%**	**64.1%**	**65.2%**	**57.0%**	**62.7%**	**63.9%**
13 (0-40)	**16 (4-40)**	**18 (6-42)**	**14 (0-40)**	**16 (4-40)**	**17 (5-40)**	**13 (0-38)**	**16 (4-40)**	**16 (4-40)**

Conclusions

- More than **1/3 of pts would not engage in ≥ 10 MET-hours/week of PA** after BC diagnosis, therefore not meeting WHO recommended PA levels.
- In this CT-treated population, there is **worsening in QoL across most domains** after BC diagnosis, persisting for over 24 months.
- Pts **achieving ≥ 10 MET-hours/week of PA** have **better mean scores** in several QoL domains over time as compared to those who do not.
- There are clusters of pts that follow **trajectories characterized by high risk of poor QoL after BC**, particularly those with comorbidities or lower income, smokers, and those receiving mastectomy. **Exposure to PA seems to significantly interact with these trajectories and to be able to modulate this risk.**
- Pts who meet WHO recommendations on PA (≥ 10 MET-hours/week) appear to **cluster preferentially** in trajectories at lower risk of poor QoL, particularly of poor global health status and poor physical function.
- The utilization of several analytic methods including exploratory clustering techniques allowed the **identification** of BC pts whose QoL will be worst affected by CT and who are **most suitable** for **dedicated interventions**, including those aimed at **increasing exposure to PA during the survivorship period**.

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