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Association between gastroduodenal ulcer and age of diagnosis of head and neck, gastroduodenal and pancreatic cancer

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TITLE: Association between gastroduodenal ulcer diagnosis and age of diagnosis of head and neck, gastrointestinal and pancreatic cancer.

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ABSTRACT

Background: Cancer is the second leading cause of death in the United States and remains a major public health problem worldwide. Epidemiological studies have demonstrated that insulin like growth factor-1 (IGF-1) is linked to ulcers and most cancers. Although studies have investigated the role of IGF1 in ulcer healing and cancer pathogenesis, the link between ulcer and cancer remains unclear. Hence, we assessed the relationship between ulcers and cancers.

Methods: This study consists of a sample of 180 cancer patients obtain by convenience sampling who were seen at Nebraska Medicine and were enrolled in the integrated cancer repository for cancer research (iCaRe^2) database. Demographics and socioeconomic data were described using descriptive statistics and data were analyzed using Linear regression and TTEST.

Results: The result of this study showed no association between ulcer diagnosis and age of cancer diagnosis. Although patients with gastroduodenal ulcer seem to be diagnosed of cancer later compared to non-gastroduodenal patients, this finding was however not significant.

Discussion: Research on the association between ulcers and cancer is scarce. This study is significant in that it will serve as a landmark for future research which may lead to establishing the link between ulcers and cancers and thus, predict or prevent certain cancer types.

INTRODUCTION

BACKGROUND

Cancer is a major public health problem worldwide and it's the second leading cause of death in the United States (Heron, Anderson & Brief, 2016). In the United States, it is estimated that about 1,762,450 new cases of cancer and 606,880 deaths would occur in 2019 (Siegel, Miller & Jemal, 2019). This study focuses on head and neck, gastrointestinal, and pancreatic cancer. Head and neck cancer include neoplasm of the oral cavity, pharynx and larynx. Head and neck cancer rank sixth among the most common cancers, accounting for approximately 6% of all cancer cases, and more than 630,000 new cases of head and neck cancer are diagnosed worldwide each year (Vigneswaran, Williams, 2014). In the United States, it is estimated that 65,410 people (48,000 men and 17,410 women) will develop head and neck cancer in 2019 and 14,620 would die from it (10,980 men and 3,640 women) (American society of clinical oncology, 2019). Although the risk of head and neck cancer is strongly associated with smoking and alcohol consumption, epidemiological data has linked elevated levels of IGF1 and head and neck cancers (Slomiany et al., 2006)

Gastrointestinal cancers are cancers involving the digestive tract. These include cancer of the esophagus, stomach, colon, rectum and pancreas (Herszenyi, Tulassay, 2010). The most common sites of GI cancer are the colon and rectum which represent over 50% of GI cancers and accounts for the fourth most common cancer type in the United States. It is estimated that about 145,600 new cases of colorectal cancer and over 51,000 deaths would occur in 2019 (SEER, 2019a) Gastric cancers account for the

second most common gastrointestinal cancer and despite its decline in incidence and mortality, has remained one of the leading cause of cancer related death worldwide (Brenner, Rothenbacher & Arndt, 2009).An estimated 97,915 people currently living with gastric cancer in the United States with this cancer account for about 1.8% of all cancer death and represent 1.6% of all new cancer cases in the United States. Surveillance epidemiology and end results program (SEER), which is an authoritative source for cancer statistics in the United States estimated that about 27,510 new cases of stomach cancer will occur, resulting in 11,140 deaths (SEER, 2016). The strongest established risk factor for gastric cancer is helicobacter pylori infection (Wroblewski, Peek & Wilson, 2010). Other identified risk factors are smoking, family history of gastric cancer, alcohol intake, and dietary factors (Brenner, Rothenbacher & Arndt, 2009). There is a similarity in risk factors of gastrointestinal and pancreatic cancers. Pancreatic cancer is a leading cause of cancer mortality and remains one of the most fatal neoplasms in the world (Ilic, Ilic, 2016). It is the third most common cancer causing death in the USA and the seventh leading cause of global cancer death (Karimi et al., 2019) .There are two main types of pancreatic cancer: adenocarcinoma that makes up about 85% of cases and pancreatic endocrine tumor that accounts for about 5% of cases (Ilic, Ilic, 2016). Based on American cancer society estimates, pancreatic cancer would account for 56,770 new cases and would cause 45,750 deaths in 2019 (American cancer society, 2019a) .Although some risk factors have been shown to be associated with pancreatic cancer, the exact cause of pancreatic cancer still remains unknown. Identified risk factors include smoking, diabetes, obesity, alcohol consumption, pancreatitis, physical inactivity, dietary factors, family history, genetics, increased IGF1 and helicobacter

pylori infection (Aier et al., 2019) The prognosis of pancreatic cancer is quite poor with an estimated overall 5 year survival rate of 8.2% (Karimi et al., 2019). Despite the improved understanding of the epidemiology pancreatic cancer it has remained a major public health issue with one of the lowest survival rates.

There is epidemiological evidence that insulin like growth factor 1 (IGF1), which is known to modulate cell growth and survival, is linked to an increased risk of certain cancers, particularly pancreatic, gastrointestinal, and head and neck cancers (Ii et al., 2011, Barnes et al., 2007, Karczewski et al., 2019). The role of IGF1 in the pathogenesis and healing of ulcer is also well known. Gastric ulceration activates expression of several growth factors including IGF-1 which accelerates gastric healing by promoting cell re-epithelization, proliferation and cox-2 expression (Nguyen et al., 2007, Howarth, 2003). More recently evidence has accrued to demonstrate that IGFs play an important role in the metastasis and spread of many cancers. The IGF-1 receptor is commonly over expressed in many cancers including head and neck cancers (HNC), as well as gastric and pancreatic cancer. Studies have identified pathways emanating from IGF-1 receptor that activates multiple signaling pathways which then result in cancer cell proliferation, differentiation, transformation, adhesion, and tumorigenicity (Pollak, 2008, LeRoith, Roberts Jr, 2003). Although several studies have investigated the role of IGF in ulcer healing and cancer pathogenesis independently, the link between ulcer and cancer remain unclear. This study aims to address this gap as well as explore the relationship between ulcer diagnosis and age of diagnosis of gastrointestinal, pancreatic and HN cancer.

AIMS

AIM 1: The main aim of this study is to investigate the relationship between ulcer diagnosis and age of head and neck, gastrointestinal and pancreatic cancer diagnosis.

HYPOTHESIS

Null hypothesis: There is no difference in the timeline of diagnosis between cancer patients with ulcers and cancer patients without ulcers.

Alternative Hypothesis: Patients with ulcers are diagnosed sooner or later of cancers compared to patients without ulcers.

MATERIALS AND METHODS:

Data source and study population

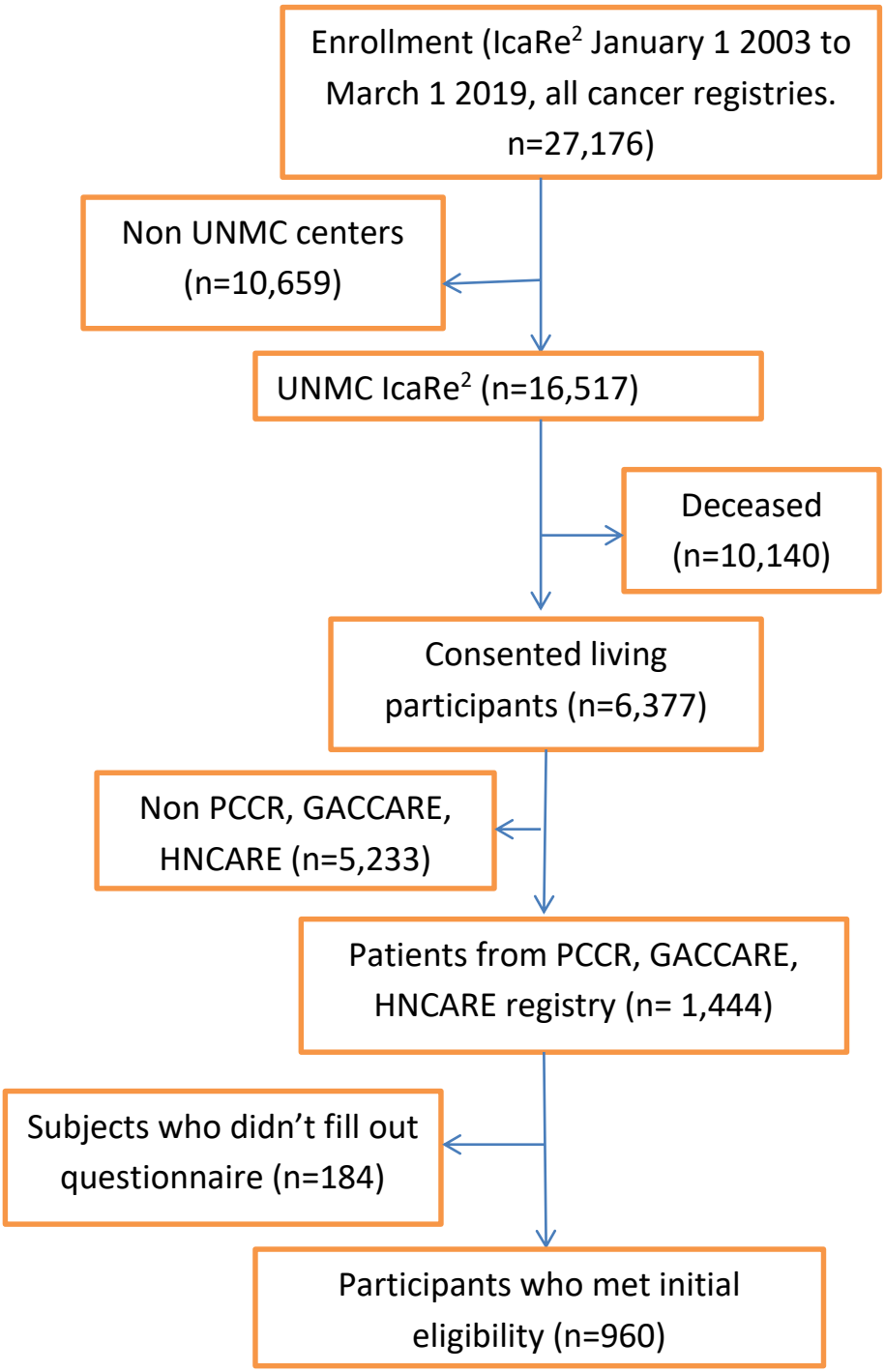
Data from the integrated cancer repository for cancer research (iCaRe^2) database was used to conduct this study. (iCaRe^2) is a multi-institutional bio specimen registry and resource created and maintained by the Fred and Pamela Buffet cancer center to collect and manage standardized, multi-dimensional, longitudinal data and bio specimen on consented adult cancer patient, high risk individuals and normal controls (ICARe^2, 2019). ICaRe^2 aims to enable comprehensive study of risk factors of cancer development and disease progression as well as enable strategies for prevention, early detection and treatment of cancer (ICARe^2, 2019). This database is a convenience sampling and includes data on quality of life, disease specific parameters, medications, treatment, surgical history, survival/outcome, socio-demographics characteristics, health behaviors, and anthropometric measures. This case control study consists of a sample

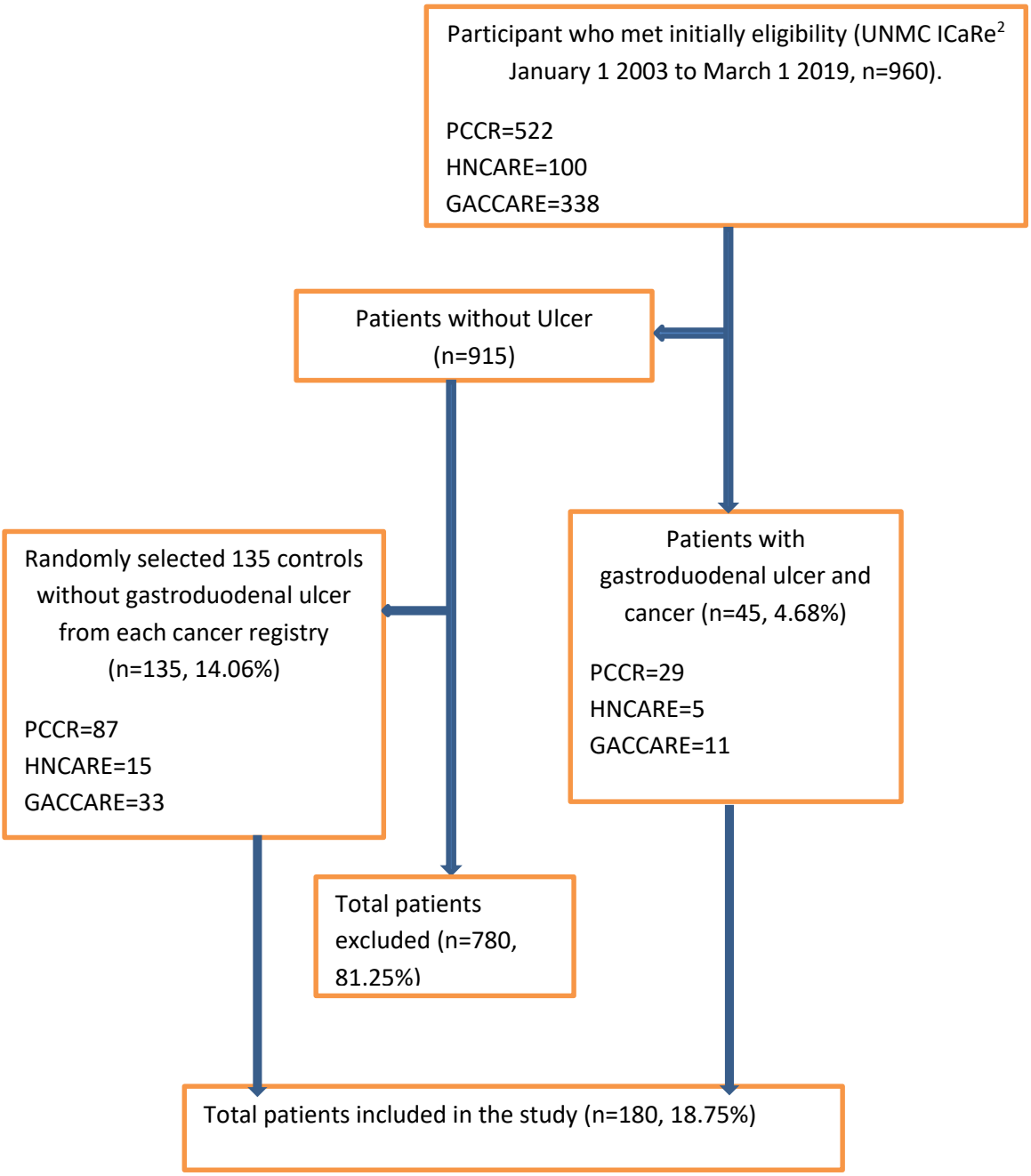
of 960 cancer patients who were seen at Nebraska medicine and enrolled in any three of the iCaRe^2 cancer registry; pancreatic cancer collaborative registry (PCCR), gastrointestinal and abdominal collaborative registry (GA CARE), and, head and neck cancer registry (HN CARE). ICaRe^2 data contains identifiers hence; this study required approval from an institutional review board and was approved by UNMC IRB. (IRB # 204-19-EP)

Eligibility Criteria

Eligibility criteria for this study included adult patients above the age of 19, with a life time diagnosis of cancer, who enrolled and provided consent in UNMC GACARE, PCCR, and HN CARE registry of the iCaRe^2 database from January 1 2003 to March 1 2019 and having a diagnosis of head and neck, gastrointestinal or pancreatic cancer and an available survey data. Subjects under the age of 19 were excluded, vulnerable subjects including pregnant women, prisoners, decisionally impaired persons and educationally disadvantaged individuals were excluded. Participants who had no data on age of pancreatic, HN and gastrointestinal cancer diagnosis were excluded.

Figure 1. A flow diagram of Eligibility participants.





NOTE:

PCCR: Pancreas care registry

HNCARE: Head and neck care registry

GACCARE: Gastrointestinal and abdominal care registry

STUDY VARIABLES

Ulcer

A diagnosis of ulcer was based on patient self-report as described in the iCaRe^2 core data dictionary and questionnaire. Specifically, in iCaRe^{2,} the diagnosis of ulcer was based on the following sequential questions: *History of peptic or stomach ulcer?*

Cancer

Diagnosis of the various cancer type used in this project was based on patient's medical data. Specifically, the diagnosis of patients with gastrointestinal cancer in the GACCARE registry was based on upper GI endoscopy and biopsy, laparoscopy, CT, and MRI. Diagnosis of pancreatic, and head and neck cancer was by biopsy of the tumor. Age at which cancer was diagnosed was also extracted from the patients medical data.

Socio-demographic variables

Age, sex, race/ethnicity, and income were collected using administered questionnaire from iCaRe^2 database. Race/ethnicity was reported on the questionnaire as White, Black/African American, Asian, American Indian or Alaska native, native Hawaiian/other pacific island, and Hispanic or Latino. Income level was categorized in to 7 groups (less than $10,000, $10,000-24,999, $25,000-44,999, $45,000-74,999, $75,000-100,000, greater than $100,000, refused)

Behavioral factors

Smoking history and alcohol consumption status were extracted from iCaRe[2] administered questionnaires and was based on the following questions; *have you ever smoked cigarettes in your life, how many cigarettes did you smoke per day, how many years did you smoke in total, cigarette stop age, do you currently drink alcohol, Alcohol start age, what was you heaviest use of alcohol?*

Body mass index

Body mass index (expressed in meter square) was extracted from the medical history. According to CDC BMI classification, (<18.50 kg/m^2) is underweight, (18.50-24.99 kg/m^2) is considered normal; (25.00-29.99 kg/m^2) is classified as overweight, and above 30 kg/m^2 obese (CDC, 2017).

STATISTICAL ANALYSIS

Duplicate data were removed and missing data excluded. All three cancer registries were merged by case id and 45 controls were randomly selected and merged to 45 cases bringing the total sample size to 90 patients. The independent variable was ulcer and was treated as a binary variable; the dependent variable was age at cancer diagnosis and treated as a continuous variable. Descriptive statistics (percentage, frequencies, mean, medians and standard deviation) were used to describe the socioeconomic and demographic variables for head and neck, gastrointestinal and pancreas cancer. Each patient age of cancer diagnosis was compared with the median age of same primary cancer diagnosis of our study population and the U.S population after adjusting the age for both sample population. The adjusted mean age of cancer

diagnosis for gastroduodenal ulcer patients was then compared to the adjusted mean age of cancer diagnosis for patient without gastroduodenal ulcer in both the U.S population and iCaRe^2 sample using a TTEST. Linear regression was also used to analyze the relationship between the adjusted mean age of cancer diagnosis for iCaRe^2 and U.S population. The analysis was conducted with SAS statistical software version 9.4, (SAS Inc., Cary, NC USA).

FOUNDATIONAL AND CONCENTRATION COMPETENCY

EPIMPH2 Apply appropriate study design and data collection methods to answer specific epidemiologic questions and address public health issues.Data would be requested and collected from iCaRe^2, and a case control study would be designed to address public health problems of several cancer types

EPIMPH3 Analyze datasets using computer software. Data collected from UNMC iCaRe^2 will be analyzed using sas software.

MPHF21 Perform effectively on interprofessional team. An open channel of communication will be maintained with capstone committee members throughout the course of the project to ensure a satisfactory project.

RESULTS

Table 1 Characteristics of study participants by ulcer status, (n=180)

Participant's characteristics	Gastroduodenal Ulcer	No gastroduodenal Ulcer	Overall	P value[e]
	No (%).	No (%).	No (%).	
Total	45 (25)	135 (75)	180 (100)	
Cancer diagnosis age, years [a]	65 (13.7)	63 (11.0)	63 (12.4)	
Enrolment age, years [a]	66 (13.4)	64 (11.1)	65 (12.2)	0.4
Gender				
Female	20 (44.4)	64 (47.4)	84 (46.7)	
Male	25 (55.6)	71 (52.6)	96 (53.3)	
BMI [b]				
Underweight	2 (4.8)	1 (1.1)	3 (2.3)	
Normal	14 (33.3)	20 (22.5)	34 (26.0)	
Overweight	15 (35.7)	28 (31.5)	43 (32.8)	
Obese	11 (26.2)	40 (44.9)	51 (38.9)	
Missing	3	46	49	
Cancer registry				
GACCARE	11 (24.4)	33(24.4)	44 (24.4)	
HNCARE	5 (11.1)	15 (11.1)	20 (11.1)	
PCCR	29 (64.5)	87 (64.5)	116 (64.5)	
Smoking [c]				
Never Smokers	10 (24.4)	39 (43.3)	49 (37.4)	
Ever Smokers	31 (75.6)	51 (56.7)	82 (62.6)	
Missing	4	44	48	
Refused	0	1	1	
Alcohol intake [d, e]				
< 1 drink/month	12 (27.9)	24 (26.4)	36 (26.9)	
>1 drink /month	31 (72.1)	67 (73.6)	98 (73.1)	
Total years of intake [e]	42.9 (13.4)	42.8 (12.5)	42.9 (13.0)	
Refuse	1	9	10	
Missing	1	35	36	
Race				
American Indian	1 (2.2)	1 (0.7)	2 (1.1)	
Asian	0	3 (2.3)	3 (1.7)	
African American	3 (6.7)	5 (3.8)	8 (4.5)	
White	41 (91.1)	124 (93.2)	165 (92.7)	
Unknown	0	2	2	

Participants characteristics	Gastroduodenal Ulcer	No gastroduodenal Ulcer	Overall	P-value
	No (%).	No (%).	No (%).	
Income				
< $10,000	3 (19.0)	0	3 (7.0)	
$10,000 - $24,999	4 (25.0)	4 (14.8)	8 (18.6)	
$25,000-$44,999	4 (25.0)	7 (25.9)	11 (25.6)	
$45,000-$74,999	2 (12.5)	5 (18.5)	7 (16.3)	
$75,000-$100,000	1 (6.25)	4 (14.8)	5 (11.6)	
$>100,000	2 (12.5)	7 (25.9)	9 (20.9)	
Refused	1	3	4	
Missing	28	105	133	

Notes.

[a, e] Age and total year of alcohol intake was presented as mean ± standard deviation, and other data were expressed as frequency (weighted %).

[b] body mass index (BMI) <18.5kg/m^2 was defined as underweight, BMI between 18.5 and 24.9kg/m^2 considered as normal, BMI between 25 and 29.9kg/m^2 as overweight and BMI ≥ 30kg/m^2 as obese.

[c] smoking status was defined base of on participant who had smoked more than 100 cigarettes.

[d] one drink was considered as one shot of liquor, a mixed drink, one glass of wine or one 12 ounce of beer per month during a 12 month period or more than 20 drinks in a lifetime.

[e] From 2 sample two test.

Table 1 shows the general characteristic of participant in the study by gastroduodenal ulcer status. Among the 180 included study participants, 45 participants had gastroduodenal ulcer and 135 participants do not have gastroduodenal ulcer. The mean enrolment age of cancer patient with gastroduodenal ulcer was 66 years and 64 years for participants without gastroduodenal ulcer. Participants without gastroduodenal ulcer seem to be more obese (44.9) than participant with gastroduodenal ulcer (26.2). There was no difference in the mean total years of alcohol intake by gastroduodenal ulcer status. Lastly 92 percent of participants in the study were white and 22.6 percent earned less than $25,000 annual income.

Table 2 Characteristics of study participants by cancer registry, (n=180)

Participants characteristics	GACCARE[e] No (%).	HNCARE[f] No (%).	PCCR[g] No (%).
Total	44	20	116
Ulcer			
No	33 (75)	15 (75)	87 (75)
Yes	11 (25)	5 (25)	29 (15)
Age, years [a]	59.9 ± 12.3	60.9 ± 13.9	64.8 ± 10.8
Gender			
Female	27 (61.4)	5 (25)	52 (45)
Male	17 (38.6)	15 (75)	64 (55)
BMI [b]			
Underweight	1 (4.2)	1 (6.7)	1 (1.1)
Normal	8 (33.3)	8 (53.3)	18 (19.6)
Overweight	6 (25.0)	4 (26.7)	33 (35.9)
Obese	9 (37.5)	2 (13.3)	40 (43.5)
Missing	20	5	24
Smoking [c]			
Never Smokers	10 (38.5)	3 (20.0)	36 (39.1)
Ever Smokers	14 (61.5)	12 (80.0)	56 (60.9)
Missing	30	5	23
Refuse	0	0	1
Alcohol intake [d, e]			
< 1 drink/month	5 (20.8)	0 (0)	31(32.6)
>1 drink /month	19 (79.2)	15 (100)	64 (67.4)
Total years of intake	39.77 (12.7)	43.71 (15.4)	44 (11.9)
Refused	0 (0)	0 (0)	10
Missing	25	5	11
Race			
American Indian	1 (2.3)	0 (0)	1(0.9)
Asian	1 (2.3)	0 (0)	2(1.7)
African American	4 (9.0)	0 (0)	4 (3.5)
White	38 (86.4)	19 (100)	108(93.9)
Unknown	0 (0)	1	1

Table 2. Continue. Characteristics of study participants by cancer registry, (n=180)

Participants characteristics	GACCARE[e] No (%).	HNCARE[f] No (%).	PCCR[g] No (%).
Total	44	20	116
Income			
< $10,000	3 (13.6)	0 (0)	0 (0)
$10,000 - $24,999	3 (13.6)	4 (28.6)	1(14.3)
$25,000-$44,999	6 (27.3)	4 (28.6)	1 (14.3)
$45,000-$74,999	3 (13.6)	2 (14.3)	2 (28.6)
$75,000-$100,000	2 (9.1)	2 (14.3)	1 (14.3)
$>100,000	5 (22.7)	2 (14.3)	2 (28.6)
Refused	1	2 (12.50)	1 (25.00)
Missing	21	4	108

Notes.

e Gaccare gastrointestinal and abdominal cancer care registry

f Hncare head and neck cancer care registry

g PCCR pancreas cancer care registry

[a, e]Age and total year of alcohol intake was presented as mean ± standard deviation, and other data were expressed as frequency (weighted %).

[b] body mass index (BMI) <18.5kg/m^2 was defined as underweight, BMI between 18.5 and 24.9kg/m^2 considered as normal, BMI between 25 and 29.9kg/m^2 as overweight and BMI ≥ 30kg/m^2 as obese.

[c] smoking status was defined base of on participant who had smoked more than 100 cigarettes.

[d] one drink was considered as one shot of liquor, a mixed drink, one glass of wine or one 12 ounce of beer per month during a 12 month period or more than 20 drinks in a lifetime.

Table 2 shows the general characteristics of participants in the study by cancer registry. Among the 180 included study participants, 44 were from gastrointestinal and abdominal cancer collaborative registry, 20 were from head and neck cancer registry and 116 participants were from pancreas cancer registry. The mean age diagnosis of participants with pancreas cancer (64.8 ± 10.8) was higher than the age diagnosis of participants with head and neck cancer (60.9 ± 13.9) and gastrointestinal cancer (59.9 ± 12.3). Among the patients studied for the various cancer types, patients with pancreas

cancer seemed to be more overweight and obese than patients with head and neck and gastrointestinal and abdominal cancer. Relative to participants from gastrointestinal and abdominal and pancreas cancer registry, participants with head and neck cancer had a higher proportion of males (75.00 %) versus 55 % for pancreas cancer and 39.6 % for gastrointestinal and abdominal cancer patients. Participants seemed to have at least one drink per month and a mean total year of alcohol intake of 44 years for head and neck and pancreas cancer and 39.8 years gastrointestinal and abdominal cancer. Alcohol intake was higher among patients with head and neck cancer (100 %) and gastrointestinal cancers (79.1 %) and lower (67.4 %) for pancreas cancer. This finding was similar to the smoking status, where 80% of head and neck cancer patient, 60.9% of pancreas cancer patient and 61.5% of patients with gastrointestinal cancer had smoke at least hundred cigarettes.

Lastly, a major proportion of participants in the study were white with Head and neck cancer (100%), pancreas cancer (93.9%) and gastrointestinal cancers (86.4%). Furthermore, 57.2% of patient diagnosed with head and neck cancer earned less than $45,000 income while 28.6% of pancreas cancer patient earned lower than $45,000.

Table 3: Median age at cancer diagnosis based on primary cancer type.

Cancer registry	Primary cancer type	Median age at diagnosis of U.S sample	Median age at diagnosis of iCaRe[2] sample	Gastroduodenal Ulcer		No Gastroduodenal Ulcer	
				n	age median	n	age median
PCCR[a]	Pancreas Cancer	70.00	63.83	29	68.15	87	63.67
GACCARE[b]	Colon Cancer Female	72.00	62.03	6	66.21	15	57.00
	Colon Cancer Male	68.00	63.00	2	68.00	13	61.77
	Rectal Cancer	63.00	50.82	2	63.66	4	50.02
	Gastric Cancer	68.00	54.98	1	40.96	1	69.00
HNCARE[c]	Lip and Oral Cavity Cancer	69.00	61.11	4	63.89	9	61.11
	Laryngeal Cancer	65.00	78.52	-	-	2	78.52
	Salivary Gland Cancer	64.00	37.43	1	27.73	1	47.13
	Oropharyngeal Cancer	63.00	58.66	-	-	3	58.66
Total		66.70	64.47	45	51.96	135	63.29

Notes.

Data for U.S median age of cancer diagnosis for lip and oral cavity, oropharyngeal, laryngeal, gastric, and pancreas are from SEER (SEER, 2019b). Data for U.S median age of cancer diagnosis colon, rectal and salivary gland cancer are from American cancer society (American cancer society, 2019b)

a PCCR pancreas cancer care registry

b Gaccare gastrointestinal and abdominal cancer care registry

c Hncare head and neck cancer care registry

Table 3 shows the number of cases per primary cancer type, the median age at diagnosis of each primary cancer type for gastroduodenal ulcer patients and patients without gastroduodenal ulcer in our study population and the United States population. There is a distinction in the median age of diagnosis of colon cancer by gender and this difference is not seen in other primary cancer types. Pancreas cancer had the highest number of cases in our sample (116 cases). Gastric, laryngeal and salivary gland cancer shared the least number of cases in our sample population (2 cases). Also the median age of diagnosis for colon, oropharyngeal, pancreas, rectal, salivary gland and gastric cancer in iCaRe[2] sample population were lower compared to the United States population.

Table 4. Association between gastroduodenal ulcers and age cancer diagnosis.

	Gastroduodenal Ulcer	No gastroduodenal ulcer	P-Value[1]
Reference population	Mean cancer age difference (SD)	Mean cancer age difference (SD)	
U.S [2]	-5.2 (13.4)	-6.8 (11.1)	0.4
iCaRe[2]	3.8 (12.4)	-0.2 (10.6)	0.2

NOTE:

1 From 2 sample t-test

2 Data for reference U.S mean age of cancer diagnosis for lip and oral cavity, oropharyngeal, laryngeal, gastric, and pancreas are from SEER (SEER, 2019b). Data for reference U.S mean age of cancer diagnosis for colon, rectal and salivary gland cancer are from American cancer society (American cancer society, 2019b)

$$\mu \text{ (ulcer)} = \frac{\sum \text{(normalize cancer diagnosis age for ulcer patient)}}{\text{Number of ulcer cases}}$$

$$\mu \text{ (no ulcer)} = \frac{\sum \text{(normalize cancer diagnosis age for non-ulcer patient)}}{\text{Number of non-ulcer cases}}$$

Table 4 shows the association between gastroduodenal ulcers and age cancer diagnosis using a 2 sample t test. Patients with no ulcer seemed to have lower mean age of cancer diagnosis for both U.S (-6.8) and iCaRe^2 (-0.2) compare to patients with gastroduodenal ulcer U.S (-5.2) and iCaRe^2 (3.8).

Table 5. Model of association between gastroduodenal ulcer and cancers iCaRe^2 .

Variables	Beta Coefficient	Standard Error	P value
Enrollment age	0.9	0.0	<0.0
Gastroduodenal ulcer	1.2	0.7	0.1

Linear regression model: Adjusted Age of cancer diagnosis (iCaRe^2 sample) = gastroduodenal ulcer (yes/no) + enrollment age.

The result suggest after adjusting for age of enrollment , the age of cancer diagnosis for patients with gastroduodenal ulcer is 1.2 year greater than patients with cancer who do not have gastroduodenal ulcer however this is not significant p value (0.1) .

Table 6. Model of association between gastroduodenal ulcer and cancers U.S.

Variables	Beta Coefficient	Standard Error	P value
Enrollment age	0.96	0.02	<0.00
Gastroduodenal ulcer	-0.03	0.49	0.95

Linear regression model: Adjusted Age of cancer diagnosis (U.S sample)= gastroduodenal ulcer (yes/no) + enrollment age.

The result suggest after adjusting for age of enrollment , the age of cancer diagnosis for patients with gastroduodenal ulcer is 0.03 year lesser than patients with cancer who do not have gastroduodenal ulcer however this is not significant p value (0.95) .

DISCUSSION

Research on the association between ulcers and cancer is scarce. The purpose of this study was to analyze the relationship between ulcer and age of cancer diagnosis as well as compare the mean age of cancer diagnosis between the ulcer and non-ulcer patients in our study population.

The results of our analysis suggest that there was no association between gastroduodenal ulcer diagnosis and age of cancer diagnosis. Our finding differ from some previous work (Bao et al., 2010), who provided the most direct evidence for ulcer

association with pancreas cancer. The study found that gastric ulcer but not duodenal ulcer increases the risk of pancreas cancer and some possible mechanism suggested is that the association found might be due to the inflammatory response seen in Helicobacter pylori infection and the ulcer healing process. Chronic inflammation generates growth a factor among which is IGF1 which might contribute to the pathology of pancreas cancer.

Findings from our study also differ from a matched case control study (Lin et al., 2015), who reported a positive association between peptic ulcer and colorectal cancer particularly among patients with helicobacter pylori infection thereby, suggesting the role played by insulin growth factor 1 in ulcer healing and cancer pathogenesis. The discrepancy between our study (Bao et al., 2010) and (Lin et al., 2015) may be largely attributed to the small sample size of our study. Data from a large United State cohort consisting of 51,529 health workers was analyzed (Bao et al., 2010) and data from 60,365 study participants was analyzed (Lin et al., 2015).

An unexpected finding of our study was the mean difference in age of cancer diagnosis for gastroduodenal ulcer patient was higher (-5.15 years) than that for non-gastroduodenal ulcer patient (-6.79 years) when age of cancer diagnosis was normalized to U.S population. However this difference was not significant (P-Value 0.42). It was also observed that the mean age of cancer diagnosis for patients with gastroduodenal in the iCaRe^2 was also higher than the age of cancer diagnosis for patient with no gastroduodenal ulcer. This finding was also not significant (p value 0.2).

The results from this study might have been different if the study had a large enough sample size.

This study is significant in that it will serve as a landmark for future research which may lead to establishing the link between ulcers and cancers and thus, predict and or prevent certain cancer types through early detection of gastroduodenal ulcers.

LIMITATIONS

The study had some limitations. First, the diagnosis of our exposure variable of interest was based patient self-report of having ulcer. iCaRe^2 questionnaire only had a check box for which patients tick yes for presence of ulcer. In the absence of ulcer there was no check box hence, we assumed all patients that didn't tick the check box had no ulcer there by introducing selection bias. Furthermore, small sample size due to a small number of patients who responded to the exposure question of interest was a limitation in this study hence, relationship between covariates and outcome variable was not studied because it would further reduce our sample size hence crude analysis was done. Also, we were limited in accessing the possibility that occurrence of gastroduodenal ulcers preceded the occurrence of cancers because of the limited number of patients that reported age of ulcer diagnosis. However the few patients that reported age of ulcer diagnosis, data show diagnosis of cancer preceded diagnosis of ulcer. Finally, due to unavailability of data, we were limited in exploring the relationship between the median age of cancer diagnosis of our sample population and the median age of cancer diagnosis among patients seen in Nebraska.

The results from this study suggest no association between gastroduodenal ulcer and pancreas, head and neck, gastrointestinal and abdominal cancer. The study was limited by sample size hence, further research with a large sample is needed to investigate both the association as well as the biologic mechanism that link gastroduodenal ulcer and cancers.

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