Effect of Pre-Treatment Combined Training on the Metabolomic Profile of the Tumor in Women with Breast Cancer: A Pilot Study

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Introduction: Breast cancer is the most common type of cancer and has the highest mortality rate among women in Brazil. On the other hand, studies have shown that engaging in physical training can enhance the effectiveness of cancer treatment and consequently reduce mortality. Physical training, especially combined training (CT) (strength and aerobic), is a promising intervention as it seems to modulate inflammatory and metabolic pathways related to the tumor, reducing its aggressiveness. Despite these indications, no study to date has investigated how CT affects tumor metabolism. Omics approaches, through metabolomic analysis, can aid in understanding metabolic pathways related to the positive effects of CT on tumors. Objectives: To determine the effect of CT performed between breast cancer diagnosis and the beginning of treatment on the metabolomic profile of the tumor in patients diagnosed with breast cancer. Methods: This pilot study sample consisted of 3 patients, with two presenting the luminal B subtype and one presenting the HER-2 positive subtype. On average, 11 CT sessions were performed, consisting of strength training (five exercises, three to four sets of 8 to 12 repetitions) and aerobic training (high-intensity interval training (HIIT) performed on a cycle ergometer, with two to five sets of two minutes at 25-50% of the load between the respiratory compensation point (RCP) and maximal aerobic power (MAP), interspersed with two minutes of active recovery at 20% of the RCP. Two breast biopsies were performed, one before (pre) and one after (post) the CT intervention period, with an average weight of 18.71 ± 9.41 mg. For metabolomic analysis, liquid chromatography coupled with mass spectrometry (LC-MS) was used. Results: Sixty-one metabolites were identified, of which seven biomarkers of the human metabolome were quantified: MG(20:1), nonadecanedioic acid, 5,9-Hexacosadiene, 3-Methoxytyrosine, phenol sulfate, 15-Di-hydroxyeicosatrienoic acid, and Actinioerythrol. The relative concentration of the metabolites MG(20:1), nonadecanedioic acid, 5,9-Hexacosadiene, 3-Methoxytyrosine, phenol sulfate, and 15-Di-hydroxyeicosatrienoic acid was significantly lower post-CT compared to pre-CT, while the relative concentration of actinieroeurythritol was relatively higher. Discussion: CT was effective in reducing the relative concentration of metabolites in tumor tissue after the intervention. The metabolites phenol sulfate, MG(20:1), and 15-Di-hydroxyeicosatrienoic acid are involved in inflammation and metabolic changes associated with cancer cell reprogramming. However, some compounds found are not described in the literature concerning cancer. Conclusion: There was a significant decrease in the metabolites MG(20:1), nonadecanedioic acid, 5,9-Hexacosadiene, 3-Methoxytyrosine, phenol sulfate, and 15-Di-hydroxyeicosatrienoic acid, and a significant increase in the metabolite Actinioerythrol after the CT intervention. These results are promising, as the significant reduction of metabolites linked to inflammation and cancer cell reprogramming, along with the increase of a metabolite with antioxidant properties, suggests the presence of biomarkers that may reflect the effectiveness of CT as an ally in cancer treatment.

Agradecimentos: We would like to express our sincere gratitude to FAPESP (São Paulo Research Foundation) for the essential financial support provided through the FAPESP Young Researcher project 2021/01424-5 and the research grant with process number 2023/02510-8. Our gratitude also extends to CEMICAMP (Center for Research in Reproductive Health of Campinas) and CAISM

(Center for Comprehensive Women's Health Care) for the infrastructure and technical support provided, which were crucial for the development of this research. We thank all collaborators and institutions involved for their commitment and valuable contributions.