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WEIGHT CONTROL AND OBESITY REDUCTION THROUGH DIET AND PHYSICAL ACTIVITY INTERVENTION IN BREAST CANCER SURVIVORS

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1. Summary of the project

The main purpose of our study is to assess the effect of a lifestyle intervention combining diet and physical activity on the weight change of breast cancer survivors, immediately after completion of the intervention, and one year after the intervention. As secondary objectives we aim to assess whether the proposed intervention may induce changes in body size and body composition, and in quality of life.

The study design proposed to achieve these objectives is a multicentre randomized controlled trial aimed to include 1000 women (500 per arm), aged 18-75 years, diagnosed with a non-metastatic breast cancer in the participating centers, after completion of the standard treatment. Participants will be assigned to either an intervention or a control group and followed for two years. Patients assigned to the control arm will continue with the usual care, including standard guidelines for weight control applied in the center. Patients in the intervention group will be involved in a 1-year lifestyle program with two components. The dietary part will aim to achieve a calorie reduction while maintaining nutritional quality; the physical activity part will include supervised sessions of moderate intensity. Data will be analyzed on an intention to treat basis using analysis of covariance.

Goals (general and specific) of the project:
The **specific aims** of the study are:

Main objective:
(1) To assess the effect of a 1-year lifestyle intervention combining diet and physical activity on the weight change of breast cancer survivors, immediately after completion of the intervention, and one year after the intervention (2 years after randomization). The purpose of the intervention is the maintenance of weight of women initially within the normal range of BMI, and achieving a clinically meaningful weight loss, defined as a ≥5% weight reduction as compared with the baseline measurement, among women with initial BMI ≥25 kg/m^2.

Secondary objectives:

(2) To assess whether the proposed intervention may induce changes in body size and body composition, determined by the following parameters: waist circumference, waist-to-hip ratio, and the percent of fat mass.

(3) To assess whether the proposed intervention is able to induce changes in quality of life.

Other objectives:

(4) To collect, process, and store blood samples from all patients. The blood samples can be used to assess changes in biomarkers related with the obesity and overweight, diet, physical activity, and the underlying biological mechanisms of weight change.

Brief synthesis of the design, procedures, and methods:

Design: Randomized Clinical trial (RCT).

Patients: women aged <76 years with a non-metastatic primary breast cancer (ICD-O C50, stages I, II, IIIA), diagnosed in the participating centres within the 3 months after completion of the standard treatment.

Randomization: random assignment to the intervention or the control (minimal intervention) group.

Collection of baseline information: anthropometric measurement (weight, height, bio-impedance, skin folds); cardio-respiratory fitness test (only in the intervention group); blood sample collection; assessment of usual diet (SUN questionnaires and 3x24h-recalls); assessment of physical activity (7-day accelerometer measurements); assessment of functional capacity (6-minutes walk test); assessment of quality of like (questionnaires SF-36, HADS, FACIT); assessment of lifestyle habits and reproductive history.

Intervention:

- Intensive phase: dietary sessions, 1-hour/week and 2 session (75 minutes each)/week of supervised physical training during 6 months.
- Semi-intensive phase: dietary sessions, 1-hour/month and 2 sessions (75 minutes each)/month of supervised physical training during 6 months; two further sessions of diet and supervised physical training will be performed during the year following the completion of the intervention.

During this period, the control group receives the usual recommendations for oncological patients.

Information collected during intervention and follow-up: The anthropometric measurements and the functional capacity (6-minutes walk test) will be assessed at 6 months. All the measurements collected at baseline (unless the CRF test, SUN questionnaire FFQ) will be collected at 12 months, immediately after completion of the intervention.
Outcome assessment: every 6 months we will measure the following anthropometric measurements: weight, height, waist and hip circumferences, body composition (via bioelectrical impedance analysis) and skin folds measurements.

2. Results

Right now, we do not have complete data to carry out an analysis to assess the objectives initially proposed. Therefore, no results have been presented at conferences, symposia, or scientific conferences, and obviously we do not have publications of the project in scientific journals either.

For several reasons explained in the final report the pace of patient recruitment was slower than expected. Although additional resources were allocated, these were insufficient and had little impact. The follow-up of recruited patients, as well as most research activities, was also completely halted in early 2020 owing to the Covid-19 pandemic. We finally closed the study with 620 patients. With the work being completed this year, we will be able to have complete data for analysis of these patients.

However, it is important to remember that, although the total number of patients included in the project is lower than initially proposed, the available data will make it possible to respond validly to the main and secondary objectives proposed in the project. Regarding the measure referring to the main objective (weight control) it was estimated that a weight reduction of 5% can be detected as significant in the intervention group with respect to control with 154 patients (77 per group) with a statistical power of 80% and an α error of 5%. This number is increased to 206 (103 per group) if the same difference is to be detected with a power of 90%. Therefore, the number of patients reached is sufficient even for subgroup analyses, such as comparisons restricted to pre- or post-menopausal women, or based on their baseline

BMI, or according to the characteristics of tumor such as stage diagnosis or type of treatment.

3. Relevance and possible future implications

As mentioned above, no results of the project are available yet. However, the expected results if our hypothesis holds true, should serve as a basis for modifying clinical practice in the management of non-metastatic (stages I to IIIa) breast cancer survivors. These patients, once they have completed their standard oncological treatment (including surgery, radiotherapy and/or chemotherapy) can also follow hormonal or immunotherapy treatment depending on the molecular characteristics of the tumor. We suggest that nutritional and physical activity support should be routinely incorporated into the management of these patients to achieve an integral approach. Although this approach should focus primarily on overweight and/or obese patients, it can be addressed to all women, including those with a BMI in the normal range, by customizing the type of intervention. This complementary therapeutic approach must be carried out by qualified and specifically trained personnel. In future studies we may consider that the onset of this nutritional and exercise support may begin during treatment, without the need to wait for the completion of radiation and / or chemotherapy, as is already being done in other countries. Finally, in addition to the empirical evidence, we also aim to provide clues for the interpretation of biological mechanisms; therefore, we will develop proposals for new projects based on blood samples collected immediately before and after the intervention of the study participants.

4. Scientific bibliography derived from the project

As previously specified, no results are yet available for publication.