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Effects of Time-Restricted Eating on Cardiometabolic and Cardiovascular Health: Study Protocol (TRES)

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ABSTRACT

This study aims to assess the safety, feasibility, and effectiveness of 10-hr Time-Restricted Eating (TRE) compared to ad libitum eating on anthropometric measurements, cardiometabolic and cardiovascular health in patients with Acute Coronary Syndrome (ACS). The Time-Restricted Eating Study (TRES) is a single-centre, pragmatic, prospective, randomised controlled trial that will include 48 patients with ACS. Participants will be randomised in a 1:1 ratio to the intervention group where eating duration is restricted to 10 hours per day or control group with no limitation of eating duration imposed. Testing is scheduled at baseline and after four weeks of intervention. The primary outcome is change in body weight after four weeks of intervention. Secondary outcomes include changes in body composition, glycaemic and lipid profiles, inflammatory markers, oxidative stress, endothelial function, arterial stiffness, blood pressure, heart rate, safety, and feasibility of TRE on patients with ACS. The study was approved by the UiTM Research Ethics Committee. Findings will be disseminated through manuscripts, reports, and presentations. Findings on the feasibility and effectiveness of TRE in patients with ACS may broaden the body of evidence for implementing TRE as a dietary intervention to prevent secondary cardiovascular diseases.

Keywords: chrononutrition, cardiovascular diseases, intermittent fasting obesity, time-restricted eating

INTRODUCTION

Coronary Artery Disease (CAD) is a subset of Cardiovascular Diseases (CVD), an umbrella of disorders related to the heart and blood vessels. Coronary artery disease is often characterised by the presence of atherosclerosis in coronary arteries. It is the leading cause of death and Disability-Adjusted Life years (DALYs) loss worldwide. The most recent data from the Global Burden of Disease (GBD) Study 2019 shows a gradual increase in the number of incidences, prevalence, mortality and DALYs related to CAD globally (Global Burden of Disease Collaborative Network 2021). Researchers and health care professionals have explored multiple diet-related strategies to improve weight, cardiometabolic health and prevention of CVD through caloric and macronutrient restriction, consumption of specific food or nutrients, adherence to selected dietary patterns as well as fasting. Continuous Calorie Energy Restriction (CER) is frequently used to manage the body weight of individuals excess weight (Rynders *et al.* 2019). However, adherence to this dietary strategy is challenging due to the daunting task of reducing caloric intake daily (Golbidi *et al.* 2017). Chrononutrition-based dietary interventions like time-restricted eating have gained popularity as a sustainable CVD prevention strategy (Katsi *et al.* 2022). Prolonged nocturnal fasting by limiting food intake to daylight hours is a simple, feasible, and

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potentially effective disease prevention strategy (Patterson & Sears 2017).

Literature suggests that Time-Restricted Eating (TRE) may be a promising alternative to weight loss and metabolic health for people who can safely tolerate fasting intervals for a certain period of the day. Studies in the preclinical setting demonstrate that TRE mitigated metabolic diseases caused by various obesogenic diets, with benefits proportional to fasting duration (Chaix *et al.* 2014; Zaman *et al.* 2023). In addition, TRE stabilised and reversed the progression of pre-existing obesity, type II diabetes, hepatic steatosis and hypercholesterolemia of mice in the study. These benefits, which may or may not be related to weight loss, frequently result in metabolic benefits. However, human data on TRE and metabolic health are limited and restricted to healthy, normal weight, overweight, or obese adults and diabetes mellitus with varying results (Manoogian *et al.* 2022). To date there is no available data on the safety and effectiveness of TRE on patients with CAD. Individuals with a history of CVD have a significantly increased risk of recurrent CVD or death (Lin *et al.* 2017). Monitoring and managing risk factors are crucial for preventing the recurrence of cardiovascular disease. We designed Time-Restricted Eating Study (TRES) to assess the safety, feasibility, and effectiveness of adopting 10-hr Time-Restricted Eating (TRE) compared to ad libitum eating on anthropometric measurements, cardiometabolic and cardiovascular health in patients with ACS.

METHODS

Study design

TRES employs investigator-led, pragmatic, single-centre, parallel, randomised, single-blinded clinical trial to assess the safety, feasibility, and effectiveness of 10-hr TRE compared to ad libitum eating on anthropometric measurements, cardiometabolic and cardiovascular health in patients with ACS. The study will be conducted at the Cardiology Department, Al-Sultan Abdullah Hospital, Selangor. The duration for the RCT is five weeks. The trial comprised of a one-week baseline period followed by four weeks of intervention phase. Participants will be randomised to either TRE or control group (ad libitum eating) and expected to follow their assigned eating duration during the four-week intervention period. The duration of the intervention is set to four weeks with the consideration that improvement in cardiometabolic health can already become evident within two to four weeks after IF-related interventions (De Cabo & Mattson 2019). After completing four weeks of intervention, all participants will return to the study site for an end-of-study visit for assessments. Recruitment of participants for this interventional study is expected to take place for 12 months or until the sample size is achieved.

Sample size

The sample size was calculated to detect the difference in the reduction of body weight of 1.0 kg in four weeks between subjects undergoing TRE compared to ad-libitum timing of eating. The formula was calculated using the formula for statistical superiority (Zhong 2009). The value 1.0 kg for δ will be used as the difference in weight that would be considered as clinically significant reduction of the parameter for four weeks of weight reduction intervention. Meanwhile, a value of 0.97 for s was taken from a previous study assessing TRE's effect on overweight patients with metabolic syndrome (Wilkinson *et al.* 2020). Sample size calculation yielded 20 samples needed for each group. Thus, the sample size required for both arms will be 40. With the consideration of approximately 20% lost to follow-up from the previously mentioned study, a total of 48 patients will be needed to be enrolled in the study to detect a significant difference in weight loss in this RCT.

Participants and eligibility

Eligible participants will be approached and invited to participate in this study. A thorough explanation of the study will be relayed along with the patient information sheet. Written and verbal informed consent will be requested from eligible patients prior to study enrolment. Clinically stable patients with ACS will be screened by investigators based on the inclusion and exclusion criteria of this study:

Inclusion criteria. 1) Adult, 18–65 years old; 2) Had history of acute coronary syndrome (ACS); 3) Clinically stable; 4) Overweight, Body Mass Index (BMI) ≥25 kg/m^2; 5) Self-reported eating window of at least 12 h per day.

Exclusion criteria. 1) Severe obesity, BMI ≥40 kg/m^2; 2) Unstable weight in the past three

months (gain or lose more than 4 kg of weight); 3) Unstable cardiovascular, renal, cardiac, liver, lung, adrenal, or nervous system disease that may compromise study validity; 4) Any medications or supplements known to affect sleep, circadian rhythms, or metabolism (exception: caffeine); 5) Pregnant or lactating women; 6) Perform overnight shift work more than one day/week on average; 7) Regularly fasted for more than 15 hours/day or having completed twelve 24-hr fasts within the past three months); 8) Active use of tobacco or illicit drug or history of treatment for alcohol abuse; 9) Type I diabetes or diabetic, treated with insulin; 10) Use of anti-obesity drugs or other drugs affecting body weight; 11) Currently enrolled in weight loss or management programmes, including surgical intervention; 12) Severe kidney failure Glomerular Filtration Rate (GFR) <30 mL/min); 13) Eating disorder or current diagnosis of uncontrolled psychiatric illness, which may impair study involvement; 14) Malignancy undergoing active treatment; 15) Had gastrointestinal surgery or impaired nutrient absorption; 16) Travelled more than two time zones away two months prior to enrolling in the trial or will travel more than two time zones away during the study period; 17) Concurrent participation in other interventional studies.

Randomisation procedure and treatment allocation

Participants will be randomly assigned to a 1:1 ratio to follow a time-restricted eating regime (consuming all meals within a 10 hours window) or to maintain their regular feeding pattern (ad libitum eating) throughout the study period, four weeks. Block randomisation of ten will be generated by statistician using an online random number generator: www.randomization.com to ensure an equal number of participants in both arms. The randomisation list will be concealed using individual, sequentially numbered, opaque, sealed envelopes, which will only be opened once a participant is enrolled to assign them to interventions. Healthcare providers and outcome assessors will not be informed of their nutrition intervention allocation. Blinding will also be done prior to laboratory assessment and statistical analysis through renumbering of samples for analysis and labelling intervention groups with non-identifying terms (Group A and B).

Study intervention

After randomisation, participants will be briefed on dietary instructions for the assigned eating duration (Figure 1). Participants in the TRE group will be asked to restrict eating to 10 hours and to be allowed to decide on the starting time of the eating period latest by 09:00 am. Participants in TRE group are required to maintain the same 10-h feeding window each day. For example, participants who begin eating at 08:30 h will be required to finish their last meal of the day by 18:30 h daily and to fast until 08:30 h of the next day. Participants will be advised to consume their main meals at constant intervals (i.e lunch at 1–2 pm). Additionally, TRE group participants will be asked to limit dietary intake to water and caloric-free beverages such as sugar-free black coffee and tea during the fasting period. Meanwhile, participants in the control group will be required to maintain their habitual period of eating throughout the intervention period. Caloric restriction will not be implemented during the intervention period, participants will be allowed ad libitum dietary intake while complying with the assigned eating period. Ten-hour TRE is adopted as the duration of TRE intervention as it is deemed more sustainable compared to shorter TRE duration. It is a safer practice as it is expected that a subpopulation of the study population may be diabetic.

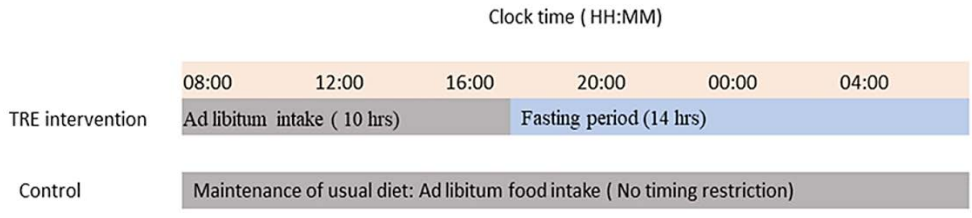

Figure 1. Eating and fasting duration during intervention

All participants in both groups will receive nutrition education regarding a heart-healthy diet through individualised counselling sessions. Heart-healthy diet consists of a dietary pattern rich in plant foods like cereals, fruits, vegetables, legumes, tree nuts, and seeds. Foods from plant origin should be eaten in large amounts and often as plants provide important nutrients, fibre, and protective substances that help with overall health, feeling full, and keeping a balanced diet. Emphasis will be given to healthy sources of protein from plants and regular consumption of fish. The diet promotes intakes of minimally processed foods, liquid plants oil and low consumption salt and added sugar. The primary intention of nutrition education is to improve the overall quality of the diet through better food selection. Additionally, participants will be advised to maintain their level of physical activity throughout the entire trial.

Study outcomes

Primary outcome. The primary outcome is a mean change in body weight (kg) from baseline to the end of four weeks of intervention.

Secondary outcomes. Secondary outcomes include a range of cardiometabolic, and cardiovascular health markers potentially associated with TRE. Secondary outcomes of interest include changes between pre- and post- 10 hr-TRE intervention for four weeks on body composition, glycaemic and lipid profiles, inflammatory markers, oxidative stress, endothelial function, arterial stiffness, blood pressure, and heart rate. Additionally, the safety and feasibility of TRE will be assessed in this study.

Study procedures

This study will be performed on identical test days for all assessments required for this study. Upon consent, patients will be provided with a Diet log (consisting of food diary and subjective appetite) and information on recording the log. Participants will be scheduled for baseline assessment the following week. They are advised to follow their habitual eating pattern, sleep, and exercise during the one-week baseline period. During the first visit (pre-intervention encounter), nutrition education regarding heart-healthy diet will be given, relevant information from participants (characteristics, medical history, and medications) will be gathered, baseline assessments will be conducted, and completed log will be collected. Intervention will begin at week 1, after baseline assessments are completed. Weekly follow-up will be conducted at week 2, 3, 4, and post-intervention will be conducted on termination visit at week 5. Summary of study activities are outlined in Table 1.

Pre-intervention measures. Baseline assessment includes anthropometric measurements, vital signs, flow-mediated dilation, brachial-ankle pulse wave velocity and blood sampling. Participants will be instructed to consume their last meal by 8:00 pm for an overnight fast and to avoid alcohol consumption or strenuous activities 24 hours prior to assessment day. Fasting blood samples will be collected by trained staff using standard institution procedures from all participants. Additionally, participants will answer questionnaires related to physical activity and sleep quality and complete a Diet log consisting of a food diary, eating time log and subjective appetite.

Intervention assignment and follow-up. Random assignment to interventions will be conducted after a 1-week baseline period at first visit. Follow-up telephone calls will be done weekly (week 2, 3, 4) for intervention monitoring, where medications, food timing and adverse events will be reviewed. Additionally, a weekly consultation during follow-up visits will take place to discuss any nutrition-related queries, with the objective to improve and maintain compliance with the intervention.

Post-intervention measures. Termination visits will be conducted four weeks post-intervention (week 5). All parameters assessed at baseline will be repeated during the termination visit.

Withdrawal of participants from a study procedure

Participants are free to withdraw from the study or procedures voluntarily at any point of the study for any reason without penalty to their continuing medical care. Additionally, participants must be withdrawn from the study by the principal investigator in consultation with the study physician for the following reasons: grade 4 clinical adverse events (requiring hospitalisation) considered causally related to TRE, pregnancy, compliance failure, poor logging or adherence to

Table 1. SPIRIT schedule of enrolment, interventions, and assessment

Timepoint	Study period (4 weeks)					Termination
	Enrolment	Baseline & allocation	Post-allocation			
	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5
Enrolment						
Eligibility screen	x					
Informed consent	x					
Allocation		x				
Interventions						
TRE 10 hr		x	x	x	x	
Ad libitum eating		x	x	x	x	
Assessments						
Demographics	x					
Clinical data	x					
Medication review	x	x	x	x	x	x
Blood pressure		x				x
Blood samples		x				x
Anthropometric measurements		x				x
Flow-mediated dilation		x				x
Brachial-ankle pulse wave velocity		x				
Food diary	x					x
Physical activity		x				x
Sleep quality		x				x
Subjective appetite	x					x
Food timing log			x	x	x	x
Adverse events			x	x	x	x

TRE: Time-Restricted Eating

the intervention, lost to follow-up, medication/s adjustment. Data collected prior to withdrawal will be used for analysis to maintain the reliability of the study. Participants who discontinue the study early will be asked to return to the study site at week 5 for end-visit assessments.

Data collection

Data collection for intervention monitoring and outcomes of study data will be gathered during pre- and post-intervention assessments and in free-living settings.

Sociodemographic and clinical data. One-off sociodemographic data will be collected after informed consent is obtained. Data includes age, ethnicity, marital status, education level, residential district, occupation, working hours, household income, household size and number of children. clinical data will include current cad diagnosis, prior history of cvd, other chronic non-

cardiovascular comorbidities, and medications. Concomitant medication use will be recorded at baseline and continued during the intervention.

Anthropometric measurements. Anthropometric measurements including weight, height, body composition and waist circumference will be conducted at pre- and post-intervention.

Resting heart rate and blood pressure. Resting heart rate (beats per minute) and blood pressure (mmHg) will be measured twice in an interval of three minutes, using a calibrated digital blood pressure monitor (OMRON HEM-907, Japan) by trained nurses. Measurement will be taken in a sitting position, on the right arm with an appropriate cuff size. Measurement will be taken after a minimum of 10 min rest. Hypertension is measured by having a systolic blood pressure of 140 mmHg or more or a diastolic blood pressure of 90 mmHg or more (MoH 2017). Resting heart rate ranges from 60 to 100 beats per minute, which is considered normal for adults.

Flow-mediated dilatation. Flow-mediated dilatation measurements will be conducted at pre- and post-intervention following an overnight fast based on the protocol specified in the literature (Corretti *et al.* 2002). Participants will lay in the recumbent position for 15 minutes in a quiet, temperature-controlled room prior to the measurements. Measurements of the right brachial artery in the longitudinal plane, approximately 2 to 4 cm above the antecubital fossa, will be performed by a single trained, blinded operator, using 5–13 MHz linear array transducer (Epiq CVX, Philips, Eindhoven, the Netherlands) operating in high-resolution B-mode. The brachial artery diameter will be measured in end-diastole from a single 2-dimensional frame. After three baseline measurements, forearm ischemia (reactive hyperemia) will be induced by inflating sphygmomanometer cuff applied to the right forearm 2 cm below the olecranon process to 50 mmHg greater than the systolic blood pressure for 5 min. As the cuff is deflated, the shear stress created will induce dilation, representing the spontaneous endothelial function. Readings will be taken at pre compression (baseline), 30 s prior to cuff release, and then every 30 s after cuff release for 2 min. FMD percentage will be calculated as (maximum diameter−baseline diameter)/baseline diameter×100.

Brachial-ankle pulse wave velocity. The measurement of brachial-ankle pulse wave velocity (baPWV) is a non-invasive technique used to assess systemic arterial stiffness by the analysis of waveforms in the brachial and tibial arteries. In the supine posture, following a brief period of rest, the SphygmoCor XCEL device (AtCor Medical) will be utilized to measure the arterial waveforms and blood pressure at both the brachial and ankle sites. The brachia and ankles will be affixed with cuffs, and a plethysmography sensor coupled to the cuffs will be used to simultaneously record pulse volume waveforms at the four extremities. Data will be collected for a duration of 10 seconds while applying a compression force of 50 mmHg. Continuous measures of blood pressure will be conducted using a typical cuff-oscillometric approach at the right arm and ankle. Subsequently, measurements will be taken at the left arm and ankle. The calculation of baPWV involves determining the time gap between the wave fronts of the brachial and ankle artery waveforms, as well as the path length from the brachia to the ankle, which is derived from the individual's body height.

Food diary. Participants will be asked to record each individual food and beverage consumed over a 24-h period (12:00 am and 11:59 pm) in a food diary for two weekdays and one weekend at baseline and at the end of the intervention. Participants are to record mealtime, food items and portion size taken on the selected days. All supplement intakes, including vitamins and minerals in the form of tablets, capsules, powder, or liquid, that might have added to the total number of calories and other nutrients will also be recorded. The food diary will be reviewed and coded by a trained dietitian using the Nutritionist Pro™ Diet Analysis software (Axxya Systems, Stafford, TX, USA) to quantify participants' average nutrient intake. Malaysian Food Composition Database (MyFCD) and the U.S. Department of Agriculture (USDA) Foods database will be used to supplement information on food items.

Questionnaires. Participants will answer the self-reported questionnaires for sleep quality (Pittsburgh Sleep Quality Index), physical activity (International Physical Activity Questionnaire), and perceived appetite (Visual analog scale) at pre-and post-intervention.

Blood test. Venous blood samples will be collected into blood tubes at pre- and post-intervention in the morning via a catheter in an

antecubital vein, following eight hours of fasting. A total of 15 mL of blood samples will be taken from subjects using a hypodermic needle and syringe by phlebotomist/certified personnel (staff nurse/doctor). Analyses include assessment of circulating levels of glucose, insulin, lipids, inflammatory markers, oxidative stress, complete blood count and future analysis, gene expression.

Intervention monitoring

Intervention monitoring will include reporting adherence to intervention and adverse events. Feasibility will be measured by the rate of participants' withdrawal from the study due to adverse effects or inability to comply with the TRE.

Adherence to intervention. Adherence to intervention will be appraised by asking participants to complete a daily meal timing log in real-time or before bedtime. Subjects will be asked to report feeding duration by imputing the time of first meal consumption and the end time of last their last meal. Compliance with the feeding duration is assumed when participants consume their meal within the identified duration with a permissible 30-minute deviation.

Safety and feasibility. The indicator for the safety of TRE used in this study will be based on the report of adverse events and complete blood count. Participants will be asked to report any adverse events weekly throughout the study period. Participants will be formally informed of the possible adverse events and serious adverse events that might occur upon participating in this intervention study. Adverse Events (AE) related to TRE include vomiting, fatigue, dizziness, headache, nausea, constipation, diarrhoea and irritability. Meanwhile, Serious Adverse Event (SAE) is considered as defined by Malaysian Guideline for Good Clinical Practice, 4th Edition, as any untoward medical occurrence that at any dose, including death, life-threatening events requiring inpatient hospitalisation or prolongation of existing hospitalisation and results in persistent or significant disability/ incapacity. Participants with AE or SAE will be given appropriate care under medical supervision until the symptoms resolve or the participant's condition becomes stable.

Data management

Paper-based Case Report Forms (CRFs) will be used to record study data. CRF will be used for each participant should be filled out by study staff as soon as assessments are carried out. The CRF will be double-checked for potential errors or missing data prior to patients leaving the study sites. All study data, including informed consent, screening assessments, physical examinations, questionnaires, and laboratory results, will be kept confidential and filed in the study office. Data entry will be completed and stored in the primary investigator's password-protected computer. Another investigator will verify data entry to ensure consistency in data collected. CRF and other study documents will be identified based on study ID. A master list consisting of study ID and identifier will be stored in the primary investigator's password-protected computer. Data monitoring committee has not been appointed for the trial because the perceived risk of damage is low.

Data analysis

All data analyses will be carried out using statistical software package SPSS software version 26 (SPSS Inc., Chicago, IL, USA). The normality of the distribution will be tested using Shapiro-Wilk for data set less than 50. Data will be presented as means (standard deviation) or medians (Interquartile range) as indicated based on its normality. All tests will be two-tailed, and p-value of <0.05 was taken to be considered statistically significant. Chi-square test (for categorical variables) and independent t-test (for continuous variables) will be used to examine differences in baseline between groups. Analysis of Covariance (ANCOVA) will be used to compare changes in study outcomes at post-intervention. Baseline data, dietary intake and physical activity, will be treated as covariates (Wan 2021). The analysis will be performed primarily based on intention-to-treat. Missing data will be imputed according to the last observation carried forward. In addition, a per-protocol analysis including only patients with no missing observations of the variable of interest will be performed. The findings of the trial will be disseminated through communication in appropriate journals and at scientific conferences.

ETHICS AND DISSEMINATION

This study will be conducted in accordance with the Declaration of Helsinki.

Written approval of the study was obtained from Universiti Teknologi MARA Ethics Committee, reference no.: REC/02/2023 (ST/MR/46). This study is registered in a clinical trial registry, ClinicalTrials.gov, identifier no.: NCT06007950. Written informed consent will be acquired prior to enrolment into the study. This protocol is prepared based on Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 (Chan *et al.* 2013). Reporting of this trial will be based on all Consolidated Standards of Reporting Trials (CONSORT) 2010.

DISCUSSION

Time-restricted eating is the chosen intermittent fasting regime in this trial due to the perceived better sustainability advantage compared to caloric restriction. Implementation of TRE aligns daily food consumption with circadian rhythm without overt attempt to reduce caloric intake. TRE research suggests that extending the duration of the daily fast to more than 12 hours may yield additional cardiometabolic benefits (Regmi & Heilbronn 2020). The proposed mechanism of actions of TRE includes the promotion of ketogenesis, attenuation of oxidative stress and alignment with circadian rhythm (Poggiogalle *et al.* 2018; De Cabo & Mattson 2019; Azemi *et al.* 2022). TRES is the first randomised clinical trial in Malaysia to explicitly assess the effectiveness of TRE on anthropometrics, cardiometabolic health, and cardiovascular health in patients with heart disease. The design of the study is predicated on previous research on the metabolic effects of TRE interventions conducted on various populations of metabolically healthy or altered participants. Exploration of the effects of TRE on vascular health, such as endothelial function and arterial stiffness, is limited but essential for preventing additional vascular impairment (Alinezhad-Namaghi *et al.* 2023).

Current TRE studies in humans typically limit eating duration to four to 12 hours during waking hours to induce fasting effects (Christensen & Kirkham 2021). This study adopts 10 hours TRE for patients with ACS after several considerations. First, as prior human study in this specific population is not available, experimenting with gradual restriction of eating duration is reasonable, taking into account the metabolic vulnerability of patients with Acute Coronary Syndrome (ACS). Annual Report of the ACS Registry 2018–2019 for Malaysians reported 93.5% of people with ACS had at least one of the common cardiovascular risk factors, with 44.2% of these patients had diabetes, 61.9% had hypertension, 36.7% had dyslipidaemia (Ahmad 2022). Secondly, study on patients with metabolic syndrome revealed mild TRE, such as limiting eating duration to ten hours, reduced adiposity and improved blood pressure, blood glucose, and blood cholesterol levels (Wilkinson *et al.* 2020). Thirdly, ten hours of TRE is assumed to be more sustainable for long-term implementation, which can be achieved by scheduling dinner earlier. Consequently, we postulate that 10-hour TRE may be advantageous for patients with ACS.

Change in body weight is identified as the primary outcome of this RCT for multiple reasons. First, excess weight is a common attribute of patients with CAD, where data from 10,507 CAD patients participating in the EUROASPIRE IV and V studies show that 80% of patients with CAD are overweight or obese. The study showed that most patients with obesity (86%) remained obese, and 14% of overweight patients had become obese at study visits (≥6 and <24 months post-hospitalisation) (De Bacquer *et al.* 2022). Secondly, an umbrella review of systematic review revealed that obesity is associated with mortality with a pooled odd ratio of 2.18, (1.10–4.34) (Harrison *et al.* 2021). Third, the sixth joint task force of the European Society of Cardiology and other societies strongly recommends weight loss in individuals with overweight and obesity to prevent cardiovascular disease prevention. Weight loss improves blood pressure levels, reduces the risk of type 2 diabetes and, therefore, reduces the risk of recurrent cardiovascular events. Fourth, body weight is easy to measure with high precision and available in most clinical studies enabling direct comparison across studies with similar interventions.

This study is expected to confirm the safety and feasibility of mild TRE in patients with ACS. Evaluation of the effectiveness of 10-h TRE offers alternative dietary intervention for secondary prevention of CVD. Additionally, based on the findings of this study, future works with a more stringent TRE regime can be challenged on patients with ACS considering TRE effects are

duration-dependent. Therefore, it is necessary to investigate whether TRE is advantageous for individuals with more adverse metabolic profiles, such as CAD.

CONCLUSION

The protocol of the TRES clinical trial was designed to determine the safety, feasibility and effectiveness of TRE on anthropometrics, cardiometabolic and cardiovascular health in patients with ACS. Data from this study may contribute to the development of a simple, safe and sustainable dietary intervention to prevent secondary cardiovascular diseases. We anticipate that our study will serve as foundations to confirm our findings in future larger studies or studies with shorter duration in this vulnerable population.

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DECLARATION OF CONFLICT OF INTERESTS

The authors have no conflict of interest.

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