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Initial Examination of the Result of Prehabilitation Of The Outcome Of Prehabilitation On Muscle Mass, Weight, And Dietary Consumption Stratified By Hand Grip Strength In Pancreatic Cancer Patients

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ABSTRACT: This intervention before surgery has been termed prehabilitation. The one known cure to pancreatic cancer is surgery. The most common surgery for pancreatic cancer, pancreaticoduodenectomy, has the highest complication rate which is why the focus was on this type of surgery. Early nutrition education and exercise intervention prior to surgery has been looked at in other types of cancers, although it has yet to be studied in pancreatic cancer patients. This is part of a larger study looking at prehabilitation on quality of life. This specific study is the preliminary analysis looking at the effect of the intervention on weight, muscle mass, and dietary intake.

This study looked at 24-Hour Recall and BIA analysis at baseline and 1 month post-surgery for individuals undergoing a pancreaticoduodenectomy. Results were also analyzed following post hoc group assignments based on baseline hand grip strength. Comparisons were made to determine if nutrition education during the prehabilitation phase was beneficial overall. This is a preliminary analysis for a larger study to help better assess if further stratification needs to occur for intervention.

Keywords: prehabilitation, muscle mass, weight, dietary consumption, hand grip strength, pancreatic cancer patients

INTRODUCTION

Pancreatic cancer accounts for 3.1% of all new cases of cancer in the Pakistan with an estimated 5307 new cases in 2016. The 5-year survival rate for pancreatic cancer is currently 7.7%. Pancreatic cancer is not easily diagnosed, therefore many patients are not diagnosed until their cancer is very advanced.

The pancreas is a major organ in the human body. This organ is located in the abdomen behind the stomach and attaches to the gall bladder and part of the intestine, which is referred to as the duodenum. The main duct of the pancreas attaches to the gallbladder by the common bile duct, and this is where bile mixes with the pancreatic enzymes before being released into the duodenum. The pancreas has many functions including producing and excreting enzymes and hormones such as insulin. Insulin is a hormone that helps the body absorb, use, and regulate glucose or blood sugar level. The enzymes produced and secreted by the pancreas are involved in breaking down the foods consumed and are often referred to as the digestive juices. These juices are mixed with the bile secreted by the gall bladder and deposited into the duodenum to aid in the digestion of food. If the pancreas is unable to produce and secrete these enzymes, the body is not able to properly digest food as well as not being able to regulate serum glucose.

Early pancreatic cancer does not present with many symptoms. It is not until the cancer starts to advance and blocks the ducts that excrete enzymes that symptoms appear. Symptoms can include jaundice, dark urine, light-colored or greasy stools, itching, weight loss, poor appetite, nausea, vomiting, stomach pain, back pain, and even diabetes or uncontrolled blood sugar levels.[2] Diagnosing can be done using (a) physical exam checking for lumps or anything else unusual; (b) history looking at patient's habits, past illnesses, and treatments; (c) blood chemical measurements looking at markers like bilirubin, tumor marker test where substances such as CA 19-9 or carcinoembronic antigen can be detected to mark for cancer; (d) MRI which uses magnet, radio waves, and computer technology to take a picture of the inside of the body; (e) CT scan which is another way of taking images of the inside of the body, but is using a computer and x-ray machines; (f) PET scan which is used to find the malignant tumor cells in the body by injecting radioactive glucose into the vein; (g) abdominal ultrasound, which is used to take images inside the abdomen by an ultrasound transducer being pressed against the skin and directing high energy sound waves into the abdomen; (h) an endoscopic ultrasound (EUS) which is when an endoscope (tube-like instrument with a light and lens on the end) is placed into the body through mouth or rectum and bounces high-energy sound waves off internal tissues to make echoes; (i) endoscopic retrograde cholangiopancreatography (ERCP) which uses x-rays to image the ducts that carry bile from the liver to the gallbladder and from gallbladder to small intestine (j) Percutaneous transhepatic cholangiography (PTC) which is used to x-ray the liver and bile ducts; (k) laparoscopy, which is a surgical procedure to look inside the body by making a small opening in the abdomen; (l) Biopsy which is a removal of cells or tissues so that they can be checked for the biochemical markers of cancer.[3]

If the cancer is found in only the pancreas, it is usually referred to as localized, and if it has spread to other areas in the body, it is referred to as regional or distant (metastasized) versus a localized tumor. Specific staging used for pancreatic cancer are Stages 0, I, II, III, and IV. Stage 0 is referred to as carcinoma in situ; this is when

A PD is a radical surgery in which a major section of the gastrointestinal (GI) tract, including the head of the pancreas, gallbladder, duodenum, and a portion of the common bile duct, is removed. The surgeon then reconnects the remaining pancreas to the stomach, small intestine, and common bile duct so that the contents of the stomach combine with bile and pancreatic enzymes to pass through the duodenum. Because of the extent of this surgery there is a very high complication rate. Because of the commonality and complication rate, this study was specifically focused on patients who underwent a PD.

Study Purpose and Specific Aims

This specific preliminary analysis is investigating increasing protein intake prior to PD and its effect on food intake, especially protein intake, measured by a 24-hour recall, and body composition, muscle mass/fat free mass (FFM) and weight, measured by bioelectrical impedance analysis (BIA). Based on previous research we hypothesize that intervening nutritionally shortly after diagnosis for resectable pancreatic cancer would minimize risk of undernutrition along with the negative effects that usually coincide [35, 36]. I also wanted to determine if these outcomes change based on a participant's HGS. Since HGS has been noted as a determinant for muscle function and nutritional status we could hypothesize that comparing groups based on HGS would indicate a change in outcomes following surgery.

Hypothesis: Nutrition education during the prehabilitation phase will increase FFM and dietary protein intake and decrease weight loss when baseline data is compared to 1 month post-surgery.

Specific Aim 1: To compare the change in FFM 1 month post-surgery to baseline FFM by assessing BIA results between participants categorized as at/above average HGS and below average HGS.

Specific Aim 2: To compare the change in body weight 1 month post-surgery to baseline weight between participants categorized as at/above average HGS and below average HGS.

Specific Aim 3: To describe dietary intake for patients undergoing PD at baseline and 1 month post-surgery.

LITERATURE REVIEW

Complications:

Each PD is patient-specific regarding the amount of GI tract removed, and thus individuals vary regarding postoperative impairments in digestion and absorption.[8] This procedure does remove a large portion of the pancreas, but this does not mean that the patient will become a diabetic. Only about 4% of patients who undergo PD will get diabetes.[9] If the patient was not diabetic prior to surgery, it is not likely this will cause them to be diabetic.

Other complications of a PD may include wound infection, bile leak, pancreatic fistula, intra-abdominal abscess, abdominal hernia, delayed gastric emptying, fat alabsorption, dumping syndrome, and difficulty tolerating a regular diet.[7, 10, 11] These complications may inhibit the patient's return to an adequate nutritional status.

A bile or pancreatic leak is caused when connection is not complete at the site of the pancreas, common bile duct, and duodenum anastomosis. This leak can cause other complications such as sepsis and abscesses. Incidence of these leaks varies based on reports and differences in surgical techniques. [13]

Pancreatic fistula is a common complication following a bile or pancreatic leak. A fistula is an abnormal passage between two hollow or tubular organs. A pancreatic fistula would be a fistula found in the pancreas with a passage to the jejunum or other surrounding organs. This can be surgically made or occur naturally at the internal incision site following the surgery. [14]

An intra-abdominal abscess usually occurs secondary to a leak where the pancreas is reconnected either with the common bile duct or small intestine. This is a collection of fluid in the abdomen that may require drainage. The incidence of an intra-abdominal abscess ranges from 1%-12%. This complication is easily controlled as long as the primary drainage or leak is resolved. [13]

Delayed gastric emptying is another major complication following a PD. The incidence is up to about 45%.[13, 16] Delayed gastric emptying is the delay in the spontaneous movement of muscles in the stomach following surgery. It is common after any abdominal surgery for the stomach to take time to adjust before functioning normally again although after a PD the time the stomach takes is increased. Delayed gastric emptying is a major source of discomfort and causes the delay in tolerating a regular diet, but it typically resolves itself within about 4-6 weeks following surgery. This complication can interfere with the normal digestion of foods and the regulation of blood sugar levels and can cause nausea, vomiting, and early satiety. [13, 17]

Fat malabsorption refers to the body's inability to utilize fat from the diet. Without certain enzymes produced and excreted by the pancreas, the body is not able to digest and absorb dietary fats from foods, which leads to fat malabsorption. This is most often seen by changes in stools. Stools that are light in color, bulky, float, and are oily are often indicators of fat malabsorption. Other symptoms include bloating and excess gas with extreme foul odor.[18] Fat malabsorption following a PD is an indicator for supplementary pancreatic enzymes. Initial fat malabsorption after surgery may resolve on its own as the gastrointestinal tract resumes adequate function and delayed gastric emptying resolves.[13] Occasionally the pancreas, even after surgery, does not produce an adequate amount of enzymes to properly digest foods. Enzyme supplements are taken orally with foods to mimic the enzymes the pancreas is supposed to produce.

Difficulty tolerating a regular diet is another complication specifically individualized for each patient. This tolerance issue may be related to any of the complications previously listed. The degree each complication can inhibit intake is dependent on how the patient feels. Delayed gastric emptying is one of the bigger complications effecting dietary tolerance. Early satiety, nausea, and vomiting can all decrease the person's desire to eat. Fat malabsorption may also cause difficulty with tolerating a regular diet because the person may feel they are not properly digesting their foods or they may feel bloated and gaseous after eating specific foods causing them to limit certain foods. Fat malabsorption can be a cause to inadequate dietary intake if they are not reporting these symptoms to their physicians in order to get the needed enzymes to supplement.

Prehabilitation:

Previous studies on other cancers have shown the benefit of initial nutrition counseling and early exercise interventions on quality of life (QOL). This initial intervention has been termed prehabilitation.[35-38]

Weight loss is an acknowledged issue in cancer patients and is known to worsen prognosis.[39, 40] Ravasco et al.[36] discusses that the treatment provided is not the only thing that affects the patient's QOL, but nutritional status and intake also play a large role. Previously, Ravasco et al. had seen that weight loss related to cancer will decrease QOL, tolerance to further treatments, and prognosis.[39-42] The high prevalence of malnutrition in cancer patients was also a concern. Ravasco et al. noted that there was a high correlation between worsening nutrition status depending on cancer staging, location, duration of disease, previous surgery or neoadjuvant therapy, along with protein energy intake.[43] Ravasco et al. measured QOL outcomes since it is able to measure the self-reported change in functional, physical, and psychological health along with the person's experiences, beliefs, expectations, and perceptions of human and financial costs to determine the effect of nutrition interventions on QOL in cancer patients.

Ravasco et al. specifically looked at 271 individuals with cancer of the head and neck, esophagus, stomach, and colon/rectum undergoing radiation therapy. This study ran for 3 months following radiation therapy and consisted of three randomized nutritional arms as follows: 1. individualized nutritional counseling, 2. ad libitum diet plus high protein supplements, and 3. ad libitum diet. Nutrition education was based on regular foods and prescribed based on dietary guidelines provided both orally and written. Individuals were provided a dietary plan that included a meal plan in quantity, type of foods, and meal distribution which was based on their individualized location of cancer, treatment they were undergoing, symptoms, nutritional status, and previous changes in weight.

Ravasco et al. did show that the individualized nutrition counseling was shown to improve outcomes on those inpatients who reported lowest QOL scores and nutritional problems during radiation therapy. The results were separated based on the type of cancer presented (esophagus, stomach, colorectal, head-neck, and the lower risk cancers such as breast, prostate, uterus, brain). QOL scores were improved or remained constant throughout the study for all cancers for the global QOL functional scale, physical function, role function, cognitive function, and social function, and emotional function. As for symptoms, fatigue appeared to worsen in the esophageal group, but all other cancers showed a decrease. Nausea, vomiting, and pain all appeared to not improve following intervention. Dyspnea, sleep disturbance, constipation, and finance appeared to be stable throughout intervention. Appetite only improved in the head-neck cancer patients and remained stable for both colorectal and low-risk cancers. For this study, dietary counseling was shown to improve overall QOL, specifically function, significantly, even with the medium individual symptoms not improving.

MATERIALS AND METHODS

Subjects:

A total of 20 participants aged ≥ 30 years were enrolled between March 2016 and January 2017 at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore Participants were newly diagnosed with pancreatic or related cancers who were deemed eligible for a PD and appropriate for exercise by the pancreatic cancer team. Participants can be newly diagnosed or following chemotherapy. Data collection occurred between March 2016 and March 2017.

This preliminary study is a subset of a much larger study titled: "Preoperative Exercise and Nutrition to Improve Pancreatic Cancer Outcomes by Targeting Sarcopenia: A Translational Pilot RCT" that is on-going at the Shaukat Khanum Memorial Cancer Hospital and Research Centre . This study is investigating increasing protein intake and physical activity prior to PD and its effect on pancreatic cancer outcomes. For this study, the purpose is to look at the impact of 2-3 weeks of protein supplementation and exercise, with or without targeted strengthening, in order to determine if targeted strengthening improves outcomes post-surgery. The specific aims are to: 1. quantify the impact of muscle strengthening on post-op outcomes, 2. determine whether novel serum and tumor biomarkers of cachexia and sarcopenia explain the impact of targeted strengthening, and 3. determine if pre-op biomarkers or physical function tests predict post-op outcomes. This study is looking at individuals 30 years of age or older with either pancreatic cancer or related pre-malignant conditions who are randomized to pre-operatively protein plus either aerobic exercise alone or aerobic exercise plus strengthening exercises. This larger study also allows subjects to participate as "assessment only" if they meet criteria which means they do not want to do the specific interventions, but are willing to do all baseline testing. Inclusion criteria include: (a) pancreatic cancer and related malignancies or pre-malignant and tentatively approved for surgical resection; (b) cognition and English language skills sufficient for consent and questionnaires; (c) age > 30 years; (d) Able to rise from a chair and walk household distances; (e) willing to be randomized to pre-operative home-based exercise and protein; (f) cleared for exercise participation by the pancreatic cancer team.

For this study, 4 assessments will be performed, and are generally on the same days as scheduled with their surgeon at the Stephenson Cancer Center. Visit 1 will occur around time of the pancreatic cancer surgical candidacy and is where eligibility will be determined and baseline testing will be done. Visit 2 is pre-operative, approximately 1-3 days prior to surgery and approximately 2-3 weeks following visit one. The third visit is post-operative and is the first post-operative visit to the pancreas clinic meeting with the surgeon, approximately 1 month post-surgery or 2 weeks post discharge from the hospital. The fourth and final visit is approximately 3-4 months post-surgery and will coincide with follow-up visit with the surgeon at the Stephenson Cancer Center.

The study will be blinded, meaning the individuals in the study who know the group assignment will not collect any data on outcomes, and participants will only know the arm of the study they are assigned to and not the difference between the two arms or the specific aspects of the protocol. The intervention materials provided, protein supplements, and exercise equipment are provided to the participants at no charge to them.

The primary outcome for this larger study is to look at: (a) performance as walking endurance and muscle strength; (b) body composition by BMI and bioimpedance; (c) post-op hospital length of stay, complications, readmissions. The larger study was powered based on QOL, specifically FACT-G.

Participants are identified in Gastrointestinal Tumor Board that occurs weekly on Wednesdays at the Shaukat Khanum Memorial Cancer Hospital and Research Centre. In Gastrointestinal Tumor Board, is an interdisciplinary team meets to determine surgical candidacy of patients based on MRI and PET scans along with blood and tissue samples. Participants are identified to be a part of this study based on inclusion listed below. Participants must be eligible for the PD surgery.

Hand Grip Strength

HGS is a useful tool to measure nutritional status. Malnutrition has been found to be an independent determinant for HGS[30]. HGS can be completed on patients independent of physical ability and is a relevant marker of functional status. To measure HGS, this study used a JAMAR Hydraulic hand dynamometer[44]. JAMAR 5-position pre-set grip position #2 for all participants were used. Measurements were obtained with participants sitting upright in a chair with their shoulder adducted and neutrally rotated, elbow flexed at a 90-degree angle, and wrist in a neutral position. The participant's wrist is in neutral radial/ulnar deviation and neutral to slight extension for comfortable gripping position. The physical therapist supported the bottom of the dynamometer for the participant so that the participant does not need to support the weight of the device while squeezing. Participants were asked to contract their hand with maximum strength, and verbal encouragement was provided. Each participant was instructed to perform 3 measures with a 30-second break between measurements; participants were also instructed when to start and stop contractions. Measurements using the dominant hand from each trial were averaged and used at baseline to determine post hoc group assignment.

For this preliminary analysis, participants were separated into groups based on comparison of their HGS as either at or above average HGS and below average HGS. Classification of average or below average is determined based on age and sex.

Table 1.0-Normative hand grip values in kilograms, from Lafayette Jamar Hand Dynamometer user manual 2003

AGE	R-HANDED	L-HANDED	R-HANDED	L-HANDED
	MALES	MALES	FEMALES	FEMALES
30-34	55.4	50.2	35.8	30.9
35-39	54.4	51.3	33.7	30.1
40-44	53.1	51.3	32.0	28.3
45-49	49.9	45.8	28.3	25.5
50-54	51.6	46.3	29.9	26.0
55-59	45.9	37.8	26.0	21.5
60-64	40.8	34.9	25.0	20.8
65-69	41.4	34.9	22.5	18.6
70-74	34.2	29.5	22.5	18.9
75+	29.8	25.0	19.4	17.1

JAMAR Hydraulic Hand Dynamometer

24-Hour Recall

Food intake was measured by a 24-hour recall. A 24-hour recall is a structured interview focused on dietary intake within a previous 24-hour period, including all foods/beverages consumed.[45] For this study, a 24-hour recall was performed both at the initial visit and at 1 month following surgery. The 24-Hour Recalls were performed by a Registered Dietitian (RD). During this interview, the participants were instructed to provide all foods and beverages consumed the previous day, including amount consumed and all ingredients, if possible. The RD is instructed to begin with a quick list of foods eaten as the participant remembers starting as the first thing consumed when they first woke up. Then the RD will question further into any forgotten foods, ingredients when made at home, restaurants if not mentioned previously, servings size, and amount eaten.

The 24-hour recalls were analyzed by FoodWorks version 15 software. Total calories, carbohydrates, protein, and fat were observed at both visits as descriptive statistics only. Total amount of protein recorded for the baseline 24-hour recall was totaled and used to measure protein supplementation needs during the intervention period.

BIA Analysis

BIA is used to measure the outcome change in weight and FFM for the purposes of this study. BIA is a non-invasive tool that is widely used for measuring body composition. This tool uses small alternating currents to measure weight, BMI, basal metabolic rate (BMR), total body water (TBW), fat mass (FM), and FFM.[46-48] BIA is a measurement which can be performed on participants unless the participant has a pacemaker, any other internal electronic devices, or cannot stand unassisted for 1 minute.

For this study, we used the Tanita TBF-310GS Total Body Composition Analyzer which is similar in appearance to a household scale. Needed information including height, age, gender, physical activity (equal to/greater than or less than 10 hours or more of intense exercise per week) was stated by the participant and input into the device for analysis. Participants were then asked to remove shoes and socks, leaving nylons on if necessary, and stand on the scale ensuring part of their feet where touching all four of the electrodes. Participants were instructed to stand still without holding on to anything for support and were instructed when to step off. Results from both visits were documented for final analysis.

Education & Supplementation

The nutrition education was created specifically for this project and included a handout along with verbal instructions on the importance of protein, foods high in protein, different ways to add protein to the diet, how to read a food label, and how to appropriately use nutritional supplements. These individual sessions are provided by the RD and last approximately 15 minutes.

Protein needs were based on a range of 1.3-1.5 grams per kilogram of body weight at time of visit (adjusted body weight if BMI >40).[49, 50] Baseline 24-hour recall was compared to the calculated range of protein needs. If current intake fell short of estimated needs, participants were instructed on supplementing protein with whey protein powder (Beneprotein) as needed starting the day after education until 5 days prior to surgery.[51] Starting 5 days prior to surgery, all participants were instructed to change from the whey protein powder to an immune-enhancing protocol (Impact AR). Impact AR is a nutritional supplement that has been shown to boost immune function while still providing 18g protein in each container.[52] This nutritional supplement is part of the standard of care in the pancreas clinic of the Stephenson Cancer Center as well is often provided post-surgery prior to discharge.

Physical therapy intervention was also included for each participant as part of the larger trial. Participants were randomized to either aerobic exercises or aerobic exercises plus strengthening: A seated aerobic intervention, stretching, and exercises for all 4 limbs to be performed either as active motion, or with weights as personalized strengthening intervention. Group 1 (aerobic group) is considered the standard care for individuals referred to physical therapy prior to surgery. This group met with a physical therapist where they were provided with a standardized home-based exercise plan. This included instructions on lower body stretching and active range of motion, and a portable upper/lower body ergometer and encouraged to achieve a target of 60 minutes of daily exercise. Individuals are instructed to spread out exercise as needed related to heart rate, and/or symptoms to self-monitoring response as noted on the Borg Rate of Perceived Exertion (RPE) scale.

Group 2 (aerobic plus strength) received the same aerobic instructions as group

This group received further counseling on individualized moderate intensity strength training. The amount of resistance is determined following baseline testing and individualized to participant needs. Group 2 received not only the portable body ergometer, but also weights to serve as the resistance and instructions on how to increase resistance.

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Figure 1.0-Participant time table

Gastrointestinal Tumor Board
- Determined if candidate for study

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Baseline seen in Pancreas Clinic
- Deemed eligible for surgery

↓

Baseline testing

Data collection:
- Hand Grip Strength
- 24-hour recall
- BIA

↓

Surgery

↓

1 month post-surgery

Data collection:
24-hour recall obtained,
BIA Analysis

Exercise intervention is not noted in outcomes for this study. Since exercises are part of the larger study, they are important to note since exercise intervention assessment may alter results.

Second Visit/1-month post-op:

The second visit assessed for this study occurred approximately 1 month following surgery. This date will vary based on when the participant is discharged from the hospital, but will be scheduled two weeks following discharge. Data collection for this visit includes BIA and 24-hour recall.

Statistical Analysis

For this preliminary analysis, participants were compared at baseline and 1 month post-surgery. Data collection occurred March 2016-March 2017. A statistician working specifically with this preliminary analysis aided in assessing the computed results. The specific aims were measured using a repeated measures ANOVA analysis of variance but power was anticipated to be inadequate due to the small sample size. Repeated measures ANOVA is known as an analysis of dependencies and is to prove cause-effect relationship between the independent variables by measuring the equality of means. All members of the sample were measured under a number of different conditions, therefore the testing of the means by repeated measures ANOVA was appropriate. Independent variables were Statistical significance was set at $p < 0.05$.

Descriptive statistics were computed for weight, in pounds %FFM, FFM in pounds, % calories from protein, % calories from fat, % calories from carbohydrates between baseline and 1 month post-surgery compared between groups (average and below average HGS). All statistical tests were performed using a 5% chance of a type 1 error.

Aim 1: Change in FFM (%FFM and FFM in pounds) between baseline and 1 month post-surgery was compared between groups (average and below average HGS) by repeated measures ANOVA.

Aim 2: Change in weight (in pounds) between baseline and 1 month post-surgery was compared between groups (average and below average HGS) by repeated measures ANOVA.

Aim 3: Mean intake (% calories from protein, fat, and carbohydrates) was compared between groups (average and below average HGS) at both time points using a repeated measure ANOVA

RESULTS

Participants:

A total of 20 participants were collected for this preliminary analysis. These were the first 20 participants of the larger study to complete HGS, 24-hour recall, and BIA analysis at baseline, and 24-hour recall and BIA analysis at one month post-surgery. Participants were excluded if they had incomplete or inaccurate data. Of these participants, 6 were above average HGS and 14 were below average HGS. As far as randomization into the exercise groups, there were 4 at or above average HGS randomized to aerobic plus strengthening and 2 participants were randomized into aerobic only exercise. Of the below average HGS participants 7 were randomized into aerobic plus strengthening exercise and 7 randomized into aerobic only exercise. The larger trial's inclusion criteria allowed participants to be enrolled either immediately into surgery following diagnosis (PP) or into surgery following neoadjuvant therapy (PC). Out of overall participants, 16 were PP while only 4 were PC. Of the at or above average HGS all participants were PP, which could indicate the possibility that neoadjuvant therapy has some effect on HGS. Of the below average HGS, 10 were PP and 4 were PC.

For 3 patients, data from visit 4 was used instead of visit 3. Visit 4 data was collected at their second follow-up visit with the surgeon at the Stephenson Cancer Center which was approximately 3 months following surgery. These original visits were excluded because either the visit was missed or data collection was incomplete. Results were still calculated based on these substitutions because of the closeness of visits and the small sample size. Two participants did not complete BIA at the 1 month post-surgery visit but were able to attain BIA at the 4th visit for the larger study. One participant was unable to complete 24-hour recall at the one month post-surgery visit because visit was scheduled at time where no RD was available, so 24-hour recall was used from the 4th visit.

Table 2.0-Average participant data at baseline

	At/Above Average HGS	Below Average HGS	Overall
Average BMI	**kg/m^2**	**kg/m^2**	**$26.5 kg/m^2$**
Average HGS Total	**32.8kg**	**25.0kg**	**23.7kg**
Average HGS Male	**51.7kg**	**29.3kg**	**33.8kg**
Average HGS Female	**23.3kg**	**19.2kg**	**20.8kg**
Male:Female	**2:4**	**8:6**	**10:10**
Age	**58.1y**	**67.9y**	**67.6y**
Aerobic:Aerobic + Strength	**2:4**	**7:7**	**9:11**
PP:PC	**6:0**	**10:4**	**16:4**

Aim 1: FFM

Mean FFM in pounds at baseline for at or above average HGS and below average HGS were 116.00 ± 28.15 pounds and 117.43 ± 27.09 pounds, respectively. Mean FFM in pounds at 1 month post-surgery for at or above average HGS and below average HGS were 112.92 ± 28.62 pounds and 113.25 ± 24.22 pounds, respectively. There was no noted difference in the change in FFM in pounds when comparing at/above average HGS participants to below average HGS (p=0.8414). When looking at the participants as a whole, there was no difference in the change in FFM in pounds from baseline to 1 month post-surgery (p=0.1266).

Mean %FFM at baseline for at or above average HGS and below average HGS were 70.67 ± 5.59% and 71.67 ± 9.93%, respectively. Mean %FFM at one month post-surgery for at or above average HGS and below average HGS were 71.87 ± 4.04% and 76.19 ± 7.94%, respectively. There is no statistical difference when comparing the at or above average HGS to the below average HGS from baseline to 1 month post-surgery (p=0.3347). Both groups showed a 3.5% increase in %FFM from baseline to 1 month post-surgery (95% CI: 0.3%, 6.7%; p=0.0328).

Aim 2: Weight

Results show that there is no difference in change of weight when comparing at or above average HGS to below average HGS (p=0.5133). Both groups shows a mean of 13.7 pounds lost from baseline to 1 month post-surgery (95% CI: 10.1, 17.4; p<0.0001).

Aim 3: Intake

Dietary intake remains low following surgery; this has not changed since previous research. When comparing the change in foods between at or above average HGS and those who are below average HGS, there was no significant change from baseline to 1 month post-surgery between groups.

Mean %calories from protein at baseline between at or above average HGS and those below average HGS were 15.37 ± 4.87% and 20.21 ±

8.18%, respectively. Mean %calories from protein at 1 month post-surgery between at or above average HGS and those below average HGS were 18.10 + 3.04% and 16.86 + 6.19%, respectively. The change in %calories from protein was not different among the two groups (p=0.1740). There was also no change in %calories from protein, regardless of group, from baseline to 1 month post-surgery (p=0.4588).

Mean %calories from fat at baseline between at or above average HGS and those below average HGS were 41.68 + 10.52% and 35.01 + 10.98%, respectively. Mean %calories from protein at 1 month post-surgery between at or above average HGS and those below average HGS were 39.90 + 5.39% and 33.84 + 8.54%, respectively. There was no difference in the change in %calories from fat among both HGS groups from baseline to 1 month post-surgery. (p=0.9233) Regardless of groups, there was no change in the %calories from fat from baseline to 1 month post-surgery (p=0.6389).

Mean %calories from carbohydrates at baseline between at or above average HGS and those below average HGS were 42.97 + 14.38% and 44.79 + 10.62%, respectively. Mean %calories from carbohydrates at 1 month post-surgery between at or above average HGS and those below average HGS were 41.97 + 7.07% and 49.33 + 9.12%, respectively. There was no difference in change in %calories from carbohydrates among both HGS groups from baseline to 1 month post-surgery (p=0.4039). Regardless of group, there was no significant difference in change from baseline to 1 month post-surgery (p=0.3412).

Table 3.0-Descriptive statistics among hand grip strength groups for both baseline and one month post-surgery follow up time points

	N	Mean	Std Dev	Median	Minimum	Maximum
FFM in Pounds						
At or Above Average HGS-Baseline/1-month post-surgery	6 6	116.00 112.92	28.15 28.62	103.75 108.75	91.00 81.50	153.00 147.00
Below Average HGS-Baseline/ 1-month post-surgery	14 14	117.43 113.25	27.09 24.22	121.75 111.25	63.00 82.50	168.50 172.00
%FFM						
At or Above Average HGS-Baseline/1-month post-surgery	6 6	70.67 71.87	5.59 4.04	69.49 72.35	64.12 65.38	79.07 76.17
Below Average HGS-Baseline/ 1-month post-surgery	14 14	71.67 76.19	9.93 7.94	73.12 76.26	53.87 54.16	85.40 85.06
Weight						
At or Above Average HGS-Baseline/1-month post-surgery	6 6	164.33 152.42	38.35 35.93	157.00 153.75	126.50 107.00	224.00 204.00
Below Average HGS-Baseline/ 1-month post-surgery	14 14	164.43 149.93	35.47 34.16	159.25 145.25	109.50 104.00	231.50 226.50
%Calories from Protein						
At or Above Average HGS-Baseline/1-month post-surgery	6 6	15.37 18.10	4.82 3.04	15.90 17.05	7.20 15.70	21.90 23.80
Below Average HGS-Baseline/ 1-month post-surgery	14 14	20.21 16.86	8.18 6.19	18.15 16.50	11.20 8.60	43.30 31.30
%Calories from Fat						

At or Above Average HGS-Baseline/1-month post-surgery	6 6	41.68 39.90	10.52 5.39	44.20 39.75	22.20 32.90	51.20 47.20
Below Average HGS-Baseline/ 1-month post-surgery	14 14	35.01 33.84	10.98 8.54	36.45 31.55	16.80 23.20	52.40 54.40
%Calories from Carbohydrates						
At or Above Average HGS-Baseline/1-month post-surgery	6 6	42.97 41.97	14.38 7.07	40.05 42.15	30.30 31.80	70.60 49.90
Below Average HGS-Baseline/ 1-month post-surgery	14 14	44.79 49.33	10.62 9.12	42.35 51.55	27.60 34.00	66.90 60.40

Figure 2.0-Fat free mass (in pounds) among HGS groups from baseline to 1 month post- surgery

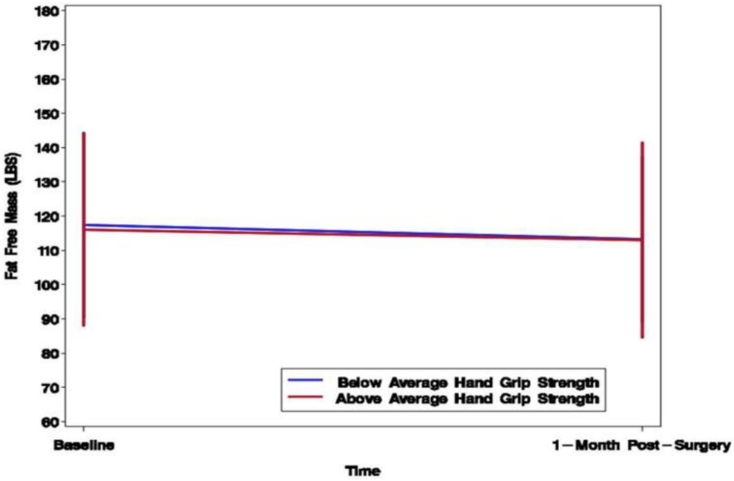


Figure 3.0-Percent FFM among HGS groups from baseline to 1 month post-surgery

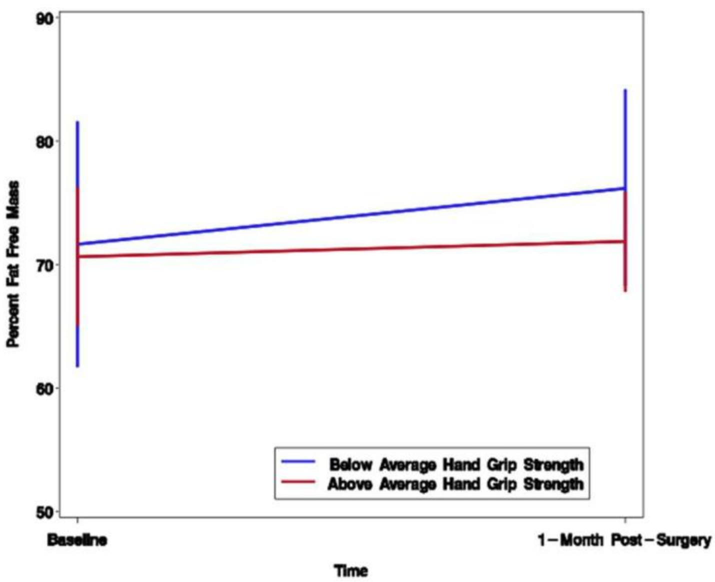


Figure 4.0-Weight (in pounds) among HGS groups from baseline to 1 month post- surgery

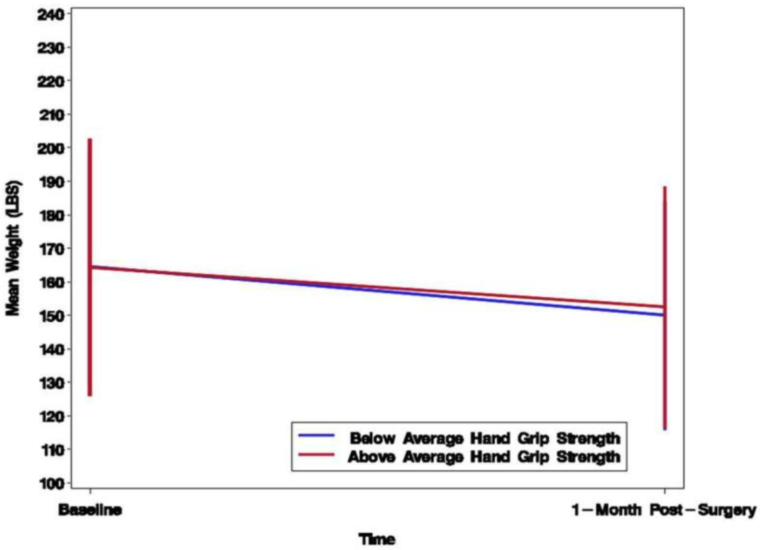


Figure 5.0-Percent calories from protein among HGS groups from baseline to 1 month post-surgery

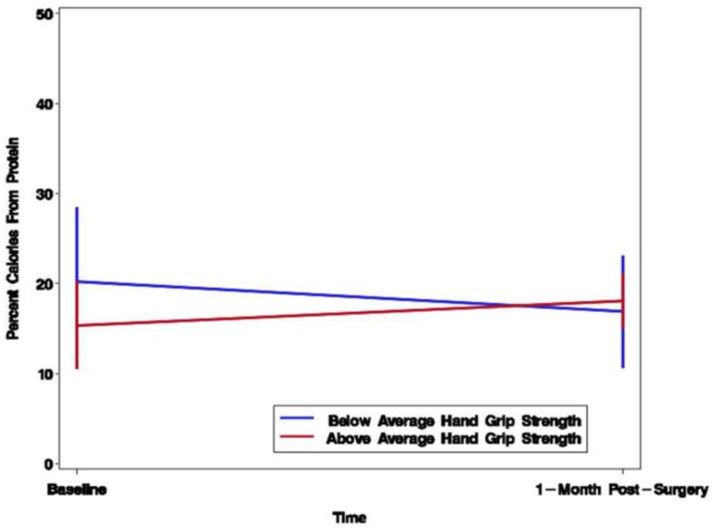


Figure 6.0-Percent calories from fat among HGS groups from baseline to 1 month post-surgery

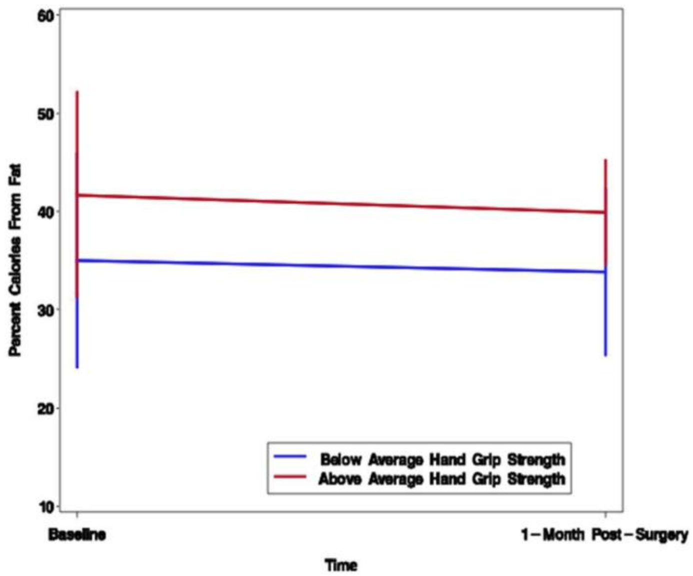
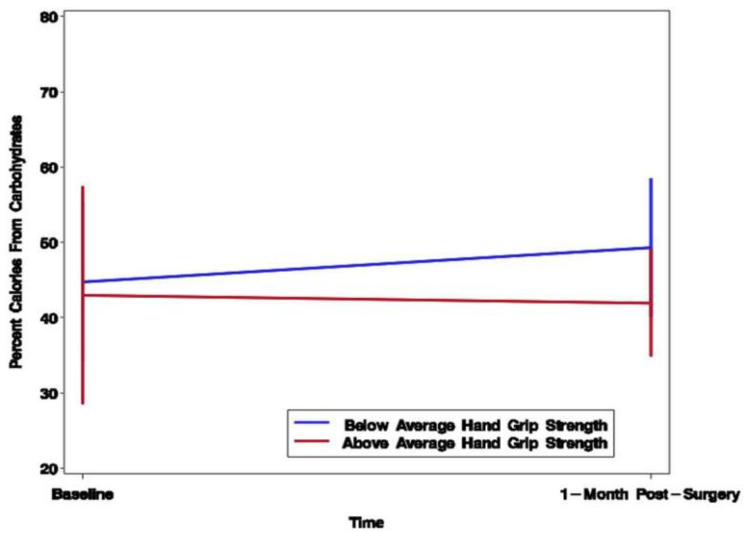


Figure 7.0-Percent calories from carbohydrates among HGS groups from baseline to 1 month post-surgery



DISCUSSION

Individuals were classified as either at or above average HGS or below average HGS at baseline. HGS has been previously used as a marker for malnutrition. Average HGS was used based on normative values for a population without any present disease markers. To my knowledge, set values for average HGS has not been determined for the cancer population at this time.

Out of the 20 participants chosen, 11 individuals were randomized into aerobic plus strengthening and 9 into aerobic only. Among the individuals classified as below average HGS, the individuals were equally distributed; 7 individuals in aerobic only and 7 individuals aerobic plus strengthening. Among individuals classified as at or above average HGS 4 individuals were aerobic plus strengthening and 2 were aerobic only. The exercise intervention may play a role in results, if strengthening causes more of an increase in FFM versus aerobic only intervention. The below average HGS group appeared to be equal in their intervention randomization, although the at or above average HGS participants were slightly skewed with 4 in aerobic plus strengthening and 2 in aerobic only, therefore it is difficult to determine if the difference in exercise intervention played a role in FFM change.

Weight loss, FFM loss, and decrease in dietary intake continue to occur post-PD despite education during the preoperative period. Figure 2.0 shows the change in FFM in pounds between the two groups from baseline to 1 month post-surgery. The below average HGS participants appear to have slightly more FFM in pounds at baseline than the at or above average HGS participants. At 1 month post-surgery, both groups appearto have the same FFM in pounds. However, these results were not statistically significant between groups or overall (p=0.8414 and p=0.1266, respectively). By looking at the lack of statistical differences there is no indication at this time that these individuals benefit from individualized interventions based on HGS. The below average HGS participants also showed a slightly bigger increase in pounds FFM. This could indicate the below average HGS participants may benefit more from the nutrition and exercise interventions. This could also indicate that no matter the classification of HGS, participants who undergo the prehabilitation program lose FFM at about the same rate. These results were regardless of exercise, with both HGS groups appearing equal in exercise randomization and assuming all exercises were completed as instructed. Although with such a small sample size this is difficult to determine.

Figure 3.0 shows the change in %FFM among participants at or above average HGS and those below average HGS from baseline to 1 month post-surgery. No statistically significant change was shown between groups with such a small sample size (p=0.3347). Both groups did have a 3.5% increase in %FFM from baseline to 1 month post-surgery (p=0.0328). Looking individually at the at or above average HGS participants, they appear to be steady from baseline to 1 month post-surgery which could mean they may benefit from an increase in intervention during the preoperative period. This could also indicate that the below average HGS participants benefitted more from the prehab intervention since it appears they gained more %FFM from baseline to 1 month post-surgery. Though, with such a small sample size, the difference between the groups is not yet clinically or statistically significant therefore no recommendations can be made.

Figures 5.0-7.0 show the change in %calories from protein, fat, and carbohydrates for both groups between baseline and one month post-surgery. The below average HGS group appears to consume more of their calories from protein and carbohydrates than fat at baseline than the at or above average HGS group. At or above average HGS participants appear to have slight increase in %calories from protein at 1 month post-surgery. Both groups seem to have stable intake of fats from baseline to one month post-surgery. Below average HGS participants appear to intake less %calories from fat throughout both time periods. Below average HGS participants appear to increase %calories from carbohydrates slightly from baseline to 1 month post-surgery. Based on data presented I could conclude that the increase in %calories from carbohydrates may be related to the decrease in %calories from protein. Although, my clinical judgment leads me to believe that the increase in calories from carbohydrates are more likely related to tolerance issues. Especially if the participants were struggling with fat malabsorption or delayed gastric emptying the participants may be able to tolerate the foods higher in carbohydrates versus those that were higher in fat or protein.

Figures 2.0-7.0 shows that there may be some slight indications of change in slope between groups at each time point and although not yet statistically significant this does have some clinical significance. Even with this preliminary analysis, there were some differences among groups classified as at or above average HGS versus those below average HGS.

One month post-surgery results for all data may be inaccurate related to the participant data included for visit 4. With small sample size visit 4 was included for 3 participants who were not able to complete data for 1 month post-surgery. All three of these individuals were below average in HGS, therefore the 1 month post-surgery results for below average HGS may be slightly positively skewed. History shows that the increase in time following surgery the lessening of the symptoms. This does not mean that functional or nutritional status are improving, but could show differences in results related to recovery time.

Potential Implications

If these results are indicative of the whole sample rather than separating based on HGS, then we could stipulate that based on this preliminary, underpowered analysis prehabilitation may be beneficial and the study should be continued to accrue to determine if these results hold true in the larger sample. Even though participants are continuing to lose weight, it appears that more weight is being lost from fat instead of FFM. If in fact participants are retaining their FFM then this could improve recovery time following surgery; therefore, participants would reach their pre-surgery FFM quicker than without the prehabilitation intervention. If participants are able to improve their FFM mass more quickly, then they may improve post-surgery outcomes.

Participants, and pancreatic cancer patients in general, often undergo to adjuvant therapy (chemotherapy, radiation therapy, chemoradiation therapy) following surgery. Following a PD patients are often malnourished and then go into adjuvant therapy; the side effects of adjuvant therapy often lead to a further nutritional decline and worsening symptoms. As seen in previous literature sarcopenia, or this further nutritional decline can worsen prognosis [5, 23].

Future Investigations

This preliminary analysis is part of a much larger trial that is ongoing at the Stephenson Cancer Center. The study hopes to gain further site locations to increase the rate at which participants are enrolled.

Based on the information gained from this study we can cautiously suggest there is a preliminary benefit of this early intervention during the prehabilitation phase such as increase in %calories from protein and %FFM mass.

Further analysis is needed to better assess change in body composition. The larger trial is gaining a new tool to assess body composition in terms of specific body compartments. This new tool will compare body fat and FFM in each part of your body instead of telling total body composition changes. This tool allows for better assessment of compartmental body measures to assess adequacy of exercise interventions since. Change in muscle mass could also be compared based on observing CT scans since all participants receive this at baseline and typically post-surgery as well.

Definitive conclusions cannot be made based on this preliminary analysis. Slight differences did appear through this preliminary analysis, with such a small sample size, although statistical significance was not achieved within this study, clinical significance is evident. Even without change in FFM in pounds, its results do indicate an increase in %FFM from baseline to 1 month post-surgery. This could indicate that the exercise intervention plus increase in protein intake are appropriate to build muscle within the 2 weeks prior to PD.

Nutrition education does cause a slight increase in %calories from protein from baseline to 1 month post-surgery, and that indicates continued education may be beneficial clinically even without statistical significance. Further investigation is warranted. From this preliminary analysis, we can determine that there are small differences in these two HGS groups that may require separate individualized interventions although further analysis in a larger sample size is needed to determine true results.

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