Impact of Intermittent Fasting on Biomarkers of Inflammation and Health-Related Quality of Life: A Feasibility Trial for Women with HR+/HER2- Early Breast Cancer

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Background

- Within one year of starting adjuvant endocrine therapy (AET), the majority struggle to return to pre-cancer weight
- At least 25-30% of women report a weight gain of ≥ 10 pounds[1,2]
- Post-treatment weight gain and increased BMI are linked to long-term sequalae such as CV disease, diabetes, QoL & psychosocial concerns, increased risk of cancer recurrence[3-7]
- Obesity is considered a pro-inflammatory state as evidenced by the decrease in adiponectin (anti-inflammatory) and elevation in inflammatory and metabolic markers[8,9]
- Prior studies have explored various diet and exercise interventions to address obesity and weight gain during AET, however their sustainability remains to be a challenge
- The Intermittent Fasting (IF) Study is a Phase II, single-arm feasibility trial evaluating the impact of intermittent fasting (IF) on biomarkers of inflammation and the Functional Assessment of Cancer Therapy-Endocrine Symptoms (FACT-ES) in women with ER-positive and HER2-negative breast cancer who are starting AET

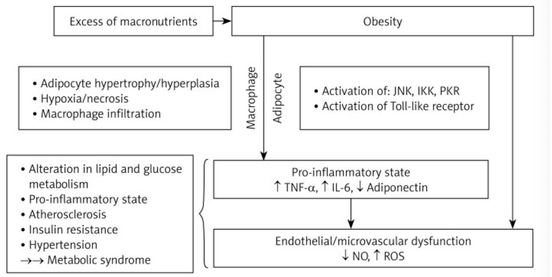


Figure 1. Mechanisms linking obesity and metabolic syndrome via inflammatory mediators.

What is Intermittent Fasting?

- Prior studies have shown that practicing time-restricted eating (TRE) has led to a decrease in several inflammatory and metabolic markers, leading to tangible improvements in CV risk and fat mass
- **Intermittent fasting (IF)**, is a type of TRE
  - Eating during a limited amount of hours and fasting at night
  - Most feasible: 10 hours of eating & 14-16 hours of fasting

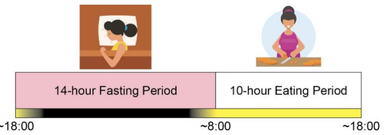
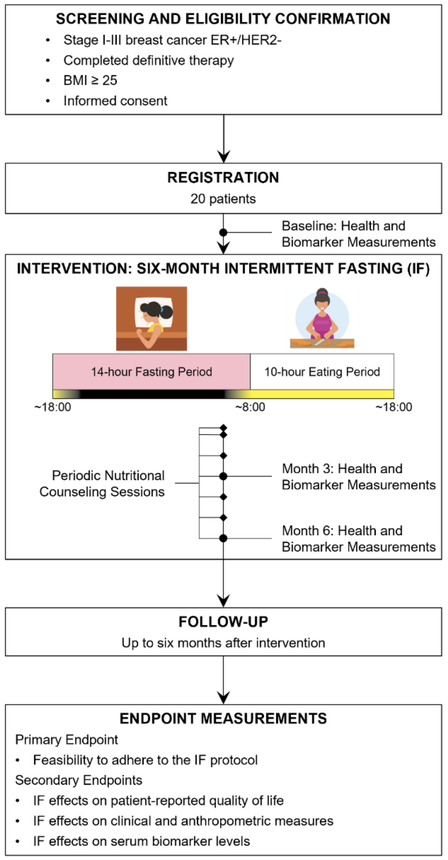


Figure 1. Daily recurring intermittent fasting intervention schema.

Methods

- Eligibility criteria:
  - Breast cancer patients ≥ 18 years old
  - Diagnosis of ER+ and HER2- localized breast cancer (Stages I-III) who completed definitive surgery +/- chemotherapy and radiation
  - BMI ≥ 25
  - ECOG performance status 0-2
  - Start intervention within 3 months of starting AET
- Exclusion criteria: history of diabetes, other diseases with fluctuation in blood sugar, dizziness, vertigo, pregnancy, breastfeeding, heavy alcohol use
- Using linear mixed-effects models, a total of 20 subjects to be accrued over 36 months

Study Schema



The Intervention

- Six-month IF regimen:
  - 14 hr nightly fasting period after dinner followed by
  - 10 hr eating period with the last meal occurring between 17:00 (5:00 pm) and 21:00 (9:00 pm)
- Nutritional counseling & assessments:
  - Meet with a dietician every other month
  - Maintain a diary and record
- Anthropometic measures, FACT-ES surveys, and biomarkers will be collected at baseline and 6 months

Biomarkers	
IGF	C-reactive Protein (CRP)
IL-6	Glycosylated Hemoglobin
Glucose	Fasting lipids
Adiponectin	ChIP-seq of H3K4me1, H3K27ac, and RNA-seq
Insulin	

Table 1. Biomarkers collected at baseline (month 0) and month 6.

Endpoints

- Primary objective: evaluate proportion of subjects who adhere to at least 80% of the IF instructions
  (follow the schedule on average 8/10 days)
- Secondary endpoints:
  - Anthropometic measures
  - FACT-ES surveys
  - Biomarkers
- The study was approved on May 16th, 2024 and enrollment began on July 31st, 2024
- At the time of submission, a total of 81 patients had been prescreened, with 13 consenting (8 accrued)

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