OREGON HEALTH & SCIENCE UNIVERSITY
SCHOOL OF MEDICINE – GRADUATE STUDIES

RETROSPECTIVE CHART REVIEW OF THE IMPACT OF PREOPERATIVE CARBOHYDRATE LOADING ON LENGTH OF STAY AND POSTOPERATIVE RECOVERY IN LIVING KIDNEY DONORS UNDERGOING LAPAROSCOPIC NEPHRECTOMY

By

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Abstract

Little research has been conducted to determine the impact of preoperative carbohydrate loading on length of hospital stay (LOS) and postoperative recovery in living kidney donors undergoing laparoscopic nephrectomy. To answer this question, we performed a retrospective chart review of electronic medical record data from subjects who previously underwent laparoscopic living donor nephrectomy at Oregon Health & Science University (OHSU). Our study population included 55 adult subjects who received preoperative carbohydrate loading and 93 adult historical control subjects who did not receive preoperative carbohydrate loading. Clinical outcomes, including LOS, length of time required to return to regular oral food and fluid intake, and incidence of postoperative gastrointestinal complications were assessed and compared between the two groups.

Preoperative carbohydrate loading significantly reduced LOS, length of time to tolerating a regular oral diet, and length of time to meeting 50% of estimated oral fluid needs after laparoscopic nephrectomy. There was no significant difference between groups in the incidence of postoperative nausea, vomiting, or ileus. Our results demonstrated the clinical benefit of preoperative carbohydrate loading in living kidney donors undergoing laparoscopic nephrectomy and support continuation of this intervention in future laparoscopic living donor nephrectomies.

Chapter 1: Specific Aims

Among living kidney donors undergoing nephrectomy, about 16.8% experience perioperative complications.[1] Gastrointestinal, bleeding, and respiratory complications as well as surgical/anesthesia-related injuries are some of the most frequent complications that occur.[1] Of the various postoperative complications, ileus is the most common.[2] The occurrence of perioperative complications contributes to an increased length of hospital stay (LOS) in living kidney donors.

Enhanced Recovery After Surgery (ERAS) programs are implemented in a number of surgical programs and are designed to promote early postoperative recovery and mitigate the stress response after surgery. ERAS protocols often involve preoperative carbohydrate loading and early allowance of oral intake postoperatively. Little research has been conducted to examine the impact of preoperative carbohydrate loading on LOS, length of time required to return to regular oral food and fluid intake, and postoperative gastrointestinal complications in living kidney donors. The utility of perioperative nutrition protocols in nephrectomy procedures is not well-established.

Kidney transplantation is the gold standard of treatment for end stage renal disease and kidneys account for a large proportion (83.1%) of the organs that individuals are currently on a waiting list to receive.[3] Living donor transplantation yields significantly better outcomes for transplant recipients when compared to deceased organ transplantation and is an important option that can substantially increase organ availability.[4] Establishing perioperative strategies to minimize or eliminate complications among living donors is a critical step in optimizing outcomes. These improvements will serve to increase the prospect and feasibility of living donation.

The main objective of this investigation is to explore the impact of preoperative carbohydrate loading on LOS, length of time required to resume a regular diet postoperatively, length of time required to meet 50% of estimated oral fluid needs postoperatively, and the incidence of gastrointestinal complications after laparoscopic nephrectomy in living kidney donors at Oregon Health & Science University (OHSU). Specifically, the investigation's overall goal is to determine whether living kidney donors who received preoperative carbohydrate loading experienced a difference in LOS, length of time required to resume a regular diet postoperatively, length of time required to meet 50% of estimated oral fluid needs postoperatively, and incidence of gastrointestinal complications after laparoscopic nephrectomy compared to historical controls who did not receive preoperative carbohydrate loading. This investigation will narrow the existing gap in the research on the efficacy of preoperative carbohydrate loading in facilitating faster recovery following laparoscopic living donor nephrectomy procedures. The results of this investigation will provide key information to guide perioperative nutrition interventions among living kidney donors.

The results will also contribute to the development of standardized nutrition protocols to improve outcomes in a variety of facilities. If results indicate that preoperative carbohydrate loading reduces LOS, length of time required to resume a regular diet postoperatively, length of time required to meet 50% of estimated oral fluid needs postoperatively, and/or incidence of postoperative gastrointestinal complications, implementation of such protocols will improve outcomes for living donors. This may make the nephrectomy procedure more acceptable and feasible for prospective donors. We hypothesize that living kidney donors who received preoperative carbohydrate

loading experienced a reduced LOS, reduced length of time to resume a regular diet postoperatively, reduced length of time to meet 50% of estimated oral fluid needs postoperatively, and fewer postoperative gastrointestinal complications compared to historical controls who did not receive preoperative carbohydrate loading.

This project is a retrospective chart review of data from patients, hereinafter referred to as subjects, who previously underwent a laparoscopic nephrectomy procedure in the Living Kidney Donor Transplant Program at OHSU in Portland, Oregon. Data in Epic electronic medical record (EMR) software will be reviewed to collect data on perioperative nutrition interventions, LOS, diet tolerance and fluid intake, and postoperative gastrointestinal complications.

The specific aims of this project are:

Specific Aim 1: To determine the impact of preoperative carbohydrate loading on LOS and incidence of postoperative gastrointestinal complications following a laparoscopic nephrectomy procedure in living kidney donors at OHSU.

Hypothesis 1: Subjects who received preoperative carbohydrate loading experienced a reduced LOS compared to historical control subjects who did not receive preoperative carbohydrate loading.

Hypothesis 2: Subjects who received preoperative carbohydrate loading experienced fewer gastrointestinal complications after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading.

Specific Aim 2: To determine the effect of preoperative carbohydrate loading on the length of time required to return to a regular oral diet and the length of time required to

meet 50% of estimated oral fluid needs following a laparoscopic nephrectomy procedure in living kidney donors at OHSU.

Hypothesis 1: Subjects who received preoperative carbohydrate loading required less time to return to a regular oral diet compared to historical control subjects who did not receive preoperative carbohydrate loading.

Hypothesis 2: Subjects who received preoperative carbohydrate loading required less time to meet 50% of estimated oral fluid needs after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading.

To our knowledge, this is one of very few investigations exploring the impact of preoperative carbohydrate loading on LOS, length of time required to return to regular oral food and fluid intake postoperatively, and incidence of postoperative gastrointestinal complications in living kidney donors. We expect results to demonstrate that preoperative carbohydrate loading reduces the following parameters: LOS, length of time required to resume a regular diet postoperatively, length of time required to meet 50% of estimated oral fluid needs postoperatively, and incidence of gastrointestinal complications after laparoscopic nephrectomy. Results will determine if an ERAS nutrition protocol is beneficial for living kidney donors and will provide a foundation for modification, refinement, and improvement of the existing protocol.

Chapter 2: Background

Introduction

According to the United Network for Organ Sharing, 7,397 living donor organ transplants were performed in the United States in 2019, a number that surpassed the previous all-time record of 6,992 in 2004.[5] Of the total living donor organ transplants performed in 2019, 6,867 were kidney transplants.[5] Living donor nephrectomy is a major abdominal procedure involving the removal of one kidney from a living organ donor for transplantation in a matched recipient. Prior to donation, potential donors undergo extensive health, compatibility, and psychosocial screening and assessment to determine suitability as a donor.[6]

Laparoscopic or hand-assisted laparoscopy are the recommended surgical approaches for living donor nephrectomy, although open nephrectomy may be performed in some clinical situations.[6] Research has demonstrated that, compared to an open nephrectomy, laparoscopic nephrectomy results in reduced recovery time and physical fatigue, decreased bodily pain, and improved physical function in donors postoperatively.[7,8] The typical length of hospital day (LOS) following nephrectomy ranges from four to six days, however, LOS is dependent on several factors, including minor and major complications.[9]

Types of Kidney Donation

Kidneys may be transplanted from either a deceased organ donor or from a living organ donor. While both deceased and living donor transplantation are viable options for individuals requiring kidney transplantation, living donor transplantation offers better outcomes for recipients as compared to deceased donor transplantation.[10,11] Within the

subgroup of living donation, there are three different donation categories: directed donation, non-directed donation, and paired exchange.[12] In a directed donation, which often takes place between friends and family members, the donor selects the individual to receive the organ. In a non-directed donation, the donated organ is provided to any individual in need and the donor does not identify a specific recipient. Such donors are also known as “good Samaritan”, “anonymous”, or “altruistic” donors. A paired exchange can be implemented when an individual is willing to donate an organ in a directed donation, but is not a match for the intended recipient. In a paired exchange, two incompatible donor-recipient pairs may enter an exchange if the donor in the first pair is a match for the recipient in the second pair, and the donor in the second pair is a match for the recipient in the first pair.[12]

Pre- and Post-Donation Evaluation and Assessment

Evaluation of a living kidney donor candidate is a multi-step process to ensure the appropriateness of the candidate and reduce risk. Prior to donation, potential donors are screened for ABO blood type and human leukocyte antigen (HLA) compatibility, abnormalities in glomerular filtration rate (GFR), albuminuria, microscopic hematuria, history of nephrolithiasis, and history of gout.[6,13] Potential donors are also screened for risk factors for chronic kidney disease (CKD) and cardiovascular disease (CVD).[6,13] Evaluation of CKD and CVD risk factors includes assessments of body mass index (BMI), screening for history of diabetes (including gestational diabetes and family history of diabetes), fasting blood glucose, glycated hemoglobin (HbA1c), fasting lipid profile, and current or prior tobacco use.[6,13,14]

Infection screening also takes place prior to donation and includes screening for human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, cytomegalovirus, Epstein-Barr virus, *Treponema pallidum* (syphilis), urinary tract infection, and other possible infections according to environmental factors and geographical location.[6,13] Further pre-donation assessments include cancer screening, screening for a family history of kidney disease, pregnancy screening, psychosocial evaluation, and participation in education and planning sessions.[6,13] Post-donation follow-up is also essential for living kidney donors. Annual measurements of blood pressure, BMI, serum creatinine and GFR estimation, albuminuria, review of healthy lifestyle behaviors, and review of psychosocial health and well-being are recommended.[6,13]

Complications Associated with Living Donor Nephrectomy

While the incidence of postoperative death following living kidney donation is minimal and 90-day all-cause mortality in living donors is low at 0.03%, the procedure does present the risk of perioperative complications.[6] In a 2016 retrospective study by Lentine et al, data on living kidney donations in the United States between 2008 and 2012 from the Organ Procurement and Transplantation Network (OPTN) registry and hospital administrative records was gathered to assess perioperative complications in living donor nephrectomies. Findings demonstrated that perioperative complications occurred in 16.8% of donors.[15] Of those complications, gastrointestinal complications were the most common, followed by bleeding, respiratory, and surgical/anesthesia-related injuries.[15] Authors also noted that patients who underwent a planned open nephrectomy were 31% more likely to experience any type of perioperative complication

when compared to patients undergoing a laparoscopic nephrectomy, and that experiencing a severe complication was twice as likely among patients who underwent a robotic nephrectomy.[15]

Of the various postoperative gastrointestinal complications following abdominal surgery, ileus is very common.[16] Postoperative ileus is defined as "…transient cessation of coordinated bowel motility after surgical intervention, which prevents effective transit of intestinal contents or tolerance of oral intake."[17] Symptoms include abdominal tenderness and a delay in passing flatus and stool following surgery.[18] Ileus may occur in any section of the gastrointestinal tract (stomach, small intestine, and/or large intestine) and is attributable to a wide range of factors, including the inflammatory response to surgery, opioid administration, autonomic disturbances, hormonal changes, and electrolyte abnormalities.[19] According to a 2019 multicenter cohort study by Garcia-Ochoa et al evaluating perioperative complications in 1,042 living kidney donors across 17 centers, ileus accounted for 34% of minor postoperative complications.[9] Because postoperative ileus prolongs LOS, preventing and reducing the duration of ileus has become a key area of interest among health professionals and researchers.[16]

An additional concern among surgical patients is postoperative nausea and vomiting (PONV). General incidence of postoperative nausea is roughly 50%, while incidence of postoperative vomiting is roughly 30%.[20] While not usually a serious medical complication, PONV is unpleasant and patients report that nausea and vomiting in the postoperative period are among the most severe and undesirable side effects experienced.[21,22] Along with the discomfort experienced by the patient, PONV prolongs LOS and increases costs for the hospital and healthcare system.[21] The central causes

of PONV are utilization of inhaled anesthetics and opioid medications.[21] Key risk factors for PONV have been identified and include female sex, non-smoker status, history of PONV or motion sickness, and younger age.[21,22] In addition, a longer duration of surgery and the specific type of surgery (including cholecystectomy, laparoscopic, and gynecological surgeries) are risk factors for PONV.[21] Identifying and implementing perioperative strategies to prevent and mitigate postoperative ileus and PONV in living kidney donors to reduce LOS, improve the patient experience, and optimize outcomes is warranted.

Physiological Response to Surgical Stress

Individuals undergoing major surgery experience surgical stress. The stress response brought about by major surgery or injury is characterized by increases in cortisol, glucagon, catecholamines, and inflammatory cytokines.[23] The stress response consists of two separate phases: the ebb phase and the flow phase. The ebb phase, which occurs first, involves decreases in cardiac output, oxygen consumption, basal metabolic rate, and glucose tolerance and may last for two to three days.[23] After the ebb phase, individuals experience the flow phase, characterized by elevations in cardiac output, respiratory rate, and oxygen consumption as well as hyperglycemia, skeletal muscle catabolism, and negative nitrogen balance.[23] The flow phase may occur over a period of days to weeks and the duration is determined by the degree of surgical stress or intensity of the injury experienced.[23] Following surgery, the metabolic rate is markedly increased. Hypermetabolism may give rise to clinical complications and prolong the recovery period following surgery by interfering with growth, healing, and preservation of homeostasis.[23]

Due to concerns regarding pulmonary aspiration, the typical preoperative nutrition protocol for elective surgery requires that patients fast starting at around midnight the night prior to the scheduled procedure.[24,25] The rationale for this is that the risk for aspiration of gastric contents and vomiting are lower following an overnight fast which induces total gastric emptying.[24] A preoperative fast of six to eight hours is generally prescribed to patients, but the fasting period is sometimes extended beyond this range as a result of schedule changes and delays in the surgical facility or medical center.[24] Longer fasting times may exacerbate the surgical stress response by raising insulin resistance, promoting reductions in lean body mass, and amplifying the acute-phase response.[24,26] Evidence suggests that a two-hour fast following clear liquids and a six-hour fast following solid foods provide sufficient time for adequate gastric emptying.[27-29]

A key metabolic change that occurs with surgical stress is an increase in insulin resistance.[24,30] Insulin resistance serves as a marker of metabolic stress, increases in proportion to the degree of physiological trauma, and is most notable on the first postoperative day.[24,31,32] Importantly, hyperglycemia in the postoperative period is associated with a higher risk of complications and higher mortality rate.[24] These risks underscore the critical role of controlling serum glucose after surgical procedures.[24] While a range of factors contribute to insulin resistance in patients undergoing elective surgery, one important factor is preoperative fasting.[24] Among healthy individuals, the normal response to a short-term fast (up to 48 hours) involves upregulation of glycogenolysis, gluconeogenesis, and fatty acid oxidation with a decline in insulin sensitivity.[24] When nutrients are consumed, healthy individuals respond with

downregulation of endogenous glucose synthesis and secretion of insulin which promotes glucose uptake.[24] Under conditions of insulin resistance, there is a reduction in glucose uptake and glycogenesis, and muscle and liver glycogen stores are diminished.[24] These changes ultimately place the patient in a more catabolic state and magnify the physiological response to surgical stress.[33]

Enhanced Recovery After Surgery Programs

Enhanced Recovery After Surgery (ERAS) programs involve a multidisciplinary team and employ multicomponent protocols aimed at increasing the quality and speed of recovery in surgical patients.[34] ERAS programs have become widely implemented and are effective in various types of surgical procedures, although ERAS was first introduced in colorectal surgeries.[34] Currently, ERAS is implemented in a range of abdominal procedures, including but not limited to, gastrectomy, laparoscopic cholecystectomy, laparoscopic ileocecal resection, nephrectomy, colorectal surgery, and gastrojejunostomy.[35-43] While ERAS programs vary between facilities and the type of procedure performed, the primary goals of ERAS are to minimize surgical stress and ameliorate the patient's stress response.[34] Primary outcomes of interest in ERAS research include LOS, perioperative complications, postoperative recovery, and readmission rates.

The various components of typical ERAS protocols are divided into four major phases: preadmission, preoperative, intraoperative, and postoperative.[34] In the preadmission period, the emphasis is on nutrition education and support, guidance and education on smoking cessation and control of alcohol intake, medical optimization, and the provision of preoperative information.[34] In the preoperative period, protocols often

involve intake of preoperative carbohydrates and preoperative prophylaxis against PONV. Patients are generally allowed to consume clear liquids, including the prescribed carbohydrate-containing beverage, up to two hours before surgery.[34] In the intraoperative phase, components include reducing invasive surgical techniques, limiting the use of drains and tubes, using regional anesthesia and opioid-sparing anesthesia, providing balanced fluids, and temperature control.[34] Finally, the postoperative phase involves early removal of drains and tubes, termination of intravenous fluids, opioid-sparing pain management, early mobilization, early oral intake of solids and liquids, and follow-up after discharge.[34]

Preoperative Carbohydrate Loading in ERAS

Within the range of ERAS protocols used in different surgical programs, various forms and quantities of oral carbohydrates are given prior to surgery (see Appendix A for a list of common preoperative carbohydrate loading products used in ERAS programs). In order to produce the desired anabolic effect and reduce insulin resistance, recommendations are for fluids providing about 12% carbohydrates mostly as maltodextrin two to three hours pre-surgery.[25,44] This form and quantity of carbohydrates reduces osmolality and prevents slowed gastric emptying, allowing for safe use prior to surgery.[44,45] The anabolic response activates postprandial glycemia, lowers glycogen degradation, and enhances glucose uptake in muscle cells which minimizes hyperglycemia.[46] Alternative options, such as standard clear liquids, juice, or sports drinks, are thought to be inferior as these fluids do not yield the desired anabolic response and are generally lower in carbohydrates (6-7% carbohydrates).[44,47] However, a 2020 randomized controlled trial by Karimian et al evaluated differences in

perioperative insulin sensitivity, complications, and time to readiness for discharge in laparoscopic colorectal surgery patients after receiving either a preoperative beverage with complex carbohydrates or a preoperative beverage with simple carbohydrates. No significant differences between the two groups were identified in the outcomes of interest, suggesting that preoperative carbohydrate loading with simple carbohydrates may be appropriate and equally as effective as complex carbohydrates.[48]

The current recommendation for preoperative carbohydrate loading products in the United States is ClearFast (CF) PreOp (ClearFast, Atlanta, GA), which provides a total of 50 grams of carbohydrates (including 44 grams of maltodextrin) as a 12% carbohydrate solution with an osmolality of 270 mOsm/kg (milliosmoles per kilogram).[49] CF PreOp also contains zinc sulfate, vitamin A, citric acid, and L-citrulline, and provides no fat or protein.[49] The total volume of the supplement is 355 milliliters (mL). Products such as Nutricia PreOp, ONS 300, ONS 400, Preload, Arginaid H_2O, and Maxijul are also utilized.[44] In some ERAS programs and studies, juice or sports drinks such as Gatorade may be used for preoperative carbohydrate loading.[42,43]

Literature Review

A small number of studies have investigated the role of preoperative carbohydrate loading and ERAS protocols in living kidney donors undergoing nephrectomy. Studies exploring the role of preoperative carbohydrate loading in abdominal procedures other than nephrectomy warrant consideration. In 2014, Smith et al published a review of 27 studies involving outcomes of 1,976 patients undergoing elective surgery and identified that the use of preoperative carbohydrate supplements resulted in shorter hospital stay.[50] However, the quality of the evidence in the review

ranged from very low to high, and there was little evidence to support the impact of preoperative carbohydrate supplements on complication rate.[50] The following sections describe the current research on ERAS and carbohydrate loading in living donor nephrectomies and other abdominal procedures. Procedures other than nephrectomy share some clinical characteristics with nephrectomy, including typical LOS, recovery period, and the anatomical areas of the body affected. The findings from such research provide further insight into the effectiveness of preoperative carbohydrate loading and ERAS protocols in elective abdominal procedures.

ERAS in Nephrectomies

In a 2015 single-center retrospective analysis by Waits et al, outcomes of 60 living donor laparoscopic nephrectomies who participated in an enhanced recovery protocol (ERP) were compared to outcomes of 60 standard of care living donor laparoscopic nephrectomies. Patients in the ERP group received 10 ounces of apple juice (36 grams of carbohydrate) two hours prior to surgery. Results demonstrated significant reductions in median LOS (from two days to one day) and narcotic use in the ERP group. No significant differences in pain scores on the first postoperative day or readmission rate between the two groups were identified.[43]

In a single-center, non-randomized, retrospective analysis by Rege et al published in 2016, outcomes of 39 patients who received CF PreOp (50 grams of carbohydrate, 12.0% carbohydrate solution) two hours before laparoscopic nephrectomy as part of an ERAS protocol were compared to 40 patients who underwent laparoscopic nephrectomy and received the standard care protocol. The patients who received the standard care protocol fasted for eight hours prior to surgery. In addition to

CF PreOp, patients in the ERAS group were allowed to consume clear liquids until two hours before surgery. A significant reduction in median LOS (from two days to one day) and significantly lower pain scores were identified in the ERAS group. Although readmission rates were lower in the ERAS group, this finding was not significant.[41]

A retrospective analysis conducted by Ricotta et al in 2019 compared outcomes of 21 adult donor laparoscopic nephrectomies in an ERAS program to outcomes of 55 adult donor laparoscopic nephrectomies prior to implementation of the ERAS program. Patients in the ERAS group consumed a regular oral diet the day prior to surgery and 500 mL of Gatorade (30 grams of carbohydrate) two to three hours pre-surgery. Significant differences were not found in LOS, readmissions, or hospital complications between the two groups. However, the subgroup of older adult donors (61-72 years of age) in the ERAS group experienced a significantly shorter LOS compared to older adult donors in the non-ERAS group.[42]

In a 2020 study by Brown et al, outcomes of 24 adult patients who underwent laparoscopic nephrectomy with a standard care protocol were compared to 57 adult patients who underwent laparoscopic nephrectomy with an ERAS protocol. The ERAS protocol included consumption of 800 mL of Nutricia PreOp (100.8 grams of carbohydrate, Nutricia Clinical Care, Trowbridge, UK) eight hours prior to surgery and 400 mL of Nutricia PreOp (50.4 grams of carbohydrate) two hours prior to surgery. After surgery, in the evening, patients resumed an unrestricted regular oral diet. Patients in the standard care protocol group fasted overnight prior to surgery. Researchers investigated differences in LOS, nausea scores, pain at rest, and pain with mobilization between the two groups and found no significant differences in any of the variables.

However, the ERAS protocol group received significantly less opiate medication than those in the standard care protocol group.[40]

ERAS in Cholecystectomy and Liver Resection

In a 2015 randomized controlled trial by Singh et al, researchers assigned 40 patients undergoing laparoscopic cholecystectomy to preoperative carbohydrate loading (group A), 40 patients to a placebo of flavored water (group B), and 40 patients to fasting beginning at midnight the night before surgery (group C). Group A consumed 400 mL of a 12.5% carbohydrate beverage between 8:00 PM and 10:00 PM the night before surgery plus 200 mL of the same beverage two hours before surgery. Primary outcomes were nausea, vomiting, and pain. The incidence of nausea in group A was significantly lower 0-4 hours after surgery compared to group B and group C, however, incidence of nausea 4-12 and 12-24 hours after surgery was not significantly different between group A and B or group A and C. When group A was compared to group B, there was a significant decrease in the incidence of vomiting in group A 0-4 hours after surgery, but no significant difference in the incidence of vomiting 4-12 or 12-24 hours after surgery between groups A and B. When comparing groups A and C, the incidence of vomiting was significantly lower in group A 0-4 and 4-12 hours after surgery, but was not significantly different between these two groups 12-24 hours after surgery. Mean score of pain in group A was significantly lower than in groups B and C at 0-4 and 4-12 hours postsurgery.[39]

In a 2005 randomized clinical trial by Hausel et al, 172 adult patients undergoing laparoscopic cholecystectomy were assigned to one of three groups: preoperative carbohydrate loading (800 mL Nutricia PreOp the evening before surgery and 400 mL

Nutricia PreOp two hours before surgery), placebo (flavored water consumed at the same time points and in equivalent volumes as the carbohydrate loading group), or fasting from midnight. Primary outcomes were PONV and pain. Across the three groups, there were no significant differences in PONV during the first 12 hours after surgery, however, during the 12-24 hours after surgery, the incidence of PONV was significantly higher in the fasting group as compared to the placebo group. No significant difference in the incidence of PONV between the carbohydrate loading group and the placebo group or between the fasting and placebo group was noted in the first 12-24 hours after surgery. Nausea scores determined by visual analogue scales (VAS) in the fasting and placebo groups were significantly higher after surgery as compared to preadmission scores, whereas there was no significant difference between preadmission and postoperative nausea scores in the carbohydrate loading group.[51]

A 2019 randomized controlled trial by Helminen et al yielded less significant results than the aforementioned study by Singh et al. Patients undergoing day-case cholecystectomy were randomized to receive either 200 mL of ProvideXtra (Fresenius Kabi, Bad Homburg, Germany) which contains 67 grams of carbohydrate and eight grams of protein two hours prior to surgery or to fast beginning at midnight the evening prior to surgery.[52] The group randomized to receive ProvideXtra was also permitted to consume food two hours after surgery. Researchers utilized VAS scores to assess thirst, hunger, mouth dryness, tiredness, pain, and nausea. Researchers also evaluated the need for postoperative analgesia and antiemetics, time to drinking, eating, first mobilization, and time to discharge. No significant differences were identified between the groups for any of the variables assessed.[37] Similar findings were reported by

Bisgaard et al (2004) in a randomized controlled trial of 86 patients undergoing laparoscopic cholecystectomy. No significant differences in general well-being, appetite, fatigue, pain, nausea, vomiting, sleep quality, or analgesic and antiemetic requirement were identified between the group of patients who received preoperative carbohydrate loading and the placebo group.[53]

In 2018, Lee et al published a randomized, double-blind, placebo-controlled trial of 141 adult patients undergoing laparoscopic cholecystectomy. Patients were randomized to one of three groups: midnight NPO (MN-NPO), no-NPO, or placebo. The MN-NPO group had all oral intake restricted after midnight the night before surgery. The no-NPO group consumed 800 mL of a clear carbohydrate beverage providing 12.8% carbohydrates and 50 calories per 100 mL with an osmolality of 290 mOsm/kg. A total of 400 mL was consumed between 8:00 PM and 10:00 PM the night before surgery and the remaining 400 mL was consumed two hours before surgery. The placebo group received flavored water in equal volumes and at the same time points as the no-NPO group. Researchers assessed preoperative and postoperative patient responses to the Quality of Recovery (QoR-40) questionnaire, which assesses emotional state, physical comfort, psychological support, physical independence, and pain. Among the three groups, no significant differences in QoR-40 scores were identified, suggesting a limited benefit to preoperative carbohydrate loading in postoperative recovery after laparoscopic cholecystectomy.[38] In contrast, Sada et al (2014), using a different assessment tool (VAS scores), identified that in patients undergoing open cholecystectomy, preoperative carbohydrate loading significantly improved thirst,

hunger, mouth dryness, nausea, and weakness when compared to placebo and preoperative fasting groups.[54]

A 2013 study by Jones et al evaluated preoperative carbohydrate loading in patients undergoing open liver resection. Researchers assessed outcomes in two groups. The first group received 125 mL of Nutricia Fortisip Compact (37.1 grams of carbohydrate per 125 mL) three times per day for the three days leading up to surgery, 800 mL of Nutricia PreOp the evening prior to surgery, and 400 mL of Nutricia PreOp at 6:00 AM the morning of surgery. The second group of patients underwent standard preoperative fasting. Compared to the fasting group, significant reductions in time to being medically fit for discharge, LOS, and rate of medical-related complications were observed in patients who received preoperative carbohydrate loading. Overall complication and morbidity rates were lower in the preoperative carbohydrate loading group, but these findings were not significant. The preoperative carbohydrate loading group resumed an oral diet significantly earlier and consumed significantly more fluids within the initial 24 hours after surgery. Additionally, the preoperative carbohydrate loading group had a significantly faster return of bowel sounds, earlier passage of flatus, and earlier opening of the bowels than the fasting group.[55]

ERAS in Colorectal Surgery

Colorectal surgeries are a key area in which the benefit of preoperative carbohydrate loading has been explored. In a 2014 study by Webster et al, patients undergoing elective colorectal surgery were randomized to a preoperative carbohydrate group or standard care group. In the preoperative carbohydrate group, patients consumed 800 mL of an oral carbohydrate solution (50 kcal/100 mL, 290 mOsm/kg)

between 7:00 PM and midnight the evening before surgery. After midnight, patients were not permitted to consume solid foods, but were permitted to consume clear liquids. At 5:00 AM the morning of surgery, patients consumed 200 mL of the same oral carbohydrate solution. Patients in the standard care group were not permitted to consume solid foods after midnight the night before surgery, but were allowed to consume clear liquids ad libitum until 5:00 AM the morning of surgery. Between the two groups, researchers identified no significant difference in mean time to readiness for discharge (4.1 days in the preoperative carbohydrate group versus 4.4 days in the standard care group), mean time to first flatus (34.5 hours versus 50.1 hours), or mean time to first bowel movement (46.2 hours versus 68.8 hours).[56]

A 2010 randomized controlled trial by Mathur et al assessed differences in LOS and time to intake of an oral diet between two groups of patients undergoing major elective colorectal surgery or hepatic resection. Patients in the preoperative carbohydrate loading group received 800 mL of Nutricia PreOp the night before surgery followed by 400 mL of Nutricia PreOp two hours pre-surgery. Patients in the placebo group received flavored water with artificial sweetener. Between the two groups, researchers did not identify a significant difference in LOS or time to intake of an oral diet.[57] A similar study by Hausel et al (2001) demonstrated a significant trend toward decreased preoperative discomfort in a sample of 252 patients undergoing either laparoscopic cholecystectomy or major colorectal surgery who received preoperative carbohydrate loading as compared to placebo and preoperative fasting.[58]

A 2006 study by Noblett et al exploring the role of preoperative carbohydrate loading in colonic resection procedures randomized patients to one of three groups and

assessed LOS, gastrointestinal function, and grip strength (measured using a dynamometer). The first group received 800 mL of water the night before surgery and 400 mL of water three hours before surgery. The second group received 100 grams of Vitaflo Preload (Vitaflo Limited, Liverpool, UK) (96 grams of carbohydrate) dissolved in 800 mL of water the night before surgery and 50 grams of Vitaflo Vitajoule (47.5 grams of carbohydrate) dissolved in 400 mL of water three hours before surgery. The third group fasted starting at midnight the night prior to surgery. Findings demonstrated a significant reduction in median time to fitness for discharge in the preoperative carbohydrate group compared to the group that received water. Though not significant, the preoperative carbohydrate group showed a trend toward shorter time to fitness for discharge as compared to the fasting group. Among the three groups, there was no significant difference in time to passage of first flatus, however, the preoperative carbohydrate group showed a trend toward earlier passage of first flatus as well as a trend toward earlier time to first bowel movement. Compared to preoperative grip strength values, patients in the fasting group were noted to have significant reductions in grip strength when reassessed at the time of discharge. Reductions in grip strength were not significant in the preoperative carbohydrate and preoperative water groups.[59]

A recent 2019 randomized controlled trial by Rizvanović et al compared clinical outcomes among patients who received preoperative carbohydrate loading or fasting prior to open colorectal surgery in 50 patients. Patients randomized to the intervention group (n=25) consumed 400 mL of a clear carbohydrate drink (12.5 g carbohydrate per 100 mL and 50 calories per 100 mL) at 10:00 PM the evening before surgery plus 200 mL of the same beverage two hours before surgery. The group randomized to fasting

underwent fasting for eight hours prior to surgery. Outcomes of interest included postoperative discharge day, time to return of intestinal sounds, time to first flatus, time to first defecation, time to oral intake, incidence of nausea and vomiting, and VAS pain scores. In the carbohydrate loading group, significant reductions in the incidence of nausea, time to first flatus, time to first defecation, and time to oral intake were observed. Additionally, the postoperative discharge day and return of intestinal sounds occurred significantly earlier in the carbohydrate loading group. For VAS pain scores and incidence of vomiting, there was no significant difference between the two groups of patients.[60]

Conclusion

Given the recent increase in the frequency of living donor nephrectomy procedures, perioperative protocols aimed at optimizing patient outcomes are essential. Such protocols may enhance the donor's experience and help to promote living donor nephrectomy as a feasible option for potential donors. An additional benefit is hospital cost reduction as a result of decreasing LOS and perioperative complications.

The current literature on the impact of preoperative carbohydrate loading in nephrectomy procedures as well as other major abdominal surgeries is limited and shows mixed results. Preoperative carbohydrate loading appears to be a safe nutrition intervention among patients undergoing abdominal surgery, but the benefit of preoperative carbohydrate loading is not consistent throughout the literature. While many studies have demonstrated significant findings that suggest a strong benefit to preoperative carbohydrate loading, other studies have found more neutral results. Additionally, there is great variation in the type, quantity, and timing of preoperative

carbohydrate intake across studies. Thus, further research is needed to identify and firmly establish the advantages of preoperative carbohydrate loading and determine the ideal preoperative protocol (including the form, quantity, and intake timing of carbohydrates) for standardization. Our study seeks to contribute to this growing body of evidence by examining outcomes of a preoperative carbohydrate loading protocol in one living kidney donor surgical program. With a sufficient number of high-quality studies, developing evidence-based, standardized protocols for preoperative carbohydrate loading in living kidney donors is possible and will guide future decisions that will improve patient outcomes.

Chapter 3: Methodology

General Design

This study was a retrospective chart review of subject data stored in electronic medical records (EMR). The medical charts of subjects who underwent laparoscopic living donor nephrectomy at the OHSU Living Kidney Donor Transplant Program between January 2012 and December 2018 were reviewed. Data collected was analyzed to address the specific aims of this study.

Preoperative Protocol

In May 2016, the OHSU Living Kidney Donor Transplant Program implemented a preoperative carbohydrate loading protocol as part of an ERAS program. Preoperative diet instructions and one or two 237-mL cartons of Ensure Clear oral nutrition supplement (Abbott Nutrition, Abbott Park, IL) were provided to subjects during an outpatient clinic visit prior to their scheduled procedure. Subjects were instructed to

consume a regular diet for the breakfast and lunch meals the day before surgery. Subjects were instructed to consume only clear liquids after the lunch meal. Depending on the surgeon performing the nephrectomy, some subjects were instructed to take 300 cc of magnesium citrate between 2:00 PM and 6:00 PM the day before surgery for bowel preparation. At midnight, subjects were instructed to consume nothing by mouth until two to four hours prior to their scheduled procedure. At that time, subjects were instructed to consume one carton (237 mL) of Ensure Clear combined with 160 mL of water for a total volume of about 400 mL. The diluted Ensure Clear was a 13.0% carbohydrate solution with an osmolality of 398 mOsm/kg and the product did not contain maltodextrin. Depending on the surgeon performing the nephrectomy, subjects may have received instructions to consume two 400-mL doses of diluted Ensure Clear. For these subjects, the first dose was consumed the evening before surgery (prior to midnight) and the second dose was consumed two to four hours before surgery.

Prior to the implementation of the ERAS protocol, subjects undergoing living donor nephrectomy at OHSU were instructed to consume only clear liquids the day before surgery. Subjects were instructed to consume nothing by mouth after midnight the night before surgery.

EMR data from subjects who underwent laparoscopic nephrectomy between May 2016 and December 2018 and received preoperative carbohydrate loading was collected and recorded. EMR data from subjects who underwent laparoscopic nephrectomy between January 2012 and April 2016 and did not receive preoperative carbohydrate loading (historical controls) was collected and recorded. Data from each of

the two groups was compared to determine the impact of preoperative carbohydrate loading on specific clinical outcome measures in living kidney donors.

Approval of the Study

This study was approved by the OHSU Institutional Review Board (IRB) (study #00022534). See Appendix B for the OHSU IRB approval letter. Because this study was a retrospective chart review, study team members received a waiver of consent and a waiver of HIPAA authorization from the OHSU IRB. All data handling and storage followed the approved IRB guidelines.

Subject Population and Description

Healthy adults 22 to 71 years of age who underwent a successful laparoscopic living donor nephrectomy at OHSU between January 2012 and December 2018 were included in this study. A total of 148 subjects met the inclusion criteria. The final analysis included 55 subjects who received preoperative carbohydrate loading and 93 historical control subjects who did not receive preoperative carbohydrate loading. All subjects met the living kidney donor patient selection criteria set forth by OHSU.

To determine living donor eligibility, subjects were screened for conditions that increase risk with living kidney donation and for absolute contraindications to living kidney donation. Conditions that increase risk are carefully considered in the selection process, but do not automatically make a potential donor ineligible. Absolute contraindications are conditions or factors that, if present, make a potential donor ineligible. Examples of conditions that increase risk include obesity, metabolic syndrome, history of mental illness, total colectomy, tobacco use, history of significant renal abnormalities, hepatitis B core antibody positive, hepatitis C positive, clotting

abnormalities, and other underlying medical conditions. Examples of absolute contraindications include blood type incompatibility, BMI above 32, age under 21 years, hypertension, kidney disease, moderate operative risk, significantly impaired glucose metabolism, previous intestinal bypass surgery, significant transmissible diseases, active or incompletely treated malignancy, and acute symptomatic infection. See Appendix C for the complete OHSU living kidney donor patient selection criteria.

Screening and Selection

Preliminary chart review for each subject was performed to screen and select subjects for inclusion (Figure 1). Subjects who underwent a laparoscopic nephrectomy at OHSU between May 2016 and December 2018 were considered for inclusion based on the criteria in Table 1a. Subjects who underwent a laparoscopic nephrectomy between January 2012 and April 2016 were considered for inclusion based on the criteria in Table 1b.

Subjects who underwent nephrectomy between May 2016 and December 2018 were screened to determine whether the nephrectomy procedure was performed laparoscopically or using an open approach. If the nephrectomy was performed laparoscopically, the subject's chart notes authored by registered dietitians during the admission for laparoscopic nephrectomy were examined for documentation of whether or not the subject had consumed Ensure Clear prior to surgery.

To assess potential historical controls for inclusion, chart review was performed for all subjects who underwent nephrectomy between January 2012 and April 2016 to determine whether the subject's nephrectomy was performed laparoscopically or using an open approach.

Figure 1: Screening and Selection Process

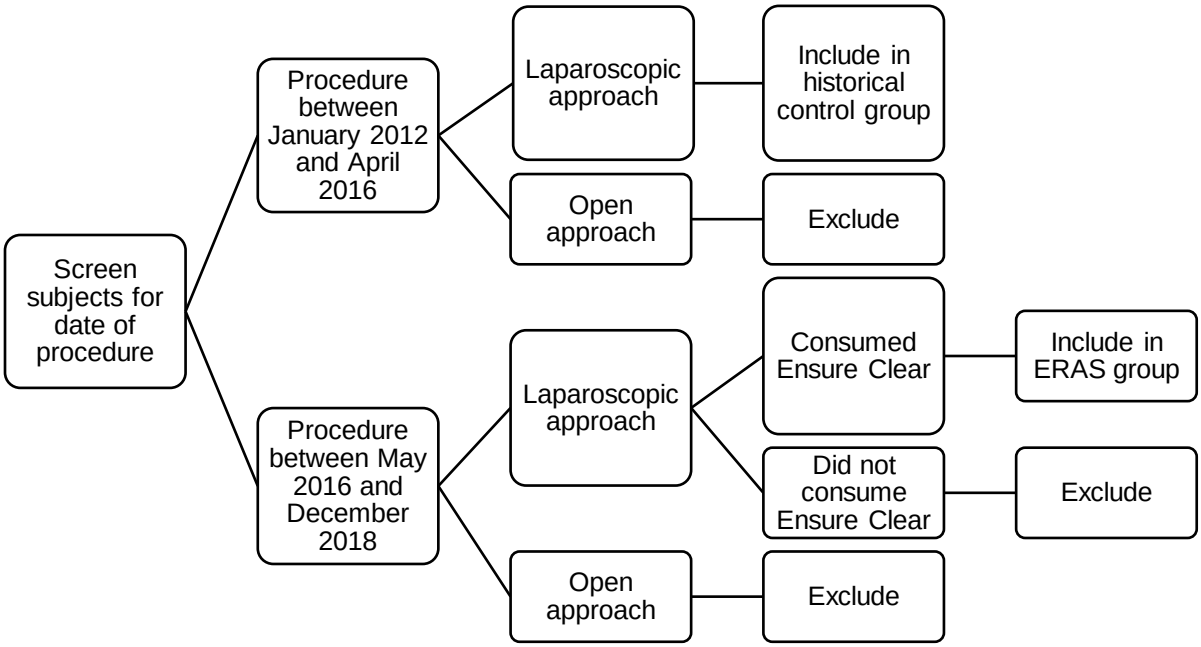

Table 1a. Inclusion and Exclusion Criteria for ERAS Subjects

Inclusion Criteria	Exclusion Criteria
1. 22 to 71 years of age 2. Nephrectomy performed at OHSU between May 2016 and December 2018 3. Subject consumed Ensure Clear before surgery 4. Nephrectomy performed laparoscopically	1. <22 or >71 years of age 2. Nephrectomy performed at OHSU before May 2016 or after December 2018 3. Subject did not consume Ensure Clear before surgery 4. Nephrectomy performed using an open approach

Table 1b. Inclusion and Exclusion Criteria for Historical Control Subjects

Inclusion Criteria	Exclusion Criteria
1. 22 to 71 years of age 2. Nephrectomy performed at OHSU between January 2012 and April 2016 3. Nephrectomy performed laparoscopically	1. <22 or >71 years of age 2. Nephrectomy performed at OHSU before January 2012 or after April 2016 3. Nephrectomy performed using an open approach

A total of 178 subjects were screened for inclusion. Between May 2016 and December 2018, 60 subjects underwent nephrectomy. Four of the subjects underwent an open nephrectomy and were excluded from the analysis. One subject did not consume Ensure Clear prior to surgery and was excluded from the analysis. A total of 55 subjects were included in the ERAS group for data collection and analysis. Between January 2012 and April 2016, 118 subjects underwent nephrectomy, 25 of which underwent open nephrectomy and were excluded from the analysis. The remaining 93 subjects underwent laparoscopic nephrectomy and were included in the historical control group for data collection and analysis.

For subjects who met the inclusion criteria described in Table 1a and Table 1b, the following data was collected and recorded from the EMR (see Appendix D for data collection form):

1. Demographic data: age on the date of procedure and sex
2. Anthropometric data: body weight and height
3. Length of hospital stay (LOS)
4. Incidence of postoperative gastrointestinal complications, including nausea, vomiting, and ileus
5. Length of time to tolerating a regular diet postoperatively
6. Length of time to meeting 50% of estimated oral fluid needs postoperatively

Demographic and Anthropometric Data

Using Epic EMR software, each subject's medical chart from the admission for laparoscopic nephrectomy was utilized to gather data. Age on the date of the procedure was collected from each subject's interval history and physical note documented on the

day of the procedure. Subject sex was collected from each subject's demographics summary located in the SnapShot tab in Epic. Preoperative body weight in kilograms and height in meters were collected from the subject's anthropometrics flowsheet in Epic. Each subject's body weight and height were used to calculate BMI.

Length of Hospital Stay

LOS was defined as the length of time between the subject's admit to inpatient order and the subject's discharge order. The date and time of these orders were used to calculate LOS. LOS was calculated in minutes and then converted into days and recorded.

Length of Time to Tolerating a Regular Diet and Length of Time to Meeting 50% of Estimated Oral Fluid Needs Postoperatively

Start time for the length of time to tolerating a regular diet and length of time to meeting 50% of estimated oral fluid needs postoperatively was either the date and time of the subject's anesthesia post-procedure evaluation chart note or the date and time of the subject's post-anesthesia care unit (PACU) handoff chart note. The anesthesia post-procedure evaluation note is authored by the anesthesiologist or certified registered nurse anesthetist. The note documents the subject's status, vital signs, pain control, and any complications or adverse events. The PACU handoff note is authored by the registered nurse in the PACU and documents the subject's status, vital signs, pain control, and any pertinent findings or additional information. Several medical charts contained both notes and the notes were typically documented consecutively and in close time proximity to one another.

The anesthesia post-procedure evaluation note was used as the start time for 54 of the subjects in the ERAS group. One subject's anesthesia post-procedure evaluation was not documented in Epic until the late afternoon on the day after the procedure (post-operative day #1). For this subject, the date and time of the PACU handoff note was used as the start time as a substitute for the date and time of the anesthesia post-procedure evaluation note. Among the control subjects, nine subjects' anesthesia post-procedure evaluations were not documented in Epic until either post-operative day #1 or post-operative day #2. Documentation of two subjects' anesthesia post-procedure evaluations were missing from the chart entirely. For these eleven subjects, the PACU handoff note was used as the start time as a substitute for the date and time of the anesthesia post-procedure evaluation note.

All chart notes documented during each subject's admission for laparoscopic nephrectomy were reviewed. The time from each subject's start time (either the anesthesia post-procedure evaluation note or the PACU handoff note) and the date and time of the first chart note documenting the subject's tolerance of a regular diet was calculated in minutes and then converted into hours. In the ERAS subjects, regular diet tolerance was not documented in one subject's chart and thus resulted in one missing data point in the analysis of the length of time to tolerating a regular diet. In the control subjects, nine subjects did not have regular diet tolerance documented in their chart, resulting in nine missing data points in the analysis of length of time to tolerating a regular diet.

Each subject's preoperative body weight was used to calculate 50% of their total estimated fluid needs using 15 mL of fluid per kilogram of body weight (15 mL/kg).

Intake and output flowsheets for each subject were reviewed to determine the date and time at which the subject had consumed at least the calculated estimated fluid needs orally. The length of time from the subject's start time (either the anesthesia post-procedure evaluation note or the PACU handoff note) and the date and time of the oral fluid intake entry indicating when the subject had met or exceeded the calculated estimated fluid needs was calculated in minutes and then converted into hours. In the ERAS subjects, two subjects either did not meet the estimated fluid needs during admission or their fluid intake was not documented in the EMR. This resulted in two missing data points in the analysis of length of time to meeting 50% of estimated fluid needs postoperatively. In the control subjects, six subjects either did not meet the estimated fluid needs during admission or their fluid intake was not documented in the EMR. This resulted in six missing data points in the analysis of length of time to meeting 50% of estimated fluid needs postoperatively.

Incidence of Gastrointestinal Complications

Incidence of nausea, vomiting, and ileus were identified by reviewing chart notes authored by physicians, physician assistants, nursing staff, registered dietitians, and clinical staff during the subject's admission. If documented, incidence of nausea, vomiting, and ileus were each recorded as 1 (occurred). If not documented, incidence of nausea, vomiting, and ileus were each recorded as 0 (did not occur).

Statistical Analysis

All statistical analyses were performed using Stata/IC 16.1 statistical analysis software. Figures were developed using Prism 9 software. For all statistical tests performed, $p<0.05$ was considered statistically significant.

Descriptive Statistics

For the ERAS and control groups, mean age, weight, height, and BMI were calculated and expressed as mean ± standard deviation (SD) for each variable. The distribution of age, weight, height, and BMI within each group was assessed for normality using the Shapiro-Wilk test. Age, weight, height, and BMI were each normally distributed. Levene's test for equality of variances was performed for age, weight, height, and BMI. An independent two-sample t-test with equal variances was performed to determine if each variable (mean age, weight, height, and BMI) differed between the two groups. The proportions of males and females in the subcategory of sex were compared between groups using a two-sample test of proportions.

LOS, Length of Time to Tolerating a Regular Diet Postoperatively, and Length of Time to Meeting 50% of Estimated Oral Fluid Needs Postoperatively

Mean LOS, mean length of time to tolerating a regular diet postoperatively, and mean length of time to meeting 50% of estimated oral fluid needs postoperatively were calculated and expressed as mean ± SD for each variable. Distribution of LOS, length of time to tolerating a regular diet postoperatively, and length of time to meeting 50% of estimated oral fluid needs postoperatively were assessed for normality using the Shapiro-Wilk test. LOS, length of time to tolerating a regular diet postoperatively, and length of time to meeting 50% of estimated oral fluid needs postoperatively were not normally distributed. Data transformations were attempted for each variable. All attempted transformations were unsuccessful in achieving a normal distribution.

A Wilcoxon Rank-Sum test was performed to determine if mean LOS, mean length of time to tolerating a regular diet postoperatively, and mean length of time to

meeting 50% of estimated oral fluid needs postoperatively differed between ERAS subjects and control subjects.

Examination of box plots of LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs revealed a small number of extreme values for each variable, necessitating further assessment of the outlying data points. Outliers within the distributions were defined using the interquartile range (IQR), first quartile (Q1), third quartile (Q3), and the plotted points on the box plot. Data points less than Q1 - (1.5)(IQR) were considered lower outliers and data points greater than Q3 + (1.5)(IQR) were considered upper outliers. Using this criteria, several outliers were identified within each group for LOS, length of time to tolerating a regular diet postoperatively, and length of time to meeting 50% of estimated oral fluid needs postoperatively. To evaluate the influence of outliers on the results of the Wilcoxon Rank-Sum tests, outliers were removed from the LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs datasets and each Wilcoxon Rank-Sum test was performed.

Incidence of Postoperative Nausea, Vomiting, and Ileus

For each subject, incidence of postoperative nausea, vomiting, and ileus were recorded as either 1 (occurred) or 0 (did not occur). Within each group, the proportion of subjects with a value of 1 for each postoperative gastrointestinal complication was calculated. For each proportion calculated, a two-sample test of proportions was performed to determine if the two groups differed with respect to the incidence of each postoperative gastrointestinal complication (nausea, vomiting, and ileus).

Table 2. Statistical Analysis Summary

Specific Aim	Hypotheses	Statistical Test
Specific Aim 1: To determine the impact of preoperative carbohydrate loading on LOS and incidence of postoperative gastrointestinal complications following a laparoscopic nephrectomy procedure in living kidney donors at OHSU.	**Hypothesis 1:** Subjects who received preoperative carbohydrate loading experienced a reduced LOS compared to historical control subjects who did not receive preoperative carbohydrate loading.	**Non-normal Distribution:** A Wilcoxon Rank-Sum test was performed to determine if mean LOS differed between the two groups.
	Hypothesis 2: Subjects who received preoperative carbohydrate loading experienced fewer gastrointestinal complications after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading.	Incidence of postoperative nausea, vomiting, and ileus for each subject within each group were recorded as either 1 (occurred) or 0 (did not occur). The proportion of subjects with a value of 1 for each postoperative gastrointestinal complication was calculated and a two-sample test of proportions was performed to compare the proportions between the two groups.
Specific Aim 2: To determine the effect of preoperative carbohydrate loading on the length of time required to return to a regular oral diet and the length of time required to meet 50% of estimated oral fluid needs following a laparoscopic nephrectomy procedure in living kidney donors at OHSU.	**Hypothesis 1:** Subjects who received preoperative carbohydrate loading required less time to return to a regular oral diet after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading.	**Non-normal Distribution:** A Wilcoxon Rank-Sum test was performed to determine if mean length of time to tolerating a regular oral diet postoperatively differed between the two groups.
	Hypothesis 2: Subjects who received preoperative carbohydrate loading required less time to meet 50% of estimated oral fluid needs after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading.	**Non-normal Distribution:** A Wilcoxon Rank-Sum test was performed to determine if mean length of time to meeting 50% of estimated oral fluid needs postoperatively differed between the two groups.

Chapter 4: Results

Screening and Selection Process

Screening and selection of subjects for inclusion in the final analysis took place as depicted in Figure 2. Following exclusion of subjects who underwent an open nephrectomy or did not consume Ensure Clear prior to surgery, data from 55 subjects in the ERAS group and 93 subjects in the control group was gathered and analyzed.

Figure 2. Inclusions and exclusions

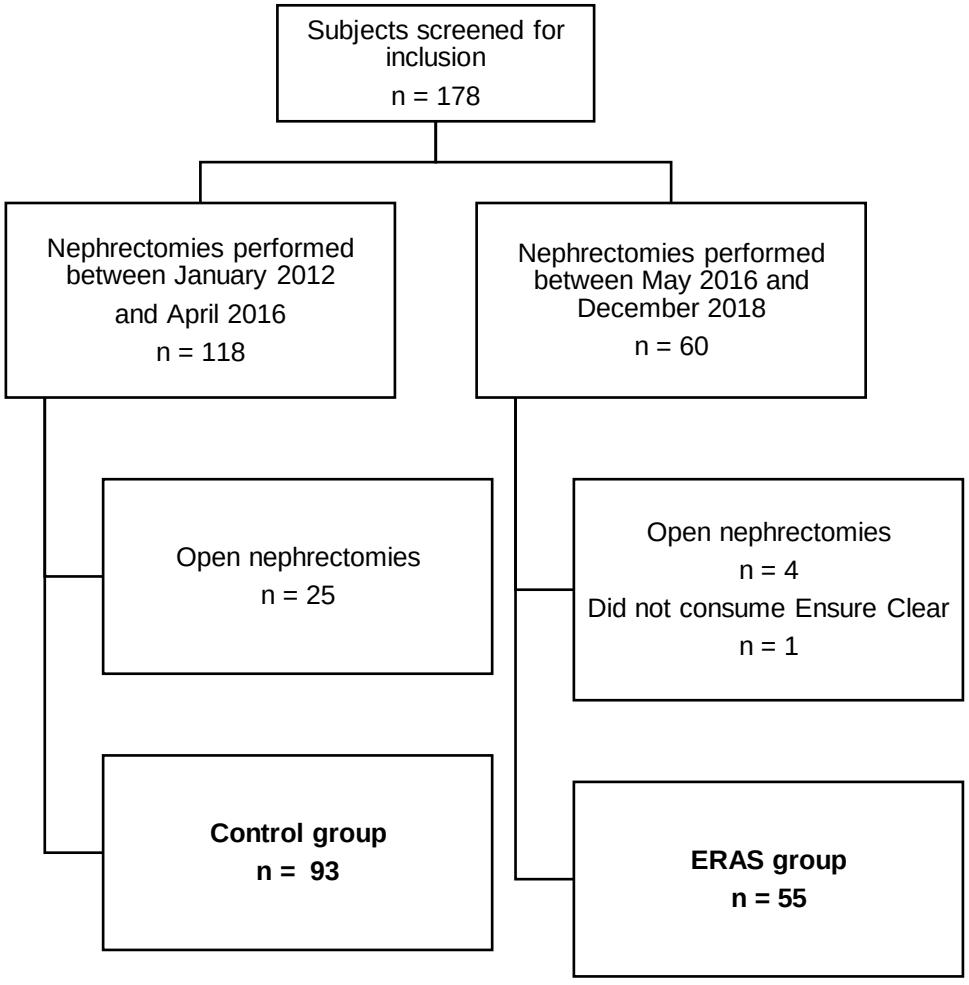

Figure 2. A depiction of the screening and selection process beginning with the total number of subjects screened for inclusion and concluding with the final groups included in the analysis. Between January 2012 and April 2016, 118 nephrectomies were performed, 25 of which were open nephrectomies and excluded from the analysis. Between May 2016 and December 2018, 60 nephrectomies were performed, four of which were open nephrectomies and excluded from the analysis. One subject did not consume Ensure Clear prior to surgery and was excluded from the analysis.

Population Description

Subject characteristics were similar between the ERAS group and the control group (Table 3). There was no significant difference between the ERAS subjects and control subjects in age, weight, BMI, or the distribution of males and females within each group. Both groups consisted of predominantly female subjects. Subjects differed significantly in height (p=0.02).

Table 3. Subject characteristics

Characteristic	ERAS subjects	Control subjects
	n = 55	n = 93
Age on procedure date (y)	41.6 ± 10.2	44.0 ± 10.9
Weight (kg)	72.2 ± 12.1	75.7 ± 13.0
Height (m)	1.67 ± 0.09*	1.71 ± 0.09
BMI (kg/m^2)	25.7 ± 3.2	25.7 ± 3.2
Sex, n (%)		
Male	12 (21.8)	34 (36.6)
Female	43 (78.2)	59 (63.4)

Table 3. A comparison of characteristics between subjects who received preoperative carbohydrate loading (ERAS subjects; n=55) and subjects who did not receive preoperative carbohydrate loading (control subjects; n=93). Results are expressed as mean ± standard deviation of the mean (SD). For each characteristic, groups were compared using an independent two-sample t-test. The proportions of male and female subjects within each group were compared using a two-sample test of proportions. * specifies a significant difference between ERAS subjects and control subjects at the p<0.05 level of significance. Subject height was significantly higher in the control group compared to the ERAS group (p=0.02).

Comparison of LOS, Length of Time to Tolerating a Regular Diet Postoperatively, and Length of Time to Meeting 50% of Estimated Oral Fluid Needs Postoperatively

Significant differences between ERAS subjects and control subjects were identified for all primary outcome variables (Table 4, Figures 3-5). LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs

were all significantly shorter in the ERAS group compared to the control group ($p<0.001$ for each comparison). Mean LOS was 2.8 days in the ERAS group and 3.9 days in the control group. Mean length of time to tolerating a regular diet was 36.5 hours in the ERAS group and 68.2 hours in the control group. Mean length of time to meeting 50% of estimated oral fluid needs was 25.3 hours in the ERAS group and 44.6 hours in the control group. There was no significant difference in estimated fluid needs between the two groups.

Table 4. Primary outcome variables

Outcome	ERAS subjects	Control subjects
LOS (d)	2.8 ± 0.8* (n = 55)	3.9 ± 1.0 (n = 93)
Time to tolerating a regular diet (h)	36.5 ± 15.6* (n = 54)	68.2 ± 24.9 (n = 84)
50% of estimated fluid needs (mL)	1083.0 ± 181.5 (n = 55)	1135.3 ± 195.6 (n = 93)
Time to meeting 50% of estimated fluid needs (h)	25.3 ± 13.0* (n = 53)	44.6 ± 19.9 (n = 87)

Table 4. A comparison of primary outcome variables, including length of hospital stay (LOS) in days, length of time to tolerating a regular diet in hours, 50% of estimated fluid needs in milliliters (mL), and length of time to meeting 50% of estimated oral fluid needs in hours between subjects who received preoperative carbohydrate loading (ERAS subjects; n=55) and subjects who did not receive preoperative carbohydrate loading (control subjects; n=93). Results are expressed as mean ± SD. Each group's mean LOS, mean length of time to tolerating a regular diet, and mean length of time to meeting 50% of estimated oral fluid needs were compared using a Wilcoxon Rank-Sum test. Each group's mean estimated oral fluid needs were compared using an independent two-sample t-test. * specifies a significant difference between ERAS subjects and control subjects at the $p<0.05$ level of significance. LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs were significantly shorter in the ERAS group compared to the control group ($p<0.001$ for each comparison).

Figure 3. Length of hospital stay (LOS) in days in ERAS subjects and control subjects

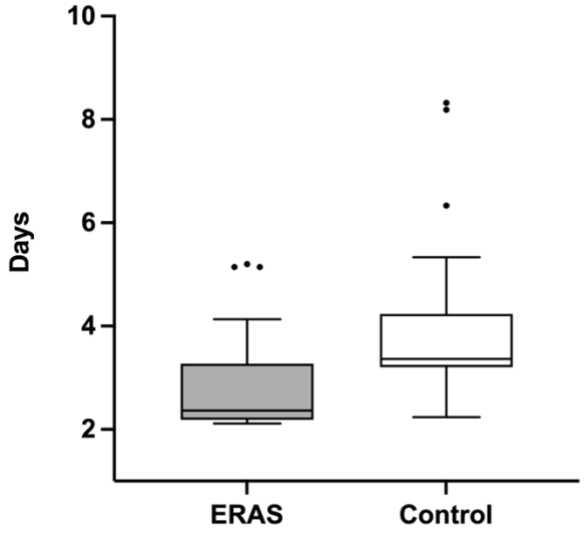

Figure 3. Length of hospital stay (LOS) in ERAS subjects (n=55) and control subjects (n=93). Box depicts quartiles of data. Bottom of box indicates the 25th percentile. Top of box indicates the 75th percentile. The line in the middle of the box indicates the median. Whiskers indicate the range of values for each group of subjects. Plotted points are outliers. LOS was significantly shorter in the ERAS group compared to the control group (p<0.001).

Figure 4. Length of time to tolerating a regular diet in hours in ERAS subjects and control subjects

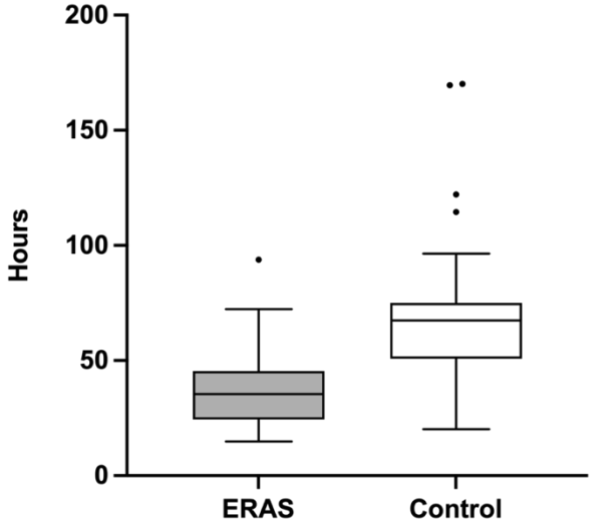

Figure 4. Length of time to tolerating a regular diet in ERAS subjects (n=54) and control subjects (n=84). Box depicts quartiles of data. Bottom of box indicates the 25th percentile. Top of box indicates the 75th percentile. The line in the middle of the box indicates the median. Whiskers indicate the range of values for each group of subjects. Plotted points are outliers. Length of time to tolerating a regular diet was significantly shorter in the ERAS group compared to the control group (p<0.001).

Figure 5. Length of time to meeting 50% of estimated oral fluid needs in hours in ERAS subjects and control subjects

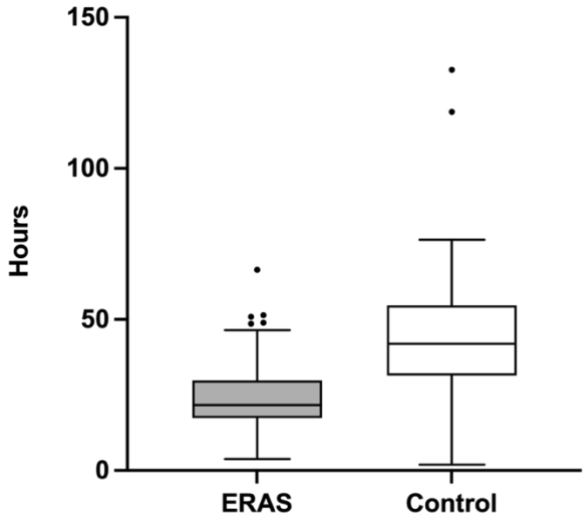

Figure 5. Length of time to meeting 50% of estimated oral fluid needs in ERAS subjects (n=53) and control subjects (n=87). Box depicts quartiles of data. Bottom of box indicates the 25th percentile. Top of box indicates the 75th percentile. The line in the middle of the box indicates the median. Whiskers indicate the range of values for each group of subjects. Plotted points are outliers. Length of time to meeting 50% of estimated oral fluid needs was significantly shorter in the ERAS group compared to the control group ($p<0.001$).

Several outliers were present within each group for LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs. After removal of outliers from the dataset, a Wilcoxon Rank-Sum test was performed for each comparison. All primary outcome variables remained significantly shorter in the ERAS group compared to the control group ($p<0.001$ for each comparison). Therefore, the presence or absence of outliers within the dataset did not influence the overall conclusions described in Table 4.

Incidence of Postoperative Gastrointestinal Complications

Incidence of nausea, vomiting, and ileus were determined through chart review and the proportion of subjects in each group who experienced each gastrointestinal complication was calculated and expressed as a percentage (Table 5). The proportion

of subjects who experienced nausea, vomiting, and/or ileus did not differ significantly between the ERAS group and the control group (Figure 6). In the ERAS group, 35 subjects (63.64%) experienced nausea, eight subjects (14.55%) experienced vomiting, and seven subjects (12.73%) experienced ileus. In the control group, 68 subjects (73.12%) experienced nausea, 14 subjects (15.05%) experienced vomiting, and 13 subjects (13.98%) experienced ileus.

Table 5. Incidence of postoperative nausea, vomiting, and ileus in ERAS subjects and control subjects

	ERAS subjects	**Control subjects**
	(n = 55)	(n = 93)
Nausea	35 (63.64)	68 (73.12)
Vomiting	8 (14.55)	14 (15.05)
Ileus	7 (12.73)	13 (13.98)

Table 5. A comparison of the incidence of postoperative gastrointestinal complications in ERAS subjects (n=55) and control subjects (n=93). Results are expressed as the number of subjects who experienced the complication and the value in parentheses is the corresponding percentage of total subjects in the group who experienced the complication. A two-sample test of proportions was performed for each complication. There was no significant difference between groups in the proportion of subjects who experienced nausea, vomiting, or ileus at the $p<0.05$ level of significance.

Figure 6. Bar graph of incidence of postoperative nausea, vomiting, and ileus in ERAS subjects and control subjects

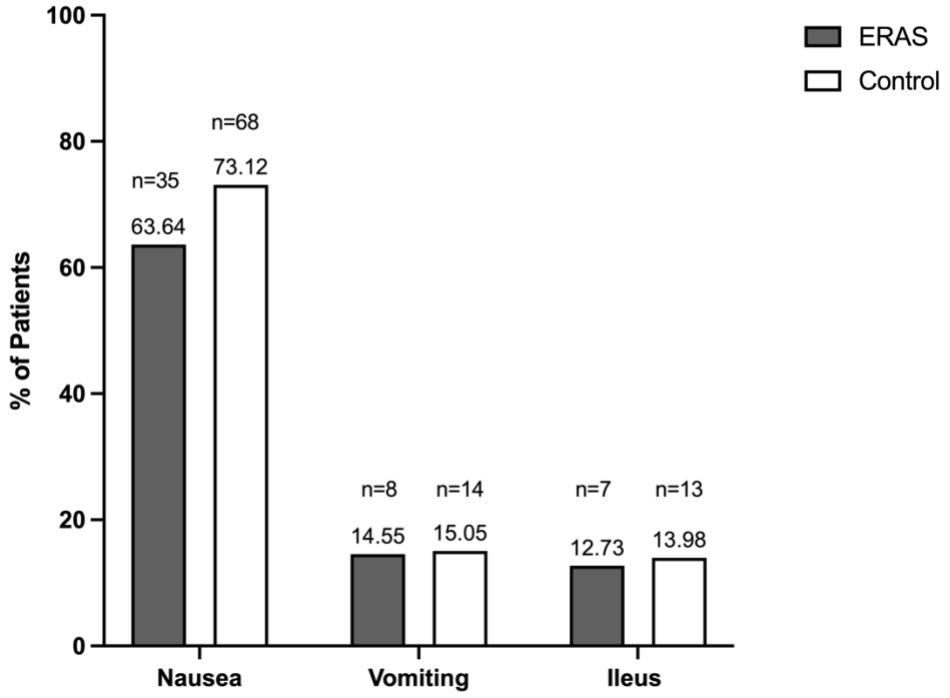

Figure 6. Bar graph of the number and percentage of subjects who experienced postoperative nausea, vomiting, or ileus in the ERAS subjects and control subjects. Values above each bar indicate the percentage of subjects who experienced the complication. The values above the percentages are the numbers of subjects in each group who experienced the complication. There was no significant difference between groups in the proportion of subjects who experienced nausea, vomiting, or ileus at the $p<0.05$ level of significance.

Summary of Findings

In this retrospective chart review, data from 55 subjects who received preoperative carbohydrate loading prior to laparoscopic nephrectomy and 93 control subjects who did not receive preoperative carbohydrate loading prior to laparoscopic nephrectomy was analyzed and the two groups were compared. There was no significant difference between groups in age, weight, BMI, or the proportions of males and females within each group. Height was significantly higher in the control group compared to the ERAS group ($p=0.02$). Preoperative carbohydrate loading significantly reduced LOS, length of time to tolerating a regular diet, and length of time to meeting

50% of estimated oral fluid needs after laparoscopic nephrectomy. There was no significant difference between the ERAS group and the control group in the incidence of postoperative nausea, vomiting, or ileus.

Chapter 5: Discussion

This study aimed to investigate the impact of preoperative carbohydrate loading on LOS, length of time required to resume regular oral food and fluid intake, and the incidence of gastrointestinal complications after laparoscopic nephrectomy in living kidney donors at OHSU. This is one of few studies examining the impact of preoperative carbohydrate loading on postoperative recovery in living kidney donors. We assessed the length of time required to return to regular oral food and fluid intake postoperatively, which other studies exploring preoperative carbohydrate loading in laparoscopic living donor nephrectomy did not assess. Ensure Clear, the preoperative carbohydrate loading product that was used in our study, has also not been examined in published studies. Our results contribute to the growing body of evidence surrounding the role of preoperative carbohydrate loading in promoting recovery after elective abdominal surgery and provide key information to guide preoperative nutrition interventions.

Compared to historical control subjects, subjects who received preoperative carbohydrate loading experienced a significantly shorter LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs after laparoscopic nephrectomy. These findings suggest that preoperative carbohydrate loading is an advantageous intervention for speeding postoperative recovery following laparoscopic nephrectomy. Tolerance of a regular oral diet and adequate oral fluid intake are key factors in the assessment of readiness for hospital discharge after major

surgery. Our results demonstrate that individuals who meet these criteria more quickly are likely to experience a shorter LOS. There was not a significant difference in the incidence of postoperative nausea, vomiting, or ileus in subjects who received preoperative carbohydrate loading when compared to historical control subjects. This finding suggests that preoperative carbohydrate loading is not effective in preventing common postoperative gastrointestinal complications after laparoscopic nephrectomy.

In several ways, our results are similar to the results of other studies examining preoperative carbohydrate loading prior to living donor nephrectomy. In our study, median LOS decreased from 3.4 days in the control group to 2.4 days in the ERAS group. Waits et al (2015) also identified a significant reduction in LOS in subjects who received preoperative carbohydrate loading compared to subjects who received the standard of care of preoperative fasting.[43] Specifically, median LOS decreased from 2.0 days to 1.0 day.[43] Rege et al (2016) also identified a reduction in median LOS from 2.0 days to 1.0 day in the study's ERAS group.[41] Similar to our finding, Brown et al (2020) did not identify a significant difference in postoperative nausea scores between the ERAS and standard care groups.[40]

In contrast to our findings, Ricotta et al (2019) identified no significant difference in LOS between the study's ERAS group and the standard care group.[42] However, authors did identify that donors 61-72 years of age in the ERAS group experienced a significantly shorter LOS compared to donors in the same age range who received standard care.[42] Brown et al (2020) did not identify a significant difference in LOS between the ERAS and standard care groups in their study.[40]

The studies by Waits et al, Rege et al, Ricotta et al, and Brown et al did not assess the length of time to tolerating a regular diet postoperatively or the length of time to meeting 50% of estimated oral fluid needs postoperatively. These studies compared additional outcome variables including narcotic use, pain scores, readmission rates, use of opiate medication, and use of preoperative IV fluids which our study did not assess. These variables could be considered in planning future studies in the OHSU surgical patient population.

Findings of studies examining the impact of preoperative carbohydrate loading on postoperative outcomes in other types of gastrointestinal surgeries such as laparoscopic cholecystectomy, colorectal surgery, and open liver resection can be compared to our study's findings. Compared to subjects randomized to preoperative fasting or preoperative water, significant reductions in time to fitness for discharge, postoperative discharge day, or LOS were identified in subjects who received preoperative carbohydrate loading in three of seven randomized controlled trials.[37,54-57,59,60] Four studies identified significant reductions in nausea and/or vomiting in subjects who received preoperative carbohydrate loading compared to preoperative fasting or placebo, whereas two studies did not find significant differences.[37,39,51,53,54,60] Compared to preoperative fasting, a shorter time to oral intake in subjects who received preoperative carbohydrate loading was identified in two of four studies.[37,55,57,60] One study's results demonstrated that, compared to preoperative fasting, subjects who received preoperative carbohydrate loading consumed more fluids in the initial 24 hours following surgery.[55]

Our study has a number of strengths. First, our control group (n=93) and ERAS group (n=55) are large compared to other studies examining preoperative carbohydrate loading in living kidney donors. Similar studies included an intervention group ranging from 22 to 60 subjects and a control group of up to 60 subjects. The relatively large size of our study groups, especially our control group, strengthened our analysis. Second, the ERAS and control subjects did not differ significantly in age, weight, BMI, distribution of males and females, or estimated fluid needs, resulting in strong comparability between groups. Third, all subjects underwent laparoscopic nephrectomy at the same surgical center. This provided consistency in the donor assessment and eligibility criteria, anesthesia and surgical procedures, EMR documentation, perioperative care processes, and hospital discharge requirements and criteria.

Several limitations related to the nature of retrospective chart review studies and secondary data analysis are present within our study. One of the most significant limitations of our study is that the laparoscopic nephrectomy procedures in the control group took place prior to the ERAS subjects' procedures. Data was collected for procedures spanning an approximately 4.3-year period (January 2012 to April 2016) for the control group and an approximately 2.7-year period (May 2016 to December 2018) for the ERAS group. Throughout this seven-year period, components of the perioperative protocols and interventions at OHSU may have evolved and improved to promote postoperative recovery. Differences in outcomes between the ERAS and control groups may not be entirely attributable to the implementation of preoperative carbohydrate loading, but rather the combined impact of preoperative carbohydrate

loading and other improvements in perioperative care that have occurred over the past several years.

Confirmation of whether subjects in the ERAS group consumed Ensure Clear prior to surgery was provided to registered dietitians by each ERAS subject after surgery, introducing the potential for recall bias and misreporting. Subjects may not have consumed the entire prescribed quantity of Ensure Clear with the recommended volume of water added, and any deviation from the prescription was not tracked or documented in the EMR. Consequently, variability in volume, carbohydrate quantity, osmolality, and timing of intake was not accounted for or analyzed. Calculations of LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs postoperatively depended on the time points provided by each subject's orders, chart notes, and fluid intake documentation in the EMR. Therefore, our results may not represent the exact time that each event occurred, but rather if and when each event was documented.

Our analysis contained a small number of missing data points due to a lack of documentation in the EMR. It is therefore unknown if and when certain subjects tolerated a regular diet and met 50% of estimated oral fluid needs during admission and how the missing data points may have impacted the results. We assessed the incidence of postoperative gastrointestinal complications (nausea, vomiting, and ileus), but could not assess the severity of these gastrointestinal complications. The interpretation of the results for this outcome is therefore limited to whether or not preoperative carbohydrate loading prevented the occurrence of postoperative gastrointestinal complications. It is possible that ERAS subjects experienced a difference in the severity of gastrointestinal

complications compared to the control group, but our study methods and the existing EMR data were not developed to assess this.

Our study population included healthy adults who underwent extensive screening and assessment by medical staff to confirm suitability as a living kidney donor. Therefore, the results of our study may not be applicable to other groups of surgical patients who are medically complex. Additionally, our study population was predominantly female and did not adequately represent males, nor did it include pediatric subjects. These factors may present challenges in applying the results to a more heterogenous and diverse patient population.

Many questions surrounding the impact of preoperative carbohydrate loading on postoperative recovery after elective abdominal surgery remain unanswered and necessitate further research. In our study, various differences in perioperative management between groups are likely present since many of the surgical procedures in the control group took place several years prior to the procedures in the ERAS group. A randomized controlled trial comparing preoperative carbohydrate loading to placebo or fasting with all other perioperative interventions identical between the two groups would be ideal. This type of study could answer the question of whether, and to what extent, preoperative carbohydrate loading is advantageous as an independent intervention. However, a randomized controlled trial may not be ethical considering that the available evidence suggests that preoperative carbohydrate loading is a safe and feasible intervention that either enhances or does not impact postoperative recovery.

A 2014 meta-analysis of 27 randomized controlled trials involving 1,976 adults undergoing elective surgery (including abdominal, orthopedic, and thyroid surgeries)

concluded that preoperative carbohydrate loading was associated with a minor reduction in LOS when compared to placebo or fasting, but did not increase or decrease the rate of postoperative complications.[50] The authors concluded that, when examining only well-conducted studies, preoperative carbohydrate loading had little to no impact on LOS and that the evidence supporting the effects of preoperative carbohydrate loading on postoperative complications was of low quality due to flaws in study design.[50] Completing a new meta-analysis that includes the more recent, higher-quality randomized controlled trials could more accurately assess the benefits of preoperative carbohydrate loading prior to elective surgery.

An additional question that should be addressed is whether or not a specific product used for preoperative carbohydrate loading provides an advantage over other products. In the existing literature, researchers have used a range of different oral nutrition supplements and beverages for preoperative carbohydrate loading, such as Nutricia PreOp, ClearFast PreOp, fruit juice, and Gatorade. Some of these products do not meet the recommendation for a 12% carbohydrate solution containing predominantly maltodextrin to minimize osmolality and prevent delayed gastric emptying.[44] However, such products still demonstrated a positive impact on postoperative recovery in some of the studies that used them.

Additionally, the currently recommended and prescribed quantity of preoperative carbohydrates in the literature and clinical guidelines is equivalent for all patients, regardless of body weight. Further research evaluating the impact of the quantity of carbohydrates prescribed for preoperative carbohydrate loading based on a subject's weight could yield a more precise method for prescribing. Additionally, evaluating

different forms of carbohydrates and electrolyte compositions in a controlled setting could provide important data to establish stronger evidence-based recommendations.

One of the key clinical challenges in managing postoperative recovery is the development of insulin resistance that follows the metabolic stress response precipitated by major surgery.[61] Though preoperative carbohydrate loading aims to reduce postoperative insulin resistance, there is a lack of research exploring the impact of preoperative carbohydrate loading on postoperative insulin resistance after living donor nephrectomy. A 2012 meta-analysis demonstrated that preoperative carbohydrate loading significantly reduced the development of postoperative insulin resistance when compared to control (preoperative fasting or placebo) in a number of surgical procedures, including colorectal, liver, inguinal hernia, and orthopedic surgeries, as well as laparoscopic and open cholecystectomy.[62]

Completing a targeted trial to compare postoperative insulin sensitivity, ideally using the gold-standard hyperinsulinemic-euglycemic clamp method, in living kidney donors who received preoperative carbohydrate loading versus controls could be extremely valuable. This type of trial could identify the impact of preoperative carbohydrate loading on postoperative insulin resistance after living donor nephrectomy. This could be expanded to evaluate the impact of preoperative carbohydrate loading on postoperative insulin resistance using various quantities and forms of carbohydrates. Findings may provide direction regarding the most effective product or formulation to use to minimize postoperative insulin resistance specifically.

Oral food and fluid intake the day prior to surgery is an unexplored area that should be investigated. Energy and carbohydrate intake the day prior to surgery,

especially at the afternoon and evening meals, likely influences the metabolic state of the individual during surgery the following day. Collecting dietary recall data from subjects to examine energy intake and macronutrient composition of meals consumed the day before surgery may reveal certain meal patterns or quantities of macronutrients that promote postoperative recovery.

Despite the fact that several unanswered questions regarding the impact of preoperative carbohydrate loading on postoperative recovery exist, the results of our study provide a number of key practice applications. In living kidney donors undergoing laparoscopic nephrectomy, preoperative carbohydrate loading with 237-mL of Ensure Clear (52 grams of carbohydrate) diluted with 160 mL of water for a total volume of roughly 400 mL and consumed two to four hours before surgery reduces LOS, length of time to tolerating a regular diet, and length of time to meeting 50% of estimated oral fluid needs postoperatively. This formulation and schedule appears to be safe and well-tolerated as no complications or adverse effects associated with Ensure Clear consumption were identified in our study population. Preoperative carbohydrate loading did not impact the incidence of postoperative nausea, vomiting, or ileus when compared to control subjects. Ultimately, our results and the results of similar studies demonstrate that preoperative carbohydrate loading is an effective intervention for accelerating postoperative recovery in living kidney donors following laparoscopic nephrectomy and should be encouraged.

Chapter 6: Conclusion

This study aimed to determine the impact of preoperative carbohydrate loading on key clinical outcomes, including LOS, length of time required to return to a regular oral diet, length of time required to meet 50% of estimated oral fluid needs, and incidence of gastrointestinal complications (nausea, vomiting, and ileus) following a laparoscopic nephrectomy procedure in living kidney donors at OHSU.

Our findings supported our hypothesis that subjects who received preoperative carbohydrate loading would experience a reduced LOS after laparoscopic nephrectomy compared to historical control subjects who did not receive preoperative carbohydrate loading. Additionally, our findings supported our hypothesis that subjects who received preoperative carbohydrate loading would require less time to return to a regular oral diet and meet 50% of estimated oral fluid needs postoperatively compared to historical controls. Our findings did not support our hypothesis that subjects who received preoperative carbohydrate loading would experience fewer gastrointestinal complications after laparoscopic nephrectomy compared to historical control subjects.

Our study demonstrated the clinical benefit and safety of preoperative carbohydrate loading in living kidney donors undergoing laparoscopic nephrectomy. Findings substantiate the value of a preoperative carbohydrate loading protocol in this population. Thus, this study supports continuation of this nutrition intervention in future laparoscopic living donor nephrectomies.

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Appendix A: Common Preoperative Carbohydrate Loading Products Used in ERAS Programs

Product	Manufacturer	Location Available	Volume (mL)	Osmolality (mOsm/kg)	Maltodextrin (g)	% Carbohydrate
PreOp	Nutricia	Europe, United Kingdom, Canada	400	285	40	12.0
PreOp	ClearFast Nutrition	United States	355	270	44	12.0
Preload	Vitaflo International	United Kingdom	400	135	47.5	13.0
Maxijul	Nutricia	United Kingdom, Europe	420	420	43.25	32.0
Ensure Pre-Surgery	Abbott	United States	296	274		16.9
Ensure Clear	Abbott	United States	237	700		21.9
Apple juice	Welch’s	United States	297	750		11.1
Gatorade	PepsiCo	United States	500	330		6.0

Appendix B: OHSU Institutional Review Board Approval Letter

APPROVAL OF SUBMISSION

January 19, 2021

Dear Investigator:

On 1/19/2021, the IRB reviewed the following submission:

IRB ID:	STUDY00022534
Type of Review:	Initial Study
Title of Study:	Retrospective chart review of the impact of preoperative carbohydrate loading on length of stay and postoperative recovery in living kidney donors undergoing laparoscopic nephrectomy
Principal Investigator:	Sandra Van Calcar
Funding:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• HIPAA WoA • Protocol V2 Clarifications • Data Form - Variables Recorded from Medical Records V2

The IRB granted final approval on 1/19/2021. The study requires you to submit a check-in before 1/17/2024.

Review Category: Exempt Category #4

Copies of all approved documents are available in the study's **Final** Documents (far right column under the documents tab) list in the eIRB. Any additional documents that require an IRB signature (e.g. IIAs and IAAs) will be posted when signed. If this applies to your study, you will receive a notification when these additional signed documents are available.

Ongoing IRB submission requirements:

- Six to ten weeks before the eIRB system expiration date, submit a check-in..
- Any changes to the project must be submitted for IRB approval prior to implementation.
- Reportable New Information must be submitted per OHSU policy.
- Submit a check-in to close the study when your research is completed.

Guidelines for Study Conduct

In conducting this study, you are required to follow the guidelines in the document entitled, "Roles and Responsibilities in the Conduct of Research and Administration of Sponsored Projects," as well as all other applicable OHSU IRB Policies and Procedures.

Requirements under HIPAA

If your study involves the collection, use, or disclosure of Protected Health Information (PHI), you must comply with all applicable requirements under HIPAA. See the HIPAA and Research website and the Information Privacy and Security website for more information.

IRB Compliance

The OHSU IRB (FWA00000161; IRB00000471) complies with 45 CFR Part 46, 21 CFR Parts 50 and 56, and other federal and Oregon laws and regulations, as applicable, as well as ICH-GCP codes 3.1-3.4, which outline Responsibilities, Composition, Functions, and Operations, Procedures, and Records of the IRB.

Sincerely,

The OHSU IRB Office

Appendix C: OHSU Living Kidney Donor Patient Selection Criteria

Clinical Transplant Services

Living Kidney Donor Transplant Program

3181 SW Sam Jackson Park Rd., Mail Code: CSB 569 Portland, Oregon 97239

Telephone #: (503) 494-8500 ·Fax #: (503) 494-4492

Email: livingdonation@ohsu.edu

Living Kidney Donor Patient Selection Criteria

I. Conditions that Increase the Risk with Kidney Donation

A. Underlying medical condition for which treatment may be nephrotoxic (i.e., rheumatoid arthritis, chronic pain)

B. Clotting abnormalities

C. Tobacco use

D. History of significant renal abnormalities (i.e., stones, pyelonephritis, cancer)

E. Hepatitis B core antibody positive

F. Metabolic Syndrome

G. Obesity

H. Past history of depression, mental illness, or substance abuse

I. Total colectomy

J. Hepatitis C Positive

II. Absolute Contraindications

A. ABO blood group incompatibility not amenable to immunomodulation; offer paired exchange

B. T or B cell crossmatch incompatibility not amenable to immunomodulation; offer paired exchange

C. BMI > 32

D. Less than 21 years old

E. Hypertension

F. Kidney disease or insufficient renal function

G. Moderate operative risk for mortality or morbidity

H. Significantly impaired glucose metabolism or history of gestational diabetes in a donor < 40 years old or if < 10

years from diagnosis

Updated 10/2018

I. Intestinal bypass surgery; < 5 years since any other bariatric surgery procedure

J. Active psychiatric conditions requiring treatment before donation, including any evidence of suicidality

K. Significant mental dysfunction

1. Inability to give informed consent

2. Inability to understand the nature of procedure

3. Inability to cooperate in medical care required following surgery

L. High suspicion of donor coercion

M. High suspicion of illegal financial exchange between the donor and recipient

N. Insufficient financial or social support

O. Active use of drugs of abuse, including alcohol

P. Significant transmissible diseases

Q. HIV positive

R. HTLV positive

S. Hepatitis B surface antigen positive

T. Active malignancy or incompletely treated malignancy

U. Evidence of acute symptomatic infection (until resolved)

V. Current inmates of correctional facilities, on parole, or legal issues pending with potential for incarceration

W. Donor decided not to proceed with surgery

III. Reference:

OHSU Kidney/Pancreas Transplant Protocol Handbook, Chapter 2.13, Pretransplant Evaluations

LaPointe Rudow, D., et al. A Clinician's Guide to Donation and Transplantation. Lenexa, KS: Applied Measurement Professionals, Inc.; 2006. Chapters 16,17; PHS Guideline for Reducing HIV, Hepatitis B Virus, and Hepatitis C Virus Transmission Through Organ Transplantation (2013).

Updated 10/2018

Appendix D: Data Collection Form

Subject Code: _____

Retrospective chart review of the impact of pre-operative carbohydrate loading on length of stay and post-operative recovery in living kidney donors undergoing laparoscopic nephrectomy

Demographic Data

Sex: _____
Age: _____

Anthropometric Data

Body weight (kg): _____
Height (m): _____
BMI: _____

LOS

LOS: _____

Postoperative Intake

Time to tolerating a regular diet: _____

Time to patient meeting 50% of estimated oral fluid needs postoperatively: _____

Incidence of Postoperative Gastrointestinal Complications

0 = did not occur
1 = occurred

Nausea: _____
Vomiting: _____
Ileus: _____

For ERAS patients only:

Number of doses of Ensure Clear consumed: _____