Implementation of a Prehabilitation Pilot Program for Individuals with Frailty Undergoing Oncologic Surgery

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BACKGROUND

As the population ages, older, frailer people represent a larger portion of the patients surgeons treat.[1] Although there is currently no agreed upon definition of frailty, it is commonly accepted that frail is a state of increased vulnerability to stressors due to decreased physiologic reserve.[2,3] Frail individuals are at increased risk for falls, disability, long term care, and death.[2] Surgery is a major stressor, to which frail individuals can be particularly vulnerable. Frailer surgical patients incur more health costs, have increased rates of mortality, experience more postoperative complications, and are more likely to have loss of independence.[4-7]

Frailty is commonly accepted as a construct capturing a group of factors that predict medical outcomes. In existing studies, pre-operative frailty screening tools inclusive of these factors have been shown to effectively predict surgical patients who are at increased risk for poor outcomes.[4,7,8] One proposed score is the Risk Analysis Index (RAI). The RAI was created as a rapid and cost-effective way to pre-operatively evaluate frailty in elective surgical patients.[9] Maine Medical Center (MMC) has recently implemented the RAI in multiple surgical clinics. To this point, MMC has only screened patients but has not yet been able to implement interventions based on a patient's status as frail.

Prehabilitation has been suggested as a way to improve outcomes for frail surgical patients. Prehabilitation is a multimodal preoperative approach to enhance patient condition, and aims to decrease rates of postoperative complications, hasten recovery, and improve overall quality of life. Prehabilitation applies methods such as improved nutrition and exercise programs to increase the physiologic reserve of a patient planned to undergo surgical intervention.[10] Some studies have suggested improved physiologic gains[11-13] and reduced rates of complications[14,15] after implementation of these programs. Current perioperative recovery pathways, in multiple surgical pathways, recommend routine use of prehabilitation programs.[16-18]

Recent efforts at MMC have used the Delphi Method to identify the ideal exercise-based prehabilitation program. Through this method, seven academic physical therapists participated in a series of three questionnaires. They came to the consensus that the prehabilitation program should focus on light cardiovascular exercise, strength training, and functional training. Further, they determined the cardiovascular training should occur for a total duration of 30-minutes daily. Additionally for strength and functional training, patients should start each exercise with 1 set of 10 repetitions, increasing to a maximum of 3 sets of 15 repetitions. The initial intensity was recommended to be 3-5/10 (*moderate* to *hard*) on the Borg Rating of Perceived Exertion (RPE) Scale and maximum intensity of 6-7/10 (RPE [*hard* to *really hard*]).[19]

We now hope to implement this prehabilitation program in the clinics at Maine Medical Center. Our long term goal is the introduce this program in all surgical specialties; but first, we plan to assess adherence, patient self-efficacy, frailty and health-related quality of life through a pilot study in the surgical oncology clinic.

In summary, frailty is a state of increased vulnerability to stressors with increased rates of poor outcomes. Surgery is one of these stressors, and previous research has therefore shown increased rates of morbidity and mortality in frail patients undergoing surgery. Prehabilitation programs can help mitigate the negative outcomes associated with frailty. We hope to implement a newly developed prehabilitation pilot program in the MMC Surgical Oncology Clinic to initially evaluate adherence, self-efficacy, and health-related quality of life.

HYPOTHESIS

Implementation of a prehabilitation program will be feasible and will improve clinical status.

SPECIFIC AIMS

We propose to pilot (N=20) and assess a new prehabilitation program for frail surgical oncology patients. We will:

1. Assess feasibility. We will:
    a. Evaluate adherence through analysis of patient maintained exercise logs.
    b. Assess self-efficacy by evaluating the relationship between pre-program self-efficacy score and adherence.
    c. Assess patient satisfaction and barriers to adherence through a post prehab program survey.

2. Assess clinical impact. We will:
    a. Evaluate health-related quality of life before and after participation in the prehabilitation program.
    b. Evaluate frailty before and after participation in the prehabilitation program.

METHODS

Study Design: Prospective cohort study

This longitudinal study will be a prospective, non-randomized, within-subject design focused on patients diagnosed with complex gastrointestinal (GI) cancer evaluated and treated at Maine Medical Center by the Surgical Oncology Service. All subjects who meet the inclusion criteria will be offered the opportunity to be enrolled; these recruitment efforts will cease when planned enrollment is complete. Participants will complete a prehabilitation exercise program through the Thinkific platform. Data on frailty, quality of life, self-efficacy and adherence will be collected through surveys and patient maintained exercise logs.

Study Population

Participants will be selected from the population of patients at the MMC Surgical Oncology Clinic. Patients at this clinic are being evaluated for surgical treatment of oncologic diseases such as colorectal or pancreatic cancer. Under normal circumstances, patients are seen for an initial consultation where a treatment plan is created. Patients either have surgery or chemotherapy up front. If the patient has surgery as the first treatment, the surgery is scheduled at that initial appointment. If the patient has chemotherapy before surgery, they will return for at least one more appointment after completion of chemotherapy. Their surgery is scheduled at this follow-up appointment. This process can span anywhere from 4 weeks to 6 months.

Yearly, this clinic evaluates 181 and 143 patients with colorectal and pancreatic cancer, respectively. Part of the goal of this study is to evaluate feasibility as well as adherence and thus, patient tolerance of the prehabilitation program. Therefore, we propose to enroll 20 patients from this population, knowing that there may be some attrition. Participants will meet the following criteria:

Inclusion Criteria-

a) Subjects ≥18 years old
b) Evaluated at MMC by surgical oncology service
c) Planned surgical intervention for gastrointestinal oncologic condition
d) Score ≥40 on RAI frailty screening
e) Physically able to participate in prehabilitation exercises
f) Home internet access and established email account
g) Able to speak and read he English language

Exclusion Criteria-

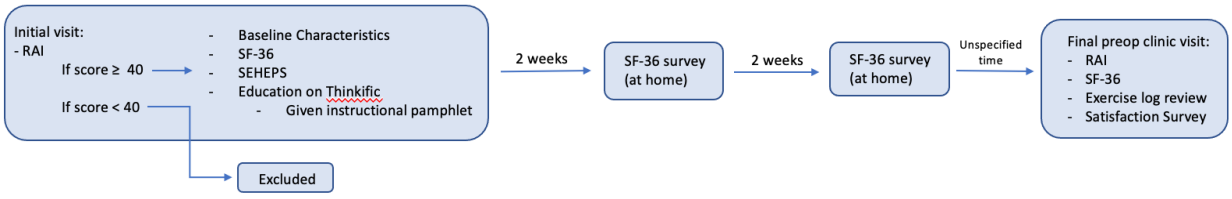
a) Patients unable to participate in exercises included in prehabilitation program
b) Patients with impaired decision making capacity as determined by the treating physician
c) Those in a high risk community: prisoners and pregnant women

d) Those who are visually impaired and unable to complete the course independently
e) Those who do not meet the above inclusion criteria

Recruitment:
Patients are screened by nursing staff for frailty at each routine clinic visit using the RAI survey as part of their standard care. By reviewing the final RAI score obtained during the initial visit to the Surgical Oncology Clinic, the attending surgeon (see key personnel form) will know clinically if the patient is considered frail and therefore if he/she is eligible for inclusion in the research study. The attending surgeon will not need to go back to review the RAI score in-depth for research purposes. In addition to the RAI score, the attending surgeon will use inclusion/exclusion criteria to evaluate each patient's eligibility for this pilot study. If the patient meets these criteria, the attending surgeon will give the patient a recruitment flyer (see attached) during the same visit to introduce the study requirements, expectations and possible benefits. The attending will answer any questions the patients may have at that time. No other recruitment, including active recruitment, will occur.

Informed Consent Process
Once the patient has read the study flyer and has been given the opportunity to have questions answered by the attending surgeon, the physician will establish their interest in participation. If interested they will be given a copy of the informed consent form (please see attached) and the physician will talk through this form with them, again, answering any questions they may have. The discussion of consent will contain information on: the purposes, procedures, and duration of the research; any reasonably foreseeable risks and benefits of the research; and how confidentiality will be maintained. Patients who agree to participate and sign the informed consent form will be considered enrolled in the study. The participant will be given a copy of the signed consent form and the original version will be maintained in study records.

Study Procedures



If patients choose to participate and subsequently provide informed consent, they will create a password protected account to the Thinkific Prehabilitation Exercise Program during this initial clinic visit. The study team will provide the participant with an instruction sheet (see attached) with the Thinkific URL to guide the creation of the account on a device in the clinic exam room. Thinkific is an online platform that Maine Medical Center utilizes for patient education. Please refer to the link below to access the specific Thinkific course that will be used in this study. This course was created through collaboration with the MaineHealth Education and Training Department and was based on Thinkific courses created for patients at MMC for other surgical specialties such as orthopedic and transplant surgery. Please see the attached screen shot of the Thinkific course welcome page. This page will further inform participants about the course layout and expectations.

After the account is created, participants will complete two electronic baseline surveys on an in room device during this initial clinic visit: the 36-Item Short Form Survey (SF-36) and the Self-Efficacy for Home Exercise Programs Scale (SEHEPS). The link for these REDCap surveys will be imbedded in Thinkific. A study team member will be available to assist in creation of the Thinkific account or completion of these initial surveys. Participants will leave their initial clinic appointment with a packet containing: a 3 pack of resistance bands, a copy of their consent form and a copy of the informational packet about the exercise program (see attached) that can otherwise be accessed through the Thinkific course.

Participants will additionally access the Thinkific account at home to complete an exercise based prehabilitation course. This course will provide video and written instruction on how to perform each exercise safely, as well as how to properly increase the intensity of the program, (e.g. resistance, number of repetitions and sets). This program will also include links to the American College of Surgeons alcohol related recommendations and the Maine QuitLink for tobacco/smoking and vaping cessation that patients may access if applicable. Participants will be instructed to perform daily exercise and keep track of their exercise in either a handwritten or electronic log (see attached document) until their surgery or until the final clinic visit if surgery is ultimately not performed. The log is available as a paper copy provided at the first visit and as a pdf embedded in the Thinkific course.

https://mainehealth.thinkific.com/courses/prehab-exercise

Repeat self-administered survey with the SF-36 will become available through a direct email link from REDCap at two and four weeks after initiation of the prehabilitation program. If participants do not complete the surveys, they will receive a reminder email, generated automatically by REDCap, at 24 and 48hrs after the initial email was sent (please see attached screen shot of emails). At the final clinic visit prior to surgery, the participant's exercise log will be collected by the study team. The participant's exercise log will either be physically brought to clinic or uploaded by the participant through the Thinkific platform prior to this final appointment. Repeat frailty screening, with the RAI, will be performed by the surgical oncology clinic nursing staff at every follow up clinic appointment until surgery as part of the patients' normal care.

Participants will complete a final self-administered SF-36 survey and a survey to assess their satisfaction with the exercise prehabilitation program anytime during the week leading up to their surgery, or the week after their final appointment if they ultimately are not a surgical candidate. The link to this final REDCap survey is embedded in Thinkific. The surgeon will remind patients at their final clinic visit to complete these surveys.

During the extent of the study, if patients have questions pertaining to the study they will be able to contact their surgeon at any time by contacting the surgical oncology clinic. If the patient has questions or concerns related to the performance of the prehabilitation program exercises, they will be directed to a licensed physical therapist.

Please reference to the attached material to view each of the following surveys:

Risk Analysis Index (RAI):
The RAI is a validated frailty screening tool that was developed and implemented at the University of Nebraska. Components of the RAI include nursing home admission, unintentional weight loss, renal failure, congestive heart failure, poor appetite, gender, shortness of breath, malignancy, age, cognition, and activities of daily living.[20]

36-Item Short Form Survey (SF-36):
SF-36 is a well-researched, self-reported measure of health which stems from the Medical Outcomes Study. It comprises 36 questions which cover eight domains of health: Limitations in physical, social or usual role activities due to physical or mental health problems, bodily pain, general mental health (psychological distress and well-being), vitality (energy and fatigue), and general health perceptions. This measure is now widely utilized by managed care organizations and by Medicare for routine monitoring and assessment of care outcomes in adult patients.[21]

Self-Efficacy for Home Exercise Programs Scale (SEHEPS):
The SEHEPS is a clinically useful tool to evaluate patients' self-efficacy in home-based musculoskeletal exercise programs. It is a 12-item patient-reported questionnaire on which patients rate their confidence in performing home-based exercise on a 7-point scale.[22]

Satisfaction Survey:
This survey was developed in house by the study team because an appropriate validated tool could not be found in the literature. It will utilize a Likert-type rating scale to assess participant satisfaction with the Thinkific platform and the video/handout instructions. Additionally, it will evaluate the participants' perceived mental and physical benefit from the program. See attached survey.

DATA COLLECTION, MANAGEMENT, AND ANALYSIS

Data Collection
Data pertaining to the patient demographics and baseline characteristics will be collected by the study team through manual extraction from Epic. Data from the participants exercise logs will be manually extracted by the study team from either the Thinkific platform or Epic depending on how the participant submitted this form (i.e. electronically on Thinkific or manually bringing the log to their appointment for uploading to Epic by the study staff). The surveys will be completed electronically in the office setting on the exam room computer or online at home through REDCap (via emailed link or a link to REDCap embedded in Thinkific). These data will automatically upload to REDCap. Please refer to the master list and data collection document submitted with this proposal for a list of variables that will be collected.

Date Management
All data will be collected and maintained in a REDCap database to which only the study team will have password protected login access. The data collected through manual extraction from EPIC will be entered into REDCap by members of the study team. Data from the RAI surveys

performed as part of routine care will be initially recorded in Epic then manually transferred into REDCap.

Data from the SF-36, SEHEPS and satisfaction survey will be directly submitted into REDCap from either an emailed link or link embedded in Thinkific. Once uploaded, the participants formula ID (first two letters of first name + first two letters of last name) and email, will help us manually link the survey entry to the master list and the second survey data collection form. Of note, the participant will only enter their email and formula ID at the beginning of the first and last surveys. The email entry is necessary to send out the 2 week and 4 week surveys. The email will also serve as a second patient identifier if participants have identical formula IDs. When more than one survey is completed on the same day, the separate surveys are linked together through REDCap. This means the participants only need to type their formula ID and email once, despite completing multiple surveys. (please see the attached email chain and document from Deanna regarding REDCap security and her support for this plan)

The exercise logs will be reviewed by the study team in Thinkific or through Epic, if the participant brought a paper log, then entered into REDCap. If participants bring a paper form of their exercise log, it will be scanned into their EPIC account by a member of the study team and the paper copy of the exercise log will be shredded after the image has been uploaded into Epic. The signed consent form will be secured in a locked file cabinet behind a locked office door in the Surgical Oncology Department at 887 Congress Street.

A master list will be maintained in REDCap separate from other study documents. Only a study ID, consisting of the first 2 letters of the first and last name, will link this master list to the two data collection files on REDCap. Once the data collection is finalized, the master list will be deleted. The limited data set that remains will then be exported as a CSV file that will be maintained as an encrypted file on a password protected MMC institution desktop. This limited dataset will be accessed only from MMC computers and only by MMC study team listed above and by members of the IRB if needed.

All regulatory documents and files associated with the study (IRB documents, HIPAA-related documentation) will be maintained for a minimum of 6 years after the final publication/report and then deleted/destroyed.

Data Analysis

Statistical analysis will be completed by the research fellow with support from CORE or statisticians. Data will be summarized using standard descriptive statistics. Continuous data will be shown as mean (standard deviation) or median [range], as appropriate, and categorical data will be shown as frequency (n, %). Paired analyses will be performed using the McNemar test for categorical data and the paired t test or Wilcoxon signed rank test for continuous data, as appropriate. Changes in survey scores over time will be assessed with repeated measures ANOVA or mixed models regression, as appropriate. Relationships among variables will be assessed by linear regression. “R” software will be used for data manipulation and all statistical analysis. As this is a pilot study, the parameters needed to support power analysis were not available. Therefore all statistical comparisons and relationships will be considered exploratory

with no anticipation of statistical significance. Statistical significance will be accepted at $p < 0.05$.

ANTICIPATED RISKS AND BENEFITS

The risks involved with participation in this study are low. One possible risk is for temporary muscular soreness. This is a risk for anyone starting a new exercise program. For those who experience it, the soreness is usually mild and can last for 24-72 hours following initial exercise sessions. Once the muscles become use to the new exercises, the soreness goes away. Further, participants will be able to contact a health care professional and a licensed physical therapist at any time during the study if they have questions or concerns. The program was explicitly designed for patient autonomy and independent use which is why the Thinkific instructions are very clear to guide the participant through every step. Despite this, patients are encourages to call with any questions. The number of phone calls will be tracked to assess the ideal program set up if implemented more widely in the future. Another risk is for loss of confidentially. Many safeguards are in place to ensure that the data is protected including: use of REDCap for storage of the master list, password protection on the desktop of the PI and co-investigators, anti-virus software on desktops, and avoidance of use of mobile devices for storing data.

We believe that most individuals will benefit by participating in this study. Participants are likely to see improvements in strength and endurance to participation in a regular exercise program. Further, these improvements may help participants recovery from surgery. This pilot study would be the first step towards offering surgical patients what is becoming standard of care. The data collected will be used to benefit patients in the future. If the results of this pilot study support our hypothesis, it is likely the prehabilitation program will be implemented widely for surgical patients at MMC. This holds the potential for a large positive impact in the future by reducing negative post-surgical outcomes. This likely has the benefit of not only improved quality of life and functionality for the patient, but also decreased healthcare utilization and cost.

POTENTIAL PROBLEMS

- Loss to follow up: As a prospective study, patients enrolled may be loss to follow up. Some reasons include if a patient transitions care to a different provider or moves. The study team will make efforts to maintain all participant and will perform phone calls if needed to re-engage participants that may have been lost. (please see phone script)
- Technology: One of the inclusion criteria for this study is home internet access and established email account. Having these does not mean a participant will be proficient in using the internet. They may struggle to access or use the technology. To try and combat this, we have made care members easily available to answer questions and help participants trouble shoot.

TIMELINE

Because this intervention is recommended in most perioperative protocols, we hope to implement this program as soon as possible. Our goal is to recruit 20 patients within three months. Each patient will participate in the prehabilitation program for at least two weeks. It is

difficult to predict how long a patient will be in the program because the duration depends on when their surgery is eventually scheduled. This is individualized, and typically ranges from two weeks to six months. We hope to complete data collection in seven months. At that time, we hope to complete data analysis and submit an abstract by July, 2022.

REFERENCES

1. 2019 profile of older americans. In: Living USDoHaHSAoC, ed2019:5-6, 17-18.
2. Sternberg SA, Schwartz AW, Karunananthan S, Bergman H, Mark Clarfield A. The identification of frailty: a systematic literature review. *Journal of the American Geriatrics Society.* 2011;59(11):2129-2138.
3. Strandberg T, Pitkälä K, Tilvis R. Frailty in older people. *European geriatric medicine.* 2011;2(6):344-355.
4. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. *Journal of the American College of Surgeons.* 2010;210(6):901-908.
5. Panayi A, Orkaby A, Sakthivel D, et al. Impact of frailty on outcomes in surgical patients: A systematic review and meta-analysis. *The American Journal of Surgery.* 2019;218(2):393-400.
6. Robinson TN, Wallace JI, Wu DS, et al. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. *Journal of the American College of Surgeons.* 2011;213(1):37-42.
7. Robinson TN, Wu DS, Stiegmann GV, Moss M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. *The American journal of surgery.* 2011;202(5):511-514.
8. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland Jr JC, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. *The American Journal of Surgery.* 2013;206(4):544-550.
9. Hall DE, Arya S, Schmid KK, et al. Development and initial validation of the risk analysis index for measuring frailty in surgical populations. *JAMA surgery.* 2017;152(2):175-182.
10. Bruns ER, van Rooijen SJ, Argillander TE, et al. Improving outcomes in oncological colorectal surgery by prehabilitation. *American journal of physical medicine & rehabilitation.* 2019;98(3):231-238.
11. Lemanu DP, Singh PP, MacCormick AD, Arroll B, Hill AG. Effect of preoperative exercise on cardiorespiratory function and recovery after surgery: a systematic review. *World journal of surgery.* 2013;37(4):711-720.
12. Moisey LL, Mourtzakis M, Cotton BA, et al. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Critical care.* 2013;17(5):1-8.
13. Singh F, Newton RU, Galvão DA, Spry N, Baker MK. A systematic review of pre-surgical exercise intervention studies with cancer patients. *Surgical oncology.* 2013;22(2):92-104.
14. Howard R, Yin YS, McCandless L, Wang S, Englesbe M, Machado-Aranda D. Taking control of your surgery: impact of a prehabilitation program on major abdominal surgery. *Journal of the American College of Surgeons.* 2019;228(1):72-80.

15. Moran J, Guinan E, McCormick P, et al. The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: a systematic review and meta-analysis. *Surgery.* 2016;160(5):1189-1201.
16. Melloul E, Lassen K, Roulin D, et al. Guidelines for Perioperative Care for Pancreatoduodenectomy: Enhanced Recovery After Surgery (ERAS) Recommendations 2019. *World J Surg.* 2020;44(7):2056-2084.
17. Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS((R))) Society Recommendations: 2018. *World J Surg.* 2019;43(3):659-695.
18. Hubner M, Kusamura S, Villeneuve L, et al. Guidelines for Perioperative Care in Cytoreductive Surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): Enhanced recovery after surgery (ERAS(R)) Society Recommendations - Part I: Preoperative and intraoperative management. *Eur J Surg Oncol.* 2020;46(12):2292-2310.
19. Borg G. *Borg's Perceived Exertion and Paine Scales.* Human Kinetics; 1998.
20. Hall DE, Arya S, Schmid KK, et al. Development and Initial Validation of the Risk Analysis Index for Measuring Frailty in Surgical Populations. *JAMA Surg.* 2017;152(2):175-182.
21. Ware JS, Cathy. The MOS 36-ltem Short-Form Health Survey (SF-36)_I. Conceptual Framework and Item Selection. *Medical Care.* 1992;30(6):473-481.
22. Picha KJL, Morgan; Heebner, Nicholas R.; Abt, John P.; Usher, Ellen L.; Capilouto, Gilson; Uhl, Tim L. The Self-Efficacy for Home Exercise Programs Scale: Development and Psychometric Properties. *Journal of Orthopaedic & Sports Physical Therapy.* 2019;49(9):647-655.