Nutritional Assessment of Chronic Pancreatitis Patients Utilizing A Web-based Food Frequency Tool: VioScreen

A Thesis

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ABSTRACT

The pancreas is the only organ which executes both exocrine and endocrine functions which promote the digestion and absorption of carbohydrates, protein, and essential fatty acids and micronutrients. Chronic pancreatitis (CP) is a disease in which the pancreatic parenchymal tissues undergo derangement and or necrosis resulting in the maldigestion and malabsorption of nutrients. The multifactorial risk of malnutrition with a myriad of nutrition deficiency related secondary complications result from these impaired physiological processes. Further complications stem from inability to appropriately diagnosis the disease until it is late stage. Due to limited nutrition research, there currently is inadequate evidence describing the dietary intakes or dietary patterns of patients with chronic pancreatitis which could enable the development of dietary interventions according to loss of pancreatic function. Previous observational studies have sought to investigate the efficacy of specific nutrients, or foods in management of CP related pain, maldigestion, and nutrient defiiciency.[1–6] However, the potential for influence and/or effect of combined dietary components upon one provides rationale for investigating effects of dietary patterns and CP treatment. The Mediterranean diet (MED) regimen has been extensively compared to the Westernized diet in relation to beneficial effects upon a host of diseases, most notably cancer.[7,8] Characteristics of the MED include high daily intakes of vegetables, fruits, legumes, nuts, fish, olive oil, non-refined cereals (whole grain rice, bread, pasta, etc.); moderate wine consumption; and low-to-moderate monthly intakes of meat and dairy products. This cross-sectional study was designed to assess the dietary intake of patients with chronic pancreatitis. The assessment was performed using a validated web-tool,

VioScreen, which provided data across 19 nutritional parameters and then subsequently compared the test results to the Healthy Eating Index (HEI), and the Mediterranean Diet (MED) Score.[9,10] The institution of HEI not only provided a baseline for nutritional interventions but additionally encompass measures to address the factors with implications tied to promotion of chronic disease. The MED score evaluated the compliance with a Mediterranean diet regimen which may provide insight into personalized optimization of nutritional intakes/treatment of CP patients.

DEDICATION

Dedicated to the one person who has had unwavering faith, encouragement, support and belief not only in our relationship, but upon any endeavor I pursue, my best friend, and husband, Monte Ryan Young.

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TABLE OF CONTENTS

Page

Abstract ii

Dedication iv

Acknowledgements v

Vita vi

List of Tables ix

List of Figures x

Chapters:

1. Introduction 1
   - Background 1
   - Statement of the Problem 4
   - Purpose of the Study 4
   - Research Objectives 5
   - Research Questions 5
   - Significance of the Study 5
   - Summary 6
   - Definition of Terms 7

2. Literature Review 9
   - Introduction 9
   - Malnutrition in Chronic Pancreatitis 9
   - Definition 10
   - Prevalence 10
   - Etiology 11
   - Diagnosis 13
   - Normal Function and Physiology 16
   - Exocrine Function of the Pancreas 16
   - Endocrine Function of the Pancreas 19
   - Pathophysiology 21
   - Nutritional Consequences 21
   - Nutritional Interventions 23
   - Dietary Patterns in Chronic Disease 30
   - Food Insecurity 32

Page

Summary 32

3. Methods 33
Research Design 33
Research Questions 33
Sample Population 33
Inclusion and Exclusion Criteria 34
Consent 35
Instruments 35
Data Collection 37
Dietary Pattern Indices and Scoring Parameters 39
Data Analysis 44
Limitations 45

4. Results and Discussion 46
Introduction 46
Research Questions 46
Population Demographics 46
Results 47
Discussion 53
Limitations 58
Implications for Research and Practice 58

5. Nutritional Assessment of Chronic Pancreatitis Patients Utilizing a Web-based Food Frequency Tool: VioScreen 61
Abstract 61
Introduction 62
Methods 65
Sample Population 66
Study Design 66
Study Instruments 66
Statistics 67
Results 67
Discussion 74
Limitations 78
Implications for Research and Practice 79

References 81
Appendix A: Chronic Pancreatitis Study Participation Letter 89
Appendix B: Chronic Pancreatitis Subject Recruitment Phone Script 91
Appendix C: Chronic Pancreatitis Subject Recruitment Face to Face Script 93
Appendix D: Demographic Questionnaire, and Two-Question Food Security Screen 95
Appendix E: Chronic Pancreatitis Study IRB 98

LIST OF TABLES

Table Page

Table 1. Pancreatic Enzyme Replacement Therapy Administration 27

Table 2. Anthropometrics and Dietary Intakes. 30

Table 3. Healthy Eating Index Scoring Assessment 41

Table 4. HEI-2010 Total and Component Scores for the U.S. Total Population, Children, and Older Adults, NHANES 2011-2012 42

Table 5. Mediterranean Diet Score Assessment 44

Table 6. HEI and MED Mean Scores, SD 48

Table 7. Lifestyle Factors 49

Table 8. Pancreas and GI Diagnoses 50

Table 9. Anthropometrics 51

Table 10. Nutrient and Vitamin Intake 52

Table 11. Estimated Calorie, Nutrient, and Food Group Intake 53

Table 12. HEI and MED Mean Scores, SD 68

Table 13. Lifestyle Factors 69

Table 14. Pancreas and GI Diagnoses 70

Table 15. Anthropometrics 71

Table 16. Nutrient and Vitamin Intake 73

Table 17. Estimated Calorie, Nutrient, and Vitamin Intake 73

LIST OF FIGURES

Figure 1. Research Design 39

Chapter 1: Introduction

Background

Chronic Pancreatitis affects 3.5 to 10 people per 100,000 in the developing world. The incidence is higher among men, and occurs between the ages of 30 and 40.[11] Chronic pancreatitis (CP) presents with the following clinical manifestations: abdominal pain, exocrine and endocrine insufficiency. The complications arise from ongoing inflammation and development of fibroids in the pancreas which result in a loss of both pancreatic function and corresponding parenchymal tissue. [12–15] The decreased functional capacity refers to the impairment of exocrine and endocrine secretory features with the ensuing development of maldigestion and malabsorption of nutrient intake. The subsequent development of related secondary complications – steatorrhea, diarrhea, unplanned weight loss, and malnutrition – compound the severity of the diseased state via increased gastrointestinal distress, and prolonged nutrient deficiencies.[13,16–20]

An initial clinical indication of chronic pancreatitis is a postprandial exacerbation of abdominal pain that radiates from lower to upper abdominal quadrants. The mechanism eliciting pain has been studied extensively but as yet is not well understood. Pain management typically begins with the administration of narcotic analgesics, or endoscopic therapies designed for large duct blockages and includes dilation, stenting, and stone dissolution. [3,21,22] Alternatively, surgery is also considered for pain management.[23–25] Unfortunately, surgical

amelioration of existing duct blockage or obstruction believed to be the correct measure for functional repair and pain management may not resolve the pain. The pain may in fact be the result of hypersensitivity and stimulation of enlarged nociceptor neurons densely populating the pancreas that are responsible for pain sensation.[22]

Malnutrition, as another secondary complication, presents additional risks regardless of the instigating factor for the disease.[13,16] Despite the myriad of complications associated with malnutrition – visual and neurodegenerative disorders related to deficiencies of Vitamin A, or metabolic bone disorders related to deficiencies of Vitamin D – current studies have primarily focused upon administration of pancreatic enzyme replace therapy (PERT) as a means to ameliorate problematic digestion and absorption.[1,6,26–30] The utilization of PERT as means to improve nutritional status is complex given the lack of a standard dosage, and the heterogeneity of functional pancreatic tissue variance within the CP patient population.[18,20,22,31] Optimal corrective actions for nutritional status in CP patients could be dramatically improved with medical nutrition therapy (including PERT) and compliance with evidence-based nutrition interventions. The continual assessment of nutritional status would provide adequate data for the Registered Dietitian and health care team to continually monitor for viable markers of malnutrition risk. Evidence based medical nutrition therapy has historically focused on the coordination of dietary intake with pancreatic enzyme supplementation and has not moved beyond this stage. Additionally, it is not a routine standard of care for the patient with CP to be referred to a Registered Dietitian except during hospitalization. Personalized nutrition counseling by physicians is hindered by limited training in nutrition counseling as well as the inability and or lack of time to accurately assess current dietary habits. Assessment of dietary intake for CP must be addressed in order to determine appropriate nutritional interventions.

The most prevalent etiology for chronic pancreatitis is excessive consumption of

alcohol.[32–34] Alcohol has the unique ability to directly and indirectly be an instigating factor for CP.[35,36] Alcohol may cause direct injury to acinar cells left vulnerable to other triggers, and indirectly through pancreatic stellate cell activation via metabolites produced by pancreatic alcohol metabolism.[36–38] While pancreatic injury does occur with chronic alcohol abuse, not all cases lead to chronic pancreatitis. Furthermore, scant data has been compiled to investigate amounts consumed, or dietary patterns and intakes, or in tandem with cigarette smoking – which elevates occurrence of CP.[32,39–43] Hence, initial treatment in this instance is the cessation of alcohol consumption and cigarette smoking.

Extensive studies have investigated the etiologies, pathologies, and traditional CP treatment, yet there is a lack of research investigating methods to definitively diagnose, and measure severity of malnutrition. Alcohol related CP predisposes the patient to greater chance of prolonged malnutrition due to direct and detrimental effects of alcohol on nutrition status.[13,44–46] Similarly, an extensive body of research reveals the influence of cigarette smoking upon dietary intake habits including excessive energy intake of empty calories in sugar-sweetened beverages and alcohol, decreased carbohydrate intakes, and higher fat consumption in comparison to nonsmokers.[47,48] Accurate assessment of dietary intake could provide data to determine correctable situations of inadequate nutritional intakes, or poor nutrition.

The most widely available techniques used to measure dietary intake include the 24-Hour Recall, Food Record or Diary, and Food Frequency Questionnaires (FFQs). The inherent biases – recall and expectation – with self-reporting dietary assessments can significantly hinder accuracy of measurement.[49–51] An alternative dietary intake instrument is the validated, web-based dietary assessment tool VioScreen Graphical Food Frequency System – which will be referred to as VioScreen.[49] VioScreen is a test which the patient completes via a computer. The test has 156 food items with photos of 3 to 6 different portion sizes.[49] The web-based program

eliminates a great deal of bias that is typically associated with pencil and paper FFQs. Additionally, the newer method reduces participant burden as completion of the survey is approximately 30 to 45 minutes, and generates immediate nutritional intake data. [49,51,52]. The burden on the patient is greatly reduced with the VioScreen, as well as a much higher rate of completion and accuracy of intakes. The utilization of VioScreen for CP patients would provide an effective tool to assess dietary intake within a nutrition assessment on a consistent and regular fashion.

Statement of the Problem

Evidence based medical nutrition therapy has historically focused on the coordination of dietary intake with pancreatic enzyme supplementation and has not moved beyond this stage. Unfortunately, it is not standard of care for the patient with CP to be referred to a Registered Dietitian except during hospitalization. Personalized nutrition counseling by physicians is hindered by limited training in nutrition counseling as well as the inability to accurately assess current dietary habits. Assessment of dietary intake for CP must be addressed in order to determine appropriate nutritional interventions.

Purpose of the study

Chronic pancreatitis (CP) is a pancreatic disease of multifactorial etiologies which result in the deleterious derangement and necrosis of pancreatic parenchymal tissue. The lack of research pertaining to dietary patterns and intakes within this patient population has prevented the recognition of malnutrition risk as well as the development of evidence based medical nutrition therapy. The goal of the study is to assess the dietary intake of patients with diagnosed CP. That said, the information garnered from the study could assist in the

development of medical nutrition therapies based upon disease severity and prevent long-term complications of malnutrition.

Research Objective

The objective of the study was to a): utilize VioScreen to describe the nutritional intakes of patients diagnosed with chronic pancreatitis, and b): to compare food frequency nutrition data obtained using VioScreen to two commonly used assessment indices, i.e., the Healthy Eating Index (HEI), and the Mediterranean Diet Score (MED).

Research Questions

- What is the average HEI score for a sample of patients with CP as measured by VioScreen FFQ?
- What is the average MED score for a sample of patients with CP as measured by VioScreen FFQ?

Significance of the Study

The multifactorial etiologies of chronic pancreatitis present a myriad of complications that promote a significant risk for malnutrition. The normal function of pancreatic exocrine and endocrine secretion is severely diminished and unable to maintain adequate nutritional health. A 2014 prospective cohort study investigated the levels of malnutrition in CP patients with specific emphasis on fat-soluble vitamin levels, and anthropometric indicators of malnutrition, i.e., BMI, and functional status. The findings revealed a prevalence in overweight status, decreased functional status, reduced lean muscle, and nutritionally deficient Vitamin A.[6] The coordinated effects of these metrics provided evidence for continued need to elucidate

potential indicators and treatment regimens for CP patients with malnutrition. The added complexities of malnutrition related complications – metabolic bone disease, visual impairment, loss of quality of life – are further exacerbated in excessive alcohol related chronic pancreatitis.[1,26,53,54]

The literature gap in treatment of CP is related to optimal dietary interventions, assessment of dietary intake and valid serum, or anthropometric indicators of malnutrition. Primary CP studies have extensively focused on alleviation of signs and symptoms without regard to amelioration of malnutrition. The deleterious effects of malnutrition beyond nutrient deficiencies relates to increased risk of morbidity and mortality. The ability to accurately and consistently assess dietary intake of CP patients would help provide insight into actual dietary patterns and habits of this disease population. Furthermore, it would provide an opportunity to determine appropriate dietary interventions to address the nutritional deficits in this patient population.

Summary

Chronic pancreatitis is a multifactorial etiology disease which is complicated by the ability to detect early onset of the disease. The loss of function via derangement of parenchymal tissue presents an environment of increased nutritional risk resulting from maldigestion and malabsorption. Unfortunately, the complexities – enhanced by heterogeneity of the disease – make it difficult to determine whether or not the underlying issues are due to abnormalities in function or structure. Despite the prevalence for the secondary complication of malnutrition in this population research has not focused on dietary interventions, but on pain management via analgesics and surgery. The institution of effective dietary assessment by a Registered Dietitian (RD) employing the VioScreen graphical food frequency questionnaire could identify nutritional

inadequacies occurring in the overall diet of the CP patient. Instead of focusing assessment on single nutritional components, or daily energy intake values the RD will be able to use the data to assess the existing dietary patterns across a larger bandwidth and targeting inadequacies existing over the entire dietary intake spectrum in comparison to nutritional indices which have shown to improve optimal overall health outcomes and increased risk for additional comorbidities, and not just single day deficiencies.

Definition of Terms

Mediterranean Diet (MED) Score: An index which measures compliance level to the Mediterranean diet.

Healthy Eating Index (HEI): A tool created by the US Department of Agriculture to measure levels of compliance with the Dietary Guidelines for Americans (DGA) set by the US federal government. The index provides insight in eating patterns and areas of nutrition where acute attention should be focused to improve dietary adequacy and habits. The most recent update to the HEI was in 2010 in concert with changes made to the DGA every 5 years.

Maldigestion: Impaired gastrointestinal digestive function that results in sufficient breakdown of food to enable adequate absorption in the the small intestines.

Malabsorption: Impaired extraction of nutrients from food by the small intestines that are excreted with stool versus delivered to tissues, organs, and muscles in support of specific functions.

Malnutrition: A condition or disorder typically related to prolonged nutritional inadequacies.

Exocrine Pancreatic Insufficiency (EPI): Inadequate production of endogenous enzyme production, secretion, and function required for digestion of nutrients.

VioScreen Graphical Food Frequency System: Also referred to as "GraFFS," or, "VioScreen". VioScreen is a computer administrated online web based graphical food frequency questionnaire. The GraFFS utilizes branching logic, an analytics engine, and an easy to use participant interface. The completed GraFFS produced data provides insight on the participants dietary patterns an well as nutrient intake and analysis of data. Additionally, the GraFFS format eliminates the opportunity for common paper questionnaire intake errors: missed questions, missing answers, or multiple responses to a single question. The computer based system provides for complex skip patterns that are not possible in pencil and paper food frequency questionnaires. GraFFS offers over 1,200 photos of up to 6 food portion sizes with text which enables enhanced accuracy of actual intakes.[49]

Chapter 2: Review of the Literature

Introduction

This literature review investigates the current research relevant to chronic pancreatitis related malnutrition. The research reviewed will describe the investigations associated with the arising complications of malnutrition in CP. Related disorders include involuntary weight loss, micronutrient deficiency related complications, visual impairment, bone mineral disorders, and overall diminished quality of life. Recent studies have shown that research is warranted to determine existing nutritional inadequacies, and the need for validated nutritional assessment markers in CP.[14,26,53–56] Additionally, research has demonstrated the potential for improved nutritional status via medical nutrition therapy provided by the Registered Dietitian.[19,20,22,57]

Malnutrition in Chronic Pancreatitis

The lack of a gold standard – functional parameter, or measurable deficiency of one required nutrient – for nutritional status assessment in chronic pancreatitis complicates the establishment of an efficacious nutritional regimen. A proactive approach to early stage disease treatment is not possible without reliable functional assessment tools and nutrition parameters related to nutritional deficiencies specific to CP. Consequently, verifiable diagnoses of CP do not typically occur until late stages of disease progression where sufficient time lapse has resulted in the development of irreversible impairment of normal pancreatic function. The physiological derangement of organ morphology precipitated by chronic duct obstruction and, or fibrosis

relates to the severe loss of parenchymal pancreatic tissue and the diminished ability of digestive enzyme secretion. These disease complications include severe abdominal pain, exocrine pancreatic insufficiency (EPI), maldigestion, malabsorption, pancreatic pseudocyst, diarrhea, and Type 3c Diabetes Miletus.[22,56,58–60] The additive effects of these complications not only elevate the risk, but reinforce the multifactorial nature of CP related malnutrition.

The clinical impairments of malnutrition have the potential for increased disease severity if there is an underlying history of chronic alcohol ingestion. Alcohol has the ability to not only be a causative factor for CP but can simultaneously and independently contribute to malnutrition including vitamin deficiencies, poor diet quality, inadequate nutritional intake, protein energy malnutrition, and increased inflammatory effects upon the upper gastrointestinal tract.[13,34,39,45,46]

Definition

Chronic Pancreatitis (CP) is the combined degenerative losses of digestive and absorptive functions resulting from irreversible inflammation, precipitous calcification, and fibrosis promoting necrosis of parenchymal tissue.[13,36,61,62] Typical medical care involves control of the ensuing gastrointestinal (GI) complications, improvement of digestive functions, drainage of pseudocysts (stent and, or lateral pancreatojujenostomy), opioids for pain management, and pancreatic enzyme replacement therapy (PERT).[21,22,63]

Prevalence

The annual incidence of CP is estimated to be 5 to 12 people per 100,000, with a prevalence of 50 per 100,000 persons in the developing world.[32] The prevalence is higher among men (occurring between the ages of 40 – 60 years of age), however the incidence is equally

proportional among men and women.[32,33]

Etiology

Historically, the literature has primarily focused on excessive alcohol intake as the leading risk factor for CP. The extensive body of research revealed both direct and indirect relationships between the promotion of irreversible and detrimental changes to pancreatic parenchymal tissue and chronic dose-dependent alcohol consumption.[35,37,64] Protein plug formation has been the main hypothesis for direct damage of alcohol on the pancreas.[37,65] Scarring, fibrosis, and atrophy of epithelial cells supported by the continued precipitation, contact, and enlargement of calculi within the small ductules.[35,36,64] The indirect toxic effects occur via oxidative and non-oxidative metabolism of alcohol by the pancreas. Oxidative metabolism produces cytotoxic metabolites and by byproducts – acetaldehyde, and reactive oxygen species (ROS). Both metabolite and toxic byproducts have been linked to activation of pancreatic stellate cells (PSC) which in turn promote fibrosis.[37,38,61,64] An environment of oxidative stress is further perpetuated by the occurrence of rapid depletion of the ROS scavenger glutathione.[41] Metabolism via the non-oxidative pathway yields a high concentration of fatty acid ethyl esters which damage the pancreatic acinar cells.[37,64] Interestingly, less than 10% of events of excessive alcohol consumption result in the development of CP.[36] Subsequent studies suggested a relationship between dose dependence, duration of alcohol consumption and tandem exposure to other risk factors necessary for the development of CP.[34,35,37,64,66] Chronic alcohol consumption in lesser quantities sufficiently diminished acinar cellular integrity to increase disease susceptibility in the face of exposure to other cytotoxic chemicals, or etiological risk factors.[67,68] The M-ANNHEIM classification system for CP assesses alcohol consumption as excessive (>80 g/day), increased (20-80 g/day), and moderate consumption

(<20 g/day).[69] Cigarette smoking has been identified as both an independent risk factor for CP and added to continued alcohol intake has been shown to heighten the likelihood of CP development.[33,41] Alternatively, continued CP investigations suggested that disease progression of the alcohol sensitized pancreas was also potentially linked to hereditary, or alcohol induced genetic derangements (SPINK1 – trypsin secretory inhibitor, CFTR – thickened secretions precipitating duct obstruction and high sweat chloride concentrations), ductal obstruction or damage, rare metabolic dysfunctions, or autoimmune conditions.[35,65,69]

The resultant complications include exocrine pancreatic insufficiency (EPI), maldigestion, malabsorption, pancreatic pseudocyst, diarrhea, steatorrhea, unplanned weight loss, diabetes mellitus (classified by the American Diabetes Association as type 3c Diabetes Mellitus) with apoptosis of cells responsible for production of insulin and glucagon.[13,31,70]

EPI presents as diminished exocrine secretion with clinical implications ranging from mild to severe symptoms which are focused upon epigastric pain – cramping, abdominal distension, and flatulence. Other severe manifestations of EPI include unplanned weight loss and steatorrhea which appear late in the progression of the disease. Steatorrhea is defined as fecal fat collection with measurement containing >7g of fat with a stool grey/yellow in color, floating in oily, greasy water.[31] Maldigestion and poor absorption of nutrients in EPI are directly correlated to the heightened risk for malnutrition and its related complications.

The loss of such function has multifactorial etiologies and may include CP, pancreatotectomy, acute pancreatitis, Cystic Fibrosis, smoking, duct morphology derangement, post-cibal asynchrony, and Zollinger-Ellinger syndrome. The underlying pathophysiology results from necrosis of parenchyma, duct secretion impairments (decreased amount, or suboptimal concentration of pancreatic juice compared to chyme), or inactivation of pancreatic enzymes due to hypersecretion of gastric acids.

Diagnosis

Accurate diagnosis of CP requires a stepwise procedure involving complimentary imaging, clinical manifestations, and functional testing.[71] The gold standard for diagnosing chronic pancreatitis is a pancreatic biopsy. The histological markers occurring in chronic pancreatitis include patchy distribution of lesions, ductal system derangement (protein plugs, calcifications, epithelial cell necrosis, acinar cell apoptosis, destruction of islet cells, infiltrates (leukocyte released cytokines) of inflammatory cells, pseudocysts, and perilobular (intralobular if obstructive) fibrosis.[36,67] However, the procedure is not the most practical given the extreme invasive nature of the assay, absence of histological CP markers in the early stages of the disease, the late onset of irreversible changes in morphology, and similar derangements in pancreatic parenchymal tissue that are non-CP related such as the effects from smoking, diabetes and end stage kidney disease and aging.[22] That said, all other diagnostic tests are measured against this gold standard diagnostic tool of CP tissue histology.[72]

The most effective alternative means of verifying a diagnosis of CP without evidence of calcifications, involves secretory testing (hormonal stimulation and resultant bicarbonate secretion and pancreatic juice components), and utilization of endoscopic retrograde cholangiopancreatography (ERCP), providing insight into existing duct function/abnormalities.[36] However, these alternative assays are no less invasive than obtaining a pancreatic histological sample, not universally available, and/or as in the case of ERCP potentially promote the development of pancreatitis. Therefore, pancreatic imaging which is non-invasive, and generates a highly defined image of the pancreas has been promoted in the confirmation of a CP diagnosis. Pancreatic imaging has significantly improved and should be simultaneously employed to visualize duct system impairments, and changes to normal organ structure. The imaging techniques utilized include: ultrasonography (US), endoscopic ultrasonography (EUS),

endoscopic retrograde cholangiopancreatography (ERCP), computed tomography CT, magnetic resonance cholangiopancreatography (MRCP), and magnetic resonance imaging (MRI). The pairing of imaging techniques enables further verification of the disease process in the event that the initial image cannot confirm or deny the diagnosis of CP. Ultrasonography (US) is typically the first imaging method selected due to lowest radiation exposure and highest affordability. However, US offers the lowest descriptive imaging potential. EUS follows an US which reveals mixed results, e.g., inconsistent organ tissue density with normal duct morphology. The complication with EUS is the fact that it is a high sensitivity and low specificity evaluation, i.e., EUS high lights non-specific alterations which may or may not be indicative of CP.[22,73] MRCP provides enhanced imaging and the potential for detailed evaluation of the duct system in relation to secretory function. While CT provides good detail of functional pancreatic tissue, and MRI illuminates the pancreatic duct system – but does not expose calcification – the more conclusive combination would be MRI paired with MRCP. Furthermore, MRCP with secretin administration promotes higher definition images of the pancreatic duct. ERCP has largely been replaced by MRCP – despite highly detailed resolution of the pancreatic duct, and the ability to consistently reveal alterations in the side branches – due to increased chance for onset of CP with that test.[22,36] Imaging techniques have improved vastly but are not without their own limitations and should be utilized with selective clinical indicators and be mindful of the potential for a false positive result. A noteworthy limitation includes the reduced sensitivity and specificity of CP diagnosis in the early stages of the disease given the lack of calcifications, ductal impairments, necrosis, and fat replacement.[74]

The imaging diagnosed CP can be supported by the quantifiable loss of pancreatic function – endocrine and exocrine – which can be measured via direct and indirect pancreatic function tests (PFTs). The consistent challenge is the PFTs lack of sensitivity and specificity for

disease indicators not appearing in early, or mild forms of CP. Moreover, dramatic loss of function with consistent complications are not evident until after a loss of 90% of parenchymal tissue.[75] Type 3c diabetes has been linked to endocrine pancreatic insufficiency (EPI). However, development of this CP related complication occurs in less than 10% of all diagnosed cases of CP, and presents late in disease.[31,59,74] Other indirect PFTs are typically performed in suspected cases of CP owing to reduced patient burden and low invasive nature. Hormonal stimulation is not involved in determining the level of exocrine function, as such, the assay is not as accurate in mild cases and reveals only moderate to severe EPI. A non-invasive assay for quantifying diminished exocrine function is the fecal elastase 1 test. The role of human pancreatic elastase (EL1) is two-fold in that along with enhancing proteolytic activity, these acinar cell produced enzymes additionally aid the intestinal transportation of cholesterol by attachment to bile acid.[74,75] The concentration of EL1 is typically 6% (170 μg/mL to 360 μg/mL) of pancreatic enzymes within the duodenum and five times greater concentration than pancreatic juice within stool samples.[74] The consistency of an individual's daily EL1 concentration within fecal samples provides a vehicle to monitor the levels of pancreas enzyme secretions. Further validating the appropriateness of EL1 as a diagnostic marker are the quantifiable sensitivity and specificity of EL1 in cases of mild, moderate, and severe exocrine pancreatic insufficiency.[31,75]

Direct PFTs are gastric hormones (cholecystokinin (CCK) and secretin) stimulated tests which measure pancreatic enzyme and bicarbonate output. Postprandial stimulation of CCK and secretin from duodenal S and I cells, respectively, promote the release of an enzyme and bicarbonate rick pancreatic juice.[31,36,74] The separate tests determine duct function via bicarbonate secretion, and acinar cell function through quantification of chymotrypsin and lipase output. The method of collecting the aspirates for these tests is highly invasive and involves collection of fluid by either a oroenteric tube, or through the endoscopes accessory

channel. Both exams are highly invasive and not well tolerated by the patient. However, in cases of suspected PC where imaging and clinical indications these invasive techniques are beneficial at revealing early onset of the disease.[31,36,74]

Currently, research is also investigating the existence of specific pancreatic secretion proteins related to pain, inflammation, and fibrosis as a means for diagnosis.[22]

Normal Function and Physiology

The pancreas is the only organ with both exocrine and endocrine functions. The majority of cells in the pancreas are exocrine acinar cells (collectively termed pancreatic acini), which produce an alkaline pancreatic juice – rich with digestive enzymes and bicarbonate – that promotes digestion of dietary nutrients.

Alongside the acini – albeit in greatly lesser percentage, or 1% of the volume of the pancreas – are the endocrine cells which occupy the pancreatic islets and are categorized as alpha, beta, delta, and F cells. The requisite functions involve secretion of glucagon by alpha cells in response to low blood glucose levels, and secretion of insulin by beta cells in response to high blood glucose levels.

Exocrine Function of the Pancreas

Digestion

The pancreas facilitates digestion in the small intestine via the secretion of digestive enzymes, and bicarbonate ions which neutralize the high acidity of the gastric chyme. The entrance of acidic gastric chyme into the duodenum stimulates the release of the gastric hormone secretin (secreted by S cells in the mucosal cells of the duodenum), which stimulates the pancreatic duct cells to secrete bicarbonate reducing the elevated pH. Exogenous fat and

protein entering the duodenum stimulate the enteroendocrine I cell release of cholecystokinin (CCK), resulting in the secretion of pancreatic juices containing the precursory digestive enzymes known as zymogens. CCK binding to receptor sites on the acinar cells induces the release of the zymogens. The digestive enzyme juice reflects the proenzymes which are, in part, responsible for carbohydrate, fat, and protein digestion. However, the utilization of the pancreatic enzymes is initially dependent on the neutralization of the gastric acids by the bicarbonate. Pancreatic stimulated secretion of bicarbonate is greatly amplified in the presence of both CCK and secretin. Digestion continues with the combination of CCK stimulated release of bile (compsed of bile salts, lecithin, bicarbonate ions, cholesterol, bile pigments, and trace metals) from the gall bladder, and pancreatic juice. The mixture proceeds via the common bile duct into the duodenum through the sphincter of Oddi.

Carbohydrate Digestion

Digestion of starch occurs with the secretion of alpha-amylase from the salivary glands in the mouth. The initial digestion involves the breakdown of polysaccharides to alpha-dextrins. The gastric acidity disables the digestive capabilities of the salivary alpha-amylase. The presence of carbohydrates in the intestinal lumen stimulates the release of CCK promoting the release of pancreatic alpha-amylase. The acinar cells within the pancreas discharge a significant volume of amylase into the lumen of the small intestine. Starch and glycogen are hydrolyzed by pancreatic alpha-amylase into disaccharide maltose, trisaccharide maltotriose, and oligosaccharides (also known as dextrins). Additionally, pancreatic bicarbonate is secreted to neutralize the acidic environment in the duodenum created by the HCL from the stomach. Starch digestion by amylase has specificity for alpha (1,4) bonds, hence it cannot cleave the predominating alpha (1,6) bonds of the dextrins. However, luminal membrane glycoprotein oligosaccharidases, and

brush border enzymes (lactase, sucrose, maltase, alpha-dextrinase, and glucosidase) are able to complete the digestive process.

Lipid Digestion

The most prevalent lipids in the western diet are triglycerides, which include primarily long chain fatty acids (LFCA). Additionally, dietary lipids include cholesterol, cholesterol esters, phospholipids, and fat-soluble vitamins A, D, E, and K. Fatty acid digestion involves a complex process beginning with the actions of lingual lipase and gastric lipase. Following the excretion of the newly formed gastric lipid emulsions into the duodenum, pancreatic lipase performs the majority of lipid digestion. Colipase, which is not activated until it is transported into the lumen of the small intestine from the pancreas, facilitates effective lipid digestion through disruption of the inhibitory effects of bile and allows access of the enzyme to the substrate. Phosopholipids are also digested in the small intestine by pancreatic lipase with subsequent activation of phospholipase in the small intestine. Cholesterol esters are converted to free cholesterol by the pancreatic secretion of cholesterol esterase.

Protein Digestion

Dietary protein must be reduced to the amino acid form before the body can adequately utilize it. Subsequent to the primary breakdown of protein in the stomach, the bulk of free amino acids are provided via hydrolysis and absorption in the small intestines. The pancreatic involvement in this process begins with the stimulation of zymogen release controlled by the hormone cholecystokinin (CCK). Once in the lumen of the small intestine, the zymogens (trypsinogen, proelastase, chymotrypsinogen, procarboxypeptidase A, and procarboxypeptidase B), are converted into proteolytic enzymes by apical membrane bound

enterokinase. Further activation is enhanced and accelerated by the ability of trypsin to convert the remaining zymogens into fully active proteases within the lumen of the small intestine. Optimization for proteolytic activity occurs with pancreatic bicarbonate secretion reducing the pH of the gastric acid in the intestinal lumen. The significance of zymogen production, and subsequent activation outside of the pancreas are safety mechanisms designed to prevent auto-digestion, or tissue damage to the organ or its ducts. Furthermore, pancreatic juice contains peptides, which inhibit the premature conversion of trypsinogen within the pancreas. The net effect of these proteolytic enzymes is the hydrolysis of proteins into free amino acids absorbed by enterocytes, and dipeptides, or tripeptides which are more readily absorbed through the apical membrane. The necessitation of multiple transport mechanisms provides efficient absorption regardless of specific peptide resistance to hydrolysis. The clinical significance of dipeptide and tripeptides absorption provides the route for feeding of patients with pancreatic insufficiency, i.e., once these peptides have been transported past the lumen they are then hydrolyzed to free amino acids within the enterocyte and transported across the basolateral membrane into circulation.[13,16,76]

Endocrine Function of the Pancreas

The pancreatic endocrine cell clusters – islets of Langerhans – occupy a volume of 1% to 2% within the pancreas. The primary role of pancreatic islet cells is the secretion of glucoregulatory hormones involved in opposing metabolic functions.[13,76,77] The specific cells responsible for the regulation of blood glucose levels (carbohydrate metabolism) are the α cells which secrete glucagon when glucose levels are low, and the β cell secretion of insulin which aid in the cellular uptake during high glucose levels. Protein and lipid metabolism are also regulated by the actions of glucagon and insulin. The remaining islet cells δ and F (or δ1) – secreting

somatostatin and pancreatic polypeptides, respectively – cells are involved in secretory regulation of insulin and glucagon.

The postprandial elevation of blood glucose following carbohydrate ingestion stimulates the β cell release of the anabolic hormone insulin. Subsequent insulin mediated signaling directs the movement of glucose cell transporters, GLUT4, to the cell membrane surface of muscle and adipose tissues resulting in the increased uptake of glucose. The heightened concentration of insulin promotes glycolysis and the storage of excess glucose while inhibiting gluconeogenesis and glycogenolysis. Excess glucose is converted into glycogen and stored within the liver and muscle tissue. [13,16,76]

The mechanism to elevate and maintain steady blood glucose levels during the post absorptive state occurs with the release of the catabolic polypeptide hormone glucagon into the blood stream by the pancreatic islet α cells. Blood stores of glucose, amino acids, and fatty acids are mobilized by glucagon. The liver is the primary site of gluconeogenesis and glycogenolysis facilitated by the actions of glucagon. Gluconeogenesis, the production of glucose from non-carbohydrate precursors, occurs from intermediate metabolites created from conversion of proteins and fatty acids. Alternatively, glucagon also promotes glycogenolysis – degradation of hepatic glycogen stores – to increase blood glucose levels. Glycogen stored within skeletal muscle can only be accessed and converted to glucose for ATP production locally due to the lack of glucagon receptors, hence, hepatic glycogen is the primary source of stored glucose when blood glucose levels are low.

Somatostatin is a peptide hormone secreted by cells within the gastrointestinal tract and by enteric nervous system neurons. The specific function of somatostatin released from pancreatic islet delta cells is to regulate the rate of absorption of food in the small intestines via

inhibitory effects on glucagon and insulin secretion.[78] Additionally, somatostatin can suppress pancreatic exocrine functions such as inhibitory effects on cholecystokinin and secretin.

Pathophysiology

The diminished function of pancreatic ducts and glandular parenchyma that are related to obstruction, dilation or constriction of ducts, fibrosis, and chronic inflammation are the pathological hallmarks of chronic pancreatitis. While the affected morphology, clinical indications, and risk factors for CP have been well studied the exact pathological mechanisms remain unclear. Past theories of CP pathogenesis include oxidative stress toxic-metabolic, duct obstruction, necrosis through fibrosis, as well as newer hypotheses – Primary Duct Hypothesis or Sentinel Acute Pancreatitis Event (SAPE) - which investigates CP respectively as being derived from an autoimmune trigger, or mechanistically as a means of compartmentalizing specific time points in a potential fibrotic development pathway.[15,36,79,80] A similarity to the various theories is not only the outcome of CP, but the requirement of persistent inflammation, abnormal location and stimulation of pancreatic stellate cell promoting fibrosis, and anti-inflammatory response.[36,79] In end stage CP, the acinar cells experience atrophy from the failing mechanisms designed to prevent zymogen activation while simultaneously mounting an intense inflammatory response within the pancreas. As a result, histological samples reveal an environment of auto digestion, loss of secretory function, and the dense growth of fibrotic tissue.[36]

Nutritional Consequences

Historically, malnutrition was perceived to be a potential instigator in the pathogenicity of chronic pancreatitis. However, research has demonstrated that it is not an etiology, nor a

contributing factor, but a multifactorial secondary complication.[43,57,81] The etiology of CP related malnutrition is not tied to a single event, but a series of complications which together amplify malnutrition related consequences that complicate the disease condition. The concomitant effects of maldigestion, malabsorption, sub-optimal nutritional intakes – amount and nutrient density – severe abdominal pain, and excessive alcohol intake provide a mechanism that contributes to the onset of malnutrition. It should also be noted that preexisting nutritional deficiencies resulting from chronic alcohol abuse prior to diagnosis CP with an alcohol related etiology may additionally contribute to malnutrition.[6,27]

Pancreatic maldigestion related complications occur when the release of gastric acids into the duodenum are not met with adequate release of bicarbonate from the pancreas, and bile acids.[13,16] The failure to correct the acidity within the duodenum results in degradation and deactivation of digestive enzymes.[58,82–84] Protein and carbohydrate metabolism is compensated respectively by gastric pepsinogen and intestinal oligosaccharides, or salivary amylase.[85] Lipase, the predominating enzyme within pancreatic juice and possessing the greatest instability in the poorly buffered duodenal acidity typical of CP, however, has little compensatory mechanisms for lipolysis beyond the pancreas. Therefore, the EPI clinical manifestations – steatorrhea, weight loss, abdominal pain, and elevated risk of fat-soluble vitamin deficiencies – resulting from fat malabsorption are the most significant complications of CP.[82,84,86]

CP diagnosed patients fearing recurrence of severe pain and gastrointestinal distress often avoid eating and this further increases their risk for malnutrition. Despite the prescription of pain medications and pancreatic enzyme replacement therapies, the patient eliminates or severely restricts calories and fat intake. The situation is further exacerbated by the common recommended reduction of dietary fat decreasing already diminished fat soluble vitamin absorption.[47,57] The clinical indications of these prolonged vitamin deficiencies promote

decreased bone mineral density and may contribute to visual and neurodegenerative impairments.[6,67]

The complications of maldigestion are intensified by the resultant occurrence of fat malabsorption. A subsequent symptom of fat malabsorption is steatorrhea which is determined by the presence of frothy, foul-smelling, stool that floats in response to high dietary fat consumption. Steatorrhea creates additional GI symptoms such as abdominal cramping and bloating.[26] The elevated risk for malnutrition secondary to malabsorption manifests as unplanned weight loss, cheilosis, glossitis, tetany, and potentially peripheral neuropathy due to diminished absorption of fat-soluble vitamins – A, D, E, and K – as well as a reduction in essential fatty acids, calcium, and magnesium.[1,6] In the prospective, controlled cohort study by Duggan et al., serum measures of vitamins A and E were deficient in CP when compared to the controls: vitamin A 9% versus 4%, and 15% versus 2%. Vitamin D (25OHD) deficiencies were similar in both groups with 36% of CP patients versus 37% of the control group. A 2013 prospective cohort study (Sikkens et al.) of 40 CP patients found deficiencies in all fat-soluble vitamins: A (3%), D (53%), E (10%), and K (63%).[26] In CP patients, Hummel et al, discovered that the expression of CYP24A1 an enzyme which degrades vitamin D is significantly elevated during inflammation.[29] The detrimental effects of prolonged nutrient deficiencies promote decreased bone health and ultimately resulting in reduced bone mineral density including osteopenia and osteoporosis.[54,55,87]

Nutritional Interventions

Current literature has primarily focused on alleviation of CP complications (pain and EPI), via surgery, pancreatic enzyme replacement therapy (PERT), endoscopic therapy, and pain medications for abdominal distress. Nutritional interventions have not been well investigated

outside of the administration of PERT strategies. However, a limited number of studies have indicated improved CP patient compliance, and improved nutrition status with medium chain triglyceride (MCT) dietary supplements, nutrition education versus MCT supplementation, low fat diets, PERT therapies, and antioxidant therapies.[2] Even more limited are recent studies investigating the resultant effects of CP with respect to dietary intakes, and nutritional status before and after the onset of disease.

The rationale for use of MCT stems from shorter chain length (6 to 10 carbon links) of these fatty acids providing the ability for intact absorption and rapid conversion into an immediate fuel source that are absorbed by intestinal cells and immediate transportation to the liver.[2,20,57,88] Additional support for MCT therapy is tied to the absorption process which does not require pancreatic exocrine secretions and reduces the potential for severe GI distress that occurs in CP.[89] MCT oil facilitates an alternative method to improve unplanned weight loss in CP patients to augment the use of PERT therapies. Available as an over the counter supplement, MCT oil can be added to juice, soups, salads, vegetables, and sauces. Adding MCT oil to food reduces the risk for potential gastric distress, emesis, nausea, gas, and as a means to mask the unpalatable taste of the oil. Initial doses for adults are recommended up to 2 tbsp (30 mL) per day.[89] However, clear benefits of using MCT oil administration is lacking in the literature and may not be superior to successful PERT therapies facilitating long chain fatty acid absorption.[90] Although compliance of MCT oil intake may be enhanced due the perception of this product as a pharmacological agent.

In 2008, a randomized control trial examined improvement of nutritional status in patients with CP via the comparison of supplemental MCT therapies versus dietary counseling with homemade foods. Throughout the study 24-hour food recalls were conducted by a Registered Dietitian. The primary outcome measured was the evaluation of changes from

baseline in body mass index (BMI). The secondary outcomes measures focused on body composition changes measured in triceps skin folds (TSF), and mid-upper arm circumference(MUAC). Researchers found that the combined dietary counseling with homemade diet was as efficacious as the supplemental MCT therapy regimen in the management of EPI with respect to decreased fecal fat of patients with CP.[57] Additionally, baseline BMI values which revealed underweight status were both improved to almost normal status at month three of the interventions: counseling BMI (kg/m^2) increased from 17.1±1.7 to 18.1±1.8, and the supplementation group increased in BMI (kg/m^2) 16.7±1.6 to 18.2±1.6. Equally significant was the improvement across both groups in energy (carbohydrates, fat and protein) at month 3 of the intervention.[57] The significant indications of this study were that supplements (expensive, foul tasting, less physiologic), could be effectively replaced by dietary counseling from a Registered Dietitian reducing the onset of clinical manifestations and risk of secondary complications (malnutrition) in CP.[19]

Intense chronic abdominal pain is the most prevalent hallmark symptom of chronic pancreatitis. The pain severity acts not only as a fear based deterrent to adequate nutritional intake but reduces the quality of life. Standard CP treatment protocols to control for pain management includes the initial response of pancreatic rest and a low-fat diet. A 2014 research study indicated that amongst 17 CP patients experiencing chronic abdominal pain who were not responsive to the typical pain therapies were placed on an elemental low-fat dietary regimen.[5] The supplement utilized in the study was a daily 80-gram dosed powder formula made up of dextrin, amino acids, soybean oil, minerals and vitamins. The preparation of the supplement was a simple dissolution in lukewarm water which promoted high participation compliance. Amelioration of abdominal pain was reported in 15 out of the 17 patients by week 8. Complete cessation of pain was reported by 67% of the group. The low-fat elemental diet was effective in

reduction of plasma CCK which in turn reduced pancreatic exocrine secretions. The clinical implication would be the reduced risk of pain.[5] A 2012, large scale Japanese study by Kataoka, et al, investigated pain and nutritional status of CP patients.[91] The 12 week intervention involved the administration of an oral low fat diet with purified amino acids – 600 kcal/day in addition to an unrestricted diet – to 594 eligible patients. The significant outcomes revealed improved BMI values in clinically designated underweight – an increase of mean BMI of 16.1 kg/m^2 to 16.7 kg/m^2,(no change overweight categories) – in addition to reduction of abdominal pain.

PERT therapy is the traditional route for management of CP related maldigestion and malabsorption of fat, and fat-soluble vitamins (A, D, E, and K). Indications for commencing PERT therapy is the designation of severe EPI (>15g/day of fecal fat).[13,27,92] However, this therapy has shown to be beneficial for normalizing micronutrient deficiencies when EPI is at moderate to mild levels of fat malabsorption (7gm to 15 gm of fecal fat). The current dosing recommendations for PERT therapy are outlined in Table 1. Adequate digestion of fat within the duodenum requires lipase in the range of 30 – 60 IU/mL of pancreatic fluid, or, <10% of the 90,000 IUs of lipase produced by a normally functioning pancreas.[22,82] Determination of enzyme administration is based on body weight and then according to fat percentage in meal consumed. The conversion for enzyme requirement is 2,000 IU per gram of fat.[82,92] Initially for severe EPI is in the range of 25,000 to 50,000 IUs. Improvement in malabsorption through PERT administration is measured through individual weight gain, body mass index, and reduction in episodes of steatorrhea.[58,82] Additional verification of PERT effectiveness is related to decreased gastrointestinal issues (flatulence, bloating, and abdominal distress). The enzymes require protection from gastric acid degradation via a pH-sensitive enteric coated capsule, or administration with a proton pump inhibitor/H_2-blocker. A 2010, double-blind randomized control trial investigated the efficacy of Pancrelipase Delayed-

PERT Administration	
Dosing Per Individual	
	Body weight
	Severity of fat malabsorption
	Dosed according to grams of fat intake
Dosing Calculation	
	2,000 lipase units per gram of fat
Dosing Per Meal	
	25,000 – 50,000 lipase units per main meals
	10,000 – 25,000 lipase units per snack
Increased up to 80,000 lipase units dependent upon disease severity, and clinical symptom response	
PERT Timing	
Prior to every meal	
Acceptable to split up over course of meal	

Table 1. Pancreatic Enzyme Replacement Therapy (PERT) Administration.

Release Capsule (CREON) for treatment of EPI in patients with CP or pancreatic surgery.[93] Verification of CP diagnosis was done by histology assessments, or imaging revealing pancreatic calcification. A five-day placebo run in trial preceded the double-blind randomized trial. Subsequently, participants were then assessed against the study inclusion criteria, and the selected eligible participants were then split into two groups: 25 receiving CREON, and 29 receiving a placebo. The PERT therapy in the study utilized CREON which were 12,000-lipase unit capsules which were taken for seven consecutive days. Each of the intervention subjects were given 6 CREON capsules (72,000 IU) per main meal, and 3 capsules (36,000 IU) per snack. The study was conducted at tightly monitored and controlled clinical facility. The study Registered Dietitian designed the dietary fat within the menu at 100g to ensure a minimum consumption of 80g of fat per day. A 72-hour stool collection was conducted at the end of the study. Coefficient of fat absorption analysis was significantly greater in the CREON group (n=24) (32.1±18.5% vs.

8.8±12.5%), compared to the placebo group (n=28) (97.7±82.3% vs 24.4±101.0%) from baseline to end of study. Patients also noted symptom improvements including diminished gastrointestinal distress, stool consistency and frequency.

The usefulness of an antioxidant approach to pain management in diagnoses of CP has become evident where other pain remedies are not appropriate – surgery, endoscopic therapy, or analgesics.[94] Additionally, opioid pain based regimens for CP have increased risk for addiction and opioid induced constipation. Vegetables, fruits, cocoa, and tea are natural food sources of antioxidants such as flavonoids, glutathione, and vitamins A, C, and E. Antioxidant therapies have been suggested for the ability to suppress the cellular damage, promotion of pancreatic inflammation, and inherent pain caused by free radicals.[95] Furthermore, the anti-inflammatory properties of antioxidants could potentially offer a mechanism to improve progression of the disease through reduction of inflammation, damage to acinar cells, and pain. While there have been RCTs with antioxidant interventions which failed to produced a reduction in pain, or possible harm, gastrointestinal distress, or increased mortality from prolonged, and or supplemented high dosed antioxidants (Vitamins A and E), adverse reactions were not observed when antioxidants were components of normal dietary intakes.[3,94] A 2015, systematic review and meta-analysis of eight studies which involved 446 patients (234 receiving the intervention and 212 controls) investigated the efficacy of antioxidants interventions in CP patients.[4] Despite significant reduction in pain occurring in the interventional groups, the studies were largely underpowered and efficacy has not been established.

Dietary intakes of specific foods – excess fat or protein – have been investigated as correlative factors in the onset and severity of alcohol induced CP. While such studies searched for associative effects, the outcomes were more indicative of alterations in dietary habits which became more restrictive with systemic complications and progression of the disease. An Italian

prospective controlled cohort study examined the dietary intakes of 40 CP subjects and 75 controls for ≥ 10 years.[47] Anthropometric data included height, weight, body mass index (kg/m^2), waist to hip ratio, and thigh circumference. Data assessment was collected via 7-Day Food Records, and 24 Hour Food Recalls conducted by Registered Dietitians. The food intake composition (fat, protein, carbohydrates, cholesterol, fiber) was analyzed by Italian National Institutes of Nutrition. The study revealed statistically significant differences in dietary habits and anthropometrics between the CP and control groups. On average, the CP group consumed just under 500 kcal/day more than the control group, and, simultaneously had BMI values which were well within the normal or health weight for height interpretation compared to the overweight status of the control group. Additionally, daily energy intake provided by carbohydrates and protein was was ≥ 71.7% for the CP group and ≥ 63.4 for the control group. Energy provided by carbohydrate sources replaced the energy provided from fat by ≥ 14.1% in the CP group. Rationale for the increased carbohydrate intake was related to fear of postprandial pain upon fat consumption, consistent (improved) carbohydrate intake to compensate for onset of T3c DM, and the recommendation of a low fat diet from the primary care physician. Table 2 contains the specific anthropometric and dietary intake data for the Vaona, et al., study.

Anthropometrics	CP Patients	Control Group
Body Mass Index (kg/m^2)	21.9 ± 3.1	26.1 ± 3.1
Weight (kg)	63.4 ± 10.6	77 ± 9.9
Height (cm)	170.1 ± 5.7	171.0 ± 6.1
Waist to Hip Ratio	0.89 ± 0.1	0.93 ± 0.1
Dietary Intake	**CP Patients**	**Control Group**
Total Energy Kcal	2585.5 ± 850.2	2104.0 ± 528.5
Carbohydrate (gm/day)	362.0 ± 168.0	250.0 ± 120.0
Protein (gm/day)	95.0 ± 33.0	88.0 ± 33.0

Table 2. Anthropometrics and Dietary Intakes

Dietary Patterns in Chronic Disease

Nutritional therapy investigations have traditionally focused on individual nutrients, foods, and food groups despite the vast literature which reveals a well balanced, nutrient dense diet promotes beneficial health and reduced risk for chronic disease. The postprandial interactions of food constituents, and/or whole food groups limit the ability to discern if the proposed health benefits result from the individual component or the combination of foods. Furthermore, dietary manipulations may also affect the effectiveness of the nutritional component in question. The examination of dietary food patterns provides insight into the combined effects produced by nutritional consumption in its entirety which is more indicative of actual eating habits – food is typically consumed in tandem not as single nutrients, or components.

A recent U.S. Department of Agriculture investigated health outcomes in chronic diseases as related to dietary patterns.[96] The systematic review defined dietary patterns according to food varieties and combinations, intake frequencies, meal size, number of meals, drinks, and nutrients. Assessment of dietary patterns were contrasted to known dietary indices,

or scoring system – the HEI, DASH Diet, Mediterranean Diet, etc. – which provided a method for analyzing the overall dietary intake. The goal of the research was to examine potential relationships between the risks for obesity, cardiovascular disease, and type 2 diabetes and selected dietary patterns and dietary guidelines. A total of 12 systematic review questions were implemented with the goal of measuring adherence to dietary guidelines via the scoring and nutritional intake indices. The dietary intake patterns which resulted in greatest risk reduction potential were the Mediterranean diet, Dietary Approaches to Stop Hypertension, and the Dietary Guidelines for Americans.

The Bamia, et al. study investigated the correlation between colorectal cancer (CRC) and adherence to the Mediterranean diet.[97] The research utilized results from a large scale European cohort study – European Prospective Investigation into Cancer and nutrition study. The subsequent number of eligible cases for this study within this larger cohort was set at 480, 308 participants out of the original 521,330 participants. The dietary patterns were obtained through food frequency questionnaires and separately assessed for one of two modified Mediterranean diet (MMDS) scoring systems. The difference in the two adaptations of the Mediterranean diet was the cut-off value of risk for CRC when comparing high to low adherence in each group. The participant follow up was for 11.6 years. The results revealed that more men (31%) had a higher adherence rate to the modified Mediterranean diet than women (29%). The relationship between CRC and adherence to the MMDS was not found to be statistically significant, however, compliance to the diet was indicated as providing modest beneficial decreased risk in CRC development.[97]

Food Insecurity

The implementation of the validated two-question food security screen – which was reliable, highly sensitive, and user friendly – is to identity situations of uncertainty in acquisition, and sufficient food nutritionally adequate stores, or the ability to obtain food items in a socially acceptable manner.[105,106] The occurrence of food insecurity encourages poorer outcomes in cases of chronic disease.

Summary

The literature investigating nutrition therapies for patients with chronic pancreatitis has largely focused on individual foods, or components within food items. Studies examining whole food patterns as a means of optimizing nutritional status in the maintenance and progression of chronic pancreatitis are scant. Additionally, dietary studies are often undertaken as a means to determine viability for pain reduction as it is a consistent complication of this disease. The secondary complications related to maldigestion and malabsorption present a heightened risk to overall nutritional status and potentially malnutrition for this population. That said, factors which amplify the potential for diminished nutritional status on top of the loss of function – inadequacy of overall diet, or failure to recognize synergistic activity of food constituents upon on one another – should be considered as routes to optimize nutritional status in such a heterogeneous population.

Chapter 3: Methods

Research Design

This thesis was a cross-sectional prospective study, analyzing data collected for a larger study at the Ohio State University Wexner Medical Center and its affiliated campuses, i.e., Martha Morehouse Medical Plaza, Gastroenterology Outpatient Endoscopy in Doan Hall clinic, and the Stoneridge Medical Services Endoscopy. The encompassing study was a cross-sectional prospective, single group, single test design. Data collection included the following: medical chart review, standard anthropometric measurements, Vioscreen Food Frequency Questionnaire, Two-Question Food Insecurity screen, and a demographic questionnaire.

Research Questions

- What is the average HEI score for a sample of patients with CP as measured by Vioscreen FFQ?

- What is the average MED score for a sample of patients with CP as measured by Vioscreen FFQ?

Sample Population

An Institutional Review Board application was submitted to the Ohio State University on August 31, 2015 and was approved on November 20, 2015. (IRB#: 2015H093) Participants with CP, according to the study inclusion criteria, were recruited through the Pancreas clinic (at the Martha Morehouse Medical Plaza (MMMP).

Inclusion and Exclusion Criteria

To participate in this study participants must fulfill the following criteria:

a. Inclusion criteria:
   i. Age >18 years
   ii. Food secure measured by the two item food security screener[16]
   iii. Ability to read English and independently operate an iPad
   iv. For participants enrolled into the CP group, a diagnosis of CP must be provided by a physician according to definition below.
b. Exclusion criteria:
   i. Inability to voluntarily provide informed consent for study (including prisoners).
   ii. Presence of other gastrointestinal diagnosis including inflammatory bowel disease, C. difficile colitis, eosinophilic esophagitis, hepatitis B or C, gastroparesis, microscopic colitis, non-alcoholic fatty liver disease/hepatic steatosis, celiac disease, short bowel syndrome, or malignancy.
   iii. History of gastrointestinal surgery, including gastric bypass
   iv. History of diagnosed eating disorder

B. Definition of CP: For the purposes of this study a diagnosis of chronic pancreatitis is established by fulfilling any **one of the following three** clinical scenarios (i.e., a or b or c):
   a. **Presence of pancreatic calcifications** - Pancreatic parenchymal or ductal calcifications (≥1) seen on abdominal imaging study
   b. **Suggestive for chronic pancreatitis** – fulfillment of any of the following 3 criteria (i.e., i or ii or iii):
      i. EUS demonstrating lobular appearing pancreas (≥3 continuous lobules) and ≥3 minor EUS criteria
         1. Minor EUS criteria (aka Rosemont criteria) include: lobular appearing pancreas (1-2 lobules), hyperechoic foci without shadowing, cysts, hyperechoic stranding, irregular main pancreatic duct contour, dilated side branches, main pancreatic duct dilation, or hyperechoic main pancreatic duct walls
      ii. EUS demonstrating ≥ 5 minor EUS criteria
      iii. Presence of ≥ 3 abnormal pancreatic duct side branches visualized on MRCP or ERCP (derived from Cambridge criteria for mild chronic pancreatitis)

   c. **Indeterminate EUS findings for chronic pancreatitis with evidence of exocrine pancreatic insufficiency (EPI)** (i.e., i + [ii or iii or iv or v])
      i. Presence of 3-4 minor EUS criteria (listed above)
      ii. Abnormal fecal fat collection (>15g fat per day)
      iii. Abnormal endoscopic pancreas function test (i.e., maximum duodenal bicarbonate concentration <80 meq/L)
      iv. Decreased serum trypsin (<20 ng/mL)
      v. Decreased fecal elastase level (<200 microgram/gram stool)[15]

Consent

Eligible participants were provided a written copy of the IRB approved consent form prior to the start of the study. The study protocol and informed consent was described in detail to the participants. (Appendix E: CP Study IRB approved consent form) There were no risks to subjects for participating in this study, aside from the possible loss of privacy from review of available medical records. All of the submitted documents – health questionnaire forms, IRB consent forms, and data generated from VioScreen FFQ – were electronically stored on an encrypted and password protected network drive with the Ohio State University Medical Center, and hard copies of said data were secured in a locked filing cabinet within the medical center office of a study coordinator. Additionally, all patient's data was de-identified via coding in place of participants actual names.

Instruments

The study used an online web-based food frequency tool, VioScreen, to collect dietary intake assessments of the study participants. VioScreen has been validated as an appropriate tool in research and clinical settings to accurately assess a patient's diet.[49] Vioscreen uniquely uses 1,200 food pictures to assist in the collection of detailed data on foods usually consumed and automatically calculates nutrient intake and food use patterns within a given population.[49] The viability and accuracy of Vioscreen has previously been compared to traditional pencil and paper food frequency questionnaires. [49] Computer based FFQs have the ability to overcome challenges – unanswered questions, questions answered with multiple responses, inability to provided adequate food choices and portion sizes – to paper questionnaires. The complications produce highly inaccurate intake measurements of energy, macro and micronutrients, and yield inexplicable skipping patterns. Additionally, the data produced by such pencil and paper FFQs

have to subsequently be entered in a dietary analysis program which further limits accuracy by errors in data entry, and leads to a delay in producing a report that is timely with meaningful results that can be given to the respondent. Vioscreen has the flexibility to provide solutions to these challenges in its ability to provide real-time and instantaneous feedback while eliminating the option to miss or incorrectly answer a question through multiple responses. The computer based FFQ provides enhanced selection of food choices and portion sizes so that the error in reporting intakes of foods and portion sizes is also greatly reduced. The study findings were that as a dietary intake instrument was it low burden on the participant, improved reporting of macronutrient intermethod reliability, and practicality as a clinical research device.[49,52]Kristal et al, evaluated the validity and reliability of Vioscreen through comparison to selected criterion measures – weighted food records and repeated 24-hour recalls – for nutrient intake analysis. The study utilized the inter-method technique to evaluate Vioscreen. A 24-hour food recall was selected as the criterion measure and performed six times by 74 study participants. Vioscreen was administered twice by all participants before and after completing the first and last of the 24-hour food recalls. The investigation revealed a higher level of intermethod reliability of Vioscreen in comparison to the traditional FFQ used in large epidemiological studies, and to the FFQ which provided the basis for Vioscreen.[49,52,98] The moderate correlational value for protein of 0.67 was the only measurement below 0.80 in the comparison between Vioscreen and the six 24-hour recalls (high correlation values were reported at 0.90 for alcohol, 0.84 for saturated fat, 0.82 for total fat, and a value just below high of 0.79 for carbohydrates). Lastly, participant feedback on user-friendliness, level of excellence, and willingness to repeat Vioscreen if asked in a future clinical setting ranged from 93% to 99%.

Data Collection

At the time of agreement to participate in this study, patients were assigned a unique study ID number. A master list of the patients' MRN's and corresponding study ID's were retained in an encrypted, electronic file on the password-protected OSU network drive, and the hard copy of study documents were stored in a locked office available only to the PI in the Division of Medical Dietetics (Atwell Hall, Room number 306). Data will be stored for period of 5 years.

The eligible CP patients were identified by the physicians in the Division of Gastroenterology, Hepatology and Nutrition. The patients were screened and determined eligible by the study inclusion/exclusion criteria. Upon verification of study participation eligibility, the patients were contacted by telephone, or in person at the pancreas clinic while they are waiting for their appointment. Subsequent to phone contact, the patient was requested to make an appointment to come into the clinic for study participation. The patients who agreed to participate were requested to present themselves one hour before their scheduled clinic visit to allow for sufficient time to fully participate in the study. Patients who agreed to participate on non clinic appointment days were duly informed of study duration. The study protocol and significance was explained in detail to the study candidate at the beginning of the study appointment. The duration of the appointment was approximately one hour in length and included: explanation of the the study, obtaining a signed consent from the patient, completion of demographic questionnaire (which includes medical history, smoking and alcohol history, and medication review), with a two-question food security survey screen (Appendix D: Demographic Questionnaire With Two-Question Food Security Survey Screen), dissemination of requisite instructions, and completion of the Vioscreen FFQ. At that time the study participant was provided with an iPad to complete the VioScreen, which on average required 30 to 45

minutes to complete. After completing the Vioscreen FFQ, copies of the IRB consent form, a one page personal health and nutrition summary (generated by the Vioscreen FFQ), and a $10.00 grocery store gift card – which they signed as received at that juncture of the study – were provided to the participants. The subjects were thanked for their participation and then discharged from the study. The original copies of the signed IRB consent form, demographic questionnaire with two-question food security survey screen, signed receipt of gift card distribution, and both Vioscreen generated reports (Personal Health and Nutrition Summary, and, Personal Health and Nutrition Report) were scanned and uploaded to the specific study encrypted and password protected network file for electronic storage, and all hard copies stored in the designated secured and locked office available only to the PI in the Division of Medical Dietetics (Atwell Hall, Room number 306) There will be no follow-up visits for the purpose of the study.

Research Questions	Data Source	Analysis
1. What is the average HEI score for a sample of patients with CP as measured by Vioscreen FFQ?	VioScreen Graphical FFQ	Descriptive mean score
2. What is the average MED score for a sample of patients with CP as measured by Vioscreen FFQ?	VioScreen Graphical FFQ	Descriptive mean score
Demographic Data Height, Weight, Body Mass Index, Diagnosis, Smoking, Alcohol, Food Security	Health Questionnaire with 2-Question Food Security Screen, and Medical Record	Categorical data will be summarized with frequencies and percentages

Figure 1. Research Design

Dietary Pattern Indices and Scoring Parameters

Healthy Eating Index

The Healthy Eating Index (HEI) is a method of assessing the nutritional intake quality via comparison to the guidelines set by the Dietary Guidelines for Americans (DGA). The DGA utilize food patterns in developing recommendations according to calorie consumption levels with restrictions on the energy provided by added sugars and solid fats.[9] The goal of the HEI is to provide an overview of dietary enhancements to improve the adequacy of the diet with respect to nutrient dense components requiring increase, food components that should be only considered in moderation (to be decreased if consumed at levels presenting risk for adverse health outcomes). Additionally, foods are scored according to variety of food constituents

(evaluating dietary patterns), and including recommendations with respect to expected energy requirements through the life cycle respective of age, and gender. The key recommendations involve increased fruit and vegetables in natural states (avoiding canned, frozen, or dried) encompassing a range of colors (especially dark green), limiting intake of refined grains (especially those high in fats, added sugar, and sodium) and replacing with whole grains by at least half, dairy to be fat free or low fat, protein sources to be lean and in variety (a mix of poultry, fish, eggs, beans, peas, soy products, and unsalted nuts and seeds), and total daily energy intake of fat to be less than 10% and in the form of mono- and polyunsaturated fats.[9,10] Further recommendations: dietary cholesterol intake <300mg/day, avoid trans fats (hydrogenated oils), decrease intake of solid fats existing in any food source and replacement by oils, selection of foods rich in calcium, vitamin D, potassium, and dietary fiber. Lastly, sodium intake limited to <2.3 gm/day, and less than <1.5 gm/day for persons over the age of 51.[9,10] Figure 2 displays the HEI component make up.

Healthy Eating Index (HEI) Calculation

The scoring for the HEI is out of a maximum of 100 points accumulated from intakes of the components included in 12 food groups. The scoring system assigns higher values for increased intake of foods required for an adequate diet, and increased values for foods to be consumed in moderation that are consumed in lower amounts. (Table 3: Healthy Eating Index Score Assessment. www.cnpp.usda.gov). Table 4 presents the most recent NHANES HEI score for the total U.S. population.

HEI-2010 Food	Max Score	Consumption level (Max Score)	Consumption level (Min Score - Zero)
Adequacy (increased intake marked by higher score)			
Total Fruit	5	≥0.8 cup eq/1,000 kcal	No fruit
Whole Fruit	5	≥0.4 cup eq/1,000 kcal	No whole fruit
Total Vegetables	5	≥1.1 cup eq/1,000 kcal	No vegetable
Greens and Beans	5	≥0.2 cup eq/1,000 kcal	No dark green vegetables, peas, or beans
Whole Grains	10	≥1.5 cup eq/1,000 kcal	No whole grains
Dairy	10	≥1.3 cup eq/1,000 kcal	No dairy
Total Protein Foods	5	≥2.5 oz eq/1,000 kcal	No protein foods
Seafood and Plant Proteins	5	≥0.8 oz eq/ 1,000 kcal	No seafood or plant proteins
Fatty Acids	10	(PUFAs & MUFAS)/SFAs ≥2.5	(PUFAs & MUFAS)/SFAs≤1.2
Moderation (decreased intake marked by higher score)			
Refined Grains	10	≤ 1.8 oz eq/1,000 kcal	≥4.3 oz eq/1,000 kcal
Sodium	10	≤1.1 gm/1,000 kCal	≥2.0 γραμσ/1,000 κχαλ
Empty Calories	20	≤19% of energy	≥50% οφ ενεργψ

Table 3: Healthy Eating Index Score Assessment

HEI-2010 Total and Component Scores1 for the U.S. Total Population, Children and Older Adults, NHANES 2011-2012			
HEI-2010 Dietary Component	Total Population	Children	Older Adults
(maximum score)	≥ 2 years (n=7,933)	2-17 years (n=2,857)	≥ 65 years (n=1,032)
	Mean Score (standard error)		
Total fruit (5)	3.00 (0.11)	3.91 (0.18)	3.84 (0.22)
Whole fruit (5)	4.01 (0.17)	4.78 (0.22)	4.99 (0.05)
Total vegetables (5)	3.36 (0.08)	2.10 (0.09)	4.16 (0.19)
Greens and beans (5)	2.98 (0.15)	0.70 (0.09)	3.58 (0.47)
Whole grains (10)	2.86 (0.13)	2.50 (0.10)	4.23 (0.34)
Dairy (10)	6.44 (0.14)	9.03 (0.22)	5.99 (0.16)
Total protein foods (5)	5.00 (0.00)	4.44 (0.13)	5.00 (0.00)
Seafood and plant proteins (5)	3.74 (0.20)	3.05 (0.17)	4.91(0.18)
Fatty acids (10)	4.66 (0.14)	3.29 (0.18)	5.60 (0.36)
Refined grains (10)	6.19 (0.15)	4.91 (0.16)	7.34 (0.31)
Sodium (10)	4.15 (0.06)	4.85 (0.25)	3.66 (0.26)
Empty calories (20)	12.60 (0.23)	11.50 (0.28)	14.99 (0.44)
Total HEI score (100)	59.00 (0.95)	55.07 (0.72)	68.29 (1.76)

Table 4. HEI-2010 Total and Component Scores1 for the U.S. Total Population, Children and Older Adults, NHANES 2011-2012

Mediterranean Diet

The Mediterranean diet has been extensively studied since the 1970s and adherence to such a dietary pattern has been linked to a significantly decreased risk in cancer, cardiovascular disease, obesity, and type 2 diabetes miletus.[7,97,99–102] Hence, the historical implication is the status of improved health status with this dietary regimen. Additional benefits conferred by adherence to the Mediterranean diet were related to reduction of inflammation and coagulation in the ATTICA study – a major epidemiological study.[103] The diet is typically presented in pyramidal form with distinctions for food groups according to frequency of intake:

monthly (red meat), weekly (sweets, eggs, potatoes, olives, pulses, nuts, poultry, and fish), daily (dairy products, olive oil, fruit/vegetables – including wild greens), non-refined cereals and products (whole grains – breads, brown rice, and pasta). Salt consumption should be at a minimum, wine consumed in moderation, and water should be continuous and plenty.

The Mediterranean Diet (MED) score, provided a scoring system to determine the level of adherence to this dietary intake pattern. The scoring was based on the weekly intakes of the following 9 types of foods: non-refined cereals (any whole grained rice, bread, or pasta), dairy (any full-fat cheese, milk, or yogurt), vegetable, legumes, fruit, animal protein sources (poultry, fish, meat and meat products), olive oil, and alcohol consumption. Potatoes are not a food listed in the Mediterranean diet per se, but offer substantial amounts of vitamins (vitamin C, B1, B2, and niacin), minerals (potassium, magnesium), carbohydrates, and fiber which will contribute to nutrient density of the meal and cardio protective effects.[100] The concern however would be excess consumption of carbohydrates in potatoes and the correlation to T2DM.

The exact scoring was done as follows: 0 – no intake reported, 1 – 5 for seldom to daily intakes, and the reverse for alcohol intake, for example, 0 intakes of alcohol would be scored a 5. The reverse scoring was applied to intakes of alcohol, poultry, red meat products, and intakes from the full fat dairy group. and Table 5 lists the detailed scoring system. The completed scores were then categorized from highest to lowest adherence to the Mediterranean diet with higher score indicating greater compliance: 45-55, 35-44, 22-34, 12-22, and 0-11.

Food Group	Intakes – recorded as servings per week, or quantity					
Non-refined grains	Never	6-Jan	12-Jul	13-18	19-31	>32
	0	1	2	3	4	5
Vegetables	Never	6-Jan	12-Jul	13-20	21-32	>33
	0	1	2	3	4	5
Legumes	Never	<1	2-Jan	4-Mar	6-May	>6
	0	1	2	3	4	5
Fruit	Never	4-Jan	8-May	15-Sep	16-21	>22
	0	1	2	3	4	5
Potatoes	Never	4-Jan	8-May	12-Sep	13-18	>18
	0	1	2	3	4	5
Olive Oil (cooking-times/week)	Never	Rare	<1	3-Jan	5-Mar	Daily
	0	1	2	3	4	5
Fish	Never	<1	2-Jan	4-Mar	6-May	>6
	0	1	2	3	4	5
Poultry	≤3	5-Apr	6-May	8-Jul	10-Sep	>10
	5	4	3	2	1	0
Dairy (Full fat)	≤ 10	15-Nov	16-20	21-28	29-30	>30
	5	4	3	2	1	0
Red Meat and meat products	≤ 1	3-Feb	5-Apr	7-Jun	10-Aug	>10
	5	4	3	2	1	0
Alcohol	<300	300	400	500	600	>700 or 0
	5	4	3	2	1	0

Table 5: Mediterranean Diet Score Assessment[102]

Data Analysis

Categorical data will be summarized with frequencies and percentages. To analyze continuous measures of dietary intake in patients with chronic pancreatitis a sample t-test will be used. If the assumption of normality of the t-tests is violated, the Wilcoxon rank-sum test will be used. Differences between categorical measures will be assessed with the chi-square test (or Fisher's exact test in the case of small sample size). All results will be presented as point

estimates with corresponding 95% confidence intervals and significance will be defined as a two-sided p-value of less than 0.05.

Limitations

The study has a number of limitations. An initial limitation is that participants' nutritional assessment was only performed with a single type of food online computer based frequency questionnaire (FFQ) and not compared to a conventional non-computer based FFQ, or compared to an alternative online computer based FFQ. A combination of alternative and similar FFQ techniques, or, multiple FFQs using the same FFQ instrument, performed by each study participant, would provide a means to account for inherent errors of over and underestimation of intakes related to self-reporting bias. The difficulty in utilizing different FFQ instrumentation (paper versus computer based) for comparison of nutritional intake assessment is the limited data examining the intra-method reliability comparing the assessments. Additionally, the inability of paper FFQ to process nutritional analysis with complex algorithms over a wider range of food items and portion sizes that exist in web based FFQ platforms.[49] Instead the study based comparison on previously published nutrition assessment measures the HEI and MED scoring systems. The second limitation are the exclusion of validated unbiased nutritional biomarkers. The biomarkers would have provided insight on nutritional deficiencies which are not subject to recall bias or expectation bias.[50–52]

Chapter 4: Results and Discussion

Introduction

The purpose of the study was to assess the dietary intake of patients with diagnosed CP. The information garnered from the study could assist in the development of medical nutrition therapies based upon disease severity and prevent long-term complications of malnutrition. This thesis was a cross-sectional prospective study, analyzing data collected for a larger study at the Ohio State University Wexner Medical Center. The encompassing study was a cross-sectional prospective, single group, single test design. Data collection included the following: medical chart review, standard anthropometric measurements, Vioscreen Food Frequency Questionnaire, Two-Question Food Insecurity screen, and a demographic questionnaire.

Research Questions

- What is the average HEI score for a sample of patients with CP as measured by Vioscreen FFQ?
- What is the average MED score for a sample of patients with CP as measured by Vioscreen FFQ?

Population Demographics

A total of 58 potential study participants were identified by the primary physician for the pancreas clinic who was also the research investigator of this study. The physician identified

the eligible participants according to the study inclusion/exclusion criteria, and had a scheduled clinic visit during the data collection time frame of January 14, 2016 to March 17, 2016. Phone call encounters were made biweekly to these eligible study participants in an attempt to recruit them for study participation in advance of their upcoming appointments, or at an alternate time on non-clinic appointment days. From these phone calls 2 participants agreed to partake in the study outside of scheduled appointments at the clinic, 5 agreed to participate during scheduled clinic appointments, 2 declined to participate, and 47 were either unreachable by phone, or did not respond to voicemail messages. Twenty-one eligible participants agreed to participate in the study upon a face-to-face encounter describing the study during their clinic appointments. A total of 27 eligible study participants (46%) completed the study, and 1 eligible study participant failed to complete more than 50% of the study and was excluded from the analysis. The study population included eighteen men with a mean age of 50.1 ± 14.1, and nine women with a mean age of 47.8 ± 20.3.

Results

The corresponding means for HEI score, and aMED score for the study sample population were, respectively, 57.17 ± 11.8, and 22.7 ± 6.2. (Table 6) The correlations between the HEI score and the aMED scores were calculated with the Pearson statistical model. The strength of the Pearson correlation between these two dietary indices in the study was moderately positive correlation or 0.532 ($p < .05$). An independent samples test (Levene's test for equality of variance, and t-test for equality of means) revealed no statistical significance in a stratification of the sample population according to gender ($p > .05$). Pearson correlations conducted for the two dietary indices subsequent to a gender stratification of the sample population revealed men (n=18) with a low positive, or weak correlation (0.357), and a very high

positive, or very strong correlation (0.806) for the women (n=9). Additionally, once stratified according to gender the mean scores for HEI and MED were, respectively, 54.8 ± 10.3 and 21.39 ± 5.5, for men, and, 63.4 ± 13.0 and 25.22 ± 7.0, for women.

Dietary Scores	Men	Women	Total
HEI	54.8 ± 10.3	63.4 ± 13.0	57.7 ± 11.8
MED	21.39 ± 5.5	25.22 ± 7.0	22.7 ± 6.2

Table 6. HEI and MED mean scores, SD

Table 7 identifies the distribution of study participants according to demographic information – lifestyle factors – consumption of smoking and alcohol, and risk of food insecurity. The proportion of current smokers amongst the two groups was higher in the male population at 86% (n=12), of which 100% (n=15) had smoked 100+ cigarettes in their lifetime, and were 67% (n=12) currently smoked 1+ pack per day. The number of current female smokers was 2 and smoked 1 to 2 packs per day. Alcohol consumption above the recommended guidelines (men 2 – 4oz drinks/day, women 1- 4oz drink/day) was more prevalent in the male group - 30% imbibing alcohol 2 – 5+ days/week over the past 12 months, 42% (n=5) consuming 4 – 7+ drinks on days of alcohol consumption, with 25% (n=3) and 17% (n=2) respectively consuming 6+ drinks weekly and daily on occasion in the past 12 months. Concurrent cigarette smoking and alcohol drinking was prevalent in all (n=6) of the clinically underweight subjects (BMI <18.5 kg/m^2), with consumption rates of 1+ packs of cigarettes per day, and a typical intake rate of 4 – 7+ drinks on days in which alcohol consumption occurred over the past 12 months. The results of the Food Insecurity Screening (Appendix: D), revealed 28% (n=5) of the study participants at risk for food insecurities and were all male. Table 8 describes relevant pancreatic histories of the study

population with regard to pancreatic diagnoses, surgeries pertaining to gastrointestinal tract, and additional gastrointestinal diagnoses.

Lifestyle Factors	Men	Women	Total
n	18	9	27
Age, mean, SD	50.1 ± 14.1	47.8 ± 20.3	49.3 ± 16.1
Alcohol consumption - current			
0<2 times per week past 12mo	13	9	22
2-5 times per week past 12mo	4	0	4
>5times per week past 12mo	0	1	1
0-3 drinks per day past 12mo	12	9	21
4-6 drinks per day past 12mo	2	1	3
7+ drinks per day past 12mo	3	0	3
6+ drinks on occasion past 12mo			
never-less than monthly	12	9	21
monthly	1	0	1
weekly	3	0	3
daily	2	0	2
Smoking Habits			
Smoked 100+ cigarettes in lifetime	15	7	22
Smokers - current	12	2	14
Unreported	3	0	0
<0.5 packs per day	1	0	1
1 pack per day	5	1	6
2 packs per day	2	1	3
4 packs per day	1	0	1
Food Insecurity Risk Score?	5	0	5

Table 7. Lifestyle Factors. Selected lifestyle factors of the study participants

Pancreas and GI Diagnoses	Men	Women	Total
n	19	9	27
Pancreatic Cyst	2	1	3
Chronic Pancreatitis	18	9	27
Surgery			
Whipple	1	2	3
Distal Pancreatography	0	1	1
Pancreas Tail/Splenectomy	0	1	1
Frey	1	0	1
TPIAT	0	1	1
ERCP	1	0	1
Other	2	0	2
GI Diagnoses			
Irritable Bowel Disease	0	1	1
Clostridium Difficile	1	0	1
Hepatitis B/C	1	0	1
NAFLD	1	0	1
Cancer	1	0	1
Eating Disorder	0	1	1
Microscopic Colitis	1	0	1
Gastroparesis	1	0	1
Eosinophilic Esophagitis	1	0	1

Table 8. Pancreatic Diagnoses. Frequency of Pancreatic and Gastrointestinal Diagnoses of the study participants

The mean Body Mass Index (BMI) (kg/m^2) of all study participants was 22.7 ± 5.2, and when separated according to gender was 23.2 ± 5.5 for men, and 21.7 ± 4.5 for women. Distribution of the sample population according to BMI (kg/m^2) clinical designations revealed 26% (n=7) of the CP patients were clinically underweight (<18.5), 52 % (n=14) were normal BMI (≥ 18.5, ≤ 24.9), 15% (n=4) were overweight BMI, and 7% (n=2) were obese BMI status (>30). The sub group of subjects with a calculated normal BMI included 43% of whom were at the low end of the normal range – > 18.5 kg/m^2 to ≤20.8 kg/m^2. Additionally, 83% of the clinically

underweight study subjects –according to BMI – presented with weight measurements which ranged from ≥ 60% to ≤ 89% of ideal body weights. Table 9 describes the anthropometrics of the study population, including Ideal Body Weight (IBW), according to Hamwi calculation.

Anthropometrics	Men	Women	Total
n	18	9	27
Height (in), mean, SD	68.2 ± 2.6	64.7 ± 3.4	67.0 ±3.3
Weight (lb) , mean, SD	153.3 ± 37.7	129.4 ± 28.4	145.4 ± 36.2
BMI (kg/m^2) , mean, SD	23.2 ± 5.5	21.7 ± 4.5	22.7 ± 5.2
IBW[1], mean, SD	155.2 ± 15.9	124.2 ± 16.9	144.8 ± 29.8

[1]Ideal Body Weight according to Hamwi calculation.

Table 9. Anthropometrics of the study population represented as means and standard deviations (SD).

Table 10 describes the mean energy intake by totals, and according to gender stratification with percentages of carbohydrate, fat, and protein intakes. The mean total energy (kcal) was 2299.4± 1986.3 for the sample population, and, stratified according to gender, 2603.8 ± 2290.6 for men, and, 1690.6 ± 1023.4 for women. The mean energy intake of 11% (n=3) of the participants measured a value similar to the required energy intake – 35 kcal/kg of Ideal Body Weight (IBW) – for this population. Fifty-nine percent (n=16) recorded mean energy intake ranging from 24% to 75% of recommended total energy requirements. The largest proportion of energy was supplied by carbohydrates (51%), and fat (32%). Saturated fat levels of consumption were above 10% of mean calories in 63% (n=17) of the participants. Total fat energy intake in 19% (n=5) was less than 25% - 30% of total calories. Calories provided by the low fat dairy/skim foods were below 2 to 3 daily servings in 96% (n=26) of the study population. Intake of calories from full fat dairy had a mean serving of 1.7 servings per week, which provided

a mean of 322.6 kcal per week. Excessive intake of empty calories from high sugar foods occurred in 33% (n=9) of the study population. The recommended consumption of fruits and vegetables (5-13 servings daily) was only achieved by 33% (n=9) of the participants, 22% (n=6) consuming <2 servings per day, and 30% (n=8) with intake <1 serving per day. Whole grain intake was revealed at <0.5 servings per day in the majority of the subjects - 48% (n=13). Intake of non-fried fish was non-existent in 37% (n=10) of all recorded diets. Fried food intake distribution in the population was at or below the recommended 0 -1servings per day in 93% (n=25) of all participant's daily intake levels. Table 11 indicates intakes across select food groups as means and energy.

Nutrient and Vitamin Intake	Men	Women	Group
n	9	18	27
Total Energy (kcal), mean, SD	2603.8 ± 2290.6	1690.6 ± 1023.4	2299.4 ± 1986.3
Range (Low-High, kcal)	497.3 - 9238.0	497.3 - 3760.1	497.3 - 9238.0
Carbohydrate. gm (%)	319.0 ± 257.0 (49%)	240.8 ± 204.8 (57%)	293.0 ± 239.8 (51%)
Protein gm (%)	98 ± 84.5 (15%)	67.1 ± 32.0 (16%)	87.7 ± 72.1 (15%)
Fat gm (%)	95.8 ± 82.3 (33%)	55.9 ± 36.2 (30%)	82.5 ± 72.1 (32%
Vitamin Intake Means	Women	Men	Total
Vitamin A (IU), mean, SD	10669.6 ± 10673.5	8644.2 ± 9796.6	9319.3 ± 9937.4
Range (Low-High)	93.0 - 33618.0	2643.0 - 35752.0	93.0 - 33618.0
Vitamin D (IU), mean, SD	345.0 ± 215.6	420.0 ± 390.2	395.0 ± 339.4
Range (Low-High)	7.0 -1284.0	58.0 - 713.0	7.0 - 1284.0
Vitamin E (IU), mean, SD	15.7 ± 12.1	27.6 ± 29.5	23.6 ± 25.4
Range (Low-High)	1.0 - 94.0	4.0 - 36.0	1.0 - 94.0
Vitamin K (mcg), mean, SD	142.0 ± 159.2	131.3 ± 230.8	134.9 ± 206.5
Range (Low-High)	2.0 - 1001.0	29.0 - 522.0	2.0 - 1001.0

Table 10. Nutrient and Vitamin Intakes. Estimated nutrient and vitamin intake quantified from the VioScreen FFQ.

Estimated Calorie and Food Group Intake Means	Men	Women	Total
n	19	8	27
Nutrients (%kcal)			
Total Fat	31.8	30.8	31.5
Sat Fat	11.8	10.3	11.4
Food Group Servings Per Day			
Fruit and Vegetable	3	6.4	4
Whole Grains	1.4	1.8	1.5
Fish	0.1	0.3	0.1
Fried Foods	0.3	0.2	0.3
Sweets	2.3	1.2	2
Low Fat/Skim	0.6	0.3	0.5
Full Fat Dairy Caloric Equivalent			
Full Fat Dairy (kcal/day)	44.5	49.3	46.1

Table 11. Nutrient and Food group intake means.

Discussion

In this study, the dietary pattern indices were based on maximum scores of 100 for the HEI score, and 55 for the MED score. The higher HEI scores indicating increased intake density of HEI food components which are focused on providing overall optimal adequacy of diet – scoring set according to optimal quantities (classified as standards or equivalents), per 1,000 calories. The mean HEI score for the sample population was 57.7, which was comparable to the most recent national average HEI Score of 59.00 (0.95) for the total U.S. population over the age of two. Gender stratification was initiated to determine if there was a significant variation between the mean HEI score of men and women. The expectation was that the women's mean HEI would be higher given that historically women tend to incorporate increased nutrient density with higher intakes of fruits and vegetables compared to men.[104] Upon stratification of the study participants according to gender the mean HEI total score for men decreased to 54.8,

and increased to 63.4 for women. The HEI has been designed to assess diet quality independent of total energy intake.[10] Separation of the HEI score from energy intake eliminated the potential bias of a high calorie intake influencing the scoring as a result of related nutrient intake.[10] Hence, although the HEI total scoring for the two independent groups of the study are just below the national average for men, and noticeably above the national average for women, the index does not address improved adequacy of diet with respect to decreased energy consumption. HEI scores reflected the density of dietary components according to intakes from optimal nutrition set by the US Dietary Guidelines. It is important to remember that patients with diagnosed CP have increased energy needs in the realm of 35 kcal/kg/day for optimal intake due to maldigestion and malabsorption of micronutrients with concomitant weight loss and poor dietary intakes.[13] That said, in this study, increased HEI scores were inconsistent with the other measure of the patient's nutritional status. For example, an HEI score of 75.5 was revealed in a study subject whose total mean energy intake was 73% of the estimated energy intake requirement, clinically underweight according to BMI, and weighed 62% of ideal body weight. Further investigation of consumption of his dietary intake (according to the recommended values set by Dietary Reference Intakes guidelines), indicated severely limited intake across all food groups.

The stratification of the MED score according to gender produced similar effects in differences between the means of each group and the group as a whole. Similar to the HEI means, the women's MED score (25.22 ± 7.0) was significantly higher than the men's mean (21.39 ± 5.5). Despite the stratification and resulting score variations, neither group presented a score reflective of high adherence to Mediterranean type dietary pattern (described in chapter 2). Although there is overlap in the components between the two indices, the foods typified by the westernized diet appear to have influenced the higher comparative score in this population.

For example, 70% of all study participants did not use olive oil for any cooking needs, 52% of red meat and meat product consumption occurred in 4 to >10 servings per week, and 85% of the study sample consumed none or less than two servings of fish per week. The MED scoring certainly could provide a description of adherence to a dietary pattern which promotes optimal health for the population and for disease prevention. Panagiotakos, et al., examined the diagnostic potential of the MED score in relation to threshold MED scores for risk development of hypertension, hypercholesterolemia, diabetes, and obesity.[100] The cutoff MED scores for these chronic diseases by gender, hypertension: men-26.5, women-26.7; hypercholesterolemia: men – 26.9, women – 26.8; diabetes: men – 25.9, women – 25.7; and, obesity: 25.8 for both men and women. The MED scores for this study population (men – 21.39 ± 5.5, women - 25.22 ± 7.0), revealed scoring which placed the male population well below the cut-off score for all four chronic diseases, and women slightly below or at the designated cut-off diagnostic value. Kastorini, et al, investigated the adherence to the Mediterranean diet in its relationship to metabolic syndrome and cardiovascular disease according to associated risk factors designated as components (1. Body weight and lipid profile, 2. Blood pressure, 3. Lipid profile, 4. Glucose profile, and 5. Inflammatory profile), which could be attenuated by adherence to a Mediterranean type diet.[103] The 10 year follow up revealed significant risk of metabolic syndrome in 80% of study participants with adherence to a Mediterranean type diet with a MED score >26. The sample population had a mean MED of 22.7 ± 6.2. The relatively low mean score can be attributed to low intakes of the MED score components fruits, vegetables, whole grains, legumes, and olive oil – 70% (n=19) reported no consumption of olive oil. However, the index does assign higher scoring for limited use of full fat dairy of which all participants received all possible points. The inflammatory effects of this disease manifest over a myriad of complications ranging form abdominal pain, maldigestion and malabsorption, and malnutrition

or under nutrition. Attenuation of these complications by the study participants could be targeted via increased adherence to the combination of foods in the MED which promote antioxidant and anti-inflammatory effects. The study population was largely deficient in dietary intakes of MED diet components – possessing nutrient density, vitamins, minerals, phytochemical, and omega three fatty acids – which act in concert to promote nutritional status. Similar to the HEI score the MED score does not reflect adequacy of energy intake levels which are increased in the CP population.

The use of Vioscreen for dietary assessment of the CP sample population provided an expedient, reliable, and valid method to collect the nutritional intake. The reporting generated not only data needed for calculation of scores for the dietary indices, but provided insight into mean total energy intakes, as well as the values corresponding to DRIs for total fat, saturated, fruits and vegetables, low fat and skim dairy products, whole grains, fish, fried foods, sweets, and alcohol consumption. It provided a good general picture of the quality of the individual's diet pattern. But as stated earlier, across the spectrum of intakes for the sample population, total energy intakes were insufficient to adequately meet the needs of this disease population. Simultaneously apparent was the wide spread insufficient intake of fruits and vegetables, low fat and skim dairy products, whole grains, and fish which were all recorded below the recommendations. Conversely, data revealed significantly excessive energy intake (n=5), as high as 427%, while still having a fairly low total fat intake of 30% (mean of 950 kcal of fat/day) in subjects who were clinically underweight (BMI <18.5 kg/m^2). This may be clinically interpreted that patients could be experiencing maldigestion and malabsorption. Additional, there may be implications that patients have suboptimal nutritional status including poor dietary habits, self-imposed dietary restrictions to avoid complications of postprandial abdominal pain, or steatorrhea.[47] The wide range – 497.3 kcal to 9238.0 kcal – in estimated energies was cause for

further investigation into the specific FFQs of patients with excessively low and high reports of energy consumption. The data revealed excessive intake of empty calorie foods (sweets and alcohol), and total fat in patients with high caloric intakes. On further investigation of the low calorie intakes sub-optimal intakes were reported across all food categories. Kristal, et al., reported underestimation of total energy and macronutrients in the range of 9% (energy), 15% (fat), 5% (carbohydrates), and 12% (protein). However, despite corrections for these underestimated amounts of energy, and macronutrients the CP study subjects were still well below elevated levels of increased energy needs.[49]

The evaluation of estimated intake of fat soluble vitamins for the group indicated excess intake of Vitamin A (9319.3 ± 9937.4 IU/day), Vitamin D (395.0 ± 339.4 IU/day), and Vitamin K (134.9 ± 206.5 mcg/day). Further investigation revealed that 80% of the study subjects consumed more than 100% (with a high of 1001%) of the Dietary Reference Intakes (DRIs) for Vitamin A. Seventy-percent of the participants consumed more than 100% (some as high as 642%), of the DRI for Vitamin D. Estimated intake of Vitamin E (23.6 ± 25.4 IU/day) were similar to values recommend by DRIs. However, serum values would be required to determine whether or not the subject was absorbing these fat soluble vitamins given the prevalence for fat malabsorption within this population.

The prevalence of cigarette smoking in the study population was over 50% (n=14) of the entire group. Studies have indicated that in addition to activating pancreatic stellate cells, continuing tissue necrosis and loss of pancreatic function, smoking perpetuates poor dietary patterns via empty calorie foods, high fat, and diminished carbohydrate intakes in direct comparison to non-smokers.[48] The addition of alcohol consumption in tandem to smoking further exacerbates diminished nutritional status via parenchymal tissue destruction along with direct negative effects upon nutritional status.[44,46] The entire sub-group of clinically underweight (BMI <18.5 kg/m^2) currently smoke and consume alcohol above recommendations.

Chronic pancreatitis patients present with further elevated risks for malnutrition upon gastrointestinal (GI) surgeries, and, or additional gastrointestinal complications which further alter gastrointestinal function (gastropareisis, micro colitis, etc.). The studied attempted to investigate additional information (GI surgeries and diagnoses), for this population in order to better understand the variation of energy intake. A modification was sent to the IRB for exclusion criteria to not restrict these criteria.

Limitations

The limitations of the study include the small sample population size, non-randomization, non-controlled, and utilization of a single instrument to measure dietary intakes. The dietary pattern was collected only once and assessed at baseline. Alterations in dietary patterns can occur over time and in response to a variety of factors – potentially indicated by the 26% (n=7) risk of food insecurity in the sample population. Furthermore, the potential for participant recall bias may produce errors of overestimation of caloric intake, and underestimation of caloric intake.

Implications for Research and Practice

Dietary assessment of patients with chronic pancreatitis has not been extensively investigated in previous literature. The attempt to determine nutritional status according to comparison of dietary intakes to HEI and MED revealed a discrepancy in the appropriateness of the indices and the CP population with regard to increased energy needs and existing food group deficiencies. A more suitable population for these two dietary measures would be a healthy, normal population as a means to improve adequacy of diet and reduce risk of disease. That said, in regards to the CP population the two dietary indices provide a baseline for

assessing nutritional intakes in this population. The data collected provides a road map to provide guidance on improving the overall quality of the diet.

Additional insight on appropriate utilization of the dietary indices was provided in examining scoring in tandem with energy intakes in subjects with the risk for food insecurity. The study population had an 18% (n=5) risk for food insecurity with MED and HEI scores at the low end of all reported scores. Despite the low dietary indices 80% (n=4) had excessive energy intakes as high as 427% of increased energy requirements. The indication was increased energy consumption and the lack of intakes across the nutrient components which compose the dietary indices. Such populations often miss meals, substitute inexpensive, non-nutritive, energy dense (high saturated fat and sugar) for nutrient dense foods. The lack of optimal nutrition exacerbates the potential of nutrient deficiencies and malnutrition.

A key component to successful dietary assessment in the CP population beyond the acquisition of accurate dietary intake data is the use of a Registered Dietitian as a component of the health care team. An effective nutritional therapy for the CP patient could be achieved with education, and thoughtful interpretation of the collected data so that the CP patient has full cognizance of how to improve nutritional status according to intakes across nutritionally beneficial food groups.

In conclusion, the study participants were predominantly thinner with the prevalence for extreme inadequacy of total calorie intakes. However, the overconsumption of high energy dense and non-nutrient dense food items was discovered, and only occurring in the population with normal and clinically underweight according to BMI in the study population. Despite the increased intakes of carbohydrates and total fat the population skewed toward clinically underweight, or the low end of normal according to BMI ranges – further suggesting maldigestion and malabsorptive complications, or was related to poor dietary choices, and a

lack of adequate food stores due to food insecurity. Limited food resources related to risk of food insecurity promote excessive intake of empty calories and may potentially contribute to the dietary choices within the study population.

Chapter 5

Nutritional Assessment of Chronic Pancreatitis Patients Utilizing A Web-based Food Frequency Tool: VioScreen

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ABSTRACT

Background Chronic pancreatitis is a disease in which the pancreatic parenchymal tissues undergo derangement and or necrosis resulting in the maldigestion and malabsorption of nutrients. The multifactorial risk of malnutrition with a myriad of nutrition deficiency related secondary complications result from these impaired physiological processes. Further complications stem from inability to appropriately diagnosis the disease until it is late stage. The aim of this study was to perform a cross-sectional analysis of dietary intakes of patients with chronic pancreatitis. The nutritional intakes were then compared to known dietary indices – adherence of which has been shown to impact the promotion of chronic disease – the Healthy Eating Index (HEI) and the Mediterranean Diet (MED), in an effort to provide insight into personalized optimization of nutritional intakes/treatment of chronic pancreatic patients. **Methods The** encompassing study was a cross-sectional prospective, single group, single test design. Data collection included the following: medical chart review, standard anthropometric measurements, Vioscreen Food Frequency Questionnaire, Two-Question Food Insecurity screen, and a demographic questionnaire. **Results The** initial assessment of mean scores for the cross sectional sample according to HEI score and MED score were, respecrtively, consistent with the most recent national mean for the U.S. population, and, low adherence to a Mediterranean type of dietary pattern. Stratification of the sample population according to gender, reflected a masking effect of poorer dietary intakes within the male subgroup. Additionally, evidence of nutritional inadequacy of dietary intakes was evident in both mean total energy intake requirements, and, across a spectrum of entire food groups. **Conclusion** The negative implications of sub-optimal caloric intakes was not reflected in the dietary indices due to the

total energy independent nature of these scoring systems. Patients with chronic pancreatitis have increased energy needs which must be taken into consideration when assessing total nutritional adequacy of dietary intakes. Furthermore, optimal nutritional therapies for this population should include addressing food group deficiencies to correct for increased estimated energy requirements.

Objective: To assess dietary intake of patients with chronic pancreatitis.

Design: Cross-sectional, single group, single test design.

Setting: A large Midwestern University Gastroenterology Outpatient clinic.

Patients: 27 patients (19 men and 8 women), ages 19 – 79.

Analysis: Sample t-test, will be used. Wilcoxon rank-sum test, chi-square test (or Fisher's exact test in the case of small sample size), Lavene's test, Spearman Correlation, p-value of less than 0.05.

INTRODUCTION

Chronic Pancreatitis affects 3.5 to 10 people per 100,000 in the developing world. The incidence is higher among men, and occurs between the ages of 30 and 40. Chronic pancreatitis (CP) presents with the following clinical manifestations: abdominal pain, exocrine and endocrine insufficiency. The complications arise from ongoing inflammation and development of fibroids in the pancreas which result in a loss of both pancreatic function and corresponding parenchymal tissue. [12–15] The decreased functional capacity refers to the impairment of exocrine and endocrine secretory features with the ensuing development of maldigestion and malabsorption of nutrient intake. The subsequent development of related secondary complications – steatorrhea, diarrhea, unplanned weight loss, and malnutrition – compound the severity of the diseased state via increased gastrointestinal distress, and prolonged nutrient deficiencies.[13,16–20]

An initial clinical indication of chronic pancreatitis is a postprandial exacerbation of abdominal pain that radiates from lower to upper abdominal quadrants. The mechanism

eliciting pain has been studied extensively but as yet is not well understood. Pain management typically begins with the administration of narcotic analgesics, or endoscopic therapies designed for large duct blockages and includes dilation, stenting, and stone dissolution. [3,21,22] Alternatively, surgery is also considered for pain management.[23–25] Unfortunately, surgical amelioration of existing duct blockage or obstruction believed to be the correct measure for functional repair and pain management may not resolve the pain. The pain may in fact be the result of hypersensitivity and stimulation of enlarged nociceptor neurons densely populating the pancreas that are responsible for pain sensation.[22]

Malnutrition, as another secondary complication, presents additional risks regardless of the instigating factor for the disease.[13,16] Despite the myriad of complications associated with malnutrition – visual and neurodegenerative disorders related to deficiencies of Vitamin A, or metabolic bone disorders related to deficiencies of Vitamin D – current studies have primarily focused upon administration of pancreatic enzyme replace therapy (PERT) as a means to ameliorate problematic digestion and absorption.[1,6,26–30] The utilization of PERT as means to improve nutritional status is complex given the lack of a standard dosage, and the heterogeneity of functional pancreatic tissue variance within the CP patient population.[18,20,22,31] Optimal corrective actions for nutritional status in CP patients could be dramatically improved with medical nutrition therapy (including PERT) and compliance with evidence-based nutrition interventions. The continual assessment of nutritional status would provide adequate data for the Registered Dietitian and health care team to continually monitor for viable markers of malnutrition risk. Evidence based medical nutrition therapy has historically focused on the coordination of dietary intake with pancreatic enzyme supplementation and has not moved beyond this stage. Additionally, it is not a routine standard of care for the patient with CP to be referred to a Registered Dietitian except during hospitalization. Personalized nutrition

counseling by physicians is hindered by limited training in nutrition counseling as well as the inability and or lack of time to accurately assess current dietary habits. Assessment of dietary intake for CP must be addressed in order to determine appropriate nutritional interventions.

The most prevalent etiology for chronic pancreatitis is excessive consumption of alcohol.[32–34] Alcohol has the unique ability to directly and indirectly be an instigating factor for CP.[35,36] Alcohol may cause direct injury to acinar cells left vulnerable to other triggers, and indirectly through pancreatic stellate cell activation via metabolites produced by pancreatic alcohol metabolism.[36–38] While pancreatic injury does occur with chronic alcohol abuse, not all cases lead to chronic pancreatitis. Furthermore, scant data has been compiled to investigate amounts consumed, or dietary patterns and intakes, or in tandem with cigarette smoking – which elevates occurrence of CP.[32,39–43] Hence, initial treatment in this instance is the cessation of alcohol consumption and cigarette smoking.

Extensive studies have investigated the etiologies, pathologies, and traditional CP treatment, yet there is a lack of research investigating methods to definitively diagnose, and measure severity of malnutrition. Alcohol related CP predisposes the patient to greater chance of prolonged malnutrition due to direct and detrimental effects of alcohol on nutrition status.[13,44–46] Similarly, an extensive body of research reveals the influence of cigarette smoking upon dietary intake habits including excessive energy intake of empty calories in sugar-sweetened beverages and alcohol, decreased carbohydrate intakes, and higher fat consumption in comparison to nonsmokers.[47,48] Accurate assessment of dietary intake could provide data to determine correctable situations of inadequate nutritional intakes, or poor nutrition.

The most widely available techniques used to measure dietary intake include the o24-Hour Recall, Food Record or Diary, and Food Frequency Questionnaires (FFQs). The inherent biases – recall and expectation – with self-reporting dietary assessments can significantly hinder

accuracy of measurement.[49–51] An alternative dietary intake instrument is the validated, web-based dietary assessment tool Vioscreen Graphical Food Frequency System – which will be referred to as VioScreen.[49] Vioscreen is a tool which the patient completes via a computer. The test has 156 food items with photos of 3 to 6 different portion sizes.[49] The web-based program eliminates a great deal of bias that is typically associated with pencil and paper FFQs. Additionally, the newer method reduces participant burden as completion of the survey is approximately 30 to 45 minutes, and generates immediate nutritional intake data. [49,51,52]. The burden on the patient is greatly reduced with the VioScreen, as well as a much higher rate of completion and accuracy of intakes. The utilization of VioScreen for CP patients would provide an effective tool to assess dietary intake within a nutrition assessment on a consistent and regular fashion.

The objective of the study was to assess dietary intakes of patients with chronic pancreatitis utilizing a validated wed tool with subsequent analysis of resultant HEI and MED scores. The 27 study participants are part of a larger ongoing study. Data was collected via the graphical food frequency questionnaire (Vioscreen), medical records, background health questionnaire, and two-question food insecurity screening questionnaire.

Methods

Prior to the initiation of this study, the study research protocol was submitted and approved by an Institutional Review Board (IRB #: 2015H0293) at the office of Sponsored Programs Office of Research at The Ohio State University.

Sample Population

All eligible study subjects were identified by the primary physician in accordance with verification of chronic pancreatitis diagnosis and the specified inclusion and exclusion criteria. Twenty-one eligible participants agreed to participate in the study upon a face-to-face encounter describing the study during their clinic appointments. A total of 27 eligible study participants (46%) completed the study, and 1 eligible study participant failed to complete more than 50% of the study and was excluded from the analysis. The study population included eighteen men with a mean age of 50.1 ± 14.1, and nine women with a mean age of 47.8 ± 20.3.

Study Design

Study participants were provided a research packet upon consent of study participation which included a copy of the IRB consent form with outline and purpose of the study, a background health questionnaire, two-question food insecurity screening questionnaire, a $10.00 grocery store gift card, and upon completion of the Vioscreen food frequency questionnaire, a one-page nutritional summary of current dietary intakes.

Study Instruments

The study used an online web-based food frequency tool, VioScreen, to collect dietary intake assessments of the study participants. VioScreen has been validated as an appropriate tool in research and clinical settings to accurately assess a patient's diet.[49] Vioscreen uniquely uses 1,200 food pictures to assist in the collection of detailed data on foods usually consumed and automatically calculates nutrient intake and food use patterns within a given population.[49] Additional data was collected via completion of demographic questionnaire (which includes medical history, smoking and alcohol history, and medication review), with a two-question food

security survey screen. The implementation of the validated food security questionnaire (FSQ) – which is reliable, sensitive, and user friendly – is to identity situations of uncertainty in acquisition, and sufficient food nutritionally adequate stores, or the ability to obtain food items in a socially acceptable manner.[105,106] The occurrence of food insecurity encourages poorer outcomes in cases of chronic disease.

Statistics

Categorical data was summarized with frequencies and percentages. To analyze continuous measures of dietary intake in patients with chronic pancreatitis a sample t-test was used. Differences between categorical measures was assessed with the chi-square test (or Fisher's exact test in the case of small sample size). All results were presented as point estimates with corresponding 95% confidence intervals and significance will be defined as a two-sided p-value of less than 0.05. Pierson correlations was used to determine relationship between dietary indices, and Levene's test for equality of variance, and t-test for equality of means was used to determine statistical significance upon the stratification of the sample population according to gender ($p > .05$).

Results

A total of 27 eligible study participants (46%) completed the study, and 1 eligible study participant failed to complete more than 50% of the study and was excluded from the analysis. The study population included eighteen men with a mean age of 50.1 ± 14.1, and nine women with a mean age of 47.8 ± 20.3.

The corresponding means for HEI score, and MED score for the study sample population were, respectively, 57.17 ± 11.8, and 22.7 ± 6.2. (Table 12) The correlations between the HEI

score and the MED scores were calculated with the Pearson statistical model. The strength of the Pearson correlation between these two dietary indices in the study was moderately positive correlation, or, 0.532 ($p < .05$). An independent samples test (Levene's test for equality of variance, and t-test for equality of means) revealed no statistical significance in a stratification of the sample population according to gender ($p > .05$). Pearson correlations conducted for the two dietary indices subsequent to a gender stratification of the sample population revealed men (n=18) with a low positive, or weak correlation (0.357), and a very high positive, or very strong correlation (0.806) for the women (n=9). Additionally, once stratified according to gender the mean scores for HEI and MED were, respectively, 54.8 ± 10.3 and 21.39 ± 5.5, for men, and, 63.4 ± 13.0 and 25.22 ± 7.0, for women.

Dietary Scores	Men	Women	Total
HEI	54.8 ± 10.3	63.4 ± 13.0	57.7 ± 11.8
MED	21.39 ± 5.5	25.22 ± 7.0	22.7 ± 6.2

Table 12. HEI and MED mean scores, SD

Table 13 identifies the distribution of study participants according to demographic information, consumption of smoking and alcohol, and risk of food insecurity. The proportion of current smokers amongst the two groups was higher in the male population at 86% (n=12), of which 100% (n=15) had smoked 100+ cigarettes in their lifetime, and were 67% (n=12) currently smoked 1+ pack per day. The number of current female smokers was 2 and smoked 1 to 2 packs per day. Alcohol consumption above the recommended guidelines (men 2 – 4oz drinks/day, women 1- 4oz drink/day) was more prevalent in the male group - 30% imbibing alcohol 2 – 5+ days/week over the past 12 months, 42% (n=5) consuming 4 – 7+ drinks on days of alcohol

consumption, with 25% (n=3) and 17% (n=2) respectively consuming 6+ drinks weekly and daily on occasion in the past 12 months. Concurrent cigarette smoking and alcohol drinking was prevalent in all (n=6) of the clinically underweight subjects (BMI <18.5 kg/m^2), with consumption rates of 1+ packs of cigarettes per day, and a typical intake rate of 4 – 7+ drinks on days in which alcohol consumption occurred over the past 12 months.

The results of the Food Insecurity Screening revealed 18% (n=5) of the study participants at risk for food insecurities and were all male.

Lifestyle Factors	Men	Women	Total
n	18	9	27
Age, mean, SD	50.1 ± 14.1	47.8 ± 20.3	49.3 ± 16.1
Alcohol consumption - current			
0<2 times per week past 12mo	13	9	22
2-5 times per week past 12mo	4	0	4
>5times per week past 12mo	0	1	1
0-3 drinks per day past 12mo	12	9	21
4-6 drinks per day past 12mo	2	1	3
7+ drinks per day past 12mo	3	0	3
6+ drinks on occasion past 12mo			
never-less than monthly	12	9	21
monthly	1	0	1
weekly	3	0	3
daily	2	0	2
Smoking Habits			
Smoked 100+ cigarettes in lifetime	15	7	22
Smokers - current	12	2	14
Unreported	3	0	0
<0.5 packs per day	1	0	1
1 pack per day	5	1	6
2 packs per day	2	1	3
4 packs per day	1	0	1
Food Insecurity Risk Score?	5	0	5

Table 13. Lifestyle Factors.

Table 14 describes relevant pancreatic histories of the study population with regard to pancreatic diagnoses, surgeries pertaining to gastrointestinal tract, and additional gastrointestinal diagnoses.

Pancreas and GI Diagnoses	Men	Women	Total
n	19	9	27
Pancreatic Cyst	2	1	3
Chronic Pancreatitis	18	9	27
Surgery			
Whipple	1	2	3
Distal Pancreatography	0	1	1
Pancreas Tail/Splenectomy	0	1	1
Frey	1	0	1
TPIAT	0	1	1
ERCP	1	0	1
Other	2	0	2
GI Diagnoses			
Irritable Bowel Disease	0	1	1
Clostridium Difficile	1	0	1
Hepatitis B/C	1	0	1
NAFLD	1	0	1
Cancer	1	0	1
Eating Disorder	0	1	1
Microscopic Colitis	1	0	1
Gastroparesis	1	0	1
Eosinophilic Esophagitis	1	0	1

Table 14. Frequency of Pancreatic and Gastrointestinal Diagnoses of the study participants

The mean BMI (kg/m^2) of all study participants was 22.7 ± 5.2, and when separated according to gender was 23.2 ± 5.5 for men, and 21.7 ± 4.5 for women. Distribution of the sample population according to BMI (kg/m^2) clinical designations revealed 26% (n=7) of the CP patients were clinically underweight (<18.5), 52 % (n=14) were normal BMI (≥ 18.5, ≤ 24.9), 15% (n=4) were overweight BMI, and 7% (n=2) were obese BMI status (>30). The sub group of subjects with a calculated normal BMI included 43% of whom were at the low end of the normal range – > 18.5 kg/m^2 to ≤20.8 kg/m^2. Additionally, 83% of the clinically underweight study subjects –according to BMI – presented with weight measurements which ranged from ≥ 60% to ≤ 89% of ideal body weights. Table 15 describes the anthropometrics of the study population.

Anthropometrics	Men	Women	Total
n	18	9	27
Height (in), mean, SD	68.2 ± 2.6	64.7 ± 3.4	67.0 ±3.3
Weight (lb) , mean, SD	153.3 ± 37.7	129.4 ± 28.4	145.4 ± 36.2
BMI (kg/m^2) , mean, SD	23.2 ± 5.5	21.7 ± 4.5	22.7 ± 5.2
IBW[1], mean, SD	155.2 ± 15.9	124.2 ± 16.9	144.8 ± 29.8

[1]Ideal Body Weight according to Hamwi calculation.
Table 15. Anthropometrics of the study population represented as means and standard deviations (SD).

Table 16 describes the mean energy intake by totals, and according to gender stratification with percentages of carbohydrate, fat, and protein intakes. The mean total energy (kcal) was 2299.4± 1986.3 for the sample population, and, stratified according to gender, 2603.8 ± 2290.6 for men, and, 1690.6 ± 1023.4 for women. The mean energy intake of 11% (n=3) of the participants measured a value similar to the required energy intake – 35 kcal/kg of Ideal Body

Weight (IBW) – for this population. Fifty-nine percent (n=16) recorded mean energy intake ranging from 24% to 75% of recommended total energy requirements. The largest proportion of energy was supplied by carbohydrates (51%), and fat (32%). Saturated fat levels of consumption were above 10% of mean calories in 63% (n=17) of the participants. Total fat energy intake in 19% (n=5) was less than 25% - 30% of total calories. Calories provided by the low fat dairy/skim foods were below 2 to 3 daily servings in 96% (n=26) of the study population. Intake of calories from full fat dairy had a mean serving of 1.7 servings per week, which provided a mean of 322.6 kcal per week. Excessive intake of empty calories from high sugar foods occurred in 33% (n=9) of the study population. The recommended consumption of fruits and vegetables (5-13 servings daily) was only achieved by 33% (n=9) of the participants, 22% (n=6) consuming <2 servings per day, and 30% (n=8) with intake <1 serving per day. Whole grain intake was revealed at <0.5 servings per day in the majority of the subjects - 48% (n=13). Intake of non-fried fish was non-existent in 37% (n=10) of all recorded diets. Fried food intake distribution in the population was at or below the recommended 0 -1 servings per day in 93% (n=25) of all participant's daily intake levels. Table 17 indicates intakes across select food groups as means and energy.

Nutrient and Vitamin Intake	Men	Women	Group
n	9	18	27
Total Energy (kcal), mean, SD	2603.8 ± 2290.6	1690.6 ± 1023.4	2299.4 ± 1986.3
Range (Low-High, kcal)	497.3 - 9238.0	497.3 - 3760.1	497.3 - 9238.0
Carbohydrate. gm (%)	319.0 ± 257.0 (49%)	240.8 ± 204.8 (57%)	293.0 ± 239.8 (51%)
Protein gm (%)	98 ± 84.5 (15%)	67.1 ± 32.0 (16%)	87.7 ± 72.1 (15%)
Fat gm (%)	95.8 ± 82.3 (33%)	55.9 ± 36.2 (30%)	82.5 ± 72.1 (32%
Vitamin Intake Means	Women	Men	Total
Vitamin A (IU), mean, SD	10669.6 ± 10673.5	8644.2 ± 9796.6	9319.3 ± 9937.4
Range (Low-High)	93.0 - 33618.0	2643.0 - 35752.0	93.0 - 33618.0
Vitamin D (IU), mean, SD	345.0 ± 215.6	420.0 ± 390.2	395.0 ± 339.4
Range (Low-High)	7.0 -1284.0	58.0 - 713.0	7.0 - 1284.0
Vitamin E (IU), mean, SD	15.7 ± 12.1	27.6 ± 29.5	23.6 ± 25.4
Range (Low-High)	1.0 - 94.0	4.0 - 36.0	1.0 - 94.0
Vitamin K (mcg), mean, SD	142.0 ± 159.2	131.3 ± 230.8	134.9 ± 206.5
Range (Low-High)	2.0 - 1001.0	29.0 - 522.0	2.0 - 1001.0

Table 16. Estimated nutrient and vitamin intake for quantified from the Vioscreen FFQ.

Nutritent and Food Group Intake Means	Men	Women	Total
n	19	8	27
Nutrients (%kcal)			
Total Fat	31.8	30.8	31.5
Sat Fat	11.8	10.3	11.4
Food Group Servings Per Day			
Fruit and Vegetable	3	6.4	4
Whole Grains	1.4	1.8	1.5
Fish	0.1	0.3	0.1
Fried Foods	0.3	0.2	0.3
Sweets	2.3	1.2	2
Low Fat/Skim	0.6	0.3	0.5
Full Fat Dairy Caloric Equivalent			
Full Fat Dairy (kcal/day)	44.5	49.3	46.1

Table 17. Nutrient and Food group intake means.

Discussion

In this study, the dietary pattern indices were based on maximum scores of 100 for the HEI score, and 55 for the MED score. The higher HEI scores indicating increased intake density of HEI food components which are focused on providing overall optimal adequacy of diet – scoring set according to optimal quantities (classified as standards or equivalents), per 1,000 calories. The mean HEI score for the sample population was 57.7, which was comparable to the most recent national average HEI Score of 59.00 (0.95) for the total U.S. population over the age of two. Gender stratification was initiated to determine if there was a significant variation between the mean HEI score of men and women. The expectation was that the women's mean HEI would be higher given that historically women tend to incorporate increased nutrient density with higher intakes of fruits and vegetables compared to men.[104] Upon stratification of the study participants according to gender the mean HEI total score for men decreased to 54.8, and increased to 63.4 for women. The HEI has been designed to assess diet quality independent of total energy intake.[10] Separation of the HEI score from energy intake eliminated the potential bias of a high calorie intake influencing the scoring as a result of related nutrient intake.[10] Hence, although the HEI total scoring for the two independent groups of the study are just below the national average for men, and noticeably above the national average for women the index does not address improved adequacy of diet with respect to decreased energy consumption. HEI scores reflected the density of dietary components according to intakes from optimal nutrition set by the US Dietary Guidelines. It is important to remember that patients with diagnosed CP have increased energy needs in the realm of 35 kcal/kg/day for optimal intake due to maldigestion and malabsorption of micronutrients with concomitant weight loss and poor dietary intakes.[13] That said, in this study, increased HEI scores were inconsistent with the other measure of the patient's nutritional status. For example, an HEI score of 75.5 was

revealed in a study subject whose total mean energy intake was 73% of the estimated energy intake requirement, clinically underweight according to BMI, and weighed 62% of ideal body weight. Further investigation of consumption of his dietary intake (according to the recommended values set by Dietary Reference Intakes guidelines), indicated severely limited intake across all food groups.

The stratification of the MED score according to gender produced similar effects in differences between the means of each group and the group as a whole. Similar to the HEI means, the women's MED score (25.22 ± 7.0) was significantly higher than the men's mean (21.39 ± 5.5). Despite the stratification and resulting score variations, neither group presented a score reflective of high adherence to Mediterranean type dietary pattern (described in chapter 2). Although there is overlap in the components between the two indices, the foods typified by the westernized diet appear to have influenced the higher comparative score in this population. For example, 70% of all study participants did not use olive oil for any cooking needs, 52% of red meat and meat product consumption occurred in 4 to >10 servings per week, and 85% of the study sample consumed none or less than two servings of fish per week. The MED scoring certainly could provide a description of adherence to a dietary pattern which promotes optimal health for the population and for disease prevention. Panagiotakos, et al., examined the diagnostic potential of the MED score in relation to threshold MED scores for risk development of hypertension, hypercholesterolemia, diabetes, and obesity.[100] The cutoff MED scores for these chronic diseases by gender, hypertension: men-26.5, women-26.7; hypercholesterolemia: men – 26.9, women – 26.8; diabetes: men – 25.9, women – 25.7; and, obesity: 25.8 for both men and women. The MED scores for this study population (men – 21.39 ± 5.5, women - 25.22 ± 7.0), revealed scoring which placed the male population well below the cut-off score for all four chronic diseases, and women slightly below or at the designated cut-off diagnostic value.

Kastorini, et al, investigated the adherence to the Mediterranean diet in its relationship to metabolic syndrome and cardiovascular disease according to associated risk factors designated as components (1. Body weight and lipid profile, 2. Blood pressure, 3. Lipid profile, 4. Glucose profile, and 5. Inflammatory profile), which could be reduced by adherence to a Mediterranean type diet.[103] The 10 year follow up revealed significant risk reduction of metabolic syndrome in 80% of study participants with adherence to a Mediterranean type diet with a MED score >26. The sample population had a mean MED of 22.7 ± 6.2. The relatively low mean score can be attributed to low intakes of the MED score components fruits, vegetables, whole grains, legumes, and olive oil – 70% (n=19) reported no consumption of olive oil. However, the index does assign higher scoring for limited use of full fat dairy of which all participants received all possible points. The inflammatory effects of this disease manifest over a myriad of complications ranging form abdominal pain, maldigestion and malabsorption, and malnutrition or under nutrition. Attenuation of these complications by the study participants could be targeted via increased adherence to the combination of foods in the MED which promote antioxidant and anti-inflammatory effects. The study population was largely deficient in dietary intakes of MED diet components – possessing nutrient density, vitamins, minerals, phytochemical, and omega three fatty acids – which act in concert to promote nutritional status. Similar to the HEI score the MED score does not reflect adequacy of energy intake levels which are increased in the CP population.

The use of Vioscreen for dietary assessment of the CP sample population provided an expedient, reliable, and valid method to collect the nutritional intake. The reporting generated not only data needed for calculation of scores for the dietary indices, but provided insight into mean total energy intakes, as well as the values corresponding to DRIs for total fat, saturated, fruits and vegetables, low fat and skim dairy products, whole grains, fish, fried foods, sweets,

and alcohol consumption. It provided a good general picture of the quality of the individual's diet pattern. But as stated earlier, across the spectrum of intakes for the sample population, total energy intake was insufficient to adequately meet the needs of this disease population. Simultaneously apparent was the wide spread insufficient intake of fruits and vegetables, low fat and skim dairy products, whole grains, and fish which were all recorded below the recommendations. Conversely, data revealed significantly excessive energy intake (n=5), as high as 427%, while still having a fairly low total fat intake of 30% (mean of 950kcal of fat/day) in subjects who were clinically underweight (BMI <18.5 kg/m^2). This may be clinically interpreted that patients could be experiencing maldigestion and malabsorption. Additional, there may be implications that patients have suboptimal nutritional status including poor dietary habits, self-imposed dietary restrictions to avoid complications of postprandial abdominal pain, or steatorrhea.[47] The wide range – 497.3 kcal to 9238.0 kcal – in estimated energies was cause for further investigation into the specific FFQs of patients with excessively low and high reports of energy consumption. The data revealed excessive intake of empty calorie foods (sweets and alcohol), and total fat in patients with high caloric intakes. On further investigation of the low calorie intakes sub-optimal intakes were reported across all food categories. Kristal, et al., reported underestimation of total energy and macronutrients in the range of 9% (energy), 15% (fat), 5% (carbohydrates), and 12% (protein). However, despite corrections for these underestimated amounts of energy, and macronutrients the CP study subjects were still well below elevated levels of increased energy needs.[49]

The prevalence of cigarette smoking in the study population was over 50% (n=14) of the entire group. Studies have indicated that in addition to activating pancreatic stellate cells, continuing tissue necrosis and loss of pancreatic function, smoking perpetuates poor dietary patterns via empty calorie foods, high fat, and diminished carbohydrate intakes in direct

comparison to non-smokers.[48] The addition of alcohol consumption in tandem to smoking further exacerbates diminished nutritional status via parenchymal tissue destruction along with direct negative effects upon nutritional status.[44,46] The entire sub-group of clinically underweight (BMI <18.5 kg/m^2) currently smoke and consume alcohol beyond set recommendations.

The evaluation of estimated intake of fat soluble vitamins for the group indicated excess intake of Vitamin A (9319.3 ± 9937.4 IU/day), Vitamin D (395.0 ± 339.4 IU/day), and Vitamin K (134.9 ± 206.5 mcg/day). Further investigation revealed that 80% of the study subjects consumed more than 100% (with a high of 1001%) of the Dietary Reference Intakes (DRIs) for Vitamin A. Seventy-percent of the participants consumed more than 100% (some as high as 642%), of the DRI for Vitamin D. Estimated intake of Vitamin E (23.6 ± 25.4 IU/day) were similar to values recommend by DRIs. However, serum values would be required to determine whether or not the subject was absorbing these fat soluble vitamins given the prevalence for fat malabsorption within this population.

Limitations

The limitations of the study include the small sample population size, non-randomization, non-controlled, and utilization of a single instrument to measure dietary intakes. The dietary pattern was collected only once and assessed at baseline. Alterations in dietary patterns can occur over time and in response to a variety of factors – potentially indicated by the 26% (n=7) risk of food insecurity in the sample population. Furthermore, the potential for participant recall bias may produce errors of overestimation of caloric intake, and underestimation of caloric intake.

Implications for Research and Practice

Dietary assessment of patients with chronic pancreatitis has not been extensively investigated in previous literature. The attempt to determine nutritional status according to comparison of dietary intakes to HEI and MED revealed a discrepancy in the appropriateness of the indices and the CP population with regard to increased energy needs and existing food group deficiencies. A more suitable population for these two dietary measures would be a healthy, normal population as a means to improve adequacy of diet and reduce risk of disease. That said, in regards to the CP population the two dietary indices provide a baseline for assessing nutritional intakes in this population. The data collected provides a road map to provide guidance on improving the overall quality of the diet.

Additional insight on appropriate use of the dietary indices was provided in examining scores in tandem with energy intakes in subjects with the risk for food insecurity. The study population had an 18% (n=5) risk for food insecurity with MED and HEI scores at the low end of all reported scores. Despite the low dietary indices, 80% (n=4) had excessive energy intakes as high as 427% of increased energy requirements. Such populations often miss meals, substitute inexpensive, non-nutritive, energy dense (high saturated fat and sugar) for nutrient dense foods. The lack of optimal nutritious exacerbates the potential of nutrient deficiencies and malnutrition.

A key component to successful dietary assessment in the CP population beyond the acquisition of accurate dietary intake data is the use of a Registered Dietitian as a component of the health care team. An effective nutritional therapy for the CP patient could be achieved with education, and thoughtful interpretation of the collected data so that the CP patient has full cognizance of how to improve nutritional status according to intakes across nutritionally beneficial food groups.

In conclusion, the study participants were predominantly thinner with the prevalence for extreme inadequacy of total calorie intakes. However, the overconsumption of high energy dense and non-nutrient dense food items was discovered, and only occurring in the population with normal and clinically underweight according to BMI in the study population. Despite the increased intakes of carbohydrates and total fat the population skewed toward clinically underweight, or the low end of normal according to BMI ranges – further suggesting maldigestion and malabsorptive complications, or was related to poor dietary choices, and a lack of adequate food due to food insecurity. Limited food resources related to risk of food insecurity promote excessive intake of empty calories and may potentially contribute to the dietary choices within the study population.

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Appendix A: Chronic Pancreatitis Study Participation Contact Letter

Contact Letter

Protocol Title: Assessment of Nutritional Intake in Chronic Pancreatitis
IRB #: 2015H0293
Principal Investigator: Dr. Marcia Nahikian-Nelms and colleagues

(Date}

{ Name} RE: *{ first name} { last name}*
{Street Address}
{City, State Zip}

Dear *{Mr., Ms, or Mrs. }*

You are being asked to participate in a research study to better understand the diets intake of people with chronic pancreatitis. We also want to compare the diets of individuals with chronic pancreatitis to individuals who do not have this condition. You may participate in this study in either capacity.

If you agree to participate you will be asked to come to the Ohio State University Wexner Medical Center for one study visit, which is expected to take approximately one hour. Your participation in the study consists of completing an online diet assessment. Information regarding your medical history will be collected with a questionnaire and by reviewing your medical records. We have enclosed a copy of the questionnaire to complete, however this will also be provided at the time of the study visit. If you would like to, you may fill it out and return in the enclosed stamped envelope.

The risks associated with this research study are minimal, which means that we do not believe that they will be any different than what you would experience at a routine clinical visit or during your daily life. You may refuse to answer any question(s) that you do not wish to answer.

Although the results of this research study are unlikely to directly benefit your health, we believe they will be of benefit to people in the future including those with chronic pancreatitis.

Please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty. Specifically, your current or future medical care at the Ohio State University Wexner Medical Center will not be jeopardized if you choose not to participate.

Contact me at 614-292-4758 if you have any questions about:
- Study tests and procedures
- Research-related injuries or emergencies
- Withdrawing from the research study
- Materials you receive

Appendix B: Chronic Pancreatitis Subject Recruitment Phone Script

Info to have before the call:

Name of patient, and whether they had previously received a dietary consult with an RD regarding diagnosis of chronic pancreatitis.

"I am calling to speak with (patient's name from chart). My name is __________ and I am working with the gastroenterology doctors, and registered dietitians at Martha Morehouse Medical Plaza, and Stoneridge Medical Center on a nutritional assessment study for patients with clinically diagnosed chronic pancreatitis. Did you receive a letter recently describing the research study and request to participate?"

If yes. – "I am calling to follow up on the participation request. We would love to have you participate in our research study. Would you be willing to participate? Would you be willing to come in one hour early prior to your next schedule appointment to complete the on-line nutritional assessment, which requires between 45 and 60 minutes? Or, you can complete the online assessment in the privacy of your own home on your personal computing device."

If no. – "I'm sorry, we may have an old address for you. One of the gastroenterology doctors may have mentioned this project to you. We are currently selecting participants for our research study that investigates the nutritional intakes of persons diagnosed with chronic pancreatitis. The study involves your input of dietary intakes into an online web tool 'VioScreen,' which will then generate a nutritional assessment of your diet. The total time to complete the assessment requires 45 to 60 minutes. The assessment can be scheduled to occur immediately prior to your next clinic appointment, or can be completed in the privacy of your home on your own personal computing device. As compensation for your time you would receive a complete nutritional analysis of your dietary intake, a free consult with one of our Registered Dietitians/study investigators to optimize your nutritional intake, and a $XX Subway Gift Card. Would you be interested in participating?"

Appendix C: Chronic Pancreatitis Subject Recruitment Face to Face Script

Script for Face-to-Face

“Hello! My name is __________ and I am working with the gastroenterology doctors, and registered dietitians at Martha Morehouse Medical Plaza, and Stoneridge Medical Center on a nutritional assessment study for patients with clinically diagnosed chronic pancreatitis. Did you see our flyers, or poster detailing the research study here in the medical center.

We are currently selecting participants for our research study that investigates the nutritional intakes of persons diagnosed with chronic pancreatitis. The study involves your input of dietary intakes into an online web tool ‘VioScreen,’ which will then generate a nutritional assessment of your diet. The total time to complete the assessment requires 45 to 60 minutes. We can schedule this to occur before your/your patient’s next clinic visit, or at your convenience in your own home on your own personal computing device.

As compensation for your time you would receive a complete nutritional analysis of your dietary intake, a free consult with one of our Registered Dietitians/study investigators to optimize your nutritional intake, and a $XX Subway Gift Card.

Would you be interested in participating?”

Appendix D: Demographic Questionnaire, and, Two-Question Food Security Survey Screen

Health Questionnaire (to be completed by study participant)
Protocol Title: Assessment of Nutritional Intake in Chronic Pancreatitis
IRB #: 2015H0293
Principal Investigator: Marcia Nahikian-Nelms, PhD,RDN,LD,CNSC

Participant's name (Last, First):___________________________

What is your height?
What is your weight? __________

Health behaviors:

Have you smoked at least 100 cigarettes in your entire life? □ Yes □ No *If yes*:

What year did you started smoking? _________

On average, how many packs do/did you smoke per day? _________

Do you currently smoke? □ Yes □ No

If No, what year did you quit? _________

How often did you have a drink containing alcohol in the past 12 months?

□ <2 times a week
□ 2-5 times a week
□ >5 times a week

How many drinks did you have on a typical day when you were drinking in the past 12 months?

□ 0-3 drinks
□ 4-6 drinks
□ 7 or more drinks

How often did you have 6 or more drinks on occasion in the past 12 months?

□ Never or less than monthly
□ Monthly
□ Weekly
□ Daily or almost daily

Pancreas History

Have you previously been diagnosed with any the following pancreas conditions?

Pancreas cyst □ Yes □ No
Pancreatitis □ Yes □ No
Pancreatic cancer □ Yes □ No

Have you ever had surgery on your esophagus, stomach or pancreas, or intestine? □ Yes □ No

If yes, what type of surgery did you have? _________

Have you ever been diagnosed with any of the following?

Inflammatory Bowel Disease □ Yes □ No
C. difficile colitis □ Yes □ No
Eosinophilic Esophagitis □ Yes □ No
Hepatitis B or C □ Yes □ No
Gastroparesis □ Yes □ No
Microscopic colitis □ Yes □ No

Non-alcoholic fatty liver disease □ Yes □ No
Celiac Disease □ Yes □ No
Short Bowel Syndrome □ Yes □ No
Cancer □ Yes □ No
Eating Disorder □ Yes □ No

Please answer the following questions:

"Within the past 12 months we worried whether our food would run out before we got money to buy more" □ Yes □ No

"Within the past 12 months the food we bought just didn't last and we didn't have money to get more."

□ Yes □ No

Appendix E: Chronic Pancreatitis Study IRB

The Ohio State University Consent to Participate in Research

Study Title:	Dietary Assessment of Chronic Pancreatitis Patients Using VioScreen
Principal Investigator:	*Marcia Nahikian-Nelms, PhD,RDN,LD, CNSC*
Sponsor:	*ChiRhoClin Research Institute*

- This is a consent form for research participation. It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- Your participation is voluntary. You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- You may or may not benefit as a result of participating in this study. Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate. If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

   The purpose of this study is to describe the dietary intake of individuals with chronic pancreatitis. It is our hope by learning more about the diets of individuals with chronic pancreatitis that we may be able to determine the best nutrition advice for these individuals.

2. How many people will take part in this study?

   100 people will take part in this study.

3. What will happen if I take part in this study?

   If you agree to participate in the study, you will need to participate in 1 visit where you will complete three activities.
   The four activities include:
   - consent
   - online dietary assessment

   At the interview, we will ask you questions about your medical history as it relates to your chronic pancreatitis. During the dietary assessment we will have you fill out an online survey. The survey will ask you questions about what you typically eat.

   Overall, it will take 30-60 minutes to complete the study.

4. How long will I be in the study?

   It is anticipated that you will be in the study for 1 hour, as we should be able to complete the data collection in one session 30-60 minutes.

5. Can I stop being in the study?

   You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

   There is a potential risk of breach of confidentiality. You will complete a questionnaire, survey and interview related to your overall health and your nutritional health. One of the surveys is an online survey.

   In order to minimize the risks, harms, and/or discomforts associated with a breach of confidentiality, data collected during the research study will be de-identified. This means that a code will be used to identify participants, as opposed to the participants' name. This is true for both hardcopy materials and the on-line survey. Finally, all research materials will be kept in a locked office, and the electronic copy will be maintained on a password-protected computer. Only the study investigators will have access to the codes linking the data to the study participant.

In order to minimize the risks, harms, and/or discomforts associated with transfers we allow you plenty of time to rest. In order to minimize the risks, harms, and/or discomforts associated with using a cushions that are not your own, you may decide not to participate in the remainder of the study.

7. What benefits can I expect from being in the study?

   There are no direct benefits to the participants.

8. What other choices do I have if I do not take part in the study?

   You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

   Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

   Also, your records may be reviewed by the following groups (as applicable to the research):
   - Office for Human Research Protections or other federal, state, or international regulatory agencies;
   - U.S. Food and Drug Administration;
   - The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
   - The sponsor supporting the study, their agents or study monitors; and
   - Your insurance company (if charges are billed to insurance).

   If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

   A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

   You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

10. What are the costs of taking part in this study?

All study procedures and questionnaires are covered by the study.

11. Will I be paid for taking part in this study?

You will be paid an honorarium of $10.00 Subway gift card.

12. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

13. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Marcia Nahikian-Nelms at 614-292-4758.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Marcia Nahikian-Nelms at 614-292-4758.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form.

Printed name of subject	Signature of subject
	AM/PM Date and time
Printed name of person authorized to consent for subject (when applicable)	Signature of person authorized to consent for subject (when applicable)
Relationship to the subject	AM/PM Date and time

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	Signature of person obtaining consent
	AM/PM Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	Signature of witness
	AM/PM Date and time

Printed name of witness	Signature of witness

________________________ AM/PM
Date and time