Summer 8-19-2016

Identifying Characteristics Associated with Ileus Development Post Coronary Artery Bypass Graft Surgery

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IDENTIFYING CHARACTERISTICS ASSOCIATED WITH ILEUS DEVELOPMENT POST CORONARY ARTERY BYPASS GRAFT SURGERY

BY

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A THESIS

Presented to the Faculty of

The University of Nebraska Graduate College

In Partial Fulfillment of the Requirements

For the Degree of Master of Science in Medical Nutrition

Medical Sciences Interdepartmental Area Graduate Program

Under the Supervision of

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University of Nebraska Medical Center

Omaha, NE

July 2016

ACKNOWLEDGEMENTS

I wish to thank my committee members whom I could not have done this without. I am forever grateful for their expertise, time and support.

Thank you Corri, Ann and Raquel.

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ABSTRACT

Background: Postoperative ileus (POI) is the period of intestinal paralysis following any surgical procedure. POI is manifested by nausea, vomiting, abdominal distention, delayed tolerance of oral diet and delayed time to flatus and stool. Little is known about POI following coronary artery bypass grafting (CABG) as no other study has focused specifically on the incidence of POI following CABG.

Purpose: The primary objective of this study is to determine the incidence of POI post CABG. The secondary aim is to evaluate baseline characteristics associated with POI following CABG.

Methods: This was a retrospective cohort study of 100 patients who underwent CABG from October 2014 to February 2015 at Nebraska Medicine. The incidence of POI was the primary outcome. Mann-Whitney U and Chi-square tests were used to compare characteristics between participants who did and did not develop POI. POI risk factors were determined using univariate logistic regression.

Results: The incidence of POI was 15%. BMI and preoperative blood glucose were risk factors for POI ($p=0.04$ and $p=0.03$, respectively). Number of days until initiation of oral diet ($p=0.014$) and number of days until advancement to a solid diet ($p=0.003$) were also significant.

Conclusion: POI is a significant complication in our population. Although further research is warranted, preoperative nutrition counseling may aid in reducing the incidence of POI by targeting weight loss and insulin sensitivity. Early postoperative oral diet may also be effective for reducing POI following CABG.

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LIST OF ABBREVIATIONS

ACS-NSQIP: American College of Surgeons' National Surgical Quality Improvement Program

CABG: Coronary Artery Bypass Graft

CVA: Cerebral Vascular Accident

GI: Gastrointestinal

LVAD: Left-Ventricular Assistive Device

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

POI: Postoperative Ileus

PPOI: Prolonged Postoperative Ileus

BMI: Body Mass Index

CT: Computed Tomography

CHAPTER 1: INTRODUCTION

A CABG is a procedure performed to improve blood flow through the circulatory system in people with coronary heart disease (characterized as a buildup of plaque in the coronary arteries)[1]. CABG is known as the most common cardiac procedure in the United States, with an estimated 395,000 performed annually[2]. Postoperative ileus (POI) is known as the period of intestinal paralysis following surgical procedures leading to multiple postoperative comorbidities, such as: nausea and vomiting, abdominal distension, intolerance of oral diet and delayed passage of flatus and stool[3]. Furthermore, POI has been associated with increased hospital length of stay, increased time to recovery, and increased mortality[3,4].

Although POI is most common following abdominal surgery, it can occur after any surgical procedure. As research is limited in regards to POI following CABG, little is known about its' incidence or associated risk factors for those who have undergone CABG. People with cardiac disease are more likely to manifest nutritional deficiencies and abnormalities compared to the general population, highlighting the importance of preventing postoperative complications, such as POI[5,6]. The gap in knowledge that exists in a population commonly characterized as nutritionally compromised warrants investigation into the incidence of POI following CABG as well as preoperative risk factors to provide a focus for preventative strategies.

The primary objective of this study is to determine the incidence of ileus development in patients post CABG. The secondary aim is to evaluate baseline characteristics associated with development of an ileus post CABG. We hypothesized a significant proportion of the study population will develop an ileus after undergoing CABG and characteristics of participants who develop an ileus post CABG will be significantly different from those who do not develop an ileus.

CHAPTER 2: REVIEW OF THE LITERATURE

CABG - Definition

CABG is performed when atherosclerotic narrowing of the coronary arteries impairs blood supply to coronary circulation through which blood is supplied to the heart[1]. The procedure involves bypassing the narrowed coronary artery or arteries with arteries or veins harvested from elsewhere in the body and grafting them to the coronary arteries[6]. Characteristics commonly found in patients preparing to undergo cardiac surgery have been reported as risk factors for POI, which raises concern on the significance of POI following CABG.

POI – Definition and Incidence

POI is known as the period of intestinal paralysis following a surgical operation, which typically results in increased patient discomfort, lengthened time to recovery, increased postoperative morbidity, increased hospital length of stay and mortality[3,4]. 'Normal' POI is considered obligatory following surgical operations and is thought to resolve with passing of flatus and stool, whereas 'prolonged' POI (PPOI) occurs with the delayed resolution of 'normal' POI and poses a much greater clinical concern[3]. POI lacks a standardized definition and method of diagnosis, as described in the literature below, leading to inconsistent reports of incidence, risk factors and effective prevention and treatment strategies. However, consensus is not lacking in regards to the significance of POI and the importance of aiming to implement strategies to decrease its' occurrence and associated complications.

Further complicating the issue is the lack of consensus regarding the significance of POI versus PPOI. A recent systematic review sought to differentiate between POI and PPOI in order to create consistency between studies. Definitions were proposed to clarify between POI and PPOI as follows: POI is known as the obligatory period of gastrointestinal dysmotility immediately following surgery, which is generally not clinically significant and is resolved with passage of flatus or stool and oral diet tolerance[7]. PPOI may last several days and is much more clinically and pathologically significant. Two or more of the following must occur on or after postoperative day 4 in order to be considered PPOI:

a) Nausea, vomiting

b) Intolerance of oral diet over the preceding 24 hours

c) Absence of flatus over the preceding 24 hours

d) Abdominal distention

e) Radiological evidence of bowel distention without mechanical obstruction

Incidence rates of POI vary greatly in the literature, not only between differing patient populations, but also between populations with similar characteristics. The wide range of reported incidence rates is thought to be largely due to the ambiguous definition and characterization of POI. Without a standardized definition of POI it is challenging to identify reliable risk factors and to compare the effectiveness of various prevention strategies[7]. The vast variety of study outcome parameters, populations and overall study design are also thought to be contributors to the wide range of incidence rates found.

After major abdominal surgery, the most common association to POI, the incidence has been noted to be between 3% and 32%[8]. Vather et al in 2015 focused on identifying risk factors for POI development in 327 patients following elective colorectal surgery and found an incidence of 26.9% in the study population[8]. Vather et al derived their definition of POI from Vather's 2014 systematic review[7] noted above. POI was diagnosed with occurrence of at least 2 of the following 5 criteria:

1. Nausea or vomiting over the preceding 12 hours.
2. Inability to tolerate a solid or semisolid oral diet over the preceding 2 mealtimes.
3. Abdominal distension.
4. Absence of flatus and stool over the preceding 24 hours.
5. Radiologic evidence of ileus on abdominal plain film or CT over the preceding 12 hours.

A study aiming to identify risk factors for POI after radical cystectomy with bilateral lymphadenectomy for bladder cancer characterized POI as the absence of bowel function causing hospitalization beyond the goal of discharge on postoperative day 6[9]. 43 of the 283 study participants (15.2%) developed POI.

Murphy et al characterized POI as a nasogastric tube or NPO (*nil per os* or "nothing by mouth") status on postoperative day 4 or later [as defined by the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) from which data for the study was collected between 2011 and 2012] and found an incidence of 14.0% succeeding elective colectomy[10]. Another study utilized the ACS-NSQIP database; however, data was collected on patients who underwent elective colon resection between 2012 and 2013[11]. Despite data being collected from the same database, POI was defined as no return of bowel function within 7 days of operation. An incidence of 12.7% was found in the study population.

Incidence after resection of colorectal cancer was described as 9.9% by Chapuis et al with POI defined as the presence of abdominal distention in the setting of absence of bowel sounds in patients who experienced nausea or vomiting and failed to pass flatus or stool for more than 3 days postoperatively[12].

Kim et al analyzed POI in patients following urologic laparoscopic surgery (with the exception of radical cystectomy due to the required manipulation of the ileum) and found an incidence of 10.8%[13]. Intolerance of a solid diet up to or after the sixth postoperative day combined with symptoms of GI distress, such as abdominal distension, nausea and vomiting and abdominal imaging consistent with obstructive or paralytic ileus was utilized as the definition for POI in the study.

Demonstrating the variation in incidence and definition of POI between differing surgical populations, Fanning and Hojat found an incidence of 0.85% after gynecologic operations, despite their definition of POI being more liberal than some studies as they defined POI as a delay in hospital length of stay by 1 day or longer due to inadequate oral intake or readmission due to nausea[14]. Furthermore, Lee et al in 2011 analyzed risk factors for POI in patients who underwent orthopedic surgery and discovered an incidence of 2.1%[15]. POI for the orthopedic population was defined as paralytic ileus lasting more than 3 days postoperatively and an association with at least two of the following: nausea and vomiting, inability to tolerate a solid diet for 24 hours and absence of flatus over a 24-hour period.

To our knowledge, no studies have focused specifically on POI following CABG. Rather, studies of cardiac populations have addressed the overarching issue of gastrointestinal (GI) complications as a whole following cardiac surgery, not exclusive to patients who have undergone CABG. Incidence rates of GI complications between 0.29% and 5.5% have been suggested after cardiac surgery, with most reporting an incidence between 1% and 2%[16]. Kurt et al. retrospectively screened 5,720 patients who underwent open-heart surgery from January 1998 to December 2002 for gastrointestinal complications with surgical consequences and discovered an incidence rate of only 0.2%[17]. When considering the relatively low incidence found by Kurt et al, it is important to note the study only included those GI complications, which required surgical intervention, which likely contributed to their low incidence.

A study by Croome et al, which aimed to compare GI complications following CABG surgery with and without use of a cardiopulmonary bypass machine, reported the incidence of GI complications to be 1.49% in the on-pump group and 0.91% in the off-pump group[18]. Of note, POI was the most common GI complication in the on-pump group with an incidence of 0.60%. The study defined GI complications as:

1. Paralytic ileus lasting 4 days of more and either requiring nasogastric suction or causing increase in length of stay (did not include transient ileus).
2. Upper GI bleed presenting with melena or hematemesis and drop of hemoglobin requiring endoscopic diagnosis.
3. Intestinal ischemia confirmed by laparoscopy, endoscopy or autopsy.

4. Acute pancreatitis presenting with abdominal pain and elevated serum amylase levels and positive ultrasound or computed tomography (CT) findings.
5. Acute cholecystitis confirmed during surgery or by endoscopic retrograde cholangiopancreatography.

In 2015, a study conducted at the University of Wisconsin-Madison Hospital and Clinics aimed to determine the effectiveness of a new postoperative bowel management protocol at decreasing the incidence of POI in their institution[19]. The study population consisted of patients who underwent continuous-flow left ventricular assist device implantation. Incidence of POI was 19% in the old regimen group compared to 4% in the new regimen group. POI was characterized with the presence of nausea, vomiting, abdominal distension, abdominal pain, no bowel movement, inability to pass flatus, lack of coordinated peristalsis on clinical examination and abdominal x-ray findings consistent with ileus.

An Australian study that analyzed the incidence of GI complications after cardiac surgery reported a GI complication incidence of 1.1% (61 patients out of 5,832) in the study population[20]. POI was included in the study with an incidence of 0.17% (10 patients developed POI), although it was not stated how POI was diagnosed or defined for the study. Patients who underwent a combined CABG and valve operation arose more frequently in the GI complication group compared to the group without GI complications (23% versus 10%, respectively; $p<0.05$).

Dong et al found an incidence of 1.4% for GI complications and 0.47% for POI in a study involving patients who underwent cardiac surgery with cardiopulmonary bypass[21]. Of the abdominal complications discovered in the study, 9.1% occurred post CABG (n=3). Furthermore, paralytic ileus accounted for 33.3% (n=11) of the total abdominal complications found.

Variation in the definition and incidence of POI is apparent. Although the incidence of GI complications appears to be relatively low in the surgical cardiac population, the reported mortality is significant with reports of mortality ranging from 11% to 72%[16]. The suggested mortality rate highlights the significance of GI complications, no matter how rare.

POI – Clinical Manifestations

Clinical manifestations of POI may include nausea, vomiting, intolerance of oral diet, poor nutritional intake, abdominal pain and distention, absent bowel sounds and delayed passage of flatus or stool[8]. Furthermore, POI has been associated with pulmonary complications, poor wound healing, delayed postoperative mobilization, prolonged hospital length of stay, mortality and increased healthcare costs[22]. Prolonged time to adequate oral intake that results in the setting of POI is suggested to contribute to impaired wound healing and immune function associated with POI[23]. With multiple complications associated with POI, it is apparent that lack of gastric motility and small and large intestine function for a prolonged period of time following surgery may pose a serious threat to patients' nutritional status, recovery time and overall well being.

These complications create a substantial burden on the patient as well as the healthcare institution. A study of 17,876 patients (in which 3,115 or 17.4% developed POI) who underwent colectomy aimed to quantify the impact of POI on hospitalization costs and found patients with POI had significantly increased hospitalization costs compared to those without POI with a mean cost of \$25,089 ± \$35,386 versus \$16,907 ± \$29,320 ($p<0.001$)[23]. The estimated total annual cost of ileus management in the United States has been suggested to be \$1.5 billion[7,24].

POI is most commonly associated with major abdominal surgery, although it can be a complication of any surgical procedure. The mechanism that causes POI may differ between types of surgical procedures, however, the clinical manifestations remain the same and result in the same clinical syndrome[24].

POI – Etiology and Pathophysiology

Typically, during the postoperative period small intestine function returns as early as 4-8 hours up to 24 hours, gastric motility returns within 24-48 hours and function of the colon returns within 48-72 hours[25]. However, colon function is much less predictable and variable compared to the function of the small intestine and stomach[7].

Research is rather inconclusive regarding the etiology and pathophysiology of POI, but the multifactorial nature of POI has been well accepted. Proposed etiologies and pathophysiologic mechanisms of POI include:

a) High catecholamine levels in non-surgical situations have been associated with decreased gastric motility. Therefore, sympathetic hyperactivity generating increased catecholamine levels following surgery has been proposed as a potential pathophysiologic mechanism of POI[22].

b) The inflammatory response to surgery[22] may cause dysmotility due to a threefold mechanism: molecules involved are smooth muscle relaxants, bowel wall edema impairs myotonic contraction and relative intestinal ischemia caused by the inflammatory state or decreased arterial blood flow[7].

c) Opiates used for analgesic purposes may have a negative effect on GI motility when opioid receptors in the GI tract are stimulated[24].

d) Electrolyte disturbances may also contribute to development of POI, with hypokalemia having the strongest association demonstrated by research[7,22].

e) Abnormal neural activity has been associated with POI, however, the exact causal mechanism is not well known at this time[7,22].

f) Non-occlusive mesenteric ischemia or arterial or venous mesenteric thrombosis may be a factor following cardiac surgery[17].

POI – Nutrition Related Treatment Strategies

Benefits of postoperative early oral feeding have received increased recognition in recent years. Da Fonseca et al. studied the effect of early oral nutrition on time of POI resolution following elective colonic surgery. The study prospectively randomized participants (n=50) into two groups: the early feeding group (liquid diet on the first postoperative day, then solid diet within twenty-four hours) and the traditional care group (NPO until presence of first flatus, liquid diet, then solid diet within twenty-four hours)[26]. Results of the study demonstrated statistically significant differences between hospital length of stay (4.0 ± 3.7 days for the early feeding group versus 7.6 ± 8.1 days for the traditional feeding group; p=0.000) and time to first flatus (1.5 ± 0.5 days versus 2.0 ±0.7 days, respectively; p= 0.019). The difference in the overall complication rate between groups was not found to be significant (p=0.480), however, two patients in the traditional feeding group developed POI compared to zero in the early feeding group (no P-value provided). The study concluded early oral nutrition may lead to decreased POI without increasing postsurgical complications.

Fujii et al also aimed to examine the benefits of early postoperative oral feeding by comparing outcomes between those who were advanced to an oral diet on postoperative day 1 versus day 2 after colorectal resection[27]. When compared to the postoperative day 2 group, those in the postoperative day 1 group tolerated a liquid diet sooner (1.2 ± 0.7 versus 2.3 ± 0.6; p<0.001), tolerated a solid diet sooner (2.3 ± 0.8 versus 3.5 ± 0.8; p<0.001), had earlier time to flatus (2.3 ± 0.7 versus 3.1 ± 1.0; p<0.001) and earlier time to defecation (3.2 ± 1.2 versus 4.2 ± 1.4; p<0.001).

A large prospective study on the safety of immediate postoperative feeding to prevent POI after gynecologic procedures also determined early postoperative feeding was safe and effective[14]. All 707 study participants were allowed immediate postoperative oral feeding, with a diet of their choice. The authors attributed their relatively low POI incidence of 1% to their protocol including immediate oral feeding. Of course, lack of a control group limits the reliability of their results.

As demonstrated by the studies outlined above, early postoperative feeding has been generally recognized as safe and feasible, despite limited evidence of significantly reduced time until POI resolution.

Some research has focused on the benefit of postoperative gum chewing. The primary outcome of a meta-analysis, which included only randomized controlled trials conducted after the year 2000, was whether chewing gum would result in decreased POI compared to the control[28]. Although the meta-analysis found a significant reduction in mean time to flatus (mean difference = -6.78 hours; 95% CI -7.64, -5.92; $p<0.01$) and time to first bowel movement (mean difference -8.38 hours, 95% CI -9.52, -7.23; $p<0.01$), the authors concluded the benefits of chewing gum were small and of limited clinical significance. Furthermore, the heterogeneity of studies included in the meta-analysis limited the significance of their results. Of note, none of the studies included were conducted on patients who had undergone cardiac surgery.

A randomized controlled trial by Noblett et al. aimed to analyze the effect of preoperative carbohydrate administration on GI function in 36 patients following elective colorectal surgery[29]. Participants were randomized into 3 groups: preoperative carbohydrate administration, preoperative water administration and preoperative fasting. Results were not significant for either time to first flatus (carbohydrate versus fasting, $p=0.3$; carbohydrate versus water, $p=0.13$) or time to first bowel movement (carbohydrate versus fasting, $p=0.2$; carbohydrate versus water, $p=0.06$) between the three groups.

POI – Other Treatment Strategies

Several treatment options have been investigated, with varying degrees of effectiveness being demonstrated. As a result of inconclusive research, treatment strategies remain experimental in many cases[8]. Increased implementation of minimally invasive surgeries in recent years has been shown to decrease the incidence of POI, however, open versus laparoscopic surgery is not always an option[8]. Methods to decrease the use of opioids, by using non-steroidal anti-inflammatory drugs (NSAIDs) as a replacement, have been shown to accelerate postoperative restoration of GI function following colorectal surgery[30]. The use of NSAIDs may also aid in reducing duration of POI by their anti-inflammatory mechanisms[22], which are believed to contribute to POI. Although some research supports the use of NSAIDs as a potential effective treatment strategy for POI, the use of NSAIDS in patients following cardiac surgery may not be warranted due to their association with adverse cardiovascular events[31].

The most promising treatment approaches have been found to be multimodal therapies, which often involve avoidance of nasogastric tube placement, epidural or regional anesthesia or analgesia, early mobilization and oral intake, frequent use of laxative agents, and use of opioid-sparing medications for pain control[22]. Despite many attempts by researchers to develop strategies to decrease the duration of POI, data is limited to determine the most effective strategies as well as the most effective multimodal strategies[22]. Further limiting the ability to determine the most effective strategies for treating POI, studies using multimodal treatment strategies seem to aim for an overall quicker recovery period and shorter hospital length of stay rather than specifically aiming to shorten the length of time until POI resolution[32]. Larger, randomized controlled trials are still needed to validate such strategies.

POI following CABG – Associated Risk Factors

There is a lack of agreement on predictive factors for POI, regardless of the type of surgery or participant population. Several studies have focused on POI following colorectal surgery and other abdominal related surgeries, and some have focused on groups of gastrointestinal complications in the surgical cardiac population rather than specifically on the development of POI. To our knowledge, research has yet to specifically focus on risk factors for POI following CABG.

A comprehensive review of 35 total studies, which focused on GI complications following CABG, found the greatest frequency of the following preoperative risk factors in the literature:

- From univariate analysis: age greater than seventy (n=10), low cardiac output (n=7), emergent surgery (n=7), chronic renal failure (n=7), chronic obstructive pulmonary disease (n=3), combined operations (n=5), preoperative use of an intraaortic balloon pump (n=5), reoperative surgery (n=4), valve operations (n=5) and female sex (n=4)[16].
- From multivariate analysis: age greater than seventy (n=4), low cardiac output (n=3), peripheral vascular disease (n=3), reoperation (n=3) and chronic renal failure (n=2)[16].

POI – Associated Risk Factors in Non-Cardiac Populations

As shown in Table I below, several varying preoperative risk factors have been identified by previous studies in non-cardiac cohorts. Although helpful, many of the identified risk factors are either difficult to attain (i.e. operation time) or are non-modifiable (i.e. age). In addition, since the studies listed involved non-cardiac surgeries, the acknowledged risk factors may not be accurately predictive of POI following CABG.

Table I. Reported Preoperative Risk Factors Associated with POI

Study	Identified Risk Factors	OR	95% CI	P-Value
Badami et al [19]	Serum Creatinine			0.05
Murphy et al [10]	Age*			
	53-63			0.013
	64-73			0.01
	74+			<0.001
	Male Gender			<0.001
	Asian Race			0.014
	BMI			
	Overweight			0.006
	Obese			0.001
	Diagnosis			

	Crohn's Disease			0.009
	Volvulus			0.001
	No Oral Antibiotics			0.001
	Smoking			0.027
	Chemotherapy			<0.001
	Ascites			0.027
	Sepsis			<0.001
	Open Surgical Approach			<0.001
	Operation Time**			
	118-159			0.001
	160-220			0.015
	221+			<0.001
Chapuis et al [12]	Male Sex	1.4	1.1-1.7	
	Respiratory Comorbidity	3.9	3.1-4.8	
	Peripheral Vascular Disease	5.5	3.9-7.8	
	Urgent Resection	3.6	2.5-5.2	
Moghadamyeghaneh et al [11]	Age			<0.01
	Male Gender			<0.01
	COPD			0.02
	Disseminated Cancer			0.01
	Minimally Invasive Approaches			<0.01
	Crohn's Disease			0.02
	Chronic Constipation			<0.01
	Serum Albumin Level			<0.01
Vather et al [8]	Male Gender	3.01	1.25-7.27	0.014
Svatek et al [9]	Age	1.09	1.02-1.16	0.008
	BMI±	1.09	1.03-1.17	0.007
Lee et al [15]	Chronic Constipation±±	35.23	7.72-160.82	<0.001
Kronberg et al [33]	Age > 60	1.89	0.89-4.02	0.1
	Narcotic Use	3.17	1.21-8.34	0.019
	Previous Abdominal Operation	2.41	1.14-5.12	0.022
Kiely et al [34]	GERD	4.864	1.104-21.426	0.037

*<53 years
**<117 minutes
±Significant association between BMI 18.5-24.9 kg/m^2 and BMI 30.0-34.9 kg/m^2
±±Only factor entered into multiple logistic regression

Characteristics of the Population

It is highly agreed upon by research that patients with heart disease who are scheduled for cardiac surgery or who have previously had cardiac surgery are more likely to manifest greater nutritional deficits compared to the general population[5,6]. Oftentimes cardiac surgery is performed under emergent conditions after diagnostic testing,[6] which has been associated with POI in non-cardiac populations. Unfortunately, in the case of emergent surgery nutrition intervention may not be feasible until after surgery, making early post-surgical intervention in a nutritionally compromised population vital.

Obesity has been accepted as an independent risk factor for cardiovascular disease, therefore, its' prevalence is relatively high in the population with cardiovascular disease[5,35]. Furthermore, overweight and obesity have been acknowledged as risk factors for poor surgical outcomes[5]. Increased BMI is also associated with systemic inflammation and insulin resistance, both of which have been associated with POI[5]. Sedentary lifestyles, undiagnosed diabetes mellitus and diets rich in fat and sugar are also common among cardiac surgery candidates[36]. The high prevalence of characteristics proposed as risk factors and etiologies of POI in cardiac surgery candidates poses a concern for POI following CABG.

A high proportion of patients in the study population analyzed by Racca et al. presented with low albumin levels[36]. Hypoalbuminemia upon admission is well known to be a risk factor for many postsurgical complications, including: wound infections, extubation failure, number and extent of postoperative complications and extended intensive care and hospital length of stay[5,36]. Albumin levels less than 3.5 g/dL have been linked to increased complications with a greater number of negative outcomes occurring with albumin levels less than 2.5 g/dL[6]. Serum albumin has also been reported to be associated with POI[11].

POI following CABG – Impact on Nutritional Status

Effective prevention and treatment of POI is of importance to nutritional care as it may contribute to significant postoperative complications, such as: increased mortality, prolonged hospital length of stay, increased catabolism and delayed initiation of enteral and oral nutrition, ultimately leading to further decline in nutritional status[22]. With lack of consensus on effective treatment strategies for POI, a need exists to further investigate reliable and modifiable preoperative risk factors, specifically for those undergoing CABG. Being able to recognize risk factors that may increase the likelihood of POI following CABG could aid in developing POI prevention strategies and early diagnosis and treatment. Since CABG procedures are often performed in emergent situations, it is even more vital to implement early diagnosis and treatment strategies to prevent further nutritional decline in a population already characterized by poor nutritional status.

CHAPTER 3: METHODS

Participants and Study Design

The institutional review board at the University of Nebraska Medical Center in Omaha, Nebraska approved this study. Data was retrospectively collected from 100 inpatient electronic medical records of all patients who underwent CABG between October 2014 and February 2015 at Nebraska Medicine. All participants met the following inclusion criteria: legal adult aged nineteen years or older and CABG surgery.

Electronic medical records were assessed for demographic and clinical data throughout the duration of each participants' hospital admission. The primary outcome of the study was the occurrence of POI. Characteristics of participants who did not develop POI were quantified in comparison to those who did develop POI.

Data Collection

Demographic data collected included: age, sex, ethnicity and mortality.

Clinical data collected included: principal problem, length of stay, readmission within thirty days post-discharge, number of vessels bypassed, BMI, response to 24-hour nurse screen, smoking status, presence of POI and postoperative time of ileus diagnosis.

Data related to participants' past medical history included: comorbidities (renal disease, diabetes, respiratory disease, other heart disease, cancer and hyperlipidemia), previous abdominal surgery and previous POI.

Postoperative time to oral diet initiation, type of initial diet and time to solid diet were diet related characteristics recorded.

Hemoglobin A1c, highest operative blood glucose, highest preoperative blood glucose and preoperative albumin lab values were recorded, if available. Hemoglobin A1c was not collected if lab was drawn greater than 1 month prior to CABG. Highest preoperative blood glucose was not collected if recorded greater than 1 day prior to CABG. Preoperative albumin was not collected if the lab value was determined greater than three days prior to CABG.

The presence of POI was determined based on results from CT of the abdomen and pelvis as read by a radiologist.

Data Analysis

Statistical analysis was performed using SPSS for Mac (version 24). Quantitative methods were used to compare patient characteristics of those who did not develop an ileus post CABG and those who did. Descriptive statistics were displayed via charts and figures for all variables to analyze results.

Continuous variables were described using means ± standard deviations. Categorical variables were displayed as frequencies and percentages. The Mann-Whitney U test was used for comparison of means for nonparametric continuous variables. The Chi-square test was used for comparison of means for nonparametric categorical variables. Nonparametric methods were used for comparison of means due to the small sample size of the group of participants who did develop an ileus. All variables, which were significant or near significant ($p < 0.150$) on comparison of means, were entered into univariate logistic regression to determine predictors of POI. The cutoff value for inclusion in univariate logistic regression was chosen based on similar studies[8,9,33]. A p-value of <0.05 was considered statistically significant for all other tests and results.

CHAPTER 4: RESULTS

Preoperative Characteristics

Of the 100 study participants who underwent CABG, 15 developed POI (15%). Table II displays participant characteristics at baseline. Statistically significant results ($p<0.05$) were not found for age, sex, ethnicity or smoking status. Of the multiple medical comorbidities examined, preexisting cardiac disease was the only condition found to be borderline statistically significant ($p=0.06$) between the two groups. Other baseline characteristics that were not found to be statistically significant include: BMI, hemoglobin A1c, highest preoperative blood glucose, highest operative blood glucose and preoperative albumin.

Table II. *Comparison of Means for Baseline Characteristics*

Characteristic	*Non-POI (n=85)*	*POI (n=15)*	*All (n=100)*	*P-Value*
Age (*y*)	63.0 ± 10.0	67.0 ± 13.0	64.0 ± 10.8	0.133
Sex, *n (%)*				1.000
Male	68 *(85)*	12 *(15)*	80	
Female	17 *(85)*	3 *(15)*	20	
Ethnicity, *n (%)*				0.427
Caucasian	73 *(86.9)*	11 *(13.1)*	84	
Hispanic	3 *(60)*	2 *(40)*	5	
African American	6 *(75)*	2 *(25)*	8	
Asian	2 *(100)*	0 *(0)*	2	
Pacific Islander	1 *(100)*	0 *(0)*	1	
Smoking Status, *n (%)*				0.241
Never	28 *(84.8)*	5 *(15.2)*	33	
Former	38 *(90.5)*	4 *(9.5)*	42	
Current	18 *(75)*	6 *(25)*	24	
Medical Comorbidity, *n (%)*				
Previous Abdominal Surgery	4 *(66.7)*	2 *(33.3)*	6	0.195
Previous POI	2 *(100)*	0 *(0)*	2	0.548
Cardiac Disease*	52 *(80)*	13 *(20)*	65	0.056
Hypertension	71 *(83.5)*	14 *(16.5)*	85	0.327
Hyperlipidemia	56 *(87.5)*	8 *(12.5)*	64	0.351

Peripheral Vascular Disease	18 *(85.7)*	3 *(14.3)*	21	0.918
Cerebral Vascular Accident	9 *(69.2)*	4 *(30.8)*	13	0.088
Respiratory	20 *(76.9)*	6 *(23.1)*	26	0.180
Chronic Kidney Disease	11 *(78.6)*	3 *(21.4)*	14	0.468
Diabetes	35 *(79.5)*	9 *(20.5)*	44	0.176
Cancer	8 *(72.7)*	3 *(27.3)*	11	0.227
BMI (*kg/m²)*	30.9 ± 9.4	33.0 ± 13.4	31.4 ± 9.45	0.113
Hemoglobin A1c (*%*)	6.1 ± 1.0 (n=55)	7.0 ± 3.0 (n=14)	6.2 ± 2.0	0.194
Highest Preoperative BG (*mg/dl*)	110 ± 36.5	140.0 ± 98.0	111.5 ± 43.3	0.094
Highest Operative BG (*mg/dl*)	160 ± 57.0 (n=75)	158.5 ± 34.0 (n=14)	160.0 ± 55.0	0.689
Preoperative Albumin (*mg/L*)	3.3 ± 0.7 (n=45)	3.5 ± 0.8 (n=11)	3.4 ± 0.7	0.495
Number of Vessels Bypassed				0.409
One	1 *(50)*	1 *(50)*	2	
Two	14 *(100)*	0 *(0)*	14	
Three	35 *(81.4)*	8 *(18.6)*	43	
Four	27 *(84.4)*	5 *(15.6)*	32	
Five	7 *(87.5)*	1 *(12.5)*	8	
Six	1 *(100)*	0 *(0)*	1	

*Other than cardiovascular diseases; included congestive heart failure, ischemic heart disease, atrial fibrillation and aortic valve insufficiency

Multiple logistic regression analysis for baseline characteristics found to be statistically significant upon comparison of means (p<0.150 for inclusion in the model) is shown in Table III. Preoperative characteristics below the cutoff for logistic regression included: age, BMI, history of CVA, cardiac disease and highest preoperative blood glucose. All parameters were entered into separate regression models. Of the variables analyzed on logistic regression, BMI (OR 1.077, 95% CI 1.00-1.156 [per kg/m^2 unit change]) and preoperative blood glucose (OR 1.011, 95% CI 1.001-1.020 [per mg/dl unit change]) were found to be risk factors for development of POI following CABG (p=0.038 and p=0.026, respectively).

Table III. *Multiple Logistic Regression for Subject Characteristics*

Characteristic	OR	95% CI	P-Value
Age (year)	1.049	0.99—1.12	0.130
BMI (per unit increase)	1.077	1.00—1.156	0.038
History of CVA (yes/no)	3.071	0.807—11.689	0.100
History of Cardiac Disease (yes/no)	4.125	0.874—19.460	0.073
Preoperative BG (per mg/dl unit increase)	1.011	1.001—1.020	0.026

Postoperative Variables

Postoperative nutrition-related practices were also compared between the two groups and results are exhibited in Table IV. The Mann-Whitney U test was used for nonparametric continuous variables and the Chi-square test was used for nonparametric categorical variables. Statistical significance was found for the number of days until initiation of oral diet (p=0.024), type of initial diet ordered (p=0.001) and number of days until advancement to a solid diet (p=0.009). The postoperative outcomes of readmission within 30 days post-discharge and mortality were not statistically significant between the two groups.

Table IV. *Comparison of Means for Postoperative Variables*

Characteristic	***Non-POI (n=85)***	***POI (n=15)***	***All (n=100)***	***P-Value***
Initiation of Oral Diet (*Days*)	1.0 ± 1.0 (n=84)	1.0 ± 1.0	1.0 ± 1.0	0.024
Type of Initial Diet, *n (%)*				0.001
Clear Liquid	82 (87.2)	12 (12.8)	94	
General	1 (100)	0 (0)	1	
Mechanical Soft	0 (0)	2 (100)	2	
Cardiac	0 (0)	1 (100)	1	
Diet not Advanced	2 (100)	0 (0)	2	
Time to Solid Diet (*Days*)	2.0 ± 0.0	2.0 ± 2.0	2.0 ± 1.0	0.009
Readmission 30 Days Post-Discharge, *n (%)*	15 (93.8)	1 (6.2)	16	0.285
Mortality, *n (%)*	6 (75)	2 (25)	8	0.409

Logistic regression analysis for postoperative practices found to be statistically significant upon comparison of means is shown in Table V. Although statistical significance did not persist on logistic regression for the type of initial diet ordered (p=1.000), the number of days until initiation of oral diet (OR 2.633, 95% CI 1.212-5.721; p=0.014) and the numbers of days until advancement to a solid diet (OR 2.295, 95% CI 1.335-3.944; p=0.003) did demonstrate statistical significance.

Table V. *Multiple Logistic Regression for Postoperative Variables*

Characteristic	OR	95% CI	P-Value
Initiation of Oral Diet (per day)	2.633	1.212—5.721	0.014
Type of Initial Diet			1.000
Time to Solid Diet (per day)	2.295	1.335—3.944	0.003

Of the participants who developed POI, as determined by CT of the abdomen and pelvis, 86% were diagnosed by day three following CABG (Figure I).

Figure I. *Number of Post-Operative Days Until POI Diagnosis*

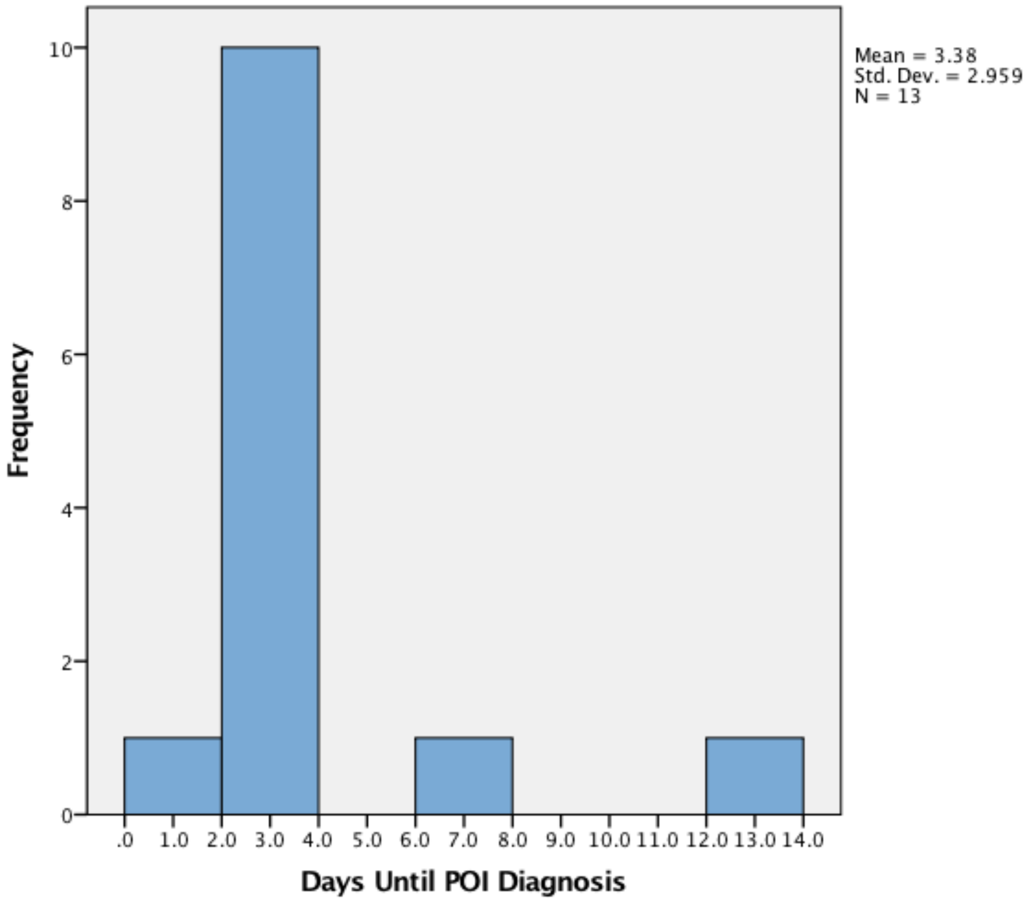
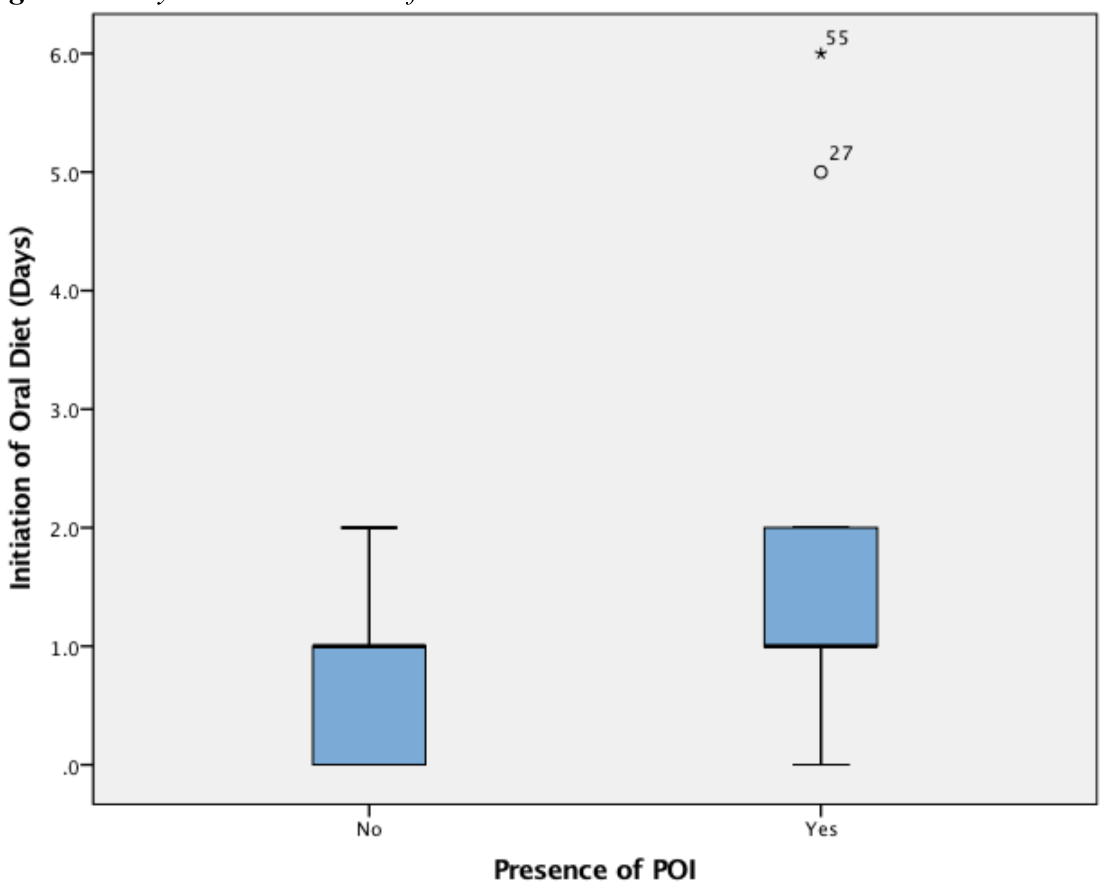


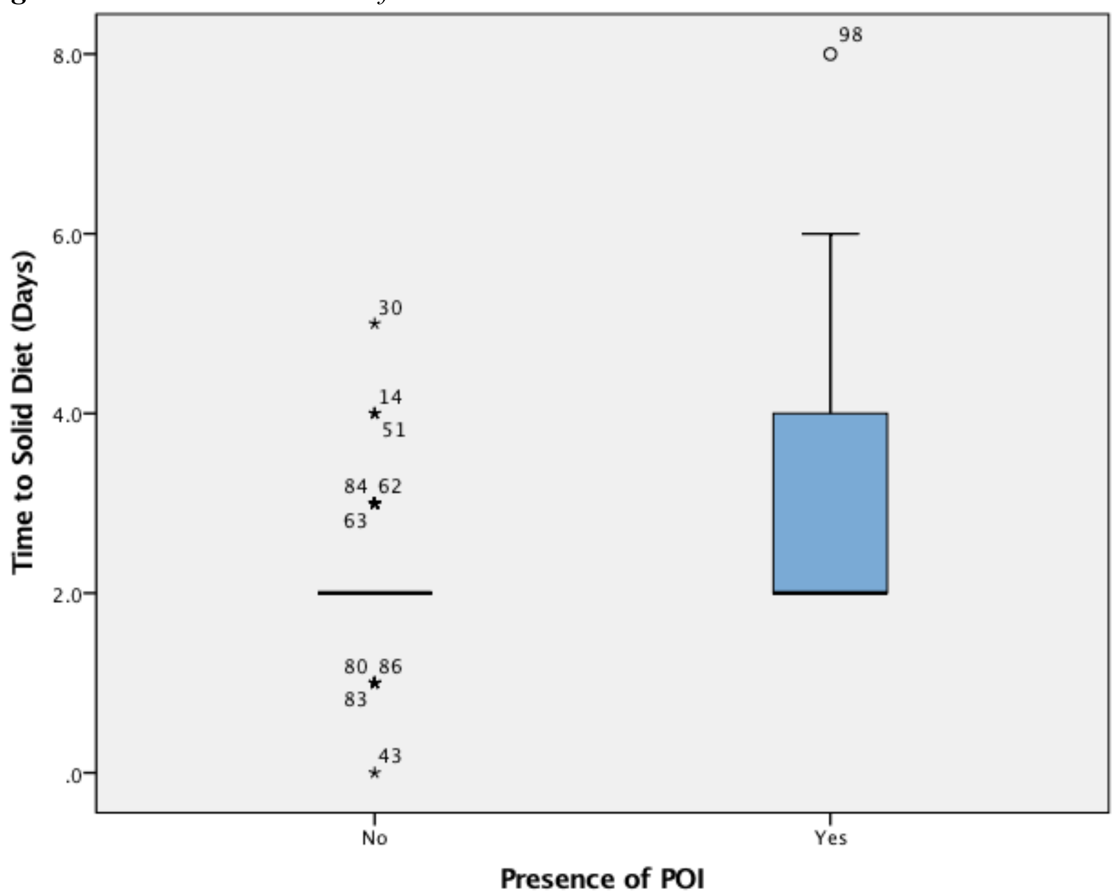
Figure II compares the difference in time to initiation of oral diet between the two groups. By postoperative day one, oral diet was initiated for 90% of participants who did not develop POI compared to only 60% for those did develop POI. Initiation of oral diet for all participants who developed POI did not occur until postoperative day 6, compared to postoperative day 2 for those who did not develop an ileus.

Figure II. *Days Until Initiation of Oral Diet*



Although 85% of participants who developed POI did have an oral diet initiated by postoperative day 2 (Figure II), only 55% of participants were advanced to a solid diet by postoperative day 2 compared to nearly 80% for those without POI (Figure III). Greater than 90% of participants without POI were advanced to a solid diet by day 3, whereas the percent of participants advanced to a solid diet who did develop POI did not reach greater than 90% until postoperative day 6.

Figure III. *Time to Initiation of Solid Diet*



CHAPTER 5: DISCUSSION

POI Incidence

The incidence of POI in the study population was 15%, much higher than previously reported by studies that focused on GI complications following cardiac surgery. A study by Croome et al, reported the incidence of GI complications to be 1.49% in the on-pump group and 0.91% in the off-pump group following CABG[18]. Although the overall incidence of GI complications in the study by Croome et al was substantially lower compared to the present study, POI was the most common GI complication in the on-pump group with an incidence of 0.60%. Ileus was defined in the study as the lack of bowel function lasting 4 days or more and either requiring nasogastric suction or causing increased length of stay (did not include transient ileus). Not diagnosing POI until postoperative day 4 likely contributed to their lower incidence compared to the present study as nearly 50% of our participants were diagnosed on postoperative day 2.

In 2006, Kurt et al found an incidence of 0.2% for GI complications following open-heart surgery[17]. However, participants were not determined to have a GI complication unless surgical intervention was needed, which likely led to their low incidence. Additionally, of the 12 participants who developed a GI complication only one was identified as an ileus.

In 2015, a study conducted at the University of Wisconsin-Madison Hospital and Clinics aimed to determine the effectiveness of a new postoperative bowel management protocol at decreasing the incidence of POI in their institution[19]. The study population consisted of patients who underwent continuous-flow left ventricular assist device (LVAD) implantation. Incidence of POI was 19% in the old regimen group compared to 4% in the new regimen group. POI was characterized with the presence of nausea, vomiting, abdominal distension, abdominal pain, no bowel movement, inability to pass flatus, lack of coordinated peristalsis on clinical examination and abdominal x-ray findings consistent with ileus. Although Badami et al diagnosed ileus when all the above criteria were met, unlike our study, the use of x-ray imaging to diagnose ileus may have led to a similar incidence of POI, in the old regimen group, to our findings.

An Australian study that analyzed the incidence of GI complications after cardiac surgery reported an incidence for POI of 0.17% (n=10), although it was not stated how POI was diagnosed or defined in the study[20]. While the incidence of POI found by Viana et al was also lower than found in our study, patients who underwent combined CABG and valve operations arose more frequently in the GI complication group compared to the group without GI complications (23% versus 10%, respectively; $p< 0.05$).

Dong et al found an incidence of 0.47% for POI in a study involving patients who underwent cardiac surgery with cardiopulmonary bypass[21]. 9.1% of the abdominal complications discovered in the study occurred post CABG (n=3). Furthermore, POI accounted for 33.3% (n=11) of the total abdominal complications found.

The method of diagnosis in our study may have contributed to the considerably higher incidence compared to previously reported incidences in the cardiac population. The use of imaging alone to diagnose POI appears to be unique since other studies that used imaging for criteria to diagnose POI required additional factors (i.e. nausea and vomiting) to make an official diagnosis. Study design may have also contributed to the difference in incidence as no other studies have focused specifically on POI following CABG.

Reported incidence rates of POI greatly vary in non-cardiovascular populations as well and seem to be highly dependent on the type of operation performed. Vather et al in 2015 reported a rate of 26.9% in their population consisting of patients who underwent elective colorectal surgery[8]. POI as defined by Vather et al was the occurrence of at least 2 of the following 5 criteria:

1. Nausea or vomiting over the preceding 12 hours.
2. Inability to tolerate a solid or semisolid oral diet over the preceding 2 mealtimes.
3. Abdominal distension.

4. Absence of flatus and stool over the preceding 24 hours.
5. Radiologic evidence of ileus on abdominal plain film or CT over the preceding 12 hours.

Fanning and Hojat found an incidence of 0.85% after gynecologic operations, despite their definition of POI being more liberal than some studies as they defined POI as a delay in hospital length of stay by 1 day or longer due to inadequate oral intake or readmission due to nausea[14].

Murphy et al in 2015 characterized POI as a nasogastric tube or NPO status on postoperative day 4 or later (as defined by the ACS-NSQIP from which data for the study was collected between 2011 and 2012) and found an incidence of 14.0% succeeding elective colectomy[10]. Another study utilized the ACS-NSQIP database, however, data was collected on patients who underwent elective colon resection between 2012 and 2013[11]. Despite data being collected from the same database, POI was defined as no return of bowel function within 7 days of operation. An incidence of 12.7% was found in the study population, despite POI not being diagnosed until postoperative day 7.

Kim et al analyzed POI in patients following urologic laparoscopic surgery (with the exception of radical cystectomy due to the required manipulation of the ileum) and found an incidence of 10.8%[13]. Intolerance of a solid diet up to or after the sixth postoperative day combined with symptoms of GI distress, such as abdominal distension, nausea and vomiting, and abdominal imaging consistent with obstructive or paralytic ileus was utilized as the definition for POI in the study.

Incidence after resection of colorectal cancer was described as 9.9% by Chapuis et al with POI defined as the presence of abdominal distention in the setting of absence of bowel sounds in patients who experienced nausea or vomiting and failed to pass flatus or stool for more than 3 days postoperatively[12].

Further demonstrating the vast variation in incidence of POI between surgical populations, Lee et al in 2011 analyzed risk factors for POI in patients who underwent orthopedic surgery and discovered an incidence of 2.1%[15]. POI for the orthopedic population was defined as paralytic ileus lasting more than 3 days postoperatively and an association with at least two of the following: nausea and vomiting, inability to tolerate a solid diet for 24 hours and absence of flatus over a 24-hour period.

Although incidence found in the present study is greater than previously found in cardiac populations, it is comparable to rates found in non-cardiac surgical populations (ranging from 9.9% to 26.9% in the literature noted above). Reported differences in the incidence of POI may be attributed to multiple factors.

Lack of consistency in the definition of POI and the method used for diagnosis of POI has been highly criticized. A majority of participants who were diagnosed with POI (84%) were diagnosed by postoperative day 3, unlike previous studies who did not consider POI diagnosis until postoperative day 4 or later[10-12,18]. To the best of our knowledge no other studies have utilized CT imaging alone to make a definitive diagnosis of POI. Identifying POI via CT of the abdomen and pelvis may have led to earlier diagnosis in the study population, as no other criteria were required POI diagnosis.

We know people with cardiac comorbidities, specifically those undergoing cardiac surgery, are more susceptible to greater nutritional deficiencies and abnormalities, such as higher BMI and insulin resistance, compared to the general population[5,6]. It is possible the study population manifested greater preoperative nutrition abnormalities than previously studied populations, potentially contributing to a higher incidence rate as well. While this notion cannot be proven, nutrition abnormalities have been associated with POI, such as: increased BMI[8,10], decreased serum albumin[11] and now increased blood glucose as demonstrated by the present study. Differences in non-nutrition related mechanisms and practices and their effect on the occurrence of POI cannot be ruled out.

Baseline Characteristics Associated with POI

Baseline characteristics found to be statistically significant or near statistically significant upon comparison of means were consistent with those previously defined in the literature, however, in the present study many of the characteristics' statistical significance did not persist upon completion of univariate logistic regression. BMI and preoperative blood glucose were the two baseline characteristics demonstrating statistical significance on univariate logistic regression.

The inflammatory response to surgery has previously been proposed as a potential etiology for the development of POI[22]. Since both obesity and insulin resistance have been associated with chronic inflammation[37] and affecting the postoperative inflammatory response, it is not surprising they may potentially have a significant impact on development of POI. Energy imbalance and excess lipid storage, which ultimately lead to obesity, cause dysfunction of a cell's endoplasmic reticulum leading to an increase of inflammatory mediators[37]. Furthermore, stress that occurs on the function of the endoplasmic reticulum as a result of energy imbalance and excess adipose tissue has been suggested to stimulate insulin resistance[37].

Firm evidence is lacking in regards to the association between BMI and POI in surgical cardiac populations. As described below, some studies lack detail regarding BMI in their study while others excluded BMI in their analysis altogether[21]. BMI was not found to be associated with GI complications following cardiac surgery in the study by Viana et al[20]. It is difficult to make a conclusion as to why BMI may have been insignificant in the study compared to similar studies as neither the mean BMI nor the exact significance level were reported. Badami et al did not include BMI in their analysis, however, they did include body surface area (BSA)[19]. Although BSA does not precisely correlate with BMI, the average BSA (indicative of a normal BMI) is suggested to be 1.7m^2 (1.6m^2 for women and 1.9m^2 for men)[38]. Badami et al found a mean BSA of 2.08m^2 ± 0.18 for those who developed POI and 2.05m^2 ± 0.2 for those who did not develop POI, indicating the study population had a higher than normal BSA. No significant difference in BSA was found between patients with and without POI following LVAD implantation (p=0.68), however, it is important to take into the consideration the narrow range in BSA for the total study population.

Literature seems to demonstrate a stronger association between POI and BMI in non-cardiac surgical populations. Murphy et al, who aimed to identify risk factors for developing POI after a colectomy, discovered 13 independent risk factors for POI with BMI being one of the strongest risk factors[10]. Overweight (BMI 25.0 – 29.9 kg/m^2) and Obesity (BMI > 30 kg/m^2) were positively correlated with the development of POI in the study (p=0.006, OR 1.25, 95% CI 1.07-1.47 and p=0.001, OR 1.32, 95% CI 1.12-1.56, respectively). Vather et al also found an association between BMI and development of POI after elective colorectal surgery (p=0.005), however, significance was only found on univariate analysis and did not persist upon logistic regression, and was therefore not used for their risk stratification system[8]. Interestingly, the mean BMI in the population studied by Vather et al was lower than that of our study (BMI 28.0 ± 7 versus 33.0 ± 13.4 for the POI groups and BMI 25.6 ± 6 versus 30.9 ± 9.4 for the non-POI groups, respectively), however, significance was still found for increasing BMI despite not having an overwhelmingly obese population. Svatek et al also found statistical significance between POI and BMI in their study involving 283 patients who underwent radical cystectomy[9]. POI developed in 10.6% of normal weight patients, 11.8% of overweight patients, 22.2% of patients with class I obesity and 30.3% of patients with class II-III obesity (BMI ≥ 35.0 kg/m^2) (p=0.014). There was not a significant difference in the presence of POI between normal weight and overweight participants. After adjusting for demographic and clinical variables on multiple logistic regression, BMI (analyzed as a continuous variable) was determined to be an independent risk factor for POI (OR 1.09, 95% CI 1.03-1.17; p=0.007) in the study population. A study by Bokey et al, which aimed to assess the association between obesity and postoperative complications following resection of rectal cancer, classified 37% of their study participants (n=255) as obese (BMI >30 kg/m^2)[39]. Although there was not a significant difference in the number of postoperative complications between obese and non-obese patients, there was a significant difference for the presence of POI between the two groups (18% versus 8%, respectively, OR 2.7; p=0.011) as well as open versus laparoscopic operations (16% versus 4%, respectively, OR 4.29; p=0.004). Upon logistic regression, the association of BMI and POI did not persist after adjusting for operative access (OR = 2.2, 95% CI 0.99-5.00; p=0.051), whereas the association between open operations did persist after adjusting for BMI (OR 3.7, 95% CI 1.2-11.1; p=0.020). Of importance, after adjusting for operative access, those who were obese were still found to be up to 5 times more likely to develop POI than those who were not obese, and at the least, only 0.01 times less likely to develop POI. In addition, 32.3% of obese participants developed POI compared to 7.6% of non-obese participants (p= 0.01) in a study involving those who underwent laparoscopic colorectal surgery, where open techniques were excluded from the study[40].

To our knowledge, the only study that found a lower BMI to be associated with POI was Lee et al, who had a cohort of patients who underwent orthopedic surgery[15]. Mean BMI in the non-POI group was 24.1 $kg/m^2 \pm 3.7$ compared to 21.8 $kg/m^2 \pm 5.1$ for the POI group (p=0.025). Multiple factors could have contributed to the contradictory results found by Lee et al. As studies on POI following orthopedic surgery are limited, differences in the baseline characteristics of the cohort may be a major contributor to their differing results. For example, the mean BMI for both groups was much lower than typically found in the cardiac population, limiting the ability for our study to find significant results in relation to decreasing BMI.

While a number of studies discovered a positive association between POI and BMI, a few studies did not find any association[11,13,20, 33,34]. The lack of association between POI and BMI may be attributed to several factors, such as: differences in operation types/operative techniques (i.e. open versus laparoscopic surgeries), differences in baseline characteristics between the various surgical populations, discrepancies in the definition of POI used, and the potential of false-positive results.

Moghadamyeghaneh et al included the presence of obesity in their analysis, however, no significance was determined (p=0.18, OR 1.08, 95% CI 0.96-1.20)[11]. Not distinguishing overweight (BMI 25.0-29.9 kg/m^2) from normal weight (BMI 18.5-24.9 kg/m^2) in their analysis may have affected the level of significance found by Moghadamyeghaneh et al, as overweight has been found to be associated with POI in studies described above. The cohort studied by Kim et al encompassed a narrow range in BMI (24.3 kg/m^2 ± 3.6), which limited the likelihood of finding a significant difference between the two groups (BMI 24.3 kg/m^2 ± 3.7 in the non-POI group and BMI 25.0 kg/m^2 ± 2.8 in the POI group, p=0.309). Chapuis et al and Dong et al, were unable to investigate the association between POI and BMI in their respective studies.

The association between BMI and the development of POI between our study and previous research appears to be inconclusive. The wide range of BMI characterized by our population (mean 31.4 kg/m^2 ± 9.45) allowed for a more reliable evaluation of BMI between groups compared to populations with little variation in BMI. Due to limited previous research specific to preoperative risk factors for POI following CABG, it is difficult to compare the results of our study with similar studies on the cardiac population.

Diabetes mellitus was not found to be associated with POI in our study, consistent with research results previously reported[8,10-12,19-21]. To the best of our knowledge no other studies have investigated the association between blood glucose levels prior to or during a surgical operation and development of POI. Furthermore, no studies to our knowledge have examined the association between hemoglobin A1c levels and POI. Although our study did not discover a significant association between hemoglobin A1c and POI, it is important to note values were missing for 31 of our 100 study participants, which likely limited the likelihood of finding statistical significance. As higher preoperative blood glucose levels were positively associated with the development of POI in our study, despite no significance found for diabetes mellitus, the question is raised regarding what impact controlled versus uncontrolled diabetes mellitus has on the probability of developing POI. An association between uncontrolled diabetes mellitus and POI is supported by our results, however, further investigation is needed.

Postoperative Characteristics

Statistical significance was found between POI and non-POI groups for the number of postoperative days until oral diet initiation, supporting the importance of early postoperative diet advancement. 30% less participants in the POI group were advanced to an oral diet by postoperative day 1 compared to the non-POI group ($p=0.014$). A majority of participants were advanced to a clear liquid diet initially, but there was not found to be a significant difference between those who were advanced to a solid diet initially and those who were advanced to a clear liquid diet. Although it is unknown what exactly participants consumed or how much they consumed on the first day of being advanced from NPO to an oral diet, in our study it appears there was a beneficial effect of stimulating the GI tract via oral intake by postoperative day 1, regardless of type of food or fluid consumed.

A study by Fujii et al aimed to examine the benefits of early postoperative oral feeding by comparing outcomes between those who were advanced to an oral diet on postoperative day 1 versus day 2 after colorectal resection[27]. When compared to the postoperative day 2 group, those in the postoperative day 1 group tolerated a liquid diet sooner (1.2 ± 0.7 versus 2.3 ± 0.6; $p<0.001$), tolerated a solid diet sooner (2.3 ± 0.8 versus 3.5 ± 0.8; $p<0.001$), had earlier time to flatus (2.3 ± 0.7 versus 3.1 ± 1.0; $p<0.001$) and earlier time to defecation (3.2 ± 1.2 versus 4.2 ± 1.4; $p<0.001$). Although there were no statistical differences found for any postoperative complications, including POI, the study concluded early oral feeding was safe and feasible.

At an institution in Korea, all patients included in the study were advanced to a clear liquid diet on postoperative day 1 and progressed to a solid diet as tolerated[15]. Since diet advancement was constant for the entire study population, the effect of early postoperative diet advancement on POI could not be analyzed, but it should be noted the study did find a relatively low incidence rate (2.1%) for their population. However, the study was conducted on patients who underwent orthopedic surgery in which the incidence has been suggested to range from 0.3% to 5.6%, depending on the type and location of surgery[41-44]. The extent to which early diet advancement potentially contributed to their incidence remains unknown.

Kim et al also included a consistent post-op diet progression regimen and was as follows: NPO status until passage of flatus was observed or until active bowel sounds were heard after which consumption of water was allowed followed by progression to soft then regular food as tolerated[13]. An incidence of 10.8% was found for the group of participants who underwent urologic laparoscopic surgery, even with POI not being diagnosed until postoperative day 6 at the earliest per their definition of POI and all participants undergoing laparoscopic surgery which has been associated with decreased incidence of POI. Data was not recorded for the number of days until ingestion of water was allowed or until participants were allowed solid food, however, it is likely some participants remained NPO later than postoperative day 1. Similar to Lee et al, postoperative care for those included in the study by Kronberg et al were allowed ice chips and popsicles immediately following surgery, clear liquids on postoperative day 1 followed by advancement to a solid diet as tolerated[33]. Despite early ingestion of clear liquids, their incidence (10.2%) was more similar to that found by Kim et al, however, their population consisted of patients who underwent colorectal surgery, which has been suggested to result in the highest incidence rates when compared to other surgeries[15]. Badami et al compared an old bowel management protocol (OBMP) to a new bowel management protocol (NBMP) where diet was advanced per patient's discretion for the OBMP compared to diet being advanced to clear liquids following extubation until the first bowel movement, then a full liquid diet until the second bowel movement followed by a regular diet for the NBMP. When diet was advanced to clear liquids following extubation (NBMP) the incidence of POI was significantly reduced from 19% in the OBMP group to 4% in the NBMP group. Since differences in administration of bowel medications and enemas also existed between the OBMP and NBMP and the lack of knowledge regarding oral intakes in the OBMP group, it is difficult to determine the impact timing of diet advancement between groups had on the occurrence of POI, however, it can be concluded a harmful effect did not exist.

Due to the retrospective nature of our study, it remains unknown as to why some participants were not advanced to a clear liquid diet by postoperative day 1. It cannot be ruled out that practitioners may have withheld an oral diet in the setting of a patient manifesting signs and symptoms of POI early on in the postoperative period or that diet was withheld until the passage of flatus or presence of bowel sounds. Differences in postoperative practices between practitioners within our institution may have also contributed to the inconsistency in the time to diet advancement.

It is apparent further studies aiming to determine the association between early postoperative diet advancement and its' effect on the development of POI are needed. Study design and inconsistent POI definitions are major contributors to the inadequacy of evidence that exists for the benefits of early oral feeding for prevention of POI. Despite the unsettled benefit of early oral feeding on POI and the need for further research, other well-known benefits of early postoperative feeding should be kept in mind, such as decreased catabolism and infectious morbidity[25]. Since early oral feeding has not been shown to be ineffective[32] or cause adverse outcomes, routine early oral feeding may be warranted.

Greater than 90% of participants who did not develop POI were advanced to a solid diet by postoperative day 3, which is also the postoperative day by which a majority of participants in the POI group were diagnosed with POI. The postponement in progression of diet for the POI group appears to have been the result of the presence of POI rather than a predictive factor for POI. Participants in the POI group who were advanced to a solid diet did not reach 100% until postoperative day 8, significantly later than the non-POI group in which 100% of participants were on a solid diet by postoperative day 5 (p=0.003). The negative impact POI can have on postoperative nutritional status was demonstrated in our study by the delay in diet advancement for those who developed POI, as withholding an oral diet is a historically common treatment strategy[22].

Study Limitations

Limitations of this study are important to take into consideration. One major limitation is the retrospective nature of the study, limiting the ability to control for all possible confounders. The small sample size of the POI group also served as a study limitation as it reduced the likelihood of finding reliable risk factors for POI following CABG, therefore, a larger sample size would have been beneficial. Since this study focused only on patients who underwent CABG, results may not be generalizable to other surgical populations.

Solely using radiologic imaging for diagnosing POI may have led to underreporting of POI incidence in our study population as others have diagnosed POI with the occurrence of GI symptoms without imaging (i.e. nausea and vomiting). It is possible some participants exhibited symptoms of POI, but since radiologic imaging it not a routine practice following CABG in our institution, POI may have been undiagnosed.

In addition, some preoperative characteristics were not available for all participants, making it challenging to identify those characteristics as preoperative risk factors for POI. Characteristics with missing data for at least one study participant included: hemoglobin A1c, highest operative blood glucose and preoperative albumin.

Application to Clinical Practice

Nutrition counseling and dietary modifications targeting weight loss and energy balance are likely to decrease insulin resistance and inflammatory mediators that may potentially lead to a greater postoperative inflammatory response. Since inflammation is known as an etiology of POI, a decrease in weight and insulin resistance may ultimately lead to a decrease in the incidence of POI in patients following CABG. In addition, obesity and insulin resistance have been well established as substantial cardiovascular risk factors as well. Although randomized controlled trials are needed to solidify the effect of insulin resistance and BMI on the development of POI, the results of this study only amplify the importance of preventative nutrition interventions to lessen the risk of cardiovascular diseases as well as progression and complications of cardiovascular conditions and surgeries.

As CABG is often performed in emergent situations, preoperative counseling may not always be possible. This emphasizes the importance of early postoperative prevention strategies in patients believed to be at high risk for POI. The results of this study demonstrate early diet advancement, regardless of type of diet, is effective at reducing the incidence of POI following CABG. Advancing diet by postoperative day 1 may be warranted for prevention of POI following CABG.

CONCLUSION

To our knowledge, this is the first study to investigate preoperative nutrition risk factors for the development of POI following CABG. The incidence found in our study, confirmed POI is a significant complication in our population of adults who have undergone CABG. Previously, data has been rather inconclusive in regards to preoperative risk factors for POI, largely due to the inconsistent definition of POI and methods used for its' diagnosis. Furthermore, data is particularly limited for POI following cardiac surgery and associated risk factors. This retrospective study determined modifiable risk factors for POI, BMI and elevated preoperative BG. Although further research is warranted, this study supports the idea that preoperative nutrition counseling could ultimately reduce the incidence of POI and its related complications, when targeted at weight loss and improved insulin sensitivity.

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