Study Protocol

FAST TRACK RECOVERY WITH A WHEY PROTEIN INFUSED CARBOHYDRATE LOADING DRINK AMONG SURGICAL GYNECOLOGIC ONCOLOGY PATIENTS: A PRAGMATIC OPENED LABELED TRIAL

NMRR Research ID:
NMRR-17-1070-36021 (II R)

Protocol number, version number and date:
FTRSG09052017, version 3, 27 September 2017

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Study site/s:
Surgical wards of National Cancer Institute.

List of Abbreviations

NCR	National Cancer Registry
BMI	Body Mass Index
IKN	Institut Kanser Negara
LOS	Length of Hospital Stay
PG-SGA	Patient Generated Subject Global Assessment
aPG-SGA	Abridge Patient Generated Subject Global Assessment
Hb	Hemoglobin
BFM	Body Fat Mass
Alb	Albumin
CRP	C-Reactive Protein
QoL	Quality of life
FTR	Fast Track Recovery
CO	Control group
CHO-P	Carbohydrate-whey protein

Research Synopsis

Study title	Fast Track Recovery With A Whey Protein Infused Carbohydrate Loading Drink Among Surgical Gynecologic Oncology Patients: A Pragmatic Opened Labeled Trial
Study Population	All patients who has been diagnosed with gynecologic oncology and undergoing surgery treatment at National Cancer Institute, Putrajaya.
Study Design	Pragmatic opened labeled trial. Participants will be randomly divided into control & intervention group during admission to hospital using random numbers. Participants were randomized into two groups: the carbohydrate-protein (CHO-P) group and conventional (CO) group. Participants were given a specific drink to their group on the evening prior to surgery and three hours before operation. The CHO-P group received 474ml (evening drink) or 237ml (3hours prior to operation drink) of a solution contain 14% whey protein, 86% carbohydrates and 0% lipids and the CO group nil-by-mouth at 12 midnight day of operation. All participants fasted for solids for 6 hours from the operation.
General Objective	To determine the impact of fast track recovery feeding with a whey protein plus carbohydrate drink in Surgical Gynecologic Oncology Patient in National Cancer Institute
Specific Objectives	a. To compare post-operation outcome between CHO-P group and conventional group. b. To compare anthropometric, biochemical and functional data between CHO-P group and conventional group c. To determine relationship between fast track recovery feeding with a whey protein plus carbohydrate drink and post-operative outcome
Study hypothesis	This hypothesis predicts there is improvement in post-operation outcome of intervention group if compare with control group of surgical gynecologic oncology patients undergoing surgery treatment in National Cancer Institute
Primary Outcome	Length of hospital stay, length of clear fluid toleration, length of solid food toleration, length of flatus, length of bowel open
Secondary outcome	Weight, fat percentage, muscle mass, PG-SGA, CRP, Albumin, handgrip strength
Sample Size	106 subjects
Study Duration	14 months

INTRODUCTION

Cancers is group of diseases which involve growth of abnormal cells. Normally, cells grow, divide and then die. Sometimes, cells mutate. They begin to grow and divide more quickly than normal cells. Rather than dying, these abnormal cells clump together to form tumors. Gynecologic oncology is a specialised field of medicine that focuses on cancers of the female reproductive system, including ovarian cancer, uterine cancer, vaginal cancer, cervical cancer, and vulvas cancer (Disaia et al. 2017).Gynecological Cancer is cancers that effect woman's reproductive system. Other types of gynecological cancers include fallopian tube cancer and placenta cancer (a pregnancy-related cancer) (Disaia et al. 2017).

In 2009, 16,437 Australians females lived with Gynecological Cancer, where 4919 new cases of Gynecological Cancer were diagnosed in year 2011. Gynecological Cancer had become the 3rd most commonly diagnosed cancer among females in Australia (Australian Institute of Health and Welfare 2014). Global Cancer Statistics (2012) shows that most common diagnosed cancer in females is cervix uteri besides stomach and colorectal cancer and become 3rd leading cause of death in females in less developed countries with 90% of cervical cancer death occurred in developing parts of the world. National Cancer Registry Report (2014), Cervix Uteri and Ovary cancer were in 10 most leading cancer and in 5 most common cancers in Malaysian females from year 2007 to 2011. There were a total of 847 cases of cervix cancer diagnosed in 2007 registered at National Cancer Registry (NCR). The incidence rate of cervical cancer increased after 30 years old and peaks at ages 65-69 years. When we compared among the major races, Indian women had the highest incidence for cervical cancer followed by Chinese and Malay. 45% of females at the point of first diagnosis with cervical cancer were already at stage 3 and 4.

Cancer cells alter energy metabolism which increase resting energy expenditure and increase metabolism of sugar, protein and lipid. Cancer patients including gynecological cancer patients' high risk being malnourished before start on any treatment. Nutrition requirement for surgery is higher if compared with normal requirement in order to support speedy recovery. For patient who went for surgery treatment, length of hospital stay (LOS) of patient after surgery may be affected impaired by nutritional status of a patient pre and post-operation. In a cohort study done in Australia among 157 Gyneacological Cancer (GC) patients, the data shows that malnutrition, low QoL scores and being diagnosed with advanced ovarian cancer are the major determinants of LOS amongst GC patients. Intervention addressing malnutrition and poor QoL may shorten LOS in GC patients (Laky et a. 2010). LOS has become surrogate marker for patient's well-being during hospital treatment and identifying

pretreatment factors associated with LOS in surgical patients may enable early intervention in order to reduce postoperative LOS (Lay et al. 2010; Caro et al. 2007). Cancer and its treatment result in severe biochemical and physiological alterations associated with a deterioration of QoL (Maria et al. 2007).

Like other cancers, first step of gynecological cancer management includes cancer diagnosis where clinical and pathological assessments taking place. Once a diagnosis and cancer stage is confirmed, oncologists determine treatment options and prognosis and to apply the appropriate research treatment protocols. The primary modalities of cancer treatment are surgery, chemotherapy and radiotherapy; these may be used alone or in combination (Feig et al. 1998). For those cancers which are well margined and operable, surgery is first treatments for gynecological cancer (Vetto et al. 1999).

Surgery, a like injury, causes skeletal muscle tissue to be broken down in order to release amino acids. These amino acids are transported to the wound to promote wound healing. Anabolism, where increased protein synthesis to repair the damaged cells as well as new blood vessels, requires protein. Optimum nutritional status peri-operation can speed up wound healing, improve immunity and ensure the better post-surgery outcome. Other than calories and carbohydrate, protein is crucial for post-surgery recovery and promotes anabolism, slows down muscle catabolism and decreases the inflammatory phase (Averd et al. 2017). Source of whey protein includes legume, dairy products and meat. Whey protein is a high quality protein that is easier to be digested and stimulates muscle protein synthesis if compared to casein. These effects may be due to the high degree of branched-chain amino acids in whey protein which directly stimulates the early cellular process involved in protein synthesis called initiation translation (Kimball et al. 2002). However, some people who are allergic to milk may be specifically allergic to whey protein. In moderate doses, whey protein does not typically cause any adverse events but consuming very high doses can cause stomach pains, cramps, reduced appetite, nausea, headache and fatigue (Vonk et al. 2003).

Conventional feeding strategy for pre- and post-operation whereby prolonged fasting or rest for both the patient and the gastrointestinal tract will delay the recovery of patients since the organic response to surgical trauma is enhanced by prolonged period of fasting. Inadequate oral intake due to delayed oral feeding caused depletion of nutrient storage in patient's body. This is because of utilization of energy which converted from protein source of body (muscle). This metabolism process is called catabolism. Patients experienced weight loss and muscle mass loss post-operatively (Balayla et al. 2004; Balayla et al. 2005).

Conventional surgery approach was questioned by professor of surgery, Henrik Kehket (1999). Hence, Kehket et al. (1999) developed multimodal perioperative protocol, named Enhanced Recovery After Surgery or Fast Track Recovery Surgery protocol. As a key of fast track recovery (FTR) programs also include a metabolic strategy to reduce perioperative stress and improve outcomes. Nutrition intervention post operation is importance. Studies of FTR program in gynecology surgery have shown that such programs significantly reduce length of hospital stay and consequently have positive economic benefits without increasing readmission and complication rates. To achieve these goals, FTR programs focus primarily on reducing perioperative stress, achieving satisfactory pain control, resumption of normal gastrointestinal function and early mobilization (Balayla et al. 2004; Balayla et al. 2005; Obermair et al. 2017; Ester et al. 2016; Averd et al. 2017).

1.2 Problem statement

While early oral feeding is preferred mode of nutrition, avoidance of any nutritional support therapy bears the risk of underfeeding during postoperative course after major surgery. To abbreviate preoperative fasting, beverage containing carbohydrates have been used and recommended in FTR program. Formula containing protein on top of carbohydrate-enriched drink proposed to improve post-operative muscle strength, reduce fatigue, anxiety and discomfort as well as lowering the endocrine-metabolic response to trauma. Whey protein contains a high level of essential amino acids especially branch-chain amino acids. These amino acids are rapidly used by skeletal muscle during stress and highly stimulate protein synthesis. Whey protein has a high degree of digestibility and rapid absorption in the small bowel. No study so far has aimed to examine the benefits of whey protein in the composition pre-operative and post-operative drinks among surgical gynecologic oncology patients.

Research Questions:

1. What are the nutritional status (anthropometry, dietary intake, muscle mass, handgrip strength and biochemical data such as CRP, serum albumin and hemoglobin level) in surgical gynecologic oncology patient in National Cancer Institute?
2. What are the post-operative outcomes (length of bowel function, length of solid food toleration and length of stay) in surgical gynecologic oncology patient in National Cancer Institute?
3. What are the differences in post-operation outcome between CHO-P group and control group?
4. Is there any relationship between fast track recovery feeding with a whey protein plus carbohydrate drink and post-operative outcome?

1.3 Objective

1.3.1 General Objective

To determine the impact of fast track recovery feeding with a whey protein plus carbohydrate loading drink in Surgical Gynecologic Oncology Patient in National Cancer Institute

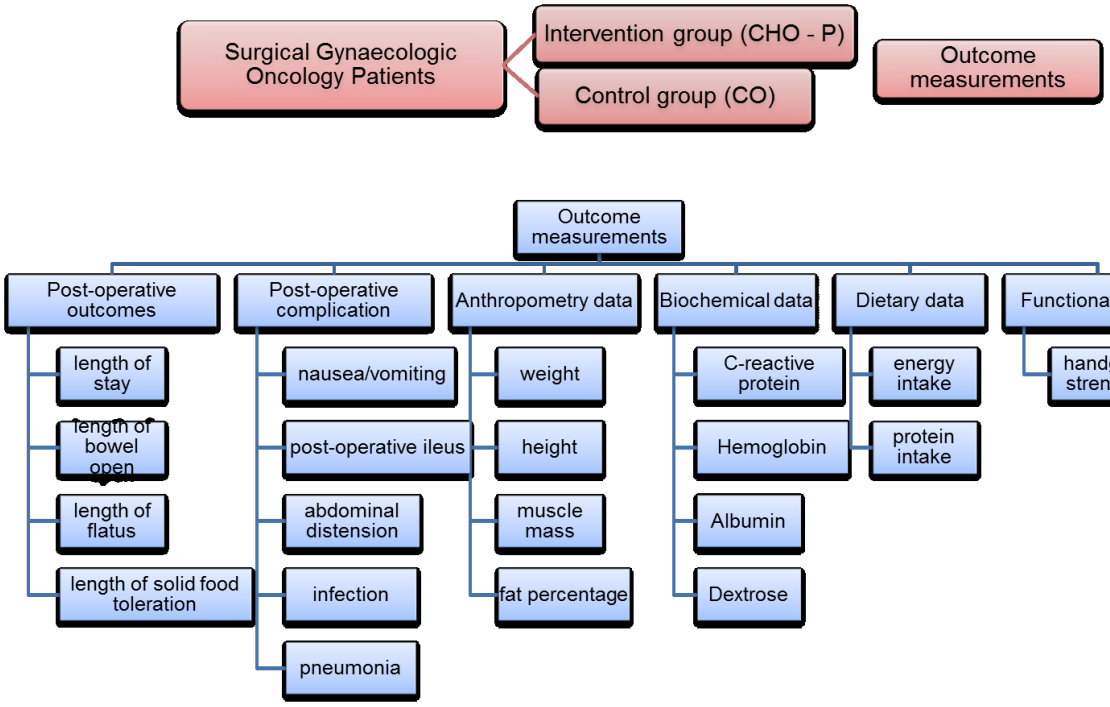
1.3.2 Specific objective

a. To compare post-operation outcome between CHO-P group and conventional group.
b. To compare anthropometric, biochemical and functional data between CHO-P group and conventional group
c. To determine relationship between fast track recovery feeding with a whey protein plus carbohydrate drink and post-operative outcome

1.4 Null Hypothesis

1. There is no difference in post-operation outcome between CHO-P group and conventional group
2. There is no relationship between fast track recovery feeding with a whey protein infused carbohydrate loading drink and post-operative outcome

Conceptual Framework



Methodology

2.1 Study Design

Pragmatic opened label trial to investigate the impact of fast track recovery feeding with whey protein plus carbohydrate drink on surgical gynecologic oncology patients in National Cancer Institute.This study will focus on impact towards post-operative outcome when whey protein contained pre-operative drink is taken in current standard operating procedure in managing surgical gynecologic oncology patients

2.2 Study Period

Recruitment and intervention period is months, 1st September 2017 to 31st October 2018.

2.3 Study Population

All surgical gynecology patients receiving surgery treatments in National Cancer Institute, Putrajaya

- Inclusion criteria
  a. Those who diagnosed with Gynecologic Cancer stage 1 to stage 4
  b. Candidates for elective operation treatments

c. Malaysian who aged more than 18 years old

- Exclusion Criteria
  a. Not a candidate for elective operation treatments
  b. Aged <18 years old
  c. Diagnosed with Diabetes Mellitus/Chronic Kidney Disease/Cardiovascular disease/Chronic liver disease
  d. Not able to provide informed consent
  e. Allergy to milk/soy/whey protein

2.4 Sample Size

Hypothesis (Equality)

$H_0: \mu_1 = \mu_2$
$H_a: \mu_1 \neq \mu_2$

Formulae for Sample Size Calculations

STEP 1

$$\text{Standard Deviation}_{\text{pooled}} = \sqrt{\frac{\sigma_1^2+\sigma_2^2}{2}} \quad [1]$$

where σ_1 = standard deviation in Group 1, and
σ_2 = standard deviation in Group 2.

$$\text{Standard Deviation}_{\text{pooled}} = \sqrt{\frac{6.50^{\,2}+\ 2.35^{\,2}}{2}}$$

$$\text{Standard Deviation}_{\text{pooled}} = 4.89$$

STEP 2

$$\text{Sample size } (n) \approx \frac{2\sigma^2\left[Z_{1-\frac{\alpha}{2}}+Z_{1-\beta}\right]^2}{(\mu_1-\mu_2)^2} \quad [1]$$

where n = sample size,
Z = level of confidence,
σ = standard deviation,
α = alpha,
β = beta,
μ_1 = mean in Group 1, and
μ_2 = mean in Group 2.

$$\text{Sample size } (n) \approx \frac{2(\ 4.89\ )^2\left[Z_{1-\frac{0.05}{2}}+Z_{1-0.20}\right]^2}{(\ 9.00\ -\ 5.60\ )^2}$$

$$\text{Sample size } (n) \approx \frac{2(\ 4.89\ )^2\left[\ (1.96)+(0.85)\ \right]^2}{(\ 9.00\ -\ 5.60\ )^2}$$

$$\text{Sample size } (n) \approx 33 \text{ samples}$$

Sample size estimation was calculated using two population means formulae[48]. Prior data indicate that the mean hospital stay of the control group was 9 (standard deviation = 6.5) and the mean of intervention group was 5.6 (standard deviation = 2.35)[51]. Thus, a minimum sample size of 33 samples per group to be able to reject the null hypothesis with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. The independent t-test statistic will be used to evaluate this null hypothesis. With an additional of 30% dropout rate, the sample size is 53 samples per group.

2.5 Withdrawal Criteria

Subjects may be withdrawn if the investigator deems that it is detrimental or risky for the subject to continue. Subjects also can withdrawal themselves in the middle of this study without any reason. Withdrawn subjects will not be replaced.

2.6 Study Tools and Parameters

All parameters and variable data will be collected throughout monitoring period and will be recorded in Data Collection Form and aPG-SGA Scoring Sheet.

Patient Generated Subjective Global Assessment (PG-SGA) is a nutritional assessment tool that can identify risk of malnutrition among cancer patients. It includes more nutritional symptoms than the one in SGA sheets, short term weight loss and numerical scoring which may reflect clinical changes over time [27]. PG-SGA component contain first four parts questionnaires reflecting history of weight and weight lost, food intake, NIS and functional ability that must be filled by patient him or herself. The next part of PG-SGA need to be filled by professionals contains assessment of metabolic demands, nutrition and disease requirement and physical exam. Abridge PG-SGA or aPG-SGA used only the first four parts questionnaire of original PG-SGA that are prove to be sufficient to be used as a useful tool for early detection and predicting outcome of cancer cachexia as shown in a cohort study with advanced cancer patients [28]. This study shows that a high score of aPG-SGA is significantly associated with lower Hb level, increased WBC Count, decreased anthropometry and physical measurement such as BMI, BFM and Handgrip Strength, a dose reduction in chemotherapy and increased mortality [28].

Valid measurement tools are scheduled calibrated Tanita Total Body Composition Analyser model SC 300 which can provide body weight in kg (up to 0.1kg), fat percentage (up to 0.1%), total muscle mass (up to 0.1kg). Subject is requested to have minimal clothing, empty pocket and stand up-right with bare foot on metal plate of scale. Scheduled calibrated SECA Height Measurement (up to 0.1cm) is used to measured height. Subject needs to be bare foot, stand up-right and face front while measuring.

Handgrip strength is measured on the non-dominant hand using Jamar hand dynamometer (Fred Sammons Inc, Burr Ridge, Illinois, USA). Handgrip strength as a surrogate marker for muscle strength in patients with cancer has been well documented elsewhere. Subjects sit with their shoulder adducted and neutrally rotated, elbow flexed at 90º, forearm in neutral position, and standard verbal instructions are given to the subjects

to squeeze the dynamometer as hard as possible for three times after an interval of 5 seconds in between grips. Average of three successive attempts is used as the final result.

The variables that being collected in the Data Collection Form are:-

1. Socio-Demographic
   a) Age
   b) Ethnic Group
   c) Education Level
   d) Occupation
2. Pre-operative data
   a) Anthropometric Data: Weight, Height, Muscle mass
   b) aPG- SGA Scoring
   c) Diet Recall via Dietary Assessment Sheet
   d) Handgrip strength
   e) Biochemical data: Hemoglobin (Hb), C-reactive protein and Albumin (Alb)
3. Post-operative Outcome
   a) Length of Hospital Stay
   b) Length of bowel function
   c) Length of solid food toleration

2.7 Study Flow

Candidates will attend Multidisciplinary Clinic (MDC) as appointment date for examination then they will get surgery appointment (admit to ward) 7-14 days after MDC date. Eligible patients will be identified from name list available in the electronic medical record. Selection of patient will be done by assigned research team member then she will approach and inform with study procedures to all potential candidates (selected based on inclusion and exclusion criteria) while they attend MDC during study period. Participants will be randomized into two groups: the carbohydrate-protein (CHO-P) group and conventional (CO) group during admission to hospital via random numbers which are issued by computer program. For the concepts of the CONSORT flow diagram are followed [50]. The Patient Information Consent Form will be given to identify eligible subjects who agreed to be recruited in the study. Subjects are allowed to bring back consent form if she keen to seek advice from family member.

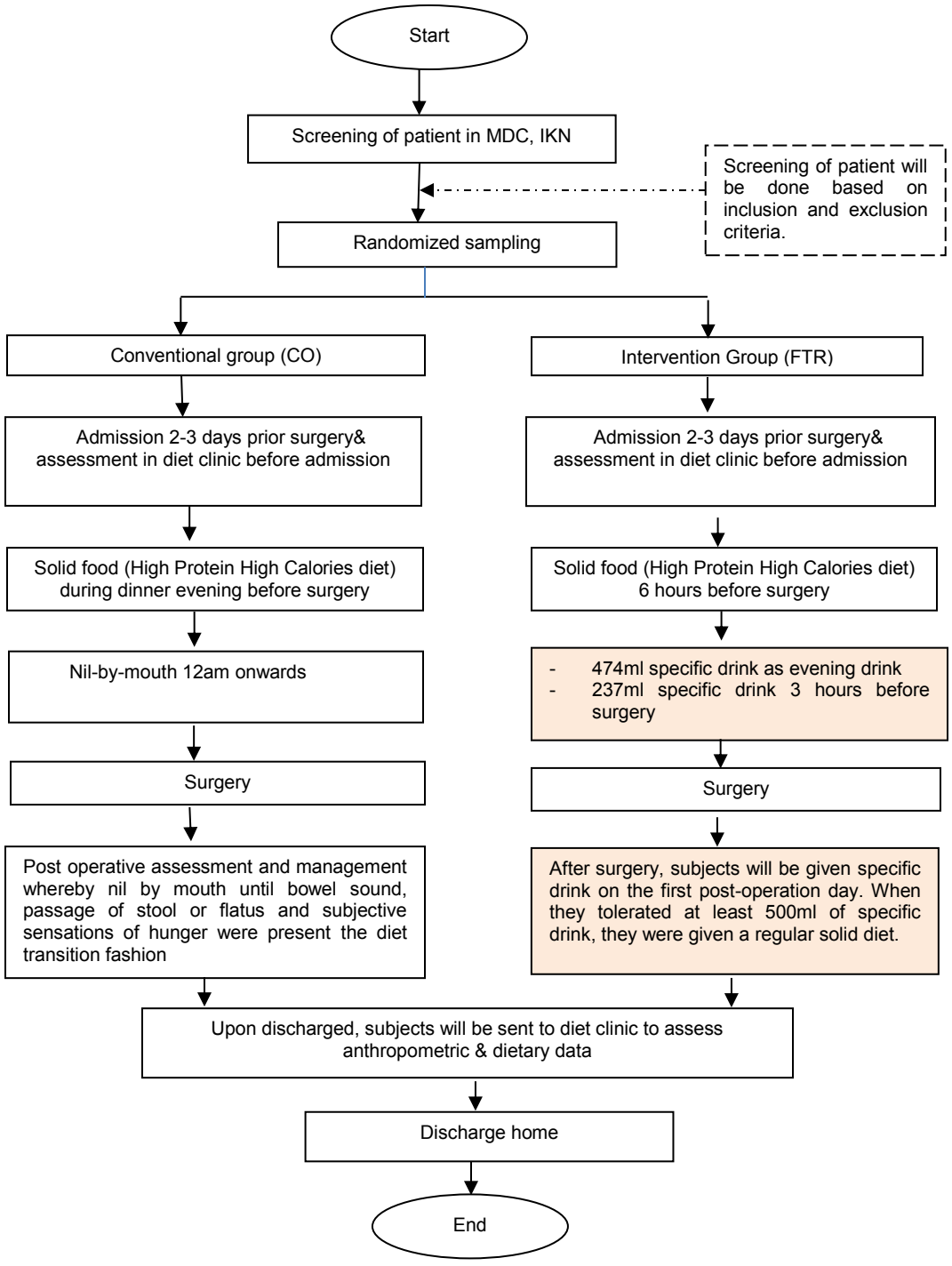
Carbohydrate-protein group: Participants will attend dietitian clinic to have anthropometry & dietary assessment on the same day of admission (before admission). Subjects are given a specific drink to their group on the evening prior to surgery and three hours before operation. The CHO-P group received 474ml (evening drink) or 237ml (3 hours prior to operation drink) of a lactose-free clear tea-colour fruit flavoured fluid

contains 14% whey protein, 86% carbohydrates and 0% lipids. Participants fast for solids for 6 hours from the operation. Participants will be given clear fluid (2 packs Resource peach) within 24 hours post-surgery (without present of bowel sound) and reviewed by dietitian. Staff nurse in-charged will monitor anesthetic risk of drinking whey protein and ensure subject to finish specific drinks prior surgery. When they tolerated at least 500ml of clear fluids, they were given a regular solid diet.

Conventional group: Participants will attend dietitian clinic to have anthropometry & dietary assessment on the same day of admission (before admission). Participants followed conventional operation procedure whereby fasting start 12am until operation. On the first day of post-operation day, participants will be reviewed by gynaecologist and dietitian. They are allowed for clear fluid once there is bowel sound. After tolerated clear fluid, they will proceed for nourishing fluid, then soft diet and they were given a regular solid diet.

On the day of operation and on the first day of post-operative day, blood samples are collected for hemoglobin, renal profile, albumin and C-reactive protein. Biochemical data will be record from electronic medical record. Upon discharge, all participants will be sent to dietitian clinic to assess anthropometry and dietary data.

Flow Chart of Research Activities



*Collection data will be collected prior to treatment and through study period.

2.8 Study Duration and Timeline

	2017																						2018						
	FEB		MAR		APR		MAY		JUNE		JULY		AUG		SEPT		OCT		NOV		DEC		JAN-SEPT		OCT		NOV		DEC
Literature review																													
Draft proposal & other documents																													
NMRR application																													
Modification on study proposal																													
Study initiation																													
Data collection and QC																													
Data entry																													
Data cleaning																													
Data analysis																													
Report writing																													
Presentation																													

The participation duration for each subject is minimum 1 week until patient is discharged

3.10 Statistical Analysis Plan

Energy and macronutrient from diet recall will be analyzed by Axxya system program Nutritionist Pro. This is diet analysis and nutrition food label software. Food in diet recall is entered into system then system will analyze and show total energy, macronutrients and micronutrient intake in kilocalories, gram and microgram.

"The analyses will be performed using IBM SPSS Statistics for Windows (Version 22.0. Armonk, NY: IBM Corp.). Descriptive statistics will be utilized for selected variables. The results will be presented as frequencies and percentage for Categorical Data. Numerical Data which is normally distributed will be presented as mean and standard deviation while median and interquartile range will be presented for Numerical Data which is not normally distributed.

Comparing Numerical Data which is normally distributed between two groups will be analyzed using the Independent t-test while Mann-Whitney test will be used if not normally distributed. Pearson's Chi-square test for Independence will be used to study association between Categorical Data and Categorical Data while Fisher's exact test will be used if assumptions of Pearson's Chi-square test for Independence are not met. Multiple logistic regressions will be used to study association between risk factors (Numerical Data/Categorical Data) and outcomes (Categorical Data). All probability values will be used two-sided and a level of significance of less than 0.05 (p-value $<$ 0.05) will be considered as statistically significant (Lang & Secic, 2006).

The aim of a clinical trial is to make a calculated judgement about the likely clinical effectiveness results that would be seen if the treatments tested were to be used for all suitable patients. The eligibility criteria for a patient entering a clinical trial should ensure that they are representative of patients suitable for the treatments being tested and compared. In a randomised trial, the set of all randomised patients is known as the ‘intention to treat population’, or the ITT population. This clinical trial study population is intended to represent suitable patients and to be reflective of what might be seen if the treatment was used in clinical practice. Therefore the ITT population should normally be the basis for inferences about the effectiveness of the treatments.

The eligibility criteria for the ITT population and treatments they receive will be clearly defined in the study protocol but in practice not everything goes perfectly to plan. Therefore, we need to plan ahead for the inconsistencies that can occur, for example, because of human error, and consider how we deal with them statistically.

One deviation from the protocol that is often experienced is when the allocated treatment is not actually received by all randomised patients; sometimes patients receive the wrong treatment or incomplete treatment. These things can, however, also happen to patients in clinical practice so they should not result in patients' exclusion from the evaluation made on the ITT population. For this same reason, patients should be analysed according to their planned (intended) treatment and not the actual treatment they received.

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Appendix A

Patient ID Information

Scored Patient-Generated Subjective
Global Assessment (PG-SGA)
History (Boxes 1-4 are designed to be completed by the patient.)

1. Weight (see Worksheet 1)

In Summary of my current and recent weight:
I currently weigh about _____ pounds
I am about _____feet _____tall.

One month ago I weighed about _____pounds
Six month ago I weighed about _____pounds

During the past two weeks my weight has:
☐ Decreased (1) ☐ Not Changed (0) ☐ Increased (0)

Box 1 ☐

2. Food Intake: As compared to my normal intake, I would rate my food intake during the past month as:

☐ Unchanged (0)
☐ More than usual (0)
☐ Less than usual (1)
I am now taking:
☐ *Normal food* but less than normal amount (1)
☐ Little solid food (2)
☐ Only liquids (3)
☐ Only nutritional supplements (3)
☐ Very little of anything (4)
☐ Only tube feedings or only nutrition by Vein (0)

Box 2 ☐

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):

☐ No problems eating (0)
☐ No appetite, just did not feel like eating (3)
☐ Nausea (1)
☐ Constipation (1)
☐ Mouth Sores (2)
☐ Things taste funny or have no taste (1)
☐ Problems swallowing (2)
☐ Pain; where? (3) _____
☐ Other* (1) _____
☐ Vomiting (3)
☐ Diarrhea (3)
☐ Dry mouth (1)
☐ Smells bother me (1)
☐ Feel full quickly (1)
☐ Fatigue (1)

***Examples: depression, money or dental problems*

Box 3 ☐

4. Activities and Function: Over the past month, I would generally rat my activity as:

☐ Normal with no limitations (0)
☐ Not my normal self, but able to be up and about with fairly normal activities (1)
☐ Not feeling up to most things, but in bed or chair less than half the day (2)
☐ Able to do little activity and spend most of the day in bed or chair (3)
☐ Pretty much bedridden, rarely out of bed (3)

Box 4 ☐

Additive Score of the Boxes 1-4 ☐ **A**

The remainder of this form will be completed by your doctor, nurse, or therapist. Thank you

5. **Disease and its Relation to Nutritional Requirements** *(See Worksheet 2)*
All relevant Diagnoses (specify)_____
Primary disease stage (circle if know or appropriate) I II III IV Other _____
Age _____

6. Metabolic Demand *(See Worksheet 3)*
7. Physical *(See Worksheet 4)*

Numerical Score from Worksheet 2 ☐ **B**
Numerical Score from Worksheet 3 ☐ **C**
Numerical Score from Worksheet 4 ☐ **D**

Global Assessment *(See Worksheet 5)*
Well-nourished or anabolic (SGA-A)
Moderate or suspected malnutrition (SGA-B)
Severely Malnourished (SGA-C)

Total PG-SGA Score
(Total Numerical Score of A+B+C+D Above) ☐
(See Triage recommendations below)

Clinician Signature_____RD RN PA MD DO Other_____Date_____

Nutritional Triage Recommendations: Additive score is used to define specific nutritional interventions including patient and family education, symptom management including pharmacologic intervention, and appropriate nutrient intervention: (food, nutritional supplements, enteral, or parenteral triage). First line nutrition intervention includes optimal symptom management.

0 – 1 No intervention required at this time. Reassessment on routine and regular basis during treatment.
2 – 3 Patient and family education by dietician, nurse, or other clinician with pharmacologic intervention as indicated by symptom Survey (Box 3) and laboratory values as appropriate
4 – 8 Requires intervention by dietician, in conjunction with nurse or physician as indicated by symptoms survey (Box 3)
≥9 Indicates a critical need for improved symptom management and/or nutrient intervention options.

Appendix B (a)– Data Collection Form

DIETITIAN CLINIC: pre-operation (on the day of admission)
BASELINE DATA

DEMOGRAPHIC DATA											
ID											
AGE		**years**									
EDUCATION LEVEL		NO EDUCATION		PRIMARY		SECONDARY		TERTIARY			
ETHNIC		MALAY		CHINESE		INDIAN					
OCCUPATION		NOT WORKING		WORKING							
ANTHROPOMETRY DATA											
HEIGHT	m		**WEIGHT**	KG							
BMI	Kg/m²										
PG-SGA SCORE			TO ATTACHED ABRIDGE PG-SGA SCORE FORM								
MUSCLE MASS			**HANDGRIP STRENGTH: 1.**		**2.**		**3.**				
CLINICAL DATA											
DIAGNOSIS											
STAGE OF CANCER											
DATE OF PLANNED SURGERY											
BIOCHEMICAL DATA											
SERUM ALBUMIN	g/dL		**Hb**	mmol/L							
C-REACTIVE PROTEIN											
NUTRITION ASSESSTMENT											
DIET RECALL TOTAL INTAKE: E- P-	BFE		MTE		LE		ATE		DE		
	BFP		MTP		LP		ATP		DP		
	SE		DIET RECALL MUST BE RECORDED IN DIETETIC CARE NOTES AND ATTACHED TOGETHER WITH THIS FORM.								
	SP										
DIET PRESCRIPTION											
ONS SUPPLEMENTATION						**PRODUCT**					
DILUTION						**FREQUENCY**					
DIETITIAN I/C											
	CHOP:										

Appendix B (b)– Data Collection Form

PROGRESS IN WARD:

DEMOGRAPHIC DATA					
ID					
AGE		**years**			
ADMISSION DATE & TIME					
Go to Dietitian clinic before admission			☐ Yes		
PRE-OPERATION					
Date & Time For Evening Drink			**TOTAL PACKS FINISHED**		
Date & Time For 3 Hours Pre-Operation Drink			**TOTAL PACK FINISHED**		
Blood (RP, Alb, Hb & CRP) day before operation	☐ **Taken (at ward)**				
Dextrose					
POST-OPERATION					
Blood (RP, Alb, Hb & CRP) day 1 operation	☐ **Taken (at recovery bay, Operation theatre)**				
Dextrose	☐ **Taken (at ward)**				
Date & Time To Start Drink (Clear Fluid)			**TOTAL TOLERATION:**		ml
Date & Time To Start Regular/Solid Diet					
Date & Time To Tolerate Regular Diet					
Date & Time To Pass Flatus					
Date & Time To bowel open					
DISCHARGE DATE & TIME					

Appendix B (c)– Data Collection Form

DIET CLINIC (OUTPATIENT) – post-operation (upon discharged)

DEMOGRAPHIC DATA										
ID										
AGE		**years**								
ANTHROPOMETRY DATA										
HEIGHT	m		**WEIGHT**	KG						
BMI	Kg/m²									
HANDGRIP STRENGTH	1. 3. 2.									
MUSCLE MASS										
BIOCHEMICAL DATA										
SERUM ALBUMIN	g/dL		**HB**	mmol/L						
CRP										
NUTRITION ASSESSTMENT										
DIET RECALL TOTAL INTAKE: E- P-	BFE		MTE		L E		AT E		DE	
	BFP		MTP		L P		AT P		DP	
	SE		DIET RECALL MUST BE RECORDED IN DIETETIC CARE NOTES AND ATTACHED TOGETHER WITH THIS FORM.							
	SP									
DIET PRESCRIPTION										
ONS SUPPLEMENTATION					**PRODUCT**					
DILUTION					**FREQUENCY**					
DIETITIAN I/C										
	CHOP:									

Participant Information Sheet and Informed Consent Form
(for adult subjects and intervention studies)

1. Title of study:

FAST TRACK RECOVERY WITH A WHEY PROTEIN INFUSED CARBOHYDRATE LOADING DRINK AMONG SURGICAL GYNECOLOGIC ONCOLOGY PATIENTS: A PRAGMATIC OPENED LABELED TRIAL

2. Name of investigator and institution:
Name and Institution of Principal investigator:
Ho Chiou Yi, National Cancer Institute, Putrajaya

Name and Institution of Co-Investigators:
Dr. Jamil Omar, National Cancer Institute, Putrajaya
Dr. Norazzam, National Cancer Institute
Dr. Zuriati Binti Ibrahim, Pensyarah Universiti Putra Malaysia
Dr. Zalina Binti Abu Zaid, Pensyarah Universiti Putra Malaysia
Dr. Zulfitri 'Azuan Bin Mat Daud, Pensyarah Universiti Putra Malaysia
Dr. Nor Baizura Binti Md Yusop, Pensyarah Universiti Putra Malaysia
Dr. Nor Azlin Binti Dahlan, National Cancer Institute
Dr. Azilah Binti Abdul Aziz, National Cancer Institute

3. Introduction:

This study is a prospective randomized pragmatic opened label trial study. There is experimental intervention being administered.

We would like to invite you to take part in our research study because you have gynecology cancer. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team members will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 5-10 minutes. Ask us if there is anything that is not clear. After you are properly satisfied that you understand this study, and that you wish to participate, you must sign this informed consent form.

Your participation in this study is voluntary. You do not have to be in this study if you do not want to. You may also refuse to answer any questions you do not want to answer. If you volunteer to be in this study, you may withdraw from it at any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled. There is no prorated payment for participation in this study.

A total of 106 subjects from multidiscipline outpatient clinic in National Cancer Institute, Putrajaya will be participating in this study. The whole study will last about 14 months. The participation duration for each subject is minimum 1 week until patient is discharged.

Probability for randomization into group A and group B are the same. If you agree to participate in the study, you will be assigned into either group A or B.
The product used in this study does not contain porcine and bovine ingredient and has been certified HALAL by Singapore Authorities. This study has been approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia.

4. What is the purpose of the study?

This study is to determine the impact of fast track recovery feeding with a whey protein infused carbohydrate drink among surgical gynecologic oncology patients in National Cancer Institute

5. What will happen if I decide to take part?

a. In this study, we will collect information on your nutritional status, physical function and hospitalization record.

b. At first, we will collect information about your medical condition from your medical record at the time of follow up in medical outpatient clinic, including your blood laboratory investigations. All blood laboratory investigations are extracted from your medical outpatient record and not taken specific to the purpose of this study.

c. A dietician will assess your nutritional status in diet clinic. Your nutritional status will be assessed using a questionnaire; dietary recall and measurements of your height, weight, body fat percentage and handgrips at the arm will be assessed. Weight, height and body fat percentage will be measured using a special scale that requires you to stand on the scale.

d. Upon admission, you have to attend to diet clinic to assess of your height, weight, body fat percentage and handgrips.
   - If you are assigned to group A, you need to be fasting at 12 midnight and only allowed to take water till 3 hours before operation.
   - If you are assigned to group B, you are allowed to take solid food as hospital served 6 hours before operation. 3 hours before operation, you will be provided 1 pack supplement (a lactose-free clear tea-colour fruit flavoured fluid contain 14% whey protein, 86% carbohydrates and 0% lipids).

   Upon discharge from ward, you have to attend to diet clinic to assess of your weight, body fat percentage and handgrips.

e. After completion of study, continuous treatment (diet intervention & oncological treatment) will be given as routine care. Study product will not be continued. But high protein nourishing fluid will only be given if indicated (malnutrition) after dietary assessment.

6. What are my responsibilities when taking part in this study?

It is important that you answer all of the questions asked by the study staff honestly and completely as well as compliance to diet advice and oral supplement as planned.

7. What are the potential risks and side effects of being in this study?

You may feel slight tired during the measurement of handgrip strength at the arm, which will resolve spontaneously after the measurement is completed. During admission to ward, branula will be set as routine care & which will cause discomfort.

Others potential risk and side effects of being in this study (group B) is intolerance towards whey protein plus carbohydrate drink provided such as nausea, diarrhea or vomiting. If such intolerance occurs by the subjects, these steps will be taken into measure:

- To substitute with carbohydrate drink only and to ask subjects to withdraw from the study
- To stop the prescription of whey protein plus carbohydrate drink and to ask subjects to withdraw from the study
- Referral to doctor if necessary

8. What are the benefits of being in this study?

There may or may not be any benefits to you. This study does provide a better understanding of the disease/condition studied. It may provide benefit for surgical gynecologic oncology patients in the future in terms of development of new dietary intervention protocol in cancer patient ongoing for surgery treatment.

9. What if I am injured during this study?

If you are injured as a result of being in this study, you should contact your investigator. In the event of a bodily injury or illness directly resulting from the study product or a medical procedure required for this study which is very minimal, you will be referred to a medical doctor as soon as possible and the expenses involve will be paid by the sponsor. The sponsor is not responsible for medical expenses due to pre-existing medical conditions, any underlying disease, any ongoing treatment process, your negligence or willful misconduct, the negligence or willful misconduct of your investigator or the study site or any third parties. You do not lose any of your legal rights to seek compensation by signing this form.

10. What are my alternatives if I do not participate in this study?

You do not have to participate in this study to get treatment for your disease or condition. Alternative treatments of routine care in dietary interventions post-surgery are available in Institut Kanser Negara and most of government hospitals. You always can get diet intervention post-surgery and usage of high protein nourishing fluid will be depending on

your daily energy and protein requirement to support post-surgery wound healing and optimize nutritional status.

11. Who is funding this research?

This study is funded by Institut Kanser Negara (sponsor).

12. Can the research or my participation be terminated early?

The research officer may due to concerns for your safety, stop the study or participation at any time. If the study is stopped early for any reason you will be informed and arrangements made for your future care. You may be asked to attend a final follow up visit.

13. Will my medical information be kept private?

All your information obtained in this study will be kept and handled in a confidential manner, in accordance with applicable laws and/or regulations. Principal investigator and co-investigator in this study only are allowed to assess to medical records and data. The identification number instead of patient identifiers will be used on subject data sheets. All data will be entered into a computer that is password protected. When publishing or presenting the results, your identity will not be revealed without your expressed consent. Individuals involved in this study and in your medical care, and governmental or regulatory authorities may inspect and copy your medical records, where appropriate and necessary.

With your permission, your family will be informed that ypur participation in this study. You will not be informed of study findings. You will be informed if new information becomes available relevant to consent. All data of study might be sent to overseas for analysis but your identity will not be exposed all the time.

14. Who should I call if I have questions?

If you have any questions about the study or you think you have a study related injury or you want information about treatment, please contact the researcher as below:

Ho Chiou Yi
Dietitian U 41
Dietetic and Food Service Department
National Cancer Institute
03-88923406
dtho@nci.gov.my

If you have any questions about your rights as a participant in this study, please contact: The Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032.

INFORMED CONSENT FORM

Title of Study: FAST TRACK RECOVERY WITH A WHEY PROTEIN INFUSED CARBOHYDRATE LOADING DRINK AMONG SURGICAL GYNECOLOGIC ONCOLOGY PATIENTS: A PRAGMATIC OPENED LABELED TRIAL

By signing below I confirm the following:

- I have been given oral and written information for the above study and have read and understood the information given.
- I have had sufficient time to consider participation in the study and have had the opportunity to ask questions and all my questions have been answered satisfactorily.
- I understand that my participation is voluntary and I can at anytime free to withdraw from the study without giving a reason and this will in no way affect my future treatment. I understand the risks and benefits, and I freely give my informed consent to participate under the conditions stated. I understand that I must follow the study doctor's instructions related to my participation in the study.
- I understand that study staff and government or regulatory authorities have direct access to my medical record in order to make sure that the study is conducted correctly and the data are recorded correctly and the data are recorded correctly. All personal details will be treated as STRICTLY CONFIDENTIAL.
- I will receive a copy of this subject information/ informed consent form signed and dated to bring home.

Subject:

Signature: I/C number:

Name: Date:

Investigator conducting informed consent:

Signature: I/C number:

Name: Date:

Impartial witness:

Signature: I/C number:

Name: Date: