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Effect of prehabilitation-related *DIET*ary protein intake on *Q*uality *o*f *R*ecovery after elective cardiac surgery (DIETQoR) study: protocol of a randomised controlled trial

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ABSTRACT

Introduction Protein malnutrition is associated with higher risks of postoperative complications, mortality, prolonged postoperative stays in hospital, slower physical and mental recovery after surgery and lower subsequent health-related quality of life. To reduce the risk of postoperative morbidity and mortality, nutritional prehabilitation programmes have been developed recently to build up patient's nutritional reserve to withstand the stress of surgery. The intervention involves nutritional screening and counselling, and increasing dietary protein intake in protein-malnourished patients in the several weeks before surgery. However, there are few well-conducted preoperative studies to examine the effect of increasing dietary protein intake on the quality of recovery of malnourished patients after elective cardiac surgery.

Method and analysis This randomised controlled trial of malnourished patients undergoing major elective cardiac surgery will compare the quality of postoperative recovery in patients with or without nutritional prehabilitation. One hundred and thirty-two patients will be randomised to receive nutritional prehabilitation (target-adjusted whey protein powder supplementation and an individualised 1 hour session/week counselling by a dietician 1 month before operation date) or standard care (no nutritional prehabilitation). Primary outcomes will be the quality of recovery after surgery (15-item Quality of Recovery) on the third postoperative day. Secondary outcomes will include days (alive and) at home within 30 days, changes in the WHO Disability Assessment Schedule 2.0, changes in health-related quality of life (EQ-5D) and Cardiac Postoperative Morbidity Survey. An outcomes assessor will be blinded to the treatment allocation. Appropriate univariate analyses, generalised estimating equations and multiple regressions will be performed for intention-to-treat and per-protocol analyses.

Ethics and dissemination The Joint CUHK-NTEC Clinical Research Ethics Committee approved the study protocol (CREC Ref. No.: 2021.703T). The findings will be presented at scientific meetings, peer-reviewed journals and to study participants.

Trial registration number ChiCTR2200057463.

STRENGTH AND LIMITATIONS OF THIS STUDY

⇒ This is the first single-centre, pragmatic, two-armed, parallel, superiority, blinded randomised controlled trial of the effect of preoperative nutritional counselling and dietary protein supplementation (nutritional prehabilitation) on the quality of recovery after surgery.
⇒ Due to the nature of the nutritional prehabilitation intervention, patients will not be blinded to the treatment allocation (nutritional prehabilitation vs no prehabilitation).
⇒ To reduce measurement bias, blinded outcome assessors will collect postintervention outcomes from the time of surgical admission until 30 days after surgery.
⇒ As study participants may change their dietary behaviour to consume adequate protein needs before surgery, a Hawthorne effect (performance bias) cannot be fully eliminated.

INTRODUCTION

Protein is an essential nutrient for good health and accounts for all building blocks in the body.[1] Elderly patients often have inadequate daily dietary protein intake, putting them at moderate to high risk of malnutrition.[2] Protein malnutrition is a state of deficiency or excess protein intake, imbalance of essential components or impaired protein utilisation that produces a measurable change in the body composition and function.[3]

In cardiac surgical patients, the prevalence of preoperative malnutrition varies widely from 17%[4] to 46%[5] depending on the screening methods used. The causes and mechanisms of preoperative malnutrition are complex in cardiac surgical patients. Key factors that may influence the prehospital

nutritional state include chronic starvation, comorbid inflammatory illnesses, age, weight loss over the preceding 6 months, low body mass index (BMI), functional status, frailty and medications.[6] A lower BMI, New York Heart Association IV class heart insufficiency, mitral valve insufficiency and renal failure are factors associated with a twofold to fourfold higher risk of preoperative malnutrition.[7]

Protein requirements are elevated in response to surgery as protein synthesis is required for immune function and wound healing.[8] However, there is no consensus among professional nutritional societies on the exact target for protein intake for surgical patients.[9] Current consensus guidelines[10 11] focus on total quantity of protein intake but it is unclear if quality of protein intake affects patient outcomes. Goldfarb and colleagues found that the mean (SD) protein intake was 1.3 (0.5) g/kg/day, 0.7 (0.3) g/kg/day and 1.3 (0.6) g/kg/day in the preoperative, early postoperative and postdischarge periods, respectively, but its effect on postoperative outcomes was unclear.[12] In another study of 100 well-nourished patients scheduled for cardiac surgery, there was no association between low preoperative protein intake (<0.98 g/kg/day) and increased risk of postoperative outcomes (organ failure, bleeding, infection, prolonged length of stay and mortality).[13]

Significance of the present study

Protein malnutrition is associated with a higher risk of postoperative complications and mortality, prolonged postoperative stays in hospital, slower physical and mental recovery after surgery and lower subsequent health-related quality of life; all factors associated with substantially higher healthcare costs.[4 5 14–17] Poor preoperative nutritional status was associated with lower physical function levels (handgrip strength, 6 min walk test (6MWT), days to independent walking after surgery) and prolonged intensive care unit (ICU) and hospital stays.[17] However, many healthcare professionals do not recognise protein malnutrition, may under-report malnutrition or poorly document patient's BMI and food intake during the patient's hospital stay.[18] This severely limits the time available before surgery for any nutritional intervention to take effect that could reduce the risk of postoperative morbidity and mortality.

In many centres, multimodal prehabilitation provides a unique opportunity to optimise the patient's physiological reserve in the 4–8 weeks before surgery to withstand the surgical stress response.[19] Multimodal prehabilitation includes individualised structured exercises (aerobic and resistance training), nutrition counselling and supplementation and psychological support (eg, standardised multimedia patient education). This study protocol focuses on nutritional prehabilitation for malnourished patients to increase their dietary protein intake for building up their nutritional reserve to withstand the stress of surgery. Whether such preoperative nutritional intervention in malnourished patients several weeks before hospital admission improves their quality of recovery (QoR) after cardiac surgery is currently unknown.

Study objectives

The primary objective of this randomised controlled trial (RCT) is to evaluate the effect of nutritional prehabilitation with high-quality dietary protein intake on the QoR after elective cardiac surgery in malnourished patients. There are several secondary objectives:

1. To determine whether dietitian-guided counselling increases preoperative dietary protein intake in malnourished patients scheduled for elective cardiac surgery undergoing nutritional prehabilitation.
2. To evaluate the effect of nutritional prehabilitation on the length of postoperative stay in malnourished patients undergoing elective cardiac surgery.
3. To describe the interaction between preoperative dietary protein intake and physical activity on QoR after elective cardiac surgery in malnourished patients undergoing nutritional prehabilitation.

METHOD AND ANALYSIS

Study design

This single-centre, pragmatic, two-armed, parallel, superiority, blinded RCT will be conducted at the Prince of Wales Hospital in Hong Kong, a university teaching hospital. Participants will be randomly allocated to either nutritional prehabilitation or usual care (no nutritional prehabilitation) with 1:1 allocation. Block randomisation with randomly selected block sizes will be performed according to a computer-generated sequence by one of the research staff not involved in the screening, recruitment or data collection. The treatment allocation will be concealed in consecutively numbered sealed opaque envelopes, to be opened by the dietician after written informed consent for the study has been obtained and after baseline Food Frequency Questionnaire (FFQ),[20] Clinical Frailty Scale (CFS)[21] and exercise capacity measurements have been conducted. The completed study will be reported with reference to the CONsolidated Standards Of Reporting Trials statement,[22] and the protocol is reported according to the Standard Protocol Items: Recommendations for Interventional Trials statement.[23] An overview of the study design is provided in figure 1.

Study setting and population

This study will be conducted at the Prince of Wales Hospital in Hong Kong, a 1807-bed tertiary hospital with a dedicated Pre-Operative Assessment Clinic (POAC) and prehabilitation facilities. All elective cardiac surgical patients will be routinely admitted to a 23-bed ICU for early postoperative care and monitoring with 1:1 nursing at all times, with an expectation of discharge from ICU to a high-dependency cardiac ward within 24 hours after surgery.[24] Adult patients undergoing major elective cardiac surgery (coronary artery bypass graft, with or without valvular repair/replacement) will be recruited. Patients will only be recruited once; only the first attempt

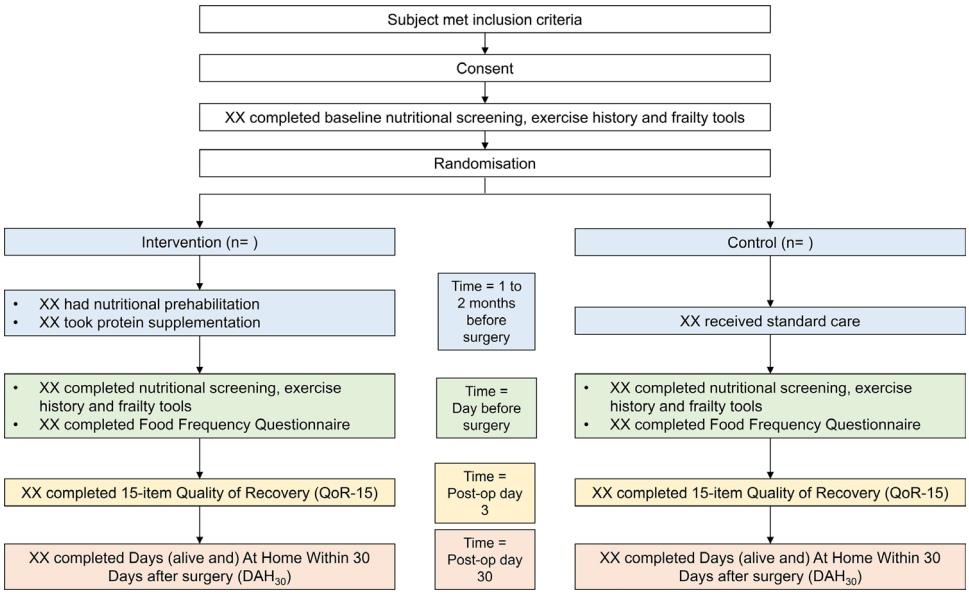

Figure 1 Patient flow diagram.

and assessment results will be recorded for patients who require follow-up or repeated surgery. The inclusion and exclusion criteria are shown in table 1. We will record the reasons for exclusion.

Screening

Patients on the elective cardiac surgery waiting list are routinely assessed at the POAC clinic several weeks before the scheduled operation date. After written informed consent, patients will complete the Malnutrition Universal Screening Test (MUST) questionnaire[25] and undertake a body composition test using a bioelectrical impedance analysis device (InBody 270, InBodyUSA, Cerritos, CA) to measure fat free mass index (FFMI) and skeletal mass index (SMI) for study eligibility determination. For the purpose of this study, preoperative malnutrition will be defined as a MUST>0 or FFMI<17 kg/m^2 for men or FFMI<15 kg/m^2 for women or SMI<7 kg/m^2 for men or SMI<5.7 kg/m^2 for women.[26]

If the inclusion criteria are met, all participants will be interviewed by a dietician to assess their usual dietary intake (frequency and usual quantity) over the past 1 month using the locally validated semiquantitative FFQ[20] at baseline. For the purpose of this study, only broad food categories with food containing protein from the 288 local food items FFQ will be used (ie, vegetables and beans, fruits, meats, fish and seafood, eggs, dairy

Table 1 Eligibility criteria for the randomised controlled trial

Inclusion criteria	Exclusion criteria
1. Adults (no age restriction) undergoing elective or non-emergent major cardiac surgery (CABG, valve surgery or combined) 2. MUST>0 or FFMI<17 kg/m^2 for men or FFMI<15 kg/m^2 for women or SMI<7 kg/m^2 for men or SMI<5.7 kg/m^2 for women 3. Patients with estimated ≥4 weeks of surgical waiting list time	1. Redo or emergency cardiac surgery 2. Major comorbidities precluding surgery, are mentally incompetent, any current disorder impairing accurate and objective completion of the malnutrition assessment and nutritional screening questionnaires, or are unable to understand Chinese or English 3. CKD not on dialysis requiring low protein diet, advanced stage CKD or end-stage renal disease on dialysis with protein requirements of 1.0–1.2 g/kg body weight/day will be excluded[44] 4. Patients with liver diseases and at risk for hepatic encephalopathy 5. Physical limitations that would preclude regular attendance to outpatient nutritional prehabilitation sessions 6. Seen by a dietician in the last 6 months 7. Patients with whey protein allergy

CABG, coronary artery bypass graft; CKD, chronic kidney disease; FFMI, fat free mass index; MUST, Malnutrition Universal Screening Test; SMI, skeletal mass index.

Table 2 Assessment overview

Assessment	Baseline	Prehospital period	Admission	POD3	POM1
Enrolment					
Eligibility screen	X				
Informed consent	X				
Malnutrition screening (MUST, FFMI, SMI)	X		X		
Demographic and comorbidity data	X				
Food Frequency Questionnaire	X		X		
Clinical Frailty Scale, 6MWT, C-VSAQ	X		X		
Randomisation	X				
Nutritional intervention					
Subjective Global Assessment, 24 hours food recall		X			
Protein supplement compliance/adverse effect		X			
Outcomes					
Primary					
15-item quality of recovery				X	
Secondary					
DAH30					X
WHODAS	X				X
EuroQol EQ-5D questionnaire	X				X
Cardiac Postoperative Morbidity Survey				X	

DAH30, days at home within 30 days of surgery; FFMI, fat free mass index; MUST, Malnutrition Universal Screening Test; 6MWT, six min walk test; POD3, postoperative day 3; POM1, postoperative 1 month; SMI, skeletal mass index; VSAQ, Chinese version of Veterans Specific Activity Questionnaire; WHODAS, WHO Disability Assessment Schedule 2.0 questionnaire.

products and beverages).[20] We will also ask patients about any other protein food items that they consume regularly but are not listed under the FFQ. Mean daily protein intake from food items consumed will be estimated using the nutrition analysis software Food Processor Nutrition Analysis and Fitness software cloud service version 11.1 (ESHA Research, Salem, USA) including local foods selected from food composition tables from China and Hong Kong. Another research staff member, blinded to treatment allocation, will use the same modified FFQ at hospital admission before surgery in all patients to compare changes in protein intake between treatment groups.

The exercise capacity and physical activity level will also be collected at baseline and immediately before surgery in all study participants (table 2). Although cardiopulmonary exercise testing (CPET) is the gold standard for measuring exercise capacity objectively, access to CPET is very limited in the prehabilitation period. Therefore, we will use the 6MWT to measure the exercise capacity. The minimal clinically important difference for 6MWT is 14.0–30.5 m in population with cardiac and pulmonary diseases.[27] The Chinese version of Veterans Specific Activity Questionnaire (C-VSAQ)[28] describes the different intensities of daily activities with corresponding metabolic equivalents (METs) on a scale ranging from 1 MET to 13 METs. Participants will be asked to indicate the highest MET that they are able to achieve routinely. The individual's exercise capacity will then be age-adjusted.[28]

Blinding

Due to the nature of the intervention and requirements of informed consent, trial participants will not be blinded to the treatment allocation. Study research personnel collecting the follow-up nutritional status and food frequency intake at hospital admission will be blinded to the treatment allocation. Outcome assessors will be blinded to the participant's group allocation.

Interventions

Control (standard care) arm

Patients in the control group will receive standard care with standardised surgical processes and perioperative care under existing protocols for preoperative patient education, standardised anaesthesia,[29] postoperative ICU sedation, analgesia and weaning from mechanical ventilation, perioperative physiotherapy and early mobilisation.[24] In brief, the control group will receive unstructured preoperative health promotion/patient education, plus physical prehabilitation provided at the treating physician's discretion. Unstructured and general health education includes information on exercise and a healthy diet without a tailored nutritional plan and no focus on protein education. Both groups will have bioelectrical

impedance analysis (FFMI and SMI) measured at baseline and immediately before surgery to determine any changes in body composition (table 2).

Intervention (nutritional prehabilitation+standard care) arm

The primary aim of the intervention is to increase protein intake using dietetic counselling and to 'top up' with whey protein powder supplements to meet the target protein intake of 1.5 g/kg/day. In addition to standard care, the nutritional prehabilitation group will receive individual 1 hour session/week counselling by a dietician, 1 month before scheduled operation date. The intervention involves a tailored approach to meet the nutritional needs of individual participants. This includes the following:

- Reviewing the patient's completed FFQ[20] to report on the amount of dietary protein intake consumed and net deficit daily protein intake
- Assessing the overall nutritional status using the Subjective Global Assessment[30] and a 24-hour diet recall at the initial visit
- Discussing why increasing dietary protein intake before surgery is important
- Educating patient about which foods contain high quality protein to eat (eg, chicken, fish, soy, lentils, nuts brown rice)[31]
- Prescribing the optimal amount of whey protein powder supplement (Beneprotein sachets) to meet the target protein intake of 1.5 g/kg/day based on actual body weight or adjusted body weight for obese patients
- Patients will be reminded via phone call 1 day before their nutritional counselling session

A Registered Dietitian (RD) will be responsible for safekeeping and dispensing of the whey protein powder supplement (Beneprotein). Participants will be given enough sachets for 1 week to consume and some backup sachets. Each sachet provides 6 g of protein (one egg equivalent). The RD will recommend that participants consume each Beneprotein sachet with 100 mL of water. They will also be given a ticked calendar and asked to bring all the used sachets, unused sachets back each week to estimate the compliance rate.

Outcome measures

Primary outcome

Quality of Recovery (QoR)

The Chinese version of the 15-item Quality of Recovery (QoR-15)[32] will be used on postoperative day 3. The QoR-15 includes the items measuring pain, physical comfort, physical independence, psychological support and emotional state.[32] The QoR-15 score ranges from 0 to 150, takes about 3 min to complete and has well-established psychometric properties.[32] A poor symptom state (recovery) after surgery has been defined at a cut-off of <118.[32] Depending on patient's postoperative status, QoR-15 assessment may be deferred if the patient is unwell or unavailable. The QoR-15 assessment will be conducted at a later date after obtaining patient's agreement. The blinded outcome assessor will record the exact date of actual QoR-15 assessment.

Secondary outcomes

Days (alive and) at home within 30 (DAH_{30}) days after surgery

The DAH is a patient-centred, generic outcome measure that will be used to measure the patient's overall recovery profile.[33] DAH is a composite measure that incorporates the details on postoperative hospital length of stay, discharge to rehabilitation centre or nursing home, hospital readmissions and postoperative deaths.[33] Three days difference is considered clinically meaningful.[34] The blinded outcome assessor will extract data from the electronic patient medical record to estimate the DAH_{30}.

Disability-free survival at 30 days after surgery

New or residual disability after surgery is of particular concern to patients and healthcare professionals.[35] In this study, the changes in disability-free survival (baseline to postoperative 1 month, table 2) will be measured using the Chinese (Hong Kong) version of the 12-item WHO Disability Assessment Schedule (WHODAS) 2.0 score that has been validated in surgical patients.[35] It will take 5 min to complete.[35] Patients will be asked to rate the difficulty in carrying out 12 specified activities on a 5-point Likert scale (0=none to 4=extreme) in the past 30 days. The total score will be converted to a scale from 0 (no disability) to 100 (maximum disability) by a blinded outcome assessor, with the following subcategories: none (0%–4%), mild (5%–24%), moderate (25%–49%), severe (50%–95%) and complete (96%–100%) disability.[35] The 25% threshold will be used to define disability; an increase in the WHODAS score≥8% from their baseline assessment will define new disability.[35]

Health-related quality of life

The changes (baseline to postoperative 1 month, table 2) in health-related quality of life will be measured using the Chinese (Hong Kong) version of the EuroQoL EQ-5D.[36] Patients will be asked to rate their mobility, self-care, usual activities, pain/discomfort and anxiety/depression on five levels (no problems, slight problems, moderate problems, severe problems and extreme problems) and to rate their health state from 0 (worst imaginable) to 100 (best imaginable). The blinded outcome assessor will use the descriptive responses to estimate the EQ-5D utilities by applying a set of Hong Kong reference weights.[36]

Cardiac Postoperative Morbidity Survey (C-POM)[37]

The C-POM score quantifies the total morbidity burden and is currently the only validated measure of postoperative morbidity after cardiac surgery. It is a composite outcome that included the following 13 morbidity types: pulmonary, infectious, renal, gastrointestinal, cardiovascular, neurological, haematological, wound, pain, endocrine, electrolyte, review and assisted ambulation. The blinded outcome assessor will collect the C-POM survey

on the third postoperative day using information from the patient's medical records.

Other variables in data collection

Using a standardised data collection form, a research assistant will collect demographic (age, gender, BMI, education level, home living support, frailty level using CFS, comorbidities), adverse protein supplement effect as measured by elevated blood urea nitrogen (BUN) concentration (BUN>24 mg/dL (8.5 mmol/L)),[38] American Society of Anesthesiologist's Physical Status, physical prehabilitation attendance, intravenous iron therapy during prehabilitation period, operation date, type of cardiac surgical procedure, duration of surgery, duration of anaesthesia, length of ICU and hospital stays. Possible contamination of control arm (ie, self-initiated changes in diet with protein supplement after providing study details) will be assessed by asking patients if they have made changes to eating habit or taken protein supplements immediately before surgery. An overview of the data collection process is shown in table 2.

Sample size

A sample size of 60 in each group will have 90% power to detect a moderate to large QoR effect (0.60) using a two group t-test with a 0.05 two-sided significance level (nQuery Advisor, version 7.0). Allowing 10% loss to follow-up, a total of 132 patients will be required.

Statistical methods

The data derived from the patient's FFQ at follow-up will be used to estimate each participant's mean protein quality score using the framework methodology outlined by Katz and colleagues.[31] The primary analysis will be an Intention to treat analysis and the secondary analysis will be a per-protocol analysis. We will consider satisfactory compliance with whey protein powder supplementation if the patient's intake is above 75% for the per-protocol analysis. Missing data will be checked and imputation of the missing data will be used to preserve power. Continuous variables will be reported as mean (SD) and median (IQR) as appropriate.

After checking for normality using Shapiro-Wilk's test, we will perform independent Student's t-test or Mann-Whitney U test as appropriately to compare group differences for the magnitude of protein intake and quality, QoR-15, postoperative length of stay and DAH_{30}. We will use a generalised estimating equation with a Gaussian distribution, identity-link, exchangeable correlation with robust SEs to estimate the mean difference (MD) in preoperative dietary protein intake and quality between treatment groups over time. Multiple regression will also be used to examine the association between dietary protein intake and physical activity with 15-item QoR; an interaction effect of dietary protein intake change and physical activity change will be included in the model, after adjusting for other potential confounders (prehabilitation exposure, change in diet quality index-international (DQI-I) score, physical activity change and frailty) using a directed acyclic graph approach in figure 2. Statistical analyses will be performed using Stata V.17 (StataCorp, College Station, TX). The two-sided level of significance will be set at $p<0.05$.

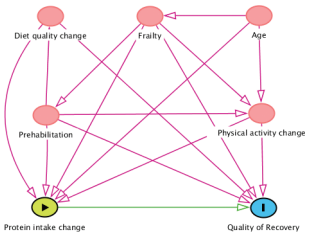

Figure 2 Directed acyclic graph using DAGitty software V.3.0. Assumptions made in the nutritional prehabilitation (exposure) and quality of recovery (outcome) relationship to identify the set of variables needed for confounding adjustment. Red circle represents ancestor of exposure and outcome. All red arrows lie on open biasing paths. Green arrow lies on open causal path.

Monitoring and data management

We will collect and manage the study data using research electronic data capture electronic data capture tools[39] hosted at The Chinese University of Hong Kong. No interim analysis has been planned. No formal data monitoring committee has been set up. There will be no formal data monitoring committee. However, the study progress and any unanticipated serious adverse events will be reported as part of an annual renewal application for local research ethics committee approval. An anonymised data set will be available after the publication of the completed study, following the deposition of the data set into The Chinese University Research Data Repository (https://researchdata.cuhk.edu.hk/).

Patient and public involvement

Patients and the public were not involved in the development of the research question, the design of the study nor did they contribute to the editing of this document for readability or accuracy.

Ethics and dissemination

Before obtaining written informed consent, the purpose of the study, procedures, risks and benefits of participation, and the time commitment involved will be explained to eligible patients by the study dietician. There will be no extra costs for patients who are allocated to the intervention group since the expenditure for every dietician consultation session will be reimbursed. We plan to disseminate the results to study participants by giving them a one-page plain language summary.

Patients may withdraw from the study without prejudice at any time during the study. Data will be kept confidential in secure offices of the Department of Anaesthesia and Intensive Care for 7 years. Approval for the project (protocol V. 1.1, 24 January 2022) was obtained from The Joint Chinese University of Hong Kong-New Territories

East Cluster Clinical Research Ethics Committee (CREC Ref. No. 2021.703-T). We will notify the local research ethics committee and clinical trials registry about any protocol modifications in a timely manner. The study will adhere to local laws, Declaration of Helsinki and institutional policies.

DISCUSSION

The American Society for Enhanced Recovery and Perioperative Quality Initiative recommends that patients at risk of malnutrition be given preoperative oral nutritional supplements (immune-nutrition containing arginine), fish oil or high protein (minimum 18 g protein/dose, 2–3 times/day) for a period of at least 7–14 days before surgery.[14] Of the 191 elective cardiac surgical patients in our recent unpublished audit, 51 (27%) had preoperative protein-malnutrition as determined by a dietician. Among these 51 patients, 38 (75%) were moderately malnourished, while the rest were severely malnourished. These findings suggest that a substantial proportion of elective cardiac surgical patients are at risk of adverse malnutrition-related postoperative events.

Few well-conducted studies in North America or Western Europe provide a sound evidence-based approach to determining the potential or actual benefits of increasing dietary protein intake in malnourished patients before any elective surgery, and especially in cardiac surgical patients. A systematic review of 15 RCTs in 3831 mixed medical and surgical patients with malnutrition showed that nutritional support (parenteral nutrition, enteral nutrition and immunonutrition) was associated with a reduction in the risk of infection (relative risk (RR) 0.58, 95% CI: 0.50 to 0.68), non-infectious complications (RR 0.74, 95% CI: 0.63 to 0.88) and a shorter length of hospital stay (MD−2.6, 95% CI: −5.1 to −0.2 days).[40]

There remain some potential study limitations. First, study participants may change their dietary behaviour to consume adequate protein needs before surgery after exposure to the information about the background and rationale of the RCT. This Hawthorne effect, a type of performance bias, may be present after study participants become more aware of the possible role of preoperative nutrition on postoperative recovery. Nevertheless, any increased in protein intake in the standard care group will likely be captured at the time of the second FFQ analysis. Second, the dietetic counselling with education on high-quality protein foods may lead to changes in overall diet quality; such changes may affect outcomes independent of protein intake. To control for the possible effect, we will adjust for the overall diet quality change using the DQI-I scores[41] derived from the FFQ responses. Third, there are varied and multiple determinants of malnutrition that cannot be completely assessed at baseline.[42] In this RCT, we will measure education level, home living support, frailty level using CFS, comorbidities but other determinants, such as socioeconomic status, mental health and isolation environment will not be measured, however the randomisation process should ensure sufficient equipoise. Finally, as objective measures of protein assimilation, such as a positive nitrogen balance, are impractical and of limited precision, we will rely on subjective assessment (ticked calendar and used sachets) to demonstrate compliance. Each participant's BUN concentration will be measured to serve as a warning marker for possible adverse effects of the increased protein intake, and as a marker of increased protein intake, although it is acknowledged that there is only a moderate correlation (r=0.50) between BUN concentration and protein intake in patients aged 60 years and above.[43]

Our intervention, an individualised tailored approach by a dietician, will establish an accurate estimate of the local prevalence of low dietary protein intake (<1.5 g/kg/day) presenting for major elective cardiac surgery. The trial will facilitate the feasibility and design of future studies of nutritional prehabilitation in all surgical patients after establishing the level of patient compliance to whey protein supplementation. The results of this RCT will enable us to establish magnitude of prehabilitation effect of increasing dietary protein intake on postoperative length of hospital stay, and improving patient-centred outcomes within 30 days after cardiac surgery, using validated and reliable tools. The trial will also generate a clearer understanding of the possible additive or synergistic effects of improved dietary protein intake with physical prehabilitation on QoR after surgery, especially in prefrail to frail patients. This should further clarify prehabilitation's effectiveness based on nutritional optimisation alone.

Trial status

The patient recruitment started on 1 September 2022. We expect patient recruitment and 1 month of follow-up to be completed by 30 August 2025.

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Competing interests None declared.

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