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Original Article

Time-restricted periodic fasting: A revolutionary approach to combat obesity by enhancing Bcl-2 pro-survival proteins

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SUMMARY

Background & Aims: Obesity is a global health issue related to many physiological functions such as apoptosis and requires specific treatment approaches, especially in nutrition or diet modification. Our study aims to investigate the effects of time-restricted periodic fasting (TRPF) on the obesity phenotype and Bcl-2 pro-survival proteins in overweight or obese adults.
Methods: A quasi-experimental study was conducted in 38 young adult men with obesity and overweight. Participants were separated into a control group (CG) and a time-restricted periodic fasting group (PFG). Anthropometric and body composition measurements measured obesity phenotype, whereas B cell

Abbreviations: BIA, Bioelectrical impedance analysis; BMI, body mass index; BW, body weight; BM, bone mass; BF, body fat; CG, control group; DBP, diastolic blood pressure; ELISA, enzyme-linked immunosorbent assay; HR, heart rate; TRPF, time-restricted periodic fasting; MM, muscle mass; SBP, systolic blood pressure; PFG, time-restricted periodic fasting group; TBW, total body water; VFL, visceral fat level; WC, waist circumference; WtHR, waist-to-height ratio.

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lymphoma 2 (Bcl-2) levels were measured by enzyme-linked immunosorbent assay (ELISA) test.
Results: A 10-day TRPF intervention could significantly reduce obesity phenotypes such as body weight (BW) ($P = 0.00$), body mass index (BMI) ($P = 0.00$), waist circumference (WC) ($P = 0.00$), waist-to-height ratio (WtHR) ($P = 0.01$), visceral fat level (VFL) ($P = 0.01$) and significantly reduced Bcl-2 levels (4.73 ± 4.96 ng/mL) compared to the pretest (5.49 ± 5.94 ng/m; $P < 0.05$). There was a significant negative correlation between Δ in Bcl-2 levels with certain obesity phenotypes such as waist hip ratio (WHR) ($\beta = -0.35$; $P < 0.05$), BMI ($\beta = -0.35$; $P < 0.05$), body fat (BF) ($\beta = -0.33$; $P < 0.05$), and visceral fat level (VFL) ($\beta = -0.34$; $P < 0.05$).
Conclusion: TRPF could reduce some parameters of obesity phenotype. These effects might be related to increased levels of Bcl-2, an anti-apoptotic parameter in young and overweight/obese adult men.

Introduction

Obesity is a global health concern which affects approximately 1 billion individuals (340 million adolescents and 650 million adults) worldwide [1]. Obesity caused by an imbalance between energy use and intake is characterized by excessive or abnormal fat accumulation. This condition is greatly related to a significant number of disorders, including cardiometabolic disease [2]. Obesity is frequently diagnosed merely based on body mass index (BMI), which does not sufficiently represent body adiposity. Consequently, assessing the clinical effectiveness of other obesity phenotypes such as abdominal adiposity (e.g., waist-height ratio, waist-hip ratio, waist circumference), and body fat may be essential to detect the cardiometabolic risk related to obesity [3].

Obesity is an intriguing subject since it also impacts mitochondrial function, which in turn influences the apoptosis process [4]. Apoptosis is essential for the maintenance of cellular balance and rapid removal of damaged or dysfunctional cells and is crucial for vital biological functions. Due to increased obesity-induced apoptosis, obesity contributes to many problems, such as pancreatic β-cell failure, fertility, and metabolic dysregulation, and is a key mechanism in disease pathogenesis [4]. Because apoptosis has a substantial impact on cell death and is a "double-edged sword" that happens under a variety of physiological and pathological situations, such as obesity, it remains a fascinating topic to explore [4–6].

B-cell lymphoma 2 (Bcl-2), a major regulator of the anti-apoptotic process, plays a crucial role as apoptotic and non-apoptotic molecules [7]. Bcl-2 can maintain mitochondrial outer membrane permeability, thereby providing antioxidant effects, preventing the action of apoptosis effectors to ensure their survival, and regulating metabolism, mitochondrial respiration, and calcium homeostasis [8–12]. Previous studies showed that obesity may activate complex 1 and nuclear factor kappa β, eventually enhancing pro-survival proteins such as Bcl-2 (Hildebrandt, Ibrahim, and Peltzer, 2023). However, some studies contradicted these findings and reported that decreased Bcl-2 levels were associated with increased body fat mass (Tinahones *et al.*, 2013).

Fasting is a non-pharmacological strategy that has a significant effect on overcoming overweight or obesity [13,14]. Fasting might be an appropriate treatment since it can also modify the PI3K/AKT pathway, which is known to be deregulated in obesity [14]. Periodic fasting (PF) and time-restriction eating are types of diet modulation that enhance metabolic function in overweight or obese individuals with few adverse effects. It is a simple and easy-to-implement lifestyle modification that

can help lower the risk of cardiometabolic disorders and reduce abdominal obesity [15–18]. Previous studies investigated the correlation between dietary manipulation and Bcl-2 to apoptosis in obesity; however, the results were contradictory [19,20]. Given the limited studies of fasting, this study aimed to analyze how PF with restricted time (TRPF) affects obesity phenotype and Bcl-2 pro-survival proteins in overweight or obese adults.

Material and methods

Study design

There were two groups in this quasi-experimental study: the control (CG) group and the treatment (PFG) group. The study used a pretest-post-test control group design. As part of the pre-and post-tests, obesity phenotype was measured by anthropometric and body composition, and Bcl-2 levels were measured in both groups before and after 10 days. Participants in the PFG underwent time-restricted periodic fasting (TRPF) for ten days, whereas the CG received no treatment. The CG and PFG were instructed to continue eating and exercising in the same ways throughout the trial.

Participants

Young adult men who met the inclusion criteria (aged $\geq$ 20 years, healthy, BMI $\geq$ 23, and had a light-moderate level of physical activity [<600MET or 600–3000 MET as measured by the Global Physical Activity Questionnaire] were included in the study. Individuals with a history of diabetes mellitus, hypertension, thyroid, heart disease, parathyroid, malignancy, alcohol consumption, smoking habit, dietary restrictions (vegetarianism and veganism), daily consumption of acetylsalicylate drugs, use of hormonal drugs, and current involvement in weight-loss programs were excluded. The participants were selected by simple random sampling. The sample size in this study was calculated based on the sample size formula according to Chow *et al.* (2018) with standard deviation and mean difference values referring to previous research [21,22].

$$n = \frac{\left(z_{\alpha/2} + z_{\beta}\right)^2 x\ SD^2}{(x_1 - x_2)^2}$$

From this formula, the minimum sample required was 11 each group, and a total of 38 participants were involved in this study.

Periodic fasting

In this study, TRPF was defined as fasting 12 hours a day for 10 days and ate twice during the restricted time: at dawn (about 06:00 am) and dinner (around 06:00 pm). To adjust diet and prevent overeating during the eating window, a 40 % daily calorie reduction (equivalent to 500–800 kcal/day) was implemented for each participant. During PF, participants in the PFG were only permitted to consume meals supplied by the authors. Fluid requirements were ensured to be at least 2 liters daily (equal to 8 glasses) and there were no additional rules on the daily meal. Participants' daily circumstances were monitored, including their food consumption and any concerns that they might have regarding fasting. Throughout the trial, the CG and PFG groups were urged to adhere to their present dietary, physical activity regimens, and exercise.

Vital sign, anthropometric, and body composition measurements

Vital sign parameters monitored in this study include systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Blood pressure parameters were measured three times. SBP and DBP were measured on the non-dominant arm using an OMRON Digital Tensimeter (Omron

Healthcare Manufacturing Vietnam Co., Ltd, Binh Duong, Vietnam), with a one-minute rest interval between readings. Anthropometric parameters consisting of body weight (BW), body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-to-hip ratio (WHR), and waist-to-height ratio (WtHR) were measured.

Anthropometric parameters, such as BW and BH, were measured while patients were standing and reported to the nearest 0.5 kg using GEA ZT-120 scales (Zhongshan Camry Electronic Co., Ltd, Guangdong, China). Based on standards from Asia-Pacific, BMI was calculated by dividing body weight by height squared (Kg/m^2) and was then categorized into multiple groups [23]. HC was measured as the largest circumference at the buttocks, AC was taken midway between the inferior margin of the last rib and the crest of the ilium in a horizontal plane, WC was measured midway between the highest point of the iliac crest and the bottom of the ribcage [24]. Body composition provides estimates of body fat (BF), muscle mass (MM), total body water (TBW), visceral fat level (VFL), and bone mass (BM), which were quantified using bioelectrical impedance analysis (BIA) Tanita BC-545N (Tanita Corporation, Tokyo, Japan) and were measured twice before and after PF treatment. Obesity Phenotype was classified according to the WHO and the Asia population [3,25,26].

Blood sampling and storage

Blood samples were collected from the antecubital vein of all participants. As much as 3 cc of blood was allowed to flow into the vacutainer and placed into a tube with ethylene diamine tetra acetic acid without additives. Blood samples were then sent to the laboratory on dry ice [27,28].

Bcl-2 quantification

Bcl-2 levels in blood samples were measured using the Human Bcl-2-like Protein 1 ELISA kit (Cat. no E4035hu, Bioassay Technology Laboratory, Zhejiang, China). All reagents, standard solutions, and samples were prepared as directed. A total of 50 μl Standard was added to the standard well, 40 μl of the sample was added to the sample well, followed by 10 μl of human BCL2L1 antibody and 50 μl of streptavidin-HRP to the sample and standard wells, and thoroughly mixed. The samples were then sealed on plates and incubated at 37 °C for 60 min. After incubation, the samples and standards were rinsed with washing buffer, and 50 μl of substrate B solution was pipetted to each well and incubated for another 10 min at 37 °C in the dark. When 50 μl of Stop Solution was applied to each well, the blue colour rapidly turned to yellow. The optical density value was assessed for each well using a microplate reader set to 450 nm within 10 min of adding the stop solution. Bcl-2 levels were reported in ng/mL [29].

Statistical analysis

Data were analyzed using IBM SPSS Statistics 26. Continuous variables or number were reported as mean ± standard deviation, whereas categorical variables were reported as percentage. The normality of data, differences in the pre- and post-test results, group differences, and correlation among variables were analyzed using Kolmogorov–Smirnov test, Paired t-test, Wilcoxon test, and correlation test, respectively. The correlation or path analysis between the variables was analyzed using SEM AMOS.

Ethical consideration

Both verbal and written information were given to all participants were informed. Before registration, all participants provided informed consent. This research was approved by the Faculty of Medicine Ethics Committee, Airlangga University, Surabaya, Indonesia (No.157/EC/KEPK/FKUA/2022) and conducted by the Declaration of Helsinki.

Results

Characteristics of the participants

A total of 38 participants completed the entire study. Table 1 shows baseline obesity phenotypes based on several measures, including general obesity (e.g., BMI), abdominal adiposity (e.g., waist-hip ratio, waist circumference, and waist-height ratio), and body fat percentage.

Table 2 displays the baseline demographic characteristics of participants in the CG and PFG groups. No significant differences in participants' characteristics in both research groups based on the Independent T-test (†) and Mann–Whitney U-test (‡) results ($P > 0.05$) (Table 2).

Effects of PF on obesity phenotype and other body composition

Table 3 shows how TRPF affects the obese phenotype and other aspects of body composition. Table 3 shows no significant differences between the pretest and posttest obesity phenotype and other body composition measures of CG group. In the meantime, TRPF intervention for 10 days might significantly lower obesity phenotypes like BW ($P = 0.00$), BMI ($P = 0.00$), WC ($P = 0.00$), WtHR ($P = 0.01$), and VFL ($P = 0.01$) in the PFG group. Significant declines were also seen in body composition metrics such as MM ($P = 0.00$), BM ($P = 0.03$), BMR ($P = 0.00$), and MA ($P = 0.04$). There were also significant differences of BW ($P = 0.00$), BMI ($P = 0.00$), WC ($P = 0.03$), MM ($P = 0.00$), BMR ($P = 0.02$), and MA ($P = 0.01$) between CG and PFG (Δ group parameters).

Effects of PF on the Bcl-2 levels

Figure 1 shows the differences in pre- and post-test bcl-2 levels in the CG and PFG after 10 days. The pre-and post-test Bcl-2 levels in CG were 13.92 ± 18.06 ng/mL and 12.91 ± 17.45 ng/mL, respectively **(Figure a)**; the difference was not significant according to the Wilcoxon signed rank test ($P = 0.05$). However, the pre-and post-test Bcl-2 levels in the PFG were 4.73 ± 4.96 ng/mL and 5.49 ± 5.94 ng/mL, respectively **(Figure b)**; the difference was significant according to the paired t-test ($P = 0.02$). Furthermore, the Mann–Whitney U-test revealed a significant difference in Bcl-2 levels (Δ group parameters) between the CG and PFG groups with a P-value of = 0.00.

Table 1
Baseline obesity phenotypes of the participants in the control (CG) and time-restricted periodic fasting (PFG) groups

Obesity phenotype	CG (n=19)	PFG (n=19)
BMI (kg/m^2)		
Overweight	3 (16 %)	0 (0 %)
Type I obesity	10 (53 %)	12 (63 %)
Type II obesity	6 (32 %)	7 (37 %)
Waist (cm)		
No Abdominal obesity (<90 cm)	11 (58 %)	13 (68 %)
Abdominal obesity (≥90cm)	8 (42 %)	6 (32 %)
WHR		
No Abdominal obesity (<0.9)	10 (53 %)	7 (37 %)
Abdominal obesity (≥0.9)	9 (47 %)	12 (63 %)
WtHR		
Normal (<0.5)	6 (32 %)	6 (32 %)
Increased Risk ((≥0.5)	13 (68 %)	13 (68 %)
Body Fat (%)		
Normoweight	3 (16 %)	0 (0 %)
Overweight	5 (26 %)	6 (21 %)
Obese	11 (58 %)	13 (68)

Body mass index (BMI); Waist Hip Ratio (WHR); Waist to height ratio (WtHR).

Table 2
Basic characteristics of participants in the control (CG) and time-restricted periodic fasting (PFG) groups

Parameters	CG (n=19)	PFG (n=19)	*P*-value
Age (yrs)	20.95 ± 0.97	20.89 ± 1.29	0.60‡
SBP (mmHg)	124.21 ± 9.47	120.95 ± 8.53	0.25‡
DBP (mmHg)	85.26 ± 10.20	86.32 ± 6.84	0.75‡
HR (bpm)	84.00 ± 12.46	87.84 ± 8.72	0.43‡
RR (x/minute)	18.84 ± 1.53	17.58 ± 1.83	0.06‡
FBG (mg/dl)	94.42 ± 10.85	100.84 ± 14.32	0.22‡
TC (mg/dl0	194.16 ± 26.17	202.42 ± 34.08	0.41ǂ
BW (kg)	82.53 ± 11,16	84.29 ± 10.62	0.61ǂ
BH (cm)	170.03 ± 6,62	169.53 ± 6.37	0.81ǂ
BMI (kg/m^2)	28.57 ± 3.76	29.22 ± 2.47	0.53ǂ
HC (cm)	96.42 ± 9.34	99.26 ± 10.44	0.38ǂ
AC (cm)	94.55 ± 9.91	95.39 ± 7.99	0.77ǂ
WC (cm)	89.21 ± 8.92	89.08 ± 7.30	1.00‡
BF (%)	25.73 ± 5.19	26.84 ± 3.35	0.44ǂ
TBW (%)	49.43 ± 4.40	48.07 ± 3.46	0.30ǂ
MM (kg)	57.58 ± 6.60	57.49 ± 6.63	0.97ǂ
BM (kg)	3.17 ± 0.33	3.13 ± 0.35	0.74ǂ
VF (level)	10.84 ± 2.99	11.03 ± 2.05	0.83ǂ
BMR (kcal)	1805.16 ± 206.91	1788.84 ± 222.97	0.82ǂ
MA (yrs)	27.53 ± 6.69	29.89 (±4.63)	0.21ǂ

Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR), body weight (BW), body height (BH), body mass index (BMI), hip circumference (HC), abdominal circumference (AC), waist circumference (WC), body fat (BF), total body water (TBW), muscle mass (MM), bone mass (BM), visceral fat level (VFL), basal metabolic rate (BMR), Metabolic age (MA). Data were reported as mean ± standard deviation. The analysis was determined based on the 10-day observation points before (pre-test) and after PF (post-test). The difference between CG and PFG data was analyzed using the independent t-test (ǂ) if data were normally distributed or Mann–Whitney U-test (‡) if the data were normally distributed.

Correlation between PF, Bcl-2, obesity phenotype, and metabolic age

The correlation between PF and the difference or delta (Δ) in Bcl-2 level, obese phenotype, and MA is displayed in Figure 2. The difference (Δ) in Bcl-2 levels was significantly positively correlated with PF (β = 0.37; $P < 0.05$). This result implied that there would likely be 0.37 changes in BCL2 Δ for each change in TRPF. The difference (Δ) in Bcl-2 levels was negatively correlated with the difference (Δ) in WHR (β = -0.35; $P < 0.05$), BMI (β = -0.35; $P < 0.05$), BF (β = -0.33; $P < 0.05$), and VFL (β = -0.34; $P < 0.05$).

The difference (Δ) in WHR (β=-0.06; $P<0.05$) and WtHR (β=-0.68; $P<0.05$) were significantly negatively correlated with the difference (Δ) in MA. This result implied that the increased difference (Δ) of WHR and WTHR would decrease for each change in difference (Δ) of MA. The differences (Δ) in BMI (β=0.05; $P<0.05$), WC (β=0.71; $P<0.05$), BF (β=0.14; $P<0.05$), and VFL (β=-0.06; $P<0.05$) were significantly positively correlated with the difference (Δ) in MA. This implied that the increased difference (Δ) of WC, BMI, BF, and VFL would increase for each change in difference (Δ) of MA.

Discussion

This study analyzed how obesity phenotypes in our study were affected by TRPF. Some participants in this study had abdominal adiposity and significant body fat (Table 1). This indicates the necessity for obesity control to lower the risk of obesity-related conditions like metabolic and cardiovascular disease [3]. The main results of this study demonstrated significant differences between the pre-test and post-test values of several obesity phenotypes, such as BW and BMI. These findings were in line with those of de Toledo *et al.* (2020), who discovered that a 10-day fasting strategy led to weight loss [22,30]. Our study also demonstrated that TRPF helped people lose weight and improved their obesity phenotype by lowering their calorie intake [31].

The PFG group also showed decreased abdominal adiposity parameters as measured by WC, WtHR, and VFL. These findings supported a previous study suggesting that TRF might help reduce abdominal

Table 3
Differences in obesity phenotype and other body composition of the control (CG) and periodic fasting (PFG) groups

Parameters	CG	*P-value* of pretest and post-test	PFG	*P-value* of pretest and post-test	*P*-Value of the difference between the groups (Δ)
Pre-BW (kg)	82.53 ± 11.16	0.08[i]	82.53 ± 11.16	0.00[†]*	0.00[ǂ]*
Post-BW	83.02 ± 11.25		81.82 ± 11.14		
Pre-BMI (kg/m^2)	28.57 ± 3.76	0.10[†]	28.57 ± 3.76	0.00[i]*	0.00[ǂ]*
Post-BMI (kg/m^2)	28.88 ± 3.61		28.38 ± 2.68		
Pre-WC (cm)	89.21 ± 8.92	0.57[i]	89.08 ± 7.30	0.00[i]*	0.03[ǂ]*
Post-WC (cm)	88.92 ± 9.20		87.21 ± 7.00		
Pre-WHR	0.93 ± 0.12	0.01[i]	0.90 ± 0.06	0.07[†]	0.32[‡]
Post-WHR	0.91 ± 0.11		0.89 ± 0.07		
Pre-WtHR	0.53 ± 0.06	0.87[i]	0.52 ± 0.04	0.01[i]*	0.05[ǂ]
Post-WtHR	0.52 ± 0.06		0.52 ± 0.04		
Pre-BF (%)	25.73 ± 5.19	0.5[i]	26.84 ± 3.35	0.05[i]	0.05[ǂ]
Post-BF (%)	25.9 ± 5.09		26.30 ± 3.30		
Pre-VFL (level)	10.84 ± 2.99	0.85[†]	10.62 ± 1.85	0.01[†]*	0.07[‡]
Post-VFL (level)	10.86 ± 2.92		10.41 ± 1.96		
Pre-MM (kg)	57.58 ± 6.60	0.86[†]	57.49 ± 6.63	0.00[i]*	0.00[‡]*
Post-MM (kg)	58.16 ± 5.92		56.60 ± 6.80		
Pre-BM (kg)	3.17 ± 0.33	1.00[†]	3.13 ± 0.35	0.03[†]*	0.16[‡]
Post-BM (kg)	3.17 ± 0.31		3.10 ± 0.35		
Pre-TBW (%)	49.43 ± 4.40	0.48[i]	49.43 ± 4.40	0.67[i]	0.89[ǂ]
Post-TBW (%)	49.19 ± 4.20		47.90 ± 3.61		
Pre-BMR (Kcal)	1805.16 ± 206.91)	0.74[i]	1788.84 ± 222.97	0.00[i]*	0.02[ǂ]*
Post-BMR (Kcal)	1802.10 (±195.60)		1758.80 ± 226.92		
Pre-MA (yrs)	27.53 (±6.69)	0.29[i]	29.89 ± 4.63	0.04[†]*	0.01[‡]*
Post-MA (yrs)	27.95 (±6.43)		29.16 ± 4.75		

Body weight (BW), body mass index (BMI), waist circumference (WC), Waist Hip Ratio (WHR); Waist to height ratio (WtHR); body fat (BF), visceral fat level (VFL), muscle mass (MM), bone mass (BM), total body water (TBW), basal metabolic rate (BMR), Metabolic age (MA). Data were presented as mean ± standard deviation. The analysis was determined based on the 10-day observation points before (pre-test) and after PF (post-test). The difference between pre-test and post-test data was analyzed using the Paired T-test if the data were normally distributed ([i]) or the Wilcoxon Test if the data were not normally distributed (†). The difference between CG and PFG data was analyzed using the independent t-test ([ǂ]) if the data were normally distributed or Mann-Whitney U-test ([‡]) if the data were not normally distributed.

obesity and minimize the risk of cardiometabolic disorders [18]. The effect of TRPF on enhancing obesity phenotype was presumed to be related to a preferential decrease in visceral adipose tissue with weight loss [32]. However, there was a notable decline in some body composition metrics in the PFG group. This demonstrated that fasting without a balanced physical activity monitoring program was unable to improve MM, BM, and BMR in overweight or obese people [19,33].

Another aim of this study was to analyze the effect of TRPF on Bcl-2 levels as an antiapoptotic parameter. This study revealed increased Bcl-2 levels in the PFG, whereas the CG had the opposite effect. Elevated Bcl-2 levels in the PFG suggested that TRPF would influence the function of anti-apoptotic proteins [20]. Figure 2 also supports this information by showing a substantial positive correlation between PF and the difference (Δ) in Bcl-2 levels. These findings were consistent with those of López-Dominguez *et al.* (2015), which suggested that diet modulation, such as caloric restriction, caused a considerable increase in the Bcl-2/Bax ratio in young and elderly mice [20]. Another study also stated that intermittent fasting upregulated the expression of other Akt and Bcl-2 as anti-apoptotic factors [34]. However, despite its insignificance, a different study asserted that intermittent fasting lowered Bcl-2 levels [19].

The PFG group showed increased Bcl-2 because 10-day TRPF might regulate the PI3K/AKT signaling pathway. Increased PI3K/AKT in obesity can result in insulin resistance, which hinders the efficient glucose uptake by cells, impairing glucose metabolism and producing too many reactive oxygen species. This disorder may then dephosphorylate GSK-3β, thereby inhibiting the anti-apoptotic function of Bcl-2 and leading to apoptosis [4]. Increasing PI3K/AKT and Bcl-2 during fasting may

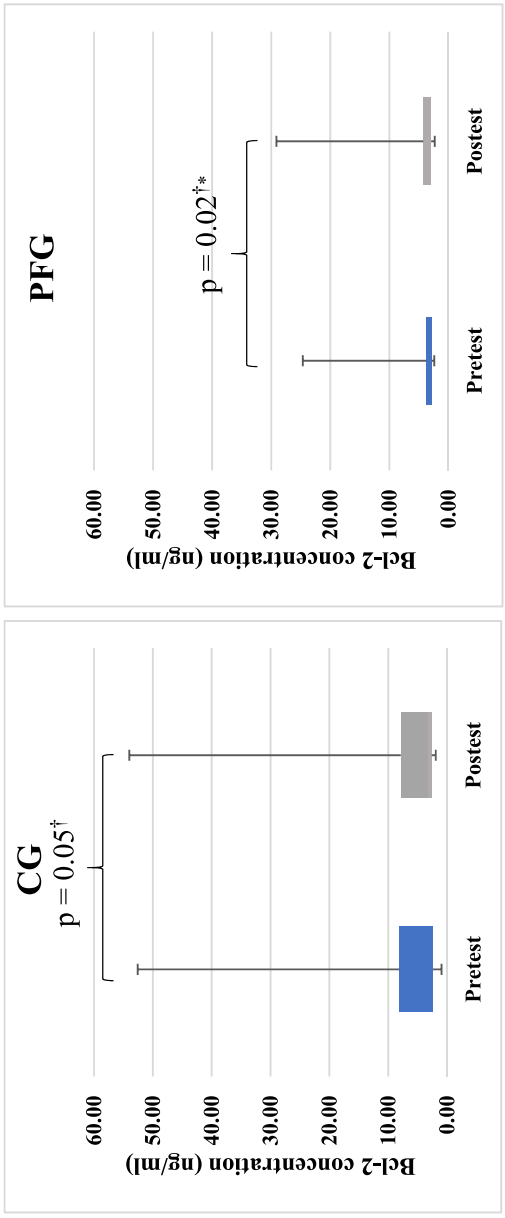

Figure 1. Differences in pre- and posttest Bcl-2 levels in the CG and PFG after 10 days. a) CG groups; b) PFG groups.

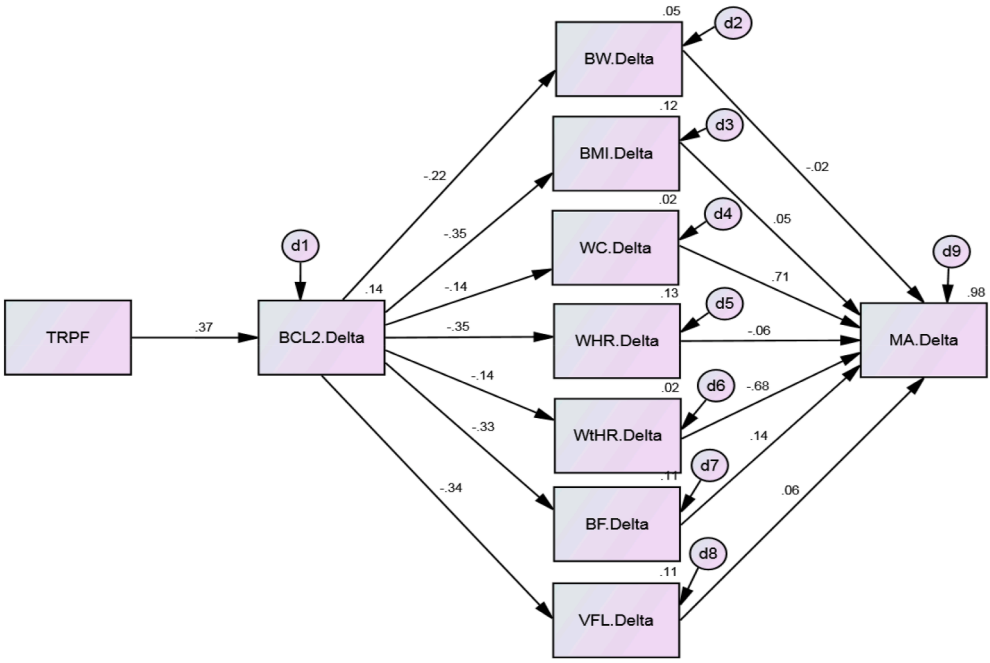

Figure 2. The correlation between PF and the difference (Δ) data from Bcl-2, obesity phenotype, and MA.

prevent obesity-related insulin resistance and type 2 diabetes mellitus that correlates with loss of β-cell mass due to β-cell apoptosis [35,36].

This study found a statistically negative correlation between Bcl-2 levels and several obesity phenotypes, including WHR, BMI, BF, and VFL (Figure 2). Therefore, increased Bcl-2 levels would decrease WHR, BMI, BF, and VFL. The result was similar to prior studies, which found that decreased Bcl-2 expression was associated with a BMI increase [5]. In obesity, low-grade chronic inflammation triggers apoptosis by downregulating Bcl-2 activation and activating caspase 3 and 7, which changes the insulin signaling pathways and can lead to insulin resistance [4,5]. We expect in this study that fasting might prevent the consequences of insulin resistance in obesity by increasing Bcl-2 levels in the group receiving TRPF [35,36].

Periodic fasting may prevent cellular senescence by reducing oxidative stress and inflammation. Previous studies have shown that calorie restriction can lower lipid peroxidation, normalize adipocyte size and morphology, reduce fatty liver, and suppress the expression of senescence-related markers such as iNOS, COX-2, Nrf2, and HO-1. However, the link between periodic fasting and increased Bcl-2 expression in this context requires further exploration. Bcl-2 maintains mitochondrial homeostasis, enhances resistance to oxidative stress, and protects cells from premature apoptosis during early metabolic stress, such as that induced by fasting. In overweight individuals, this mechanism may contribute to reduced cellular senescence [36,37].

The improvement of obesity phenotype parameters in this study will further impact metabolic age, which indirectly shows the cellular or tissue condition of each individual [37–39]. However, additional study was needed to completely comprehend the different mechanisms involved in fasting and cell death, from upstream regulators to final apoptotic effectors [20].

This study proved that TRPF could improve obesity phenotype parameters and increase levels of antiapoptotic proteins. However, the small number of participants remained a limitation in this study. The influence of TRPF must be further investigated to analyze other obesity phenotypes such as metabolic health parameters, phenotyping visceral obesity with imagen techniques, skeletal muscle mass, or a combination of body fat amount and distribution [4]. As obesity is a complex phenomenon,

the effect of TRPF on the cell death markers, signaling pathways, effectors, and other hallmarks must be investigated. This study was an informative study that revealed novel information on how TRPF can affect the obesity phenotype and Bcl-2 as prosurvival proteins in overweight or obese adults.

Conclusion

TRPF could reduce some parameters of the obesity phenotype. These effects might be related to the increased levels of Bcl-2, an anti-apoptotic protein in overweight or obese young adult men. Diet modification, particularly TRPF, was feasible for treating obesity, improving health, and preventing the development of obesity-related disorders. However, other approaches, such as monitoring physical activity, must be implemented with diet modifications.

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Declaration of competing interest

The authors declared no conflict of interest.

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