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[Carmen Vega](#) , [Esteban Barnafí](#) , César Sánchez , Francisco Acevedo , Benjamin Walbaum , [Alejandra Parada](#) , Nicolás Rivas , [Tomás Merino](#) *

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Article

Calorie Restriction and Time-Restricted Feeding: effective interventions in overweight or obese patients undergoing radiotherapy treatment with curative intent for cancer

Carmen Vega ¹, Esteban Barnafi ², César Sánchez ³, Francisco Acevedo ³, Benjamin Walbaum ³, Alejandra Parada ⁴, Nicolás Rivas ² and Tomás Merino ^{1,*}

¹ Cancer Center UC, Red de Salud Christus-UC, Santiago 8330032, Chile

² Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago 8331150, Chile

³ Department of Hematology-Oncology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago 8330077, Chile

⁴ Department of Health Sciences, Nutrition and Dietetics Program, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago 78204360, Chile

* Correspondence: tomasmerinolara@gmail.com

Abstract: Breast and prostate cancer lead incidence rankings in Chile, with obesity and overweight as important risk factors involved in prognosis. Nutritional interventions have shown to be beneficial therapies in patients with cancer, improving anthropometric and biochemical measurements. This study investigates the feasibility and effectiveness of Calorie Restriction and Time-Restricted Feeding in overweight or obese patients undergoing curative radiotherapy for breast and prostate cancer. The research was conducted as a prospective, interventional, non-randomized clinical trial, involving 27 participants, of whom 23 completed the study. Findings indicate that both interventions are feasible and effective. Notably, Time-Restricted Feeding demonstrated superior adherence and more significant improvements in weight loss and metabolic parameters. A mean weight reduction of 3.6 kg and waist circumference decrease of 4.9 cm was observed across participants. Serum levels of glucose, insulin, LDL, HDL and TG showed an average reduction, indicating positive metabolic changes. Results suggest that Time-Restricted Feeding could be a superior beneficial dietary intervention for cancer patients undergoing radiotherapy, due to its ease of adherence and positive impact on metabolic health. This research contributes to the growing evidence on the role of nutritional interventions in cancer treatment and underscores the need for more extensive studies to validate these findings.

Keywords: intermittent fasting; cancer; curative; radiotherapy; calorie restriction; time-restricted feeding; diet; nutrition; overweight; obese

1. Introduction

In the last decade, cancer and cardiovascular diseases have established themselves as the first cause of morbidity and mortality collectively, with over 18 million new cases of cancer being registered only in 2020 [1]. These pathologies share common risk factors such as sedentary lifestyle, poor diet, obesity, tobacco and alcohol consumption [2]. Notably, overweight and obesity are modifiable risk factors present in 74.2% of the Chilean population [3], and are particularly impactful due to their implication in the origin of various types of cancer [4]. Breast cancer and prostate cancer are of significant interest as they lead the incidence of new cancer cases among Chilean women and men, respectively [1].

Due to the implication of weight and nutrition in incidence and prognosis in cancer [5 - 7], numerous nutritional interventions such as Calorie Restriction (CR), Ketogenic Diet (KD) [8] and Intermittent Fasting (IF) (defined in Table 1), have been investigated to elucidate their impact as beneficial therapies in cancer [9]. IF is one of the most frequently cited diet patterns in 2023 among

Americans aged 18 to 80 years according to the International Food Information Council survey [10]. CR is frequently applied in overweight people and, despite showing great results when applied in short-term duration (< 6 months), it tends to have a lot of difficulties with adherence when following it for extended periods of time [11].

Table 1. Nutritional interventions definitions and different approaches to IF [11]. In this study we analyzed CR and IF. Specifically, the Time Restricted Feeding (TRF) approach. We also define other approaches so the reader understands crucial differences between nutritional interventions and key aspects of the various approaches of IF.

Intervention	Approach	Definition
Intermittent Fasting		Periods of voluntary abstinence from food and drink [11]. There are various ways to approach IF. Most of them have no caloric restriction associated, or have caloric restriction for short periods of time.
	TRF	Fasting that requires limiting the consumption of calories to a window of time, typically between 4 and 12 h daily
	5:2	Two days per week, 24 hours each day, a very low calorie diet is applied.
	B2	Two large meals are eaten per day: breakfast between 06:00 a.m. and 10:00 a.m., and lunch between 12:00 p.m. and 04:00 p.m. No dinner.
Calorie Restriction		Nutritional intervention where the focus is in reducing energy intake, but keeping adequate nutrition [12]. In general, 10 - 30% of restriction is accepted as having beneficial effects and being tolerable [13, 14].
Ketogenic Diet		Diet primarily consists of high fat intake, moderate protein consumption, and low carbohydrate intake. The macronutrient distribution typically ranges from approximately 55% to 60% fat, 30% to 35% protein, and 5% to 10% carbohydrates [15].

The pathophysiological reasoning behind the effectiveness of these nutritional interventions has long been researched and explained [16 - 18]. There are preclinical studies that establish the impact from IF and CR on glucose regulation, resistance to stress and inflammation suppression [19]. Despite showing promising results in regression of tumor volume and radiosensitivity of tumors in mice preclinical models [20 - 23], clinical trials are a must to determine the effect of these interventions on patients with cancer [24]. Unfortunately, available evidence on this matter is lacking and even international guidelines (ACS, NCCN, ESPEN or ASCO) don't have a conclusive stance on their application [25 - 28].

The recommendations from these guidelines on breast and prostate cancer were reviewed and summarized in **Table 2**.

Table 2. Summary of recommendations from international guidelines. ACS (American Cancer Society). NCCN (National Comprehensive Cancer Network). ESPEN (The European Society for Clinical Nutrition and Metabolism). ASCO (American Society of Clinical Oncology).

ACS	Published in 2022. Focuses mostly on BMI, dietary patterns, specific food avoidance and physical activity.
NCCN	Published in 2022. Similar to ACS, it focuses mostly on BMI, dietary patterns, specific food avoidance and

	physical activity. No mention of intermittent fasting or caloric restriction at all in their guidelines.
ESPEN	Published in 2021. Does not recommend fasting unless there is evidence of a benefit.
ASCO	Published in 2022. Mentions intermittent fasting as an intervention, but refrains from recommending it as there is insufficient evidence and points to 5 systematic reviews. These reviews revised 177 articles, where only 7 talk about any kind of weight loss intervention and of these, 5 of them investigated short term fasting finding it to be well tolerated and having beneficial effects.

A 2020 literature review [29] found 9 clinical trials which focused on radiotherapy and a KD. These studies suggested that KD may have a beneficial effect, but the small numbers of patients in these cohorts, absence of control groups, and in 3 studies KD not being the only variable associated with response to RT, prevented them from drawing definitive conclusions.

A recent paper from June 2023 by Kalam et al. [30] synthesized results from 23 studies dating 2020 onwards where various methods of IF were used. Studies involving IF found rates of severe toxicity decreased. Those combining fasting and KD found it was well tolerated and decreased toxicity. Others investigating Fasting-mimicking Diets, a low-calorie diet that is low in protein and carbohydrates but high in unsaturated fat, found it increased ketone bodies and improved plasma glucose, but had variable compliance and conflict of interest. Lastly, TRF showed the highest degree of adherence, and helped decrease fatigue, improved visceral adipose tissue, whole-body fat mass, cardiometabolic outcomes, anxiety, and depression.

A systematic review on the impact of IF on breast cancer from January 2023 by Anemoulis et al. [31] which included studies from 2009 to 2021, failed to conclude there were beneficial effects from IF on Quality of Life (QoL), response after chemotherapy or an improvement on symptoms. They did, however, find that there could be a beneficial effect on chemotherapy related adverse effects based on markers of DNA and leukocyte damage but require further validation.

The lack of evidence in this area of research and variety of nutritional interventions make it so that it is often overseen and difficult to gauge their real impact. Important international guidelines published in 2021 and 2022, such as ACS and NCCN, have no dedicated space for IF, TRF or CR in the entirety of their guidelines, whereas ESPEN or ASCO group it together with other recommendations that, while they may have in common the modification of food intake, have different objectives and ways to implement.

In practice, many patients show interest in a dietary modification that could increase their chances of success in treatment. A recent study evaluating CR and radiotherapy in breast cancer patients found that up to 75% would be part of a CR study [32]. However, adherence to dietary interventions is variable, and can be explained by several reasons such as: depression, stress, previous weight loss attempts or negative perceptions of diet and exercise [33, 34]. On the other hand, regular and frequent attendance at nutritional controls, physical exercise, educational materials and feeling control over what they eat are factors that favor adherence [35, 36].

A prospective, interventional, non-randomized clinical trial was built. It assesses the feasibility and effectiveness of CR and TRF in patients with breast or prostate cancer, overweight or obese, undergoing curative radiotherapy. CR and TRF were chosen due to their history, ease of application and as previously exposed, supporting evidence in their favor.

The main objective of this clinical trial is to evaluate the feasibility and effectiveness of either CR or TRF in prostate and breast cancer patients who are under curative radiotherapy treatment.

In this novelty clinical trial we seek to establish guidelines for future works in this area which can be easily reproducible and improved upon, and thus build the foundations for effective and efficient interventions such as TRF or CR.

To our knowledge it is the first published work of this kind in developing countries, and showed consistent results in favor of the intervention.

2. Materials and Methods

We defined a prospective, interventional, non-randomized clinical trial that assesses the feasibility and effectiveness of CR and TRF in patients with breast or prostate cancer, body mass index (BMI) >25 and treated with curative radiotherapy. A summary of the main characteristics of the cohort can be found in Table 3.

Table 3. Summary of main characteristics of patient cohort. Clinical characteristics of patients along the staging of their cancer. Number of people in each intervention. Changes in biochemical and anthropometric values before and after intervention in the complete cohort.

General			
	Male patients		2
	Female patients		21
	Mean Age (y)		53,1
	Mean Height (m)		1,57
Cancer			
	Breast		21
	Prostate		2
Stage			
Breast Cancer	0		1
	I		13
	II		2
	III		2
	N/A		3
Prostate Cancer	Recurrence		2
Intervention			
	TRF		7
	CR		16
Mean serum levels		Before	After
	Glucose	94,4	93,6
	Insulin	16,8	14,8
	LDL	119,7	111,6
	HDL	47,8	47,4
	TG	189,0	176,6

Mean Anthropometry		Before	After
	Weight (kg)	77,2	73,6
	Waist Circ. (cm)	95,8	90,9

Inclusion criteria:

- ≥ 18 years old
- Breast cancer or hormone-sensitive prostate cancer diagnosed by biopsy
- Overweight or obesity defined as BMI ≥ 25 kg/m² and 30 kg/m² respectively
- Indication of radiotherapy with a curative intent.

Exclusion criteria:

- BMI < 25 kg/m²
- Patients undergoing nutritional treatment or malnutrition
- Patients with diabetes mellitus using insulin
- Diagnosis of vascular ischemia, uncontrolled thyroid disease, mental illness without medical supervision, liver disease or malabsorption syndromes (inflammatory bowel disease, celiac disease)
- Patients with gastric by-pass or gastric sleeve
- Use of corticosteroids or anti-depressants
- Moderate or high level of physical activity.

If the patient was a suitable candidate, during the initial consultation the details of the study along with its risks and benefits were explained. Patients who accepted to be part of the study signed an informed consent and were distributed between CR and IF according to their preferences.

The following steps were taken with each patient to ensure a thorough procedure:

Step 1: Initial Evaluation

- Nutritional evaluation: baseline measurement of weight, BMI, waist circumference, along with serum levels of glucose, basal insulin and lipid were performed.
- Quality of life (QoL): QoL was assessed through the EORTC-c30 questionnaire with all patients, and additionally the EORTC QLQ - BR23 questionnaire in breast cancer and the Expanded Prostate Cancer Index Composite (EPIC 2.0) in prostate cancer, if appropriate, which were taken at the same time as the EORTC-30.
- Physical activity: international physical activity questionnaire (IPAQ) from the World Health Organization (WHO).
- Eating habits: a 24-hour food survey and consumption trend was used to determine the patient's eating habits (Supplementary Material, "Supplementary Spreadsheet 1").

Step 2: Intervention

Each intervention was defined to start 2 weeks before the patient's oncologic treatment, and last for 12 weeks.

Once nutritional evaluation was done, participants were then assigned to TRF or CR according to their preferences. Patient distribution can be seen in Figure 1.

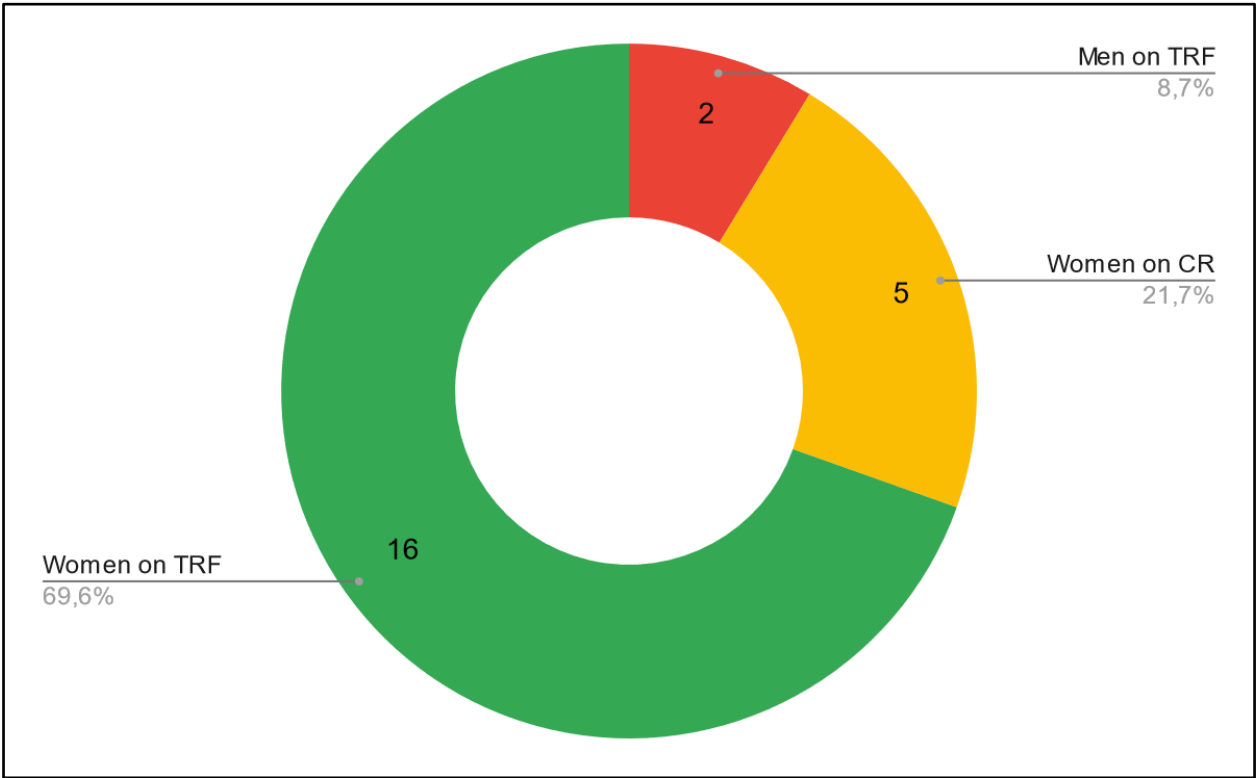


Figure 1. Patient distribution according to sex (Male and Female) and chosen nutritional intervention (TRF or CR).

Nutritional guidelines were made and personalized for each patient according to their group, following certain rules:

- A. The **TRF group** had a sugar and saturated fat free diet with caloric intake according to the patient's total energy expenditure, distributed in 8 hours of food intake and 16-hour daily fast.
- B. The **CR group** was based on the Obesity Society guidelines, with a total caloric intake 25% less than total energy expenditure. This was distributed in 4 meals and 1 snack according to the following proportions: 55% for carbohydrates, 15% protein and 30% fat, without sugar or saturated fat.
- C. Every patient, independent of their group, was tasked with a dairy registry of what they ate.

Step 3: Monitoring

Throughout the investigation, the following parameters were closely monitored:

- A. Treatment adherence: patients were called once a week and their dairy diet registry was evaluated according to their corresponding group, where important concepts related to their intervention were reinforced.
- B. Anthropometric changes: every 4 weeks every patient's weight and waist circumference were measured.
- C. Toxicity: once a week during their consultation with radiation oncology, acute toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

Step 4: Final Evaluation

12 weeks after having started the intervention, and at least 4 weeks after finishing oncologic treatment, the following were measured:

- A. Acute Toxicity
- B. Weight and waist circumference

- C. Fasting glucose, basal insulin and lipid profile.
- D. QoL with EORTC-c30, EORTC QLQ - BR23 (for breast cancer) and the EPIC 2.0 (for prostate cancer)

3. Hypothesis

CR or TRF are feasible and effective interventions in overweight and obese patients with breast or prostate cancer undergoing curative radiotherapy.

4. Primary objectives

Evaluate feasibility and effectiveness of CR and TRF in overweight and obese patients with cancer under curative radiotherapy.

5. Secondary Objectives

- A. Assess adherence, defined as a reduction in body weight of at least 5% compared to baseline and in at least 50% of the recruited patients.
- B. Establish which intervention (CR or TRF) has better adherence.
- C. Assess the impact on quality of life in patients under nutritional interventions
- D. Assess differences in weight and waist circumference in patients under nutritional interventions
- E. Assess differences in serum levels of fasting glucose, basal insulin and lipid profile in patients under nutritional interventions
- F. Assess acute toxicity grade ≥ 2 in patients under nutritional interventions

6. Results

27 patients were recruited from April 2021 to May 2023. Two patients withdrew from the trial before treatment and one patient did not receive radiotherapy (as seen in Figure 2). At the end of May 2023, 23 patients had completed 12 weeks of follow up of which 21 were women and 2 were men.

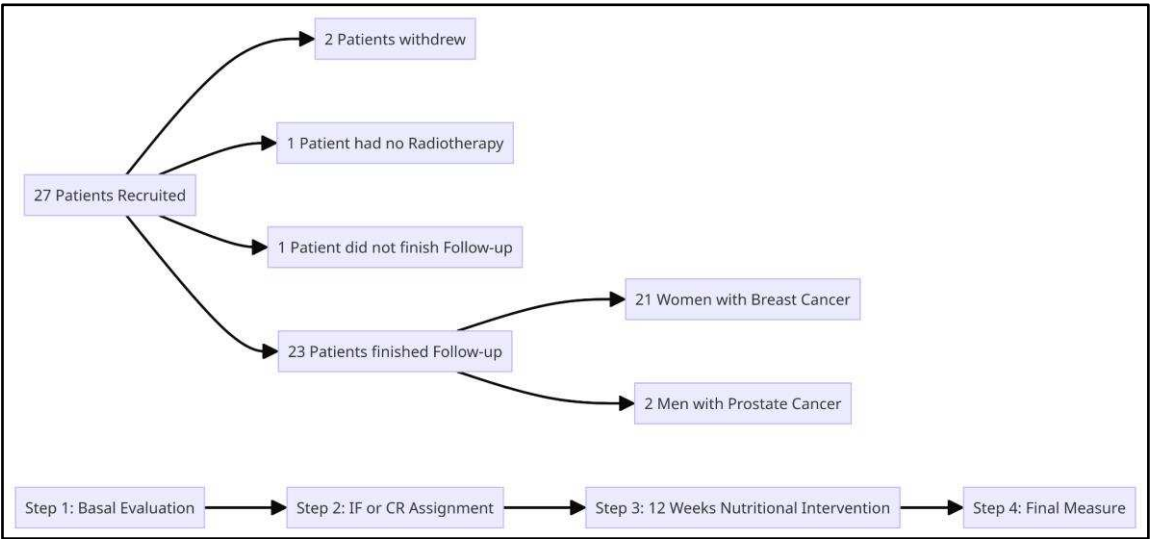


Figure 2. General outline of the study. Figure showing an easier to visualize representation of the cohort of the study and the steps taken to ensure the intervention was a thorough and replicable success.

Of the 24 patients available for analysis, 22 were women with breast cancer with luminal ductal carcinoma being the most common histologic subtype. From the 22 women with breast cancer, 14 received some kind of chemotherapy (neoadjuvant, adjuvant or both), and 19 received endocrine

therapy. All 22 patients underwent whole breast radiotherapy (+-regional nodal irradiation) and 11 received simultaneous integrated boost to the tumor bed up to 45,75 Gy.

Of the 24 patients available for analysis, 2 were men with prostate cancer and a Gleason score of 6 and 7. Both of them underwent surgery and had initiated androgen deprivation therapy. They received a dose of 51 Gy in 17 fractions to the prostate bed or equivalent EQD2.

Table 4 provides detailed clinical characteristics of patients separated by intervention, along with changes in biochemical and anthropometric measures before and after the intervention.

Table 4. Expanded table of the cohort of patients. Shows characteristics of the cohort and results from the study, differentiated by intervention type (TRF or CR). Clinical characteristics of patients and their cancer (sex, cancer type and molecular subtype), differences in measures before and after the intervention, and percentage of adherence in both breast and prostate cancer.

General				
Male				2
	TRF			2
	CR			0
Female				21
	TRF			5
	CR			16
Type				
Breast				
	DCIS			1
	CDI			18
	CLI			3
	Poorly Differentiated			1
Prostate				
Adenocarcinoma	Gleason 3 + 3			1
	Gleason 3 + 4			1
Molecular Subtypes				
Breast	Luminal			18
	Triple Negative			3
Mean Serum Levels by Intervention		Before	After	Difference (%)
TRF				
	Glucose	94,43	93,86	-0,61
	Insulin	15,58	11,93	-23,45
	LDL	122,23	127,00	3,90
	HDL	48,43	48,86	0,88

	TG	180,29	142,14	-21,16
CR				
	Glucose	94,38	93,45	-0,98
	Insulin	17,26	16,28	-5,71
	LDL	116,93	103,90	-11,14
	HDL	47,88	46,64	-2,57
	TG	195,75	193,86	-0,97
Mean Anthropometry by Intervention		Before	After	Difference (%)
TRF				
	Weight (kg)	75,11	70,23	-6,50
	Waist Circ. (cm)	94,21	88,07	-6,52
CR				
	Weight (kg)	78,09	75,07	-3,87
	Waist Circ. (cm)	96,47	92,36	-4,26
Loss of 5% or more of initial weight (True adherence)			Yes	No
Breast Cancer				
	TRF (n = 5)		5	0
	CR (n = 16)		7	9
Prostate Cancer				
	TRF (n = 2)		0	2
	CR (n = 0)		0	0

Notable results before and after the intervention are as following:

- A. There was a reported loss of 5% or more of the initial weight in 52,1% of patients (12/23).
- B. Within the patients with breast cancer, 100% of those who chose TRF showed true adherence (5 out of 5), whereas only 43.75% (7 out of 16) showed true adherence in the CR group.
- C. Within the patients with prostate cancer, 0% showed true adherence in the TRF group (0 out of 2).
- D. There was a mean reduction in weight of 3.6 kg and waist circumference of 4.9 cm.
- E. Serum levels of glucose, insulin, LDL, HDL and TG showed a mean reduction of 0.6 mg/dL, 2.0 uU/mL, 8.1 mg/dL, 0.4 mg/dL and 12.4 mg/dL respectively (Figure 3).

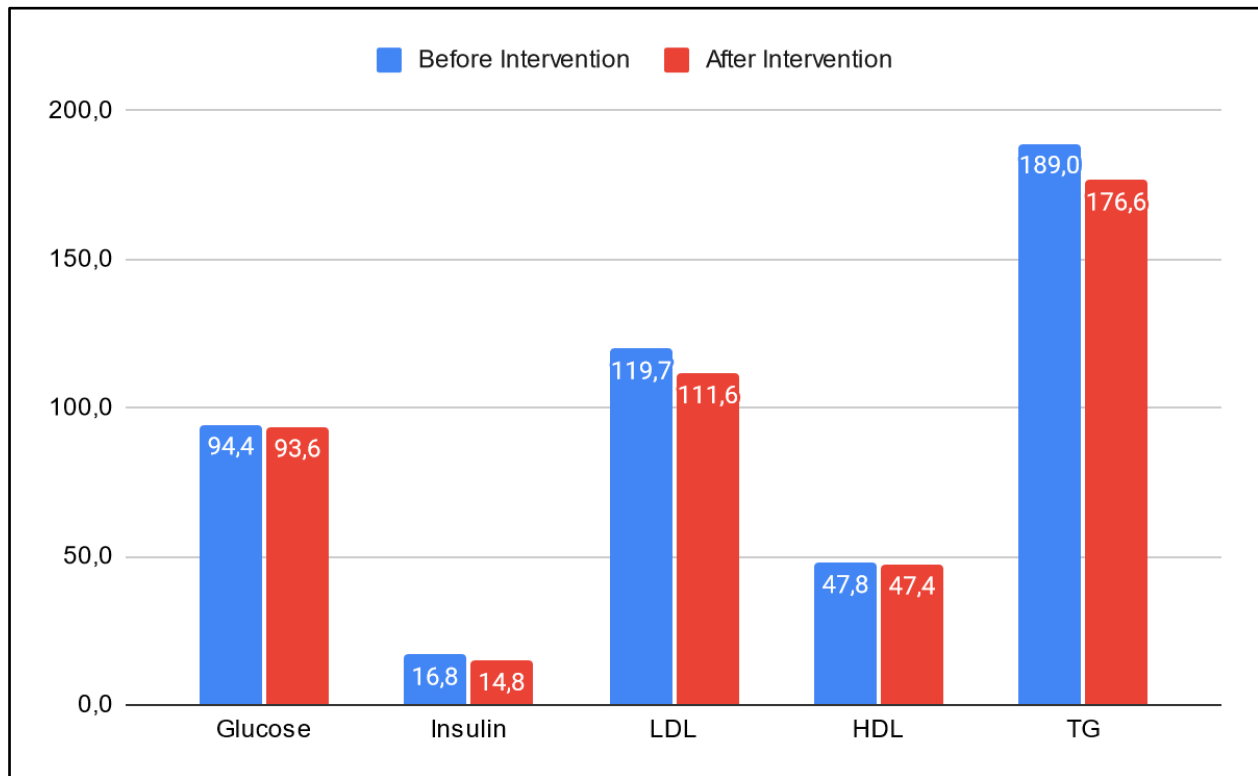


Figure 3. Differences in biochemical measurements before and after the intervention. Shows changes in all our patients, independent of their clinical characteristics and chosen intervention. All measurements show a decrease after this study's intervention was implemented.

Differences between interventions are as following (as seen in Table 5, and better visualized in Figure 4):

- A. Anthropometric measures: patients in the TRF group lost 61.8 % more weight and reduced their waist circumference by 49.5% more in comparison to those in the CR group (6.50% and 6.52% vs 3.87% and 4.26%, respectively).
- B. Glucose and insulin: TRF showed a reduction 38% smaller than the CR group in mean serum glucose levels (0.57 vs 0.92), but a 270% bigger decrease in their mean serum insulin level, in comparison to the CR group (3.65 vs 0.99).
- C. LDL and HDL: in mean serum levels of LDL, the TRF group showed an increase of 3.9%, whereas the CR group showed a decrease of 11.14%. On the other hand, the TRF group showed an increase of 0.88% in their mean serum levels of HDL, whereas the CR group showed a reduction of 2.57%.
- D. TG: the TRF group showed a decrease in their TG mean serum levels 1900% higher than those in the CR group (21.16% vs 0.97% reduction, respectively).
- E. Adherence: of the 12 patients who showed true adherence, all 12 were women. 5 were on the TRF group (5 out of 7 patients in the TRF group) and 7 were on the CR group (7 out of 16 patients in the CR group). None of the men showed true adherence.

Table 5. Changes in anthropometric and biochemical measurements post intervention.

Differences before and after treatment quantified in quantity (QD) and in percentage (PD) relative to each intervention's average levels.

	TRF		CR		
	QD	PD (%)	QD	PD (%)	TRF:CR

Glucose	-0,57	-0,61	-0,92	-0,98	- 38,0
Insulin	-3,65	-23,45	-0,99	-5,71	270,8
LDL	4,77	3,90	-13,03	-11,14	-
HDL	0,43	0,88	-1,23	-2,57	-
TG	-38,14	-21,16	-1,89	-0,97	1915,1
Weight (kg)	-4,89	-6,50	-3,02	-3,87	61,8
Waist Circ. (cm)	-6,14	-6,52	-4,11	-4,26	49,5

*On column TRF:CR, by using the following formula:.

$$\frac{(QD\ of\ TRF) - (QD\ of\ CR)}{QD\ of\ CR} * 100$$

we seek to demonstrate what percentage of QD-CR, QD-TRF represents. As an example, the decrease in insulin levels due to TRF (which is 3.65 points) is 270% of the decrease in insulin due to CR (which is 0.99 points). LDL and HDL were not evaluated due to the fact they increased with TRF and decreased with CR.



Figure 4. Differences in anthropometric and biochemical measurements between interventions. Both TRF and CR show a decrease in the measure of glucose, insulin, TG, waist circumference and weight. TRF had a bigger drop than CR on waist circumference, weight, and levels of insulin and TG; while CR shows a larger drop in glucose level than TRF. On the other hand, TRF led to an increase in LDL and CR decreased it, while CR led to a decrease in HDL while TRF increased it.

7. Discussion

Our findings show that 52.1% of patients lost 5% or more of the initial weight, which shows that a nutrition intervention of these characteristics is not only feasible and attains true adherence from

participants, but is also effective in reducing metabolic parameters in a short period of time (12 weeks).

Compared with other publications, our results are consistent with the available literature. TRF showed similar results to existing articles [30]: high degree of adherence, decrease in weight, and improvement of blood glucose and insulin levels. Our differences in the result of blood glucose levels may be explained by the low adherence of both men in the TRF group. The differences with the study from Harvie [37] may be explained due to the fact they used another approach of IF which focuses on the amount of calories consumed (2 days of 650-1000 kcal/day before chemotherapy infusion) rather than the window of time they are consumed within.

Of interest is the differences of findings with the systematic review from Anemoulis et al. [31]. This could be explained due to the type of IF approaches utilized in the studies considered, where only one of them specified the use of TRF, and the others were variations of calorie restricting approaches of IF: one included Ramadan-fasting patients, one used a FMD, while the others employed varied hours of fasting before and after chemotherapy. This reinforces the need for clear and established definitions of IF and its different approaches, and also an urgent necessity of evidence in this field.

Our findings are similar in adherence, weight loss and insulin levels in both interventions. We found that both TRF and CR managed to improve mean serum glucose, insulin, and TG levels. We also found that TRF was a vastly superior intervention in comparison to CR when it came to improving insulin and TG levels, but more research is required to further cement these findings in international literature.

Not only did these interventions as a group achieve true adherence, but 100% of the patients with breast cancer in the TRF group showed true adherence in comparison to only 43.75% adhering in the CR group, despite previous literature indicating breast cancer patients favored a CR approach [30].

We believe these findings to be due to how TRF does not restrict the amount of calories in a certain day, but rather restricts the timing of meals to 4 - 12 hours a day (8 hours in this study) and thus may be easier to carry on in cancer patients busy with the whole therapeutic process. Further research is needed on this aspect.

Despite both interventions showing positive results, it seems TRF as a nutritional intervention has both better adherence, improved anthropometric values and metabolic serum levels.

In this novel clinical trial, we propose a straightforward and easy to replicate method with which to reclude patients and further study nutritional interventions besides TRF or CR, which we believe can provide the base for future nutritional intervention studies and open a window into other aspects of nutritional interventions such as impact on toxicity reduction which, although seen in animals [38, 39], has yet to be reproduced and further explored in human participants.

To our knowledge it is the first published work of this intervention in developing countries and showed consistent efficacy of the intervention.

Limitations of our work include but aren't limited to: limited number of participants, a relatively short period of surveillance, adherence of patients to the guidelines given, the low number of prostate cancer patients in our cohort and the lack of prostate patients in the CR group, only evaluating the TRF approach of IF, and the absence of a control group.

This work could be improved by an increase in the number of participants and specifically the number of prostate patients, an increase in the time of surveillance, employing other nutritional interventions, recruiting more types of cancer patients, measuring blood levels of inflammatory response markers, recruiting only patients with cancer in early stages, having a more homogeneous cohort, the inclusion of a control group, or the incorporation of feedback from participants.

8. Conclusions

Cardiovascular diseases and cancer lead incidence and mortality rates worldwide, sharing common risk factors such as overweight and obesity. These play an important role in the origin of

breast and prostate cancer, and thus different interventions have been investigated to establish a faithful and reproducible way to improve weight in cancer patients.

The theory behind the benefit of diet and weight loss in cancer has been largely studied and established in preclinical studies, but clinical studies that show these results in practice are few in between and limited in their approach. This could be attributed to the numerous interventions in existence and a lack of agreement on definitions, establishing which ones are best, and also a lack of patients on which these interventions have been measured thoroughly.

Two of these interventions are TRF and CR. These nutritional interventions were chosen due to their historical relevance and evidence supporting them. Our findings are consistent with the literature, with TRF displaying better results in terms of adherence, weight loss and metabolic parameters, whereas CR still proves to be beneficial but has worse adherence and glucose, insulin and lipid profile levels in comparison to TRF.

Differences with literature can be explained due to heterogeneity on application of IF and its different approaches, lacking a formal definition. This leads to large differences in fasting hours, number of fasting days and the existence or not of a caloric restriction.

QoL and acute toxicity were also evaluated, but are currently under analysis and will be published in another manuscript.

We propose a series of steps through which metabolic parameters, anthropometry and quality of life can be measured. These steps are simple to apply and reproducible. We hope this helps establish concrete and well established definitions of the various fasting regimes, and motivates other researchers to further investigate and build the foundation of what we believe is a low-cost and effective way to lose weight and improve metabolic parameters.

Supplementary Materials: The following supporting information has been uploaded together with the manuscript: **Supplementary Spreadsheet 1:** 24- hour Reminder Survey.

Author Contributions: Conceptualization, Carmen Vega and Tomás Merino; Data curation, Esteban Barnafi and Nicolás Rivas; Funding acquisition, Carmen Vega; Investigation, Carmen Vega, Alejandra Parada and Nicolás Rivas; Methodology, Carmen Vega and Tomás Merino; Project administration, Carmen Vega; Resources, César Sánchez, Francisco Acevedo, Benjamin Walbaum and Tomás Merino; Supervision, Carmen Vega and Francisco Acevedo; Validation, Tomás Merino; Visualization, Esteban Barnafi; Writing – original draft, Esteban Barnafi; Writing – review & editing, Carmen Vega, Esteban Barnafi and Tomás Merino.

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Institutional Review Board Statement: This study was conducted with the approval of the Comité Ético Científico de Ciencias de la Salud UC (CEC-Salud UC). This Committee adheres to the ethical principles of Pontificia Universidad Católica de Chile, which considers respect for the dignity of the human person in any condition as a fundamental axis. This Committee also complies with the Good Clinical Practice Guidelines defined by the International Conference on Harmonization (GCP-ICH); and with Chilean laws 19.628; 20.120; 20.584 and 20.850 that modify the Health Code.

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study after the procedure and the steps involved were explained.

Data Availability Statement: All statements and conclusions made within this article have been made with the data and information contained within the provided supplements (tables and figures). No other data was used.

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