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Novel multimodal intervention for surgical prehabilitation on functional recovery and muscle characteristics in patients with non-small cell lung cancer: study protocol for a randomised controlled trial (MMP-LUNG)

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ABSTRACT

Introduction Lung cancer is the leading cause of cancer-related deaths. Patients with stage I-III non-small cell lung cancer (NSCLC) are candidates for surgical resection; however, patients with low muscle mass, myosteatosis, malnutrition or reduced functional capacity preoperatively have a higher risk of postoperative morbidity. Prehabilitation is a care process aiming to enhance functional capacity before surgery to improve surgical outcomes. Study objectives are to test the effect of prehabilitation interventions of a mixed-nutrient supplement (NUT) alone or its combination with exercise (MM, multimodal prehabilitation), compared with placebo-control (CTL), in NSCLC patients on change in functional capacity pre-surgery and post-discharge, muscle mass and myosteatosis, postoperative health-related quality of life (HRQoL), complications and length of hospital stay. We hypothesise that a multi-nutrient supplement, with or without exercise, will be of benefit.

Methods and analysis Randomised controlled trial of three parallel arms: 168 patients with operable NSCLC at nutritional risk are randomised 1:1:1 to CTL, NUT or MM. Patients in the NUT and MM groups receive a nutritional supplement consisting of whey protein, leucine, vitamin D and fish oil 4–6 weeks preoperatively and 6 weeks post-discharge. The exercise programme (MM) consists of daily moderate-intensity aerobic activity and resistance training 3 days/week. The following is assessed at baseline, preoperatively and week six post-discharge: functional capacity using the 6 min walk test, muscle mass and myosteatosis using D3-creatine dilution and peripheral quantitative CT, and HRQoL using the Functional Assessment of Cancer Therapy-Lung. Intention-to-treat analysis of covariance will compare between-group differences adjusted for baseline variables. Postoperative functional recovery will be tested by logistic regression. Between-group differences in clinical outcomes will be tested, applying Bonferroni correction.

Ethics and dissemination This trial is approved by the McGill University Health Centre Research Ethics Board (2022–7782). Results will be published in open-access peer-reviewed journals and conference presentations.

Trial registration details NCT05955248.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Low muscle mass, functional capacity and malnutrition are associated with greater risk of adverse surgical outcomes in patients with cancer. Multimodal prehabilitation improves functional capacity before surgery, and patients deemed at higher surgical risk demonstrate improved postoperative outcomes following such programmes.

WHAT THIS STUDY ADDS

⇒ A novel multi-nutrient supplement, made of whey protein, leucine, vitamin D and fish oil, with and without exercise, could improve preoperative functional capacity, recovery and postoperative outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ If the hypothesis is confirmed, patients could be systematically screened for malnutrition at diagnosis and referred to the prehabilitation clinic accordingly, hence optimising better resource management. In addition, nutritional interventions could be used with or without exercise to improve outcomes in those patients.

INTRODUCTION

Background

Lung cancer is the most frequently diagnosed cancer in Canada and is the leading cause of cancer deaths.[1] Lung cancer can be divided into small cell lung cancer and non-small cell lung cancer (NSCLC). The latter is the most

common, accounting for 88% of cases.[1] Recent advances in systemic therapy, including the introduction of immunotherapy in the neoadjuvant setting, have expanded the use of surgery as a curative option for patients with stage I-III NSCLC. However, patients with lung cancer are at particular risk of low muscle mass due to ageing, their catabolic disease state, smoking and symptoms that reduce food intake. The association between low preoperative muscle mass,[2 3] poor muscle quality (myosteatosis),[4–7] poor functional capacity[8] and malnutrition[9] with increased risks of perioperative complications and worse long-term outcomes, including mortality, has been widely reported in the literature.

Prehabilitation is defined as "a process from diagnosis to surgery, consisting of one or more preoperative interventions of exercise, nutrition, psychological strategies and respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve postoperative outcomes, and facilitate recovery".[10] While preoperative exercise alone has been found to improve surgical outcomes in patients with lung cancer,[11] it is increasingly recognised that multimodal prehabilitation, including nutrition, exercise and anxiety management, may offer additional benefits. Prehabilitation interventions contribute to improvements in preoperative functional and exercise capacity[12–17] and consistently show higher rates of postoperative functional recovery, in multiple cancer populations.[11 16–18] In terms of postoperative outcomes, studies demonstrating benefits typically target higher-risk patients, based on age, baseline functional capacity or physical status such as per the American Society of Anesthesiologists score.[13 19] Additionally, patients at greater risk of malnutrition based on Patient-Generated Subjective Global Assessment (PG-SGA) scores showed greater improvements in preoperative functional capacity with multimodal prehabilitation.[20 21] However, those at very high risk of malnutrition often do not respond to prehabilitation, possibly due to metabolic changes restricting adherence to exercise and decreased nutrient availability.[20]

Malnutrition is common in cancer patients at diagnosis,[9] likely due to a combination of reduced food intake and underlying metabolic derangements. This condition is associated with poor muscle mass, strength and function[22] and is a risk factor for poor surgical outcomes and mortality.[9] Adaptive mechanisms caused by malnutrition reduce energy expenditure by decreasing basal metabolic rate and function,[22] thus potentially limiting the ability of those patients to perform unimodal exercise interventions. Studies exploring the effect of nutritional supplements alone on cancer surgical recovery most often use protein as a standalone component.[23] Yet, leucine,[24] omega-3 fatty acids[25] and vitamin D[26] may also contribute to improving muscle health and functional capacity. The use of a multi-nutrient supplement may have additive beneficial effects on surgical outcome measures and muscle parameters. A supplement combining those nutrients has been used in a study of frail older adults, but given the advanced age of study participants, the trial was deemed non-feasible and was interrupted.[27] A pilot study in surgical patients with lung cancer,[28 29] however, demonstrated feasibility and promising results. Thus, a larger trial is warranted to support the use of such multi-nutrient supplement.

Rationale

The preoperative period is an opportune time to actively engage and empower patients in improving their functional, nutritional and mental status in anticipation of the surgical stress. As opposed to exercise, the role of nutrition in prehabilitation has been much less studied. Optimisation of dietary supplements provided may improve functional capacity before surgery as well as postoperative outcomes, especially in malnourished patients. In addition, the effect of prehabilitation on skeletal muscle mass and myosteatosis is unknown and remains to be explored.

Objectives

In a randomised control trial (RCT), we aim to test the effect of a multimodal prehabilitation intervention (MM) lasting 4–6 weeks prior to surgery and 6 weeks following hospital discharge, which combines a mixed-nutrient supplement with structured exercise training or the supplement alone (NUT) against a placebo (CTL) on the following pre- and postoperative outcomes in surgical patients with NSCLC at nutritional risk: The preoperative change in functional capacity, measured with the 6 min walk test (6MWT), the recovery of functional capacity 6 weeks after discharge, postoperative QoL, complications, muscle mass, strength and quality, and hospital length of stay.

We hypothesise that functional capacity will increase more in both the MM and NUT groups preoperatively, and more of these participants will recover their baseline functional capacity by week 6 compared with the CTL group. We also hypothesise that the intervention groups (MM and NUT) will have better postoperative self-reported HRQoL; fewer postoperative complications; an attenuated loss in muscle mass, strength and quality perioperatively; and a shorter length of stay.

METHODS AND ANALYSIS

This trial was approved by the McGill University Health Centre (MUHC) Research Ethics Board (REB 2022–7782), Montreal, Quebec, Canada, and registered on ClinicalTrials.gov (NCT05955248).

Study design

This is a prospective 10 to 12-week randomised controlled trial of three parallel arms: control (CTL), multi-nutrient supplement (NUT) and multimodal intervention (MM);

double-blinded, placebo-controlled for supplement. It is a single-centre trial taking place at the MUHC-Montreal General Hospital, located in Montreal, Quebec, Canada. The study will follow Consolidated Standards of Reporting Trial guidelines and is designed to minimise bias according to the Cochrane Collaboration's tool.[30]

Population and recruitment

We are aiming to enrol 168 males and females (≥45 y) with NSCLC stages I, II or IIIa, at nutritional risk (PG-SGA >2), scheduled for surgery. Exclusion criteria are prior recent (<2 months) neoadjuvant therapy (chemo-, radio- and or immunotherapy), PG-SGA score <3, inability to perform or comorbidities contraindicating exercise (defined as VO_2peak<10 mL O_2/kg/min), inability to walk (wheelchair use), allergy to milk or seafoods, hypercalcaemia (total serum Ca >2.60 mmol/L or ionised Ca >1.30 mmol/L), hypervitaminosis D (serum 25(OH) D >375 nmol/L), glomerular filtration rate <30 mL/min/1.73 m^2) and insufficient understanding of English or French to provide informed consent. Patients taking prior omega-3 FA supplements will be asked to withhold them during the study; those taking vitamin D will continue unless serum 25(OH)D >80 nmol/L.

Participant recruitment was initiated in June 2023 and is expected to conclude in December 2026. The study takes place at the MUHC-Montreal General Hospital. Potential participants are identified by four thoracic surgeons during their initial appointment with them and approached by the study coordinator for a pre-screening interview. During this discussion, the study coordinator interviews patients on potential exclusion criteria, such as food allergies and appetite and weight loss for malnutrition risk. Patients who are deemed eligible and are also interested in participating in the study are scheduled for a first visit at the perioperative programme (POP) clinic for their baseline assessment. The informed consent form is sent by email to read ahead of the first visit. For eligible patients who decline to participate, the reason for declining and their age is documented.

During the first visit, the study procedures, requirements, risks and benefits are explained verbally, and sufficient time is given to read and discuss the consent form. Consenting participants complete the PG-SGA questionnaire assessing weight loss, dietary intake, symptoms, performance, disease state (that may affect nutritional requirements), metabolic stressors (fever or use of corticosteroids) and a nutrition-focused physical exam is completed to confirm eligibility. Patients with a PG-SGA score of >2 are categorised at nutritional risk and deemed eligible to participate in the study. Patients with low nutritional risk (scores ≤2) were excluded from the study and subsequently referred to the POP clinic for off-trial clinical counselling. To maximise retention, participants are visited the day after their surgery and given a get well soon card.

Randomisation

Participants are randomised in a 1:1:1 ratio to receive a mixed-nutrient supplement (NUT) alone, NUT combined with exercise (MM, multimodal prehabilitation) or placebo-control (CTL), using a randomisation scheme by permuted block of three, within each stratum of sex and functional capacity (< or ≥ 450 m on the 6MWT), as individuals who are less fit at baseline have greater risks of complications[31 32] and tend to improve more with prehabilitation.[33] Group allocation was generated by the Research Institute-MUHC biostatistician and is concealed using sequentially numbered sealed envelopes. Given that the baseline 6MWT result is used in the randomisation scheme, envelopes are opened by the study coordinator after the test is performed. Considering the nature of the intervention, participants and study personnel are blinded to the NUT and CTL group, while the MM group is not blinded. Supplements are packaged by the supplier (Gruppo Nutrition Inc, ON, Canada) in coded-labelled sachets (for powder) and bottles (for oil). The supplier has disclosed the code to a research person not associated with the trial. Research staff prepare boxes of supplements (or placebo) according to coded group allocation. All participants are instructed not to self-supplement with commercially available products, to minimise the risk of group contamination.

If any adverse event occurs for which a participant should be unblinded, the participant would be contacted by the external research person aware of group allocation for unblinding.

Intervention

The intervention lasts from 4 days after the baseline assessment for surgery (estimated 4 to 6 weeks pre-surgery) until 6 weeks post hospital discharge, for a total of about 10–12 weeks. Additionally, psychosocial screening is performed using the Hospital Anxiety and Depression Scale (HADS),[34] and any participant with scores of seven or higher for anxiety or five or higher for depression is referred for psychosocial counselling by a trained psychosocial nurse for anxiety management. Relaxation and breathing techniques are taught and prescribed to be performed two to three times/week at home. Finally, all participants receive individualised counselling from a registered dietitian to optimise their diet, with a focus on protein-rich foods to meet dietary protein intake of 1–1.2 g/kg/day and energy intake of 25–30 kcal/kg/day. Dietary counselling also includes individualised tips to alleviate nutrition impact symptoms (loss of appetite, constipation, etc). Participants randomised to CTL and NUT receive education on the benefits of a healthy diet and physical activity but without specific tips on precise types and duration of exercises. All participants from the study follow the Enhanced Recovery After Surgery protocol[35] as it is the standard of care at the MUHC. As such, participants receive a carbohydrate-loading drink to consume 2 hours before surgery, to reduce postoperative

insulin resistance and surgery-related catabolism.[35] Early ambulation and oral feeding are ubiquitously initiated within 24 hours of surgery.[35]

The NUT group is provided with an active supplement containing 10 or 20 g of whey protein isolate (dose determined individually with the goal of reaching a total intake ≥1.5 g/kg/d), 3 g of leucine and 800 IU of vitamin D3 to be consumed twice daily: once before breakfast and once at bedtime. In addition, this group receives 15 mL of fruit-flavoured fish oil containing 2120 mg eicosapentaenoic acid (EPA) and 1320 mg docosahexaenoic acid (DHA). In turn, the CTL group is receiving an isocaloric placebo supplement with the same physical aspect, flavour and packaging as the active supplement. Maltodextrin (10 or 20 g) is the placebo for protein powder and sunflower oil (15 mL), the placebo for fish oil. Placebo is ingested at the same time points as the active supplement.

The MM group receives the active supplement and a resistance and aerobic exercise programme. During the 4 to 6 weeks prior to surgery, participants have 1 weekly in-person kinesiologist-supervised session and biweekly at home sessions. The training consists of (1) 30 min per day of cumulated aerobic exercise of their preferred type (walking, machine or other), at a moderate intensity of 12–15 on a Borg scale of 6 to 20, including a 5 min warm up and cool down and (2) 30 min, 3 times per week, of resistance exercise targeting major muscle groups with the use of a Theraband or body weight. These are instructed to be performed in 2 sets of 8–12 repetitions for each exercise, with the intensity becoming 'difficult' to perform (rate of perceived exertion of 5–6/10) by the end of the set. The programme is individualised based on initial assessments and in line with American College of Sport Medicine standards.[36] Technique, intensity and progression are monitored weekly; intensity or duration is increased weekly, if tolerated. Patients are given an information booklet containing instructions and figures showing all elements of the programme and a Borg scale to assist in determining appropriate exercise intensity at home. Non-exercising NUT and CTL participants are contacted weekly by phone to provide equivalent monitoring time and encouragement.

After discharge, MM participants follow a customised weekly home-based programme similar to the preoperative training with an on-site supervised session at week 3. During the postoperative exercise session, participants perform preoperative exercises free of resistance in the active range of motion, and based on pain tolerance, resistance is progressively increased. Home sessions are monitored with weekly telephone or video calls for follow-up and adjustments by the study kinesiologist.

Assessment visits

There are three standardised site visits for assessment: baseline, within 1 week of surgery and 6 weeks after hospital discharge (figure 1). Additional site visits for supervised exercise training are planned weekly during

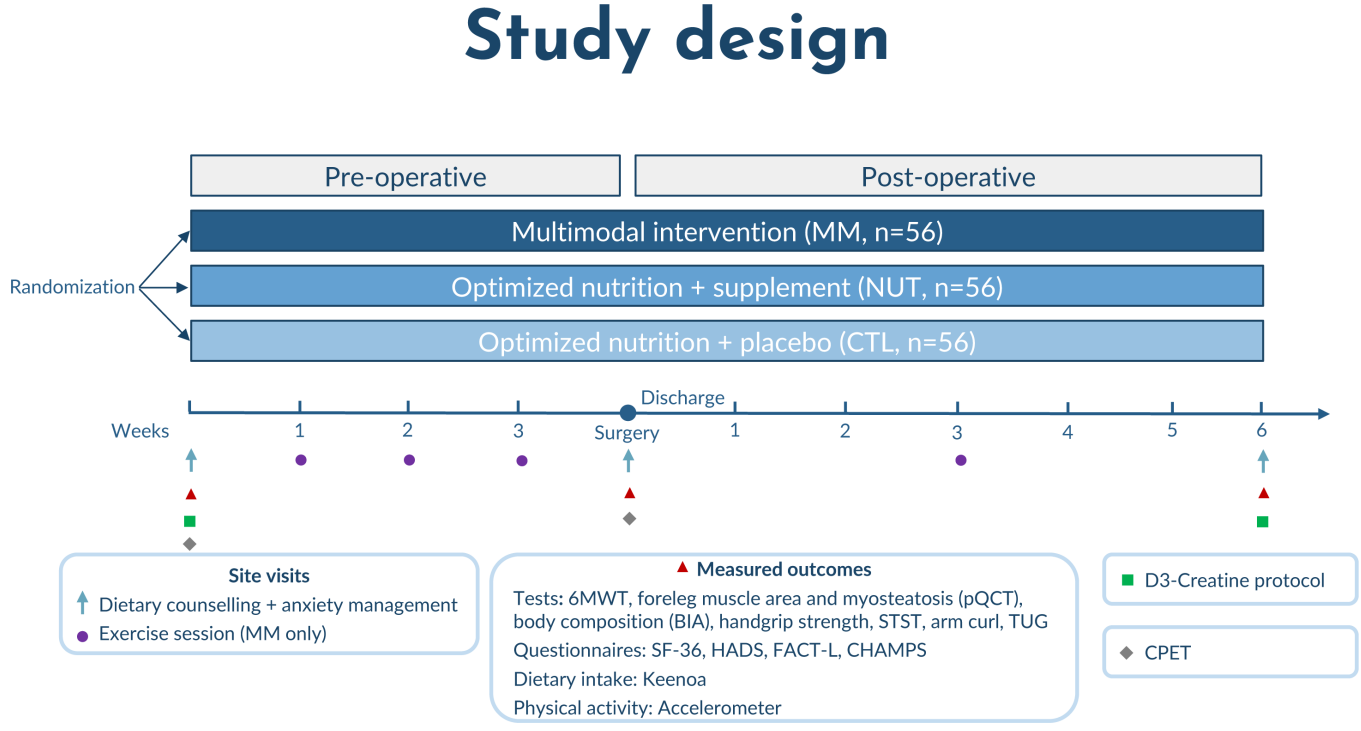

Figure 1 Study design. 6MWT, 6 min walk test; BIA, bioelectrical Impedance Analysis; CHAMPS, Community Healthy Activities Model Programme for Seniors; CTL, placebo-controlled group; FACT-L, Functional Assessment of Cancer Therapy – Lung; MM, multimodal intervention; NUT, active supplement intervention; SF-36, 36-Item Short Form Survey; STST, sit-to-stand test; TUG, timed up-and-go test.

preoperative weeks. An additional preoperative visit may be required if surgery is delayed.

Study outcome assessment

Primary outcome

As the primary outcome, functional capacity is assessed using the 6MWT following the American Thoracic Society guidelines[37] and will be analysed as the change in preoperative functional walking capacity and postoperative functional walking capacity. Participants are instructed to walk as far as possible during 6 min on a 20 m linear corridor (turning around at each end), and the total distance achieved on the first trial is recorded, in metres (± 1 m).[38] A standardised script is used by the assessor indicating the time remaining at each minute while also providing motivational cues. For example, after minute 1: 'You are doing well. You have 5 minutes to go'. After minute 2: 'Keep up the good work. You have 4 minutes to go'. This test assesses the submaximal level of exercise capacity; it integrates balance, speed and endurance and reflects the fitness levels required to perform activities of daily living.[38] Results from the 6MWT predict postoperative complications,[39] length of stay[39] and survival[8] in surgical NSCLC patients. A within-person difference of 14 m is considered clinically meaningful (19 m between groups) in abdominal surgery patients,[40] and 20 m is the estimated measurement error of the test among community-dwelling elderly.[41]

Secondary outcomes

Secondary outcomes include changes in muscle strength, total skeletal muscle mass, foreleg muscle cross-sectional surface area and myosteatosis (radiodensity), body weight and composition, quality of life scores (QoL) and self-reported functional assessment. They also include hospital length of stay (LOS) and the number and severity of postoperative complications. For muscle strength and functional outcomes, handgrip strength is measured as a maximal voluntary isometric contraction on both sides in alternation, using the Jamar hydraulic dynamometer, in kg. The maximal strength of three trials is recorded.[42] Leg strength is assessed using the 30 s sit-to-stand test, as the number of complete stands from a chair without help from the arms.[43] Arm strength is measured using the 30 s arm curl test, using a seven-pound (3.18 kg) weight for males and five-pound (2.27 kg) weight for females, scored by counting the number of repetitions performed during the assigned time, with their back against the chair and without swinging the weight.[44] The Timed-up-and-Go is measured as the time (in seconds) required to stand from a chair without arms, walk three metres, turn, and walk back to sit.[45] Total body skeletal muscle mass is determined using the validated deuterated creatine (D3Cr) dilution method,[46] measured at baseline and at 6 weeks post-discharge. This method involves the ingestion of a 30 mg dose of stable isotope deuterium-labelled creatine followed by assessment of D3Cr levels in a fasting urine sample 3–6 days later (4 days in the present study).[47] Results from the D3Cr dilution method are strongly related to physical performance, mobility, falls and mortality in older adults.[48–51] Samples will be analysed using liquid chromatography-tandem mass spectrometry, as described.[51] Foreleg muscle area and myosteatosis are analysed using peripheral quantitative computed tomography (pQCT) (Stratec XCT2000, Stratec Medizintechnik GmbH, Pforzheim, Germany) of the non-dominant foreleg at the 66% tibial length, at each assessment visit. Image analysis is performed using the BoneJ software.[29] Health-related QoL is measured using the 36-item Short Form Health Survey, which includes eight subscales of health and is validated in surgical populations.[52] The disease-specific Functional Assessment of Cancer Therapy–Lung[53] is also used as a disease-specific HRQoL outcome assessment. The HADS is used to assess preoperative and postoperative anxiety and depression. Hospital LOS, defined as the number of days from surgery to discharge, and 30-day postoperative complications graded by severity using the Clavien–Dindo classification[54] and comprehensive complication index[55] will be recorded from medical charts. For body composition, total fat mass,[56] total and segmental fat-free mass,[56] total and segmental skeletal muscle mass[57] and phase angle are estimated by bioelectrical impedance (seca mBCA 515), after voiding, removal of any jewellery, in light clothing without shoes.

Other outcomes

Other outcomes include changes in dietary intake, biomarkers, exercise tolerance, pulmonary function (forced expiratory volume (FEV1), forced vital capacity), self-reported physical activity level score, physical activity, anxiety/depression score, nutritional status (PG-SGA score) and adverse events. Dietary intake is assessed with 4 day food diaries using the validated Keenoa food diary,[58] which is an intelligent image-based mobile application. Food diaries are reviewed by the study dietitian, and dietary data, including nutrient intakes and food groups, is derived from the application. Participants who are not comfortable with using a mobile app are asked to perform a written 4 day food diary which is reviewed and entered onto Keenoa by the study dietitian. Nutritional status is assessed using the PG-SGA.[59] Exercise capacity is measured during cardiopulmonary exercise testing, at both baseline and preoperative assessments, on an electromagnetically braked cycle ergometer with breath-by-breath gas exchange collected throughout an incremental load exercise protocol until volitional exhaustion. Peak oxygen consumption (VO2) and VO2 at the anaerobic threshold is collected following the Perioperative Exercise Testing and Training Society consensus guidelines.[60] Pulmonary function is assessed by spirometry as the forced vital capacity and forced expiratory volume in 1 s (FEV1). Biomarkers (serum albumin, pre-albumin, complete blood count including haemoglobin, C-reactive

protein, serum 25(OH)D) are analysed by the MUHC Clinical Laboratory following standard procedures. All adverse events will be recorded and documented.

Adherence to intervention is assessed using both self-reported and objective methods. Self-reported physical activity is assessed using the Community Healthy Activities Model Programme for Seniors questionnaire.[61] Actual physical activity levels are assessed from counts measured by accelerometry (Actigraph wGT3X-BT) with activity monitors worn at the waist for 4 days after each assessment visit (baseline assessment is performed before intervention begins). Adherence to dietary supplements is self-reported in a logbook and confirmed from serum 25(OH)D concentrations (for the powder supplement) and from increments in EPA and DHA proportions of the plasma phospholipid fatty acid profile (for the oil supplement). The former are measured by the MUHC Clinical Laboratory and the latter by gas chromatography-flame ionisation as described.[62]

Data management

Each participant is assigned a unique identification number at enrolment. Research data are kept on paper case report forms (CRF) and Research Electronic Data Capture (REDCap) server only accessible to selected research personnel. An electronic file linking contact information, names and study identifiers is held by the study coordinator and principal investigator. This file is password protected and stored on a secure server (McGill OneDrive). Most research data are collected electronically, but some participants prefer completing questionnaires on paper. Paper copies of the CRFs and questionnaires are stored in binders in a secure office environment. Data captured on the paper CRFs and REDCap are entered by trained member(s) of the research team and double-checked by another research member to ensure data quality.

The information collected for research purposes will be kept strictly confidential. Paper documents will be stored in a locked filing cabinet, in a locked room. The study will comply with the Data Protection Act, which requires data to be anonymised as soon as it is practical to do so. All study data will be de-identified, and the code will be maintained by the study principal investigator and coordinator. Study data will be stored at the MUHC in a password-protected computer and retained for a period of 7 years after study completion and then destroyed. Participant's identity is also protected when using the Keenoa mobile application.

Sample size and statistical analysis

Our sample size of 168 was based on data from a secondary analysis of malnourished lung cancer patients (n=162),[21] aiming for a conservative meaningful difference of 21 m (SD±33) in the 6MWT in those at nutritional risk (PG-SGA score>2), between MM and CTL with a power of 80% and a significance level of 0.025 (Bonferroni correction for two comparisons, two-tailed), giving 40 per group.[63] Accounting for 30% loss to follow-up and exclusion after randomisation (cancelled surgery or stage IV diagnosis), we will need to randomise 168 participants. For the primary outcome, we will use intention-to-treat analysis of covariance to compare between-group differences in preoperative data, conditioned for baseline data, including predefined covariates: age, sex, body mass index[64 65] and surgical approach.[38] The hypothesis of full recovery from the intervention at 6 weeks post-discharge (ie, 6MWT returning to or exceeding baseline, yes/no) will be tested by X^2 tests and logistic regression. Between-group differences in postoperative outcomes will be evaluated with two-sided Student t-test, Wilcoxon signed rank test or proportion tests as appropriate. Bonferroni corrections will be applied. Missing data will be handled with multiple imputations.

Patient and public involvement

Feedback and comments from our pilot study participants[28 29] and patient partners of the PeriOperative clinic were considered in the study design. More specifically, they commented on the acceptability and burden of the intervention, including supplement taste and texture, intensity of the exercise programme, number and duration of site visits and assessment tests to guide our final study design. Participant experience from prior studies conducted from our research group guided the selection of outcomes to include self-reported HRQoL in addition to postoperative recovery without complications. Since the study onset, a participant partner has been recruited and will contribute to co-creating and adapting dissemination material to the public and patient communities.

ETHICS AND DISSEMINATION

This trial was reviewed and approved by the McGill University Health Centre Research Ethics Board (REB 2022–7782). Any subsequent modifications of the protocol and consent forms will be reviewed and approved by MUHC REB. Participants currently enrolled in the trial during an amendment will be asked to sign the new consent form before continuing participation. Independent trial auditing may occur at any time, at the discretion of the MUHC REB and the Research Institute of the MUHC Quality Assurance Programme. The final trial dataset will remain with the principal and co-investigators. Results will be disseminated primarily through peer-reviewed publications in open-access medical journals and conference presentations, targeting medical researchers, clinicians and policymakers. Additionally, we aim to reach future clinicians, including dietitians, kinesiologists, pharmacists and physicians, through conference presentations and teaching, ensuring the widespread dissemination of knowledge. Furthermore, we intend to engage the general public by publishing our findings in the media and giving public lectures.

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Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by McGill University Health Centre Research Ethics Board (REB 2022-7782). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. No data are available.

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