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ORIGINAL RESEARCH

Metabolic Conditions and Organ Dysfunctions Risk Factors for Gastrointestinal Cancer in Hypertensive Patients: A Case-Control Study in China

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Background: The associations of metabolic conditions, chronic organ dysfunctions and acidic food consumption with the risk of gastrointestinal cancer are unknown among individuals with primary hypertension. We sought to identify risk factors for gastrointestinal cancer in this population.

Methods: We conducted a case-control study among individuals who had primary hypertension and were later diagnosed with a type of gastrointestinal cancer, and those who had primary hypertension and were not diagnosed with gastrointestinal cancer at a local hospital from January 2020 to January 2024. We compared sociodemographic, lifestyle, dietary, and medical characteristics between the groups using data extracted from electronic medical records. Univariate and multivariate logistic regression were used to find associations with risk factors.

Results: We identified 125 cases of gastrointestinal cancer and 544 controls who were cancer-free. There were significant associations between overall gastrointestinal cancer and hyperlipidemia (OR, 3.37; 95% CI, 1.98–5.72), diabetes mellitus (OR, 2.58; 95% CI, 1.64–4.07), chronic renal failure (OR, 2.45; 95% CI, 1.43–4.20), alcohol consumption (OR, 2.35; 95% CI, 1.49–3.70), heart failure (OR, 2.13; 95% CI, 1.36–3.33), and higher-grade hypertension (OR, 1.97; 95% CI, 1.41–2.74).

Conclusion: In this retrospective study of patients who had primary hypertension, we identified several comorbid conditions as indicators for gastrointestinal cancer, including hyperlipidemia, diabetes mellitus, chronic renal failure, alcohol consumption, heart failure, and higher-grade hypertension.

Keywords: gastrointestinal cancer, hypertension, risk factors, metabolic conditions, organ failures, diet

Introduction

Gastrointestinal (GI) cancers account for a quarter of all new cancer cases and a third of all cancer-related deaths globally.[1] In Asia, esophageal, gastric, and liver cancers have the highest incidences among major GI cancers, followed by colorectal and pancreatic cancers. Although the incidences and mortalities of esophageal, gastric, and liver cancers have been decreasing, those of colorectal cancer have been on the rise.[1] The incidence of colorectal cancer in China has increased from 14.25 cases per 100,000 in 1990 to 25.27 cases per 100,000 in 2016, and is predicted to increase by more than 50% from the latter by 2025.[2] Furthermore, the incidence of colorectal cancer in the population aged 15–49 years has seen an over-two-fold increase over the same period.[2] The resulting vast numbers of GI cancer-related deaths are expected to aggravate the cancer burden in China, therefore, primary prevention is of utmost importance.[3]

Behavioral risk factors of GI cancers such as cigarette smoking, alcohol consumption, and physical inactivity have been well-established.[4–6] Chronic metabolic conditions, such as obesity, diabetes, and hyperlipidemia are increasingly recognized as contributing factors. These metabolic conditions frequently coexist with hypertension,[7] a condition that affects a significant portion of the population, particularly older adults. However, the relationship between hypertension and GI cancer risk, as well as the role of related comorbidities, has not been thoroughly explored.[8,9]

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This study provides a novel perspective by focusing on hypertensive patients, who are at higher risk for metabolic conditions and organ dysfunctions that may increase their susceptibility to GI cancers. Compared with studies that examine GI cancer in the general population, our focus on hypertensive patients is clinically significant because these individuals are more likely to have comorbidities that interact with cancer risk factors differently.[10] Understanding the cumulative impact of these conditions can help identify high-risk individuals for more targeted screening and prevention strategies. Additionally, recent research has highlighted the importance of dietary factors in GI cancer risk, with both risk factors, including red meat, processed meat, and high cholesterol intake, and protective factors, such as fruits, vegetables, dietary fiber, and fish, being identified.[11,12] However, it remains unclear whether high-acidity or fermented foods, commonly consumed in many Asian diets, also contribute to cancer risk.[12]

In light of these gaps, we conducted a retrospective case-control study among hypertensive patients in a tertiary hospital to explore the associations between metabolic conditions, organ dysfunctions, and GI cancer risk. By focusing on this patient population, we aim to provide new insights into the risk factors specific to hypertensive individuals, thus contributing to more effective cancer prevention strategies for this high-risk group.

Methods

Study Design

This is a retrospective case-control study of patients who visited Zibo Central Hospital. We performed a search in the electronic health record system among patients who received medical care at the hospital between 2020 to January 2024. Patients who met the following inclusion criteria were identified as cases: (1) were diagnosed with one of four types of GI cancer during the study period, namely, esophageal cancer, gastric cancer, colon cancer, and rectal cancer; (2) were 18 years or older at the time of cancer diagnosis; (3) were diagnosed with primary hypertension prior to the study period. Diagnoses of GI cancer were identified based on the International Classification of Diseases, Tenth Revision (ICD-10), using the codes C15, C16, C18, C19 and C20. Diagnosis of primary hypertension was identified from the chart of diagnoses included in a patient's electronic health record. Controls were defined as patients who did not have a diagnosis of GI cancer or any other type of malignancy by the end of the study period, had a diagnosis of primary hypertension prior to the study period, and were 18 years or older. The control subjects were not matched to the cases for age or sex. Patients were excluded if they had a diagnosis of hereditary GI cancer, secondary or malignant hypertension, or severe physical or mental illness. The screening process yielded a total of 669 subjects, including 125 cases and 544 controls. This study was approved by the Ethics Committees of Zibo Central Hospital.

Study Variables

Demographic information (eg age, sex, ethnicity, education level, employment status, and marital status) and lifestyle characteristics (eg Body mass index (BMI), smoking status, and alcohol consumption) were extracted from patient registration forms. Medical history (eg primary hypertension, diabetes, hyperlipidemia, *H. pylori* infection, fatty liver disease, and history of psychological trauma within the past ten years) were extracted from the diagnoses and medical history sections.

Dietary patterns (eg salt consumption, high-fat diet, and consumption of acidic foods such as fermented cabbage, sour soups, vinegar, and yoghurt) were collected from personal history. To define "acidic food consumption", we considered regular, sustained intake rather than isolated or occasional consumption. Participants were categorized as regular consumers if they reported consuming these foods at least once per week over a period of six months or longer. This threshold was set to capture habitual dietary patterns that may contribute to gastrointestinal health outcomes.

Hypertensive severity, control status, and the presence of vascular complications (such as cardiac, cerebral, aortic, renal, and/or retinal diseases secondary to hypertension) were identified according to case records. The amount of salt consumption per day, preference for a high-fat diet, and significant consumption of certain types of acidic food were self-reported information in personal history.

Definitions of Medical Conditions

Diabetes Mellitus: Defined as fasting plasma glucose ≥ 126 mg/dL, 2-hour OGTT plasma glucose ≥ 200 mg/dL, random plasma glucose ≥ 200 mg/dL with hyperglycemic symptoms, or use of anti-diabetic medication.

Chronic Kidney Disease: Diagnosed as eGFR < 60 mL/min/1.73 m^2 for ≥ 3 months, or albuminuria > 30 mg/g creatinine.

Primary Hypertension: Defined according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines as systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 80 mmHg, measured on at least two separate occasions, or current use of antihypertensive medication.

Hyperlipidemia: Defined as total cholesterol ≥ 240 mg/dL, LDL-C ≥ 160 mg/dL, triglycerides ≥ 200 mg/dL, or patients currently on lipid-lowering medication.

Fatty Liver Disease: Diagnosed via imaging (ultrasound/CT) showing hepatic steatosis, or liver biopsy confirming fat accumulation.

Retinal Arteriolosclerosis: Diagnosed by fundus photography or ophthalmoscopy, indicating arteriolar narrowing or arteriovenous nicking.

Statistical Analysis

Descriptive analyses were performed to reveal any differences between case and control groups in demographic information, lifestyle characteristics, dietary patterns, medical history, and hypertension-related variables. The Chi-square test was used to compare the distributions of categorical variables, and the Student *t*-test and ANOVA for continuous variables. A two-sided *P*-value of < 0.05 was adopted for statistical significance. Explanatory variables that were found to have statistically significant differences between study groups during univariate analyses were carried into multivariable regression analyses. A multivariable logistic regression analysis was performed for overall GI cancer diagnosis. Further multivariable logistic regression analysis was performed for each of the four types of GI cancer. Adjusted odds ratios (OR), 95% confidence intervals (95% CI), and corresponding p-values were reported for the multivariable models. SPSS 26.0 software was used to perform statistical analysis.

Results

Sociodemographic Characteristics

Of the total 669 subjects included in the study, 125 (18.7%) were GI cancer cases. Median age of the study sample was 58 (range, 35–83) years. Among the subjects, 380 (56.8%) were female. Sociodemographic characteristics of the two groups were summarized in Table 1. There were no significant differences in gender, age, and BMI between cases and controls ($P > 0.05$). Nor were there differences in ethnicity, education level, employment status, and marital status ($P > 0.05$). History of psychological trauma within the past 10 years had similar frequencies in the two groups. Though these sociodemographic factors were not the primary focus of our risk factor analysis, they were included to ensure the two groups were comparable in terms of basic population characteristics and to control for potential confounding variables.

Dietary and Lifestyle Risk Factors

The presence of *H. pylori* infection was significantly more frequent (57.6% vs 47.1%, P = 0.03) among the GI cancer cases. Patients diagnosed with GI cancer were more likely to be alcohol drinkers (65.6% vs 41.2%, $P < 0.001$), but were not more likely to be cigarette smokers. Both higher salt intake (4.80 ± 1.36 vs 4.56 ± 1.0, $P = 0.03$) and a high-fat diet (60.0% vs 50.0%, $P = 0.04$) were more prevalent among GI cancer cases. In the preferences for acidic food, GI cancer cases were more likely to report consumption in significant quantities of sour fermented cabbage (32.0% vs 23.0%, $P = 0.04$) and sour-tasting soup (36.0% vs 26.7%, $P = 0.04$); however, there were no significant differences in the consumption of yoghurt or vinegar between the groups ($P > 0.05$). These variables were reported in Table 2.

Table 1 Sociodemographic Characteristics of GI Cancer Cases with Primary Hypertension and Non-GI Cancer Controls with Primary Hypertension

Variable	Control (n=544)	GI Cancer (n=125)	χ^2/t	*P*
Gender (%)			1.443	0.230
Male	241(44.3)	48(38.4)		
Female	303(55.7)	77(61.6)		
Age (years)	58.17±8.18	57.74±9.93	0.500	0.617
BMI (kg/m²)	22.42±2.93	22.77±2.73	−1.234	0.218
Ethnicity (%)			0.562	0.453
Han	483(88.8)	108(86.4)		
Minority	61(11.2)	17(13.6)		
Education Level (%)			3.830	0.147
Primary School	153(28.1)	37(29.6)		
Middle School	293(53.9)	57(45.6)		
College and above	98(18.0)	31(24.8)		
Occupation (%)			0.078	0.780
Employed	319(58.6)	75(60.0)		
Retired/Unemployed	225(41.4)	50(40.0)		
Marital Status (%)			4.282	0.118
Married	406(74.6)	84(67.2)		
Divorced	106(19.5)	28(22.4)		
Widowed	32(5.9)	13(10.4)		
Major psychological trauma in the past 10 years (%)			1.374	0.241
No	390(71.7)	83(66.4)		
Yes	154(28.3)	42(33.6)		

Notes: Values are reported as frequency (percentages) or mean ± standard deviation.
Abbreviations: GI, Gastrointestinal; BMI, Body mass index;.

Table 2 Dietary and Lifestyle Risk Factors of GI Cancer Cases with Primary Hypertension and Non-GI Cancer Controls with Primary Hypertension

Variable	Control (n=544)	GI Cancer (n=125)	χ^2/t	*P*
***H. pylori* (%)**			4.519	0.034
Negative	288(52.9)	53(42.4)		
Positive	256(47.1)	72(57.6)		
Alcohol consumption (%)			24.43	<0.001
No	320(58.8)	43(34.4)		
Yes	224(41.2)	82(65.6)		
Smoking (%)			2.300	0.129
No	430(79.0)	91(72.8)		
Yes	114(21.0)	34(27.2)		
Salt intake (g)	4.56±1.02	4.80±1.36	−2.228	0.026
High-fat diet (%)			4.071	0.044
No	272(50.0)	50(40.0)		
Yes	272(50.0)	75(60.0)		
Acidic food (%)				
Yoghurt	371(68.2)	93(74.4)	1.839	0.175
Sour soup	145(26.7)	45(36.0)	4.366	0.037
Pickled cabbage	125(23.0)	40(32.0)	4.453	0.035
Vinegar	384(70.6)	84(67.2)	0.555	0.456

Note: Values are reported as frequency (percentages).

Table 3 Hypertension Classification and Blood Pressure Control-Related Variables in GI Cancer Cases with Primary Hypertension and Non-GI Cancer Controls with Primary Hypertension

Variable	Control (n=544)	GI Cancer (n=125)	χ^2/t	*P*
Blood Pressure (mmHg)	152.49±14.55	154.8±14.38	−1.608	0.108
Time Since Hypertension Diagnosis (months)	73.85±6.13	74.15±5.99	−0.506	0.613
Hypertension Classification (%)			25.108	0.000
II	168(30.9)	24(19.2)		
II	292(53.7)	58(46.4)		
III	84(15.4)	43(34.4)		
Hypertension Medication Usage (%)			2.713	0.100
Irregular/Untreated	92(16.9)	29(23.2)		
Regular	452(83.1)	96(76.8)		
Medication Treatment (%)				
ACEI	328(60.3)	68(54.4)	1.462	0.227
ARB	386(71)	83(66.4)	1.007	0.316
Beta-blockers	284(52.2)	57(45.6)	1.775	0.183
Calcium channel blockers	234(43.0)	51(40.8)	0.204	0.652
Diuretics	389(71.5)	85(68.0)	0.605	0.437
Blood Pressure Control Status (%)			4.418	0.036
Ideal	296(54.4)	55(44.0)		
Not ideal	248(45.6)	70(56.0)		

Notes: Values are reported as frequency (percentages) or mean ± standard deviation.

State of Primary Hypertension

Average systolic blood pressure among GI cancer cases were (154.8 ± 14.4) mm Hg, and time of diagnosis on average was 74.2 ± 6.0 months prior to the study period. There was a significant difference in the distribution of hypertension classes between the two groups ($P < 0.001$), and the relative frequency of grade III hypertension was higher among cases (34.4% vs 15.4%). Proportions of patients who regularly took antihypertensive medicine were not significantly different between the groups, nor were the choice of antihypertensive therapies. However, the relative frequency of patients who failed to maintain a satisfactory control of their blood pressure was significantly higher among GI cancer cases (56.0% vs 45.6%, $P = 0.04$). The data were summarized in Table 3.

Hypertension-Associated Complications

We compared the relative frequencies of cardiac, cerebral, arterial, and renal complications among cases and controls (Table 4). We found that heart failure (52.8% vs 35.7%, $P < 0.001$) and chronic renal failure (28.8% vs 13.2%, $P < 0.001$) were significantly more likely to be present among GI cancer cases, so were atherosclerosis (37.6% vs 28.3%, p=0.04) and benign nephrosclerosis (19.2% vs 12.3%, $P = 0.04$). We found no significant differences in the prevalence of left-sided cardiomegaly, angina, myocardial infarction, cerebral infarction, cerebral hemorrhage, hypertensive encephalopathy, aortic dissection, and malignant nephrosclerosis between cases and controls ($P > 0.05$).

Other Diseases

GI cancer cases were more likely to be diabetic (65.6% vs 42.6%, $P < 0.001$), have hyperlipidemia (81.6% vs 58.6%, $P < 0.001$), and have fatty liver disease (34.4% vs 23.3%, $P = 0.01$) compared to controls (Table 5). There was no significant difference in the percentages of patients with retinal arteriolosclerosis between the groups ($P > 0.05$).

Adjusted Analysis of GI Cancer Risk Factors

Multifactorial analysis showed that hyperlipidemia, diabetes mellitus, chronic renal failure, alcohol consumption, heart failure, and hypertension classification were significantly associated with increased odds of GI cancer (Table 6). Further

Table 4 Prevalence of Hypertension-Associated Complications in GI Cancer Cases with Primary Hypertension and Non-GI Cancer Controls with Primary Hypertension

Variable	Control (n=544)	GI Cancer (n=125)	χ^2	*P*
Heart (%)				
Left ventricular hypertrophy	181(33.3)	41(32.8)	0.010	0.919
Angina	201(36.9)	55(44.0)	2.139	0.144
Myocardial infarction	120(22.1)	33(26.4)	1.086	0.297
Heart failure	194(35.7)	66(52.8)	12.555	<0.001
Stroke (%)				
Cerebral infarction	164(30.1)	47(37.6)	2.615	0.106
Cerebral hemorrhage	108(19.9)	32(25.6)	2.029	0.154
Hypertensive encephalopathy	125(23.0)	36(28.8)	1.885	0.170
Arteries (%)				
Atherosclerosis	154(28.3)	47(37.6)	4.175	0.041
Aortic dissection	77(14.2)	24(19.2)	2.019	0.155
Kidneys (%)				
Benign nephrosclerosis	67(12.3)	24(19.2)	4.099	0.043
Malignant nephrosclerosis	60(11.0)	17(13.6)	0.659	0.417
Chronic renal failure	72(13.2)	36(28.8)	18.190	<0.001

Note: Values are reported as frequency (percentages).

Table 5 Prevalence of Diabetes, Fatty Liver Disease, Hyperlipidemia, and Retinal Arteriolosclerosis in GI Cancer Cases with Primary Hypertension and Non-GI Cancer Controls with Primary Hypertension

Variable	Control (n=544)	GI Cancer (n=125)	χ^2	*P*
Retinal Arteriolosclerosis (%)			3.432	0.180
No	265(48.7)	65(52.0)		
Yes	71(13.1)	22(17.6)		
Not checked	208(38.2)	38(30.4)		
Diabetes (%)			21.501	0.000
No	312(57.4)	43(34.4)		
Yes	232(42.6)	82(65.6)		
Fatty Liver (%)			6.553	0.010
No	417(76.7)	82(65.6)		
Yes	127(23.3)	43(34.4)		
Hyperlipidemia (%)			22.97	0.000
No	225(41.4)	23(18.4)		
Yes	319(58.6)	102(81.6)		

Note: Values are reported as frequency (percentages).

analysis also revealed that fatty liver disease was significantly associated with a higher risk of GI cancer (OR, 1.689; 95% CI, 1.101–2.590, $P < 0.05$), along with diabetes mellitus (OR, 2.459; 95% CI, 1.628–3.714, $P < 0.001$) and hyperlipidemia (OR, 3.021; 95% CI, 1.852–4.930, $P < 0.001$) (Table S1). Elevated levels of serum lipid markers were associated with 3.4 times greater odds of developing GI cancer (OR, 3.37; 95% CI, 1.98–5.72) compared to normal levels of serum lipids. Diabetes mellitus was associated with a 2.6-fold increased odds of developing GI cancer (OR, 2.58; 95% CI, 1.64–4.07). The odds of being diagnosed with GI cancer were significantly higher in patients who suffered from chronic renal failure (OR, 2.45; 95% CI, 1.43–4.20) or heart failure (OR, 2.13; 95% CI, 1.36–3.33). Alcohol drinkers had 2.3

Table 6 Adjusted Odds Ratios and 95% Confidence Intervals of GI Cancer

Variable	*B*	*S.E.*	*Wald*	*P*	*OR*	*95% CI*	
						Lower Limit	Upper Limit
Alcohol consumption	0.854	0.232	13.561	0.000	2.349	1.491	3.701
Hypertension classification	0.677	0.169	16.052	0.000	1.968	1.413	2.741
Heart failure	0.754	0.229	10.811	0.001	2.125	1.356	3.331
Chronic renal failure	0.896	0.276	10.566	0.001	2.449	1.427	4.204
Diabetes	0.948	0.232	16.651	0.000	2.580	1.636	4.067
Hyperlipidemia	1.213	0.270	20.135	0.000	3.365	1.980	5.716
H. pylori	0.367	0.229	2.572	0.109	1.444	0.922	2.262
Salt intake	0.143	0.102	1.945	0.163	1.153	0.944	1.410
High-fat diet	0.386	0.231	2.789	0.095	1.472	0.935	2.316
Sour soup	0.423	0.244	3.016	0.082	1.527	0.947	2.461
Pickled cabbage	0.389	0.252	2.394	0.122	1.476	0.901	2.417
Blood pressure control status	0.195	0.230	0.718	0.397	1.216	0.774	1.909
Atherosclerosis	0.409	0.240	2.901	0.089	1.506	0.940	2.412
Benign nephrosclerosis	0.609	0.314	3.764	0.052	1.839	0.994	3.403
Fatty liver	0.421	0.246	2.94	0.086	1.524	0.942	2.466

Abbreviations: *B*, beta coefficients. *S.E.*, standard error. *Wald*, Wald Chi-square value. *P*, p-value. *OR*, odds ratios. *95% CI*, 95% confidence intervals.

times greater odds of receiving a GI cancer diagnosis compared to non-drinkers (OR, 2.35; 95% CI, 1.49–3.70). Being classified as higher-grade hypertension was significantly associated with an almost 2-fold increased odds of developing GI cancer compared to being classified as lower-grade hypertension (OR, 1.97; 95% CI, 1.41–2.74).

Adjusted Analysis by Type of Cancer

Among the 125 cases of GI cancer, there were 35 cases of esophageal cancer, 34 cases of gastric cancer, 37 cases of colonic cancer, and 18 cases of rectal cancer. We carried out further multivariable logistic regression analysis for each of the four types of GI cancer included in this study. The variables that were found to have significantly different distributions between cases and controls were carried forward to this stage of analysis.

Among the 35 esophageal cancer cases, there were 10 tumors located cervically, 13 tumors located thoracically, and 12 tumors located abdominally. Fourteen and 21 cases had I/II and III/IV staging, respectively. Fifteen cases had surgery, of whom 18 cases recovered their blood pressures to preoperative levels. For esophageal cancer, hyperlipidemia, diabetes mellitus, heart failure, and hypertension classification were significant risk factors (Table 7), with hyperlipidemia being the most dominant (OR, 5.80; 95% CI, 1.99–16.91), followed by diabetes (OR, 2.99; 95% CI, 1.40–6.38).

Table 7 Adjusted Odds Ratios and 95% Confidence Intervals of Esophageal Cancer

	B	*S.E.*	*Wald*	*P*	*OR*	*95% CI*	
						Lower Limit	Upper Limit
Alcohol consumption	0.576	0.369	2.435	0.119	1.779	0.863	3.670
Hypertension classification	0.579	0.263	4.836	0.028	1.785	1.065	2.991
Heart failure	0.781	0.366	4.548	0.033	2.184	1.065	4.479
Chronic renal failure	0.554	0.468	1.402	0.236	1.74	0.696	4.351
Diabetes	1.095	0.387	8.01	0.005	2.989	1.400	6.378
Hyperlipidemia	1.757	0.546	10.355	0.001	5.797	1.988	16.905

Abbreviations: *B*, beta coefficients. *S.E.*, standard error. *Wald*, Wald Chi-square value. *P*, p-value. *OR*, odds ratios. *95% CI*, 95% confidence intervals.

Among the 34 gastric cancer cases, there were 4 tumors located in the antrum, 11 tumors located in the pylorus, 6 tumors located in the angular notch, and 13 tumors located in the body. Twenty-one and 13 cases had I/II and III/IV staging, respectively. Twenty-one cases had surgery, of whom 16 cases recovered their blood pressures to preoperative levels. Multifactorial analysis showed that chronic renal failure, alcohol consumption, hyperlipidemia, and diabetes mellitus were found to be associated with significantly increased odds of developing cancer (Table 8), with chronic renal failure (OR, 3.74; 95% CI, 1.70–8.20) and alcohol consumption (OR, 3.20; 95% CI, 1.47–7.01) both being associated with over 3-fold increase in the odds of developing cancer.

In our analysis for colon cancer, there were 7 tumors located in the ileocecum, 8 tumors located in the ascending colon, 13 tumors located in the transverse colon, 4 tumors located in the descending colon, and 5 tumors located in the sigmoid colon. Seventeen and 20 cases had I/II and III/IV staging, respectively. Twenty-two cases had surgery, of whom 24 cases recovered their blood pressures to preoperative levels. Multifactorial analysis showed that alcohol consumption, chronic renal failure, hyperlipidemia, diabetes mellitus, heart failure, and hypertension classification were all found to be significant risk factors for cancer development (Table 9). Among them, alcohol consumption (OR, 3.50; 95% CI, 1.62–7.57) and chronic renal failure (OR, 3.06; 95% CI, 1.40–6.69) were the most significant indicators.

In the analysis for rectal cancer, 7 and 11 cases had I/II and III/IV staging, respectively. Five cases had surgery, of whom 9 cases recovered their blood pressures to preoperative levels. We identified hyperlipidemia, diabetes mellitus, heart failure, and hypertension classification as significant indicators of cancer development (Table 10), with hyperlipidemia (OR, 5.60; 95% CI, 1.24–25.31) and diabetes (OR, 4.60; 95% CI, 1.45–14.65) being the most important ones. Of note, hyperlipidemia, diabetes mellitus and hypertension classification were consistent risk factors for both combined GI cancer and the four individual types of GI cancer in this hypertensive patient population.

Table 8 Adjusted Odds Ratios and 95% Confidence Intervals of Gastric Cancer

	B	*S.E.*	*Wald*	*P*	*OR*	*95% CI*	
						Lower Limit	**Upper Limit**
Alcohol consumption	1.165	0.399	8.502	0.004	3.204	1.465	7.010
Hypertension classification	0.555	0.277	4.001	0.045	1.742	1.011	3.001
Heart failure	0.416	0.376	1.225	0.268	1.517	0.725	3.171
Chronic renal failure	1.319	0.401	10.816	0.001	3.738	1.704	8.203
Diabetes	0.763	0.379	4.046	0.044	2.145	1.020	4.513
Hyperlipidemia	0.912	0.428	4.543	0.033	2.490	1.076	5.759

Abbreviations: *B*, beta coefficients. *S.E.*, standard error. *Wald*, Wald Chi-square value. *P*, p-value. *OR*, odds ratios. *95% CI*, 95% confidence intervals.

Table 9 Adjusted Odds Ratios and 95% Confidence Intervals of Colon Cancer

	B	*S.E.*	*Wald*	*P*	*OR*	*95% CI*	
						Lower Limit	**Upper Limit**
Alcohol consumption	1.254	0.393	10.192	0.001	3.504	1.623	7.567
Hypertension classification	0.600	0.266	5.103	0.024	1.823	1.083	3.068
Heart failure	0.76	0.360	4.459	0.035	2.139	1.056	4.332
Chronic renal failure	1.118	0.399	7.833	0.005	3.059	1.398	6.692
Diabetes	0.802	0.370	4.692	0.030	2.230	1.079	4.609
Hyperlipidemia	1.030	0.426	5.840	0.016	2.801	1.215	6.456

Abbreviations: *B*, beta coefficients. *S.E.*, standard error. *Wald*, Wald Chi-square value. *P*, p-value. *OR*, odds ratios. *95% CI*, 95% confidence intervals.

Table 10 Adjusted Odds Ratios and 95% Confidence Intervals of Rectal Cancer

	B	*S.E.*	*Wald*	*P*	*OR*	*95% CI*	
						Lower Limit	**Upper Limit**
Alcohol consumption	0.620	0.517	1.436	0.231	1.859	0.674	5.124
Hypertension classification	0.825	0.383	4.648	0.031	2.281	1.078	4.829
Heart failure	1.087	0.519	4.386	0.036	2.966	1.072	8.203
Chronic renal failure	0.770	0.625	1.518	0.218	2.160	0.634	7.357
Diabetes	1.526	0.591	6.670	0.010	4.601	1.445	14.652
Hyperlipidemia	1.723	0.769	5.019	0.025	5.604	1.241	25.31

Abbreviations: *B*, beta coefficients. *S.E.*, standard error. *Wald*, Wald Chi-square value. *P*, p-value. *OR*, odds ratios. *95% CI*, 95% confidence intervals.

Discussion

In this retrospective case-control study of hypertensive patients at a tertiary hospital, we found that hyperlipidemia, diabetes mellitus and higher-grade hypertension were significant risk factors for all four types of GI cancer that we investigated, namely, esophageal, gastric, colon and rectal cancers. Additionally, alcohol consumption was significantly associated with increased risk of gastric and colon cancers, but were not significant risk factors for esophageal and rectal cancers, contrary to prior research. We also identified heart failure and chronic renal failure as significant comorbid illnesses that may act as indicators of increased GI cancer risk. These findings suggested that metabolic conditions and other comorbid diseases may perform a role in helping to identify patients who may benefit from GI cancer screening.

This study is one of the few that focuses specifically on hypertensive patients, examining how metabolic conditions and organ dysfunctions, including heart and renal failure, influence GI cancer risk. While previous research has explored general risk factors for GI cancer, few have investigated these specific risk factors within the hypertensive population. Our findings suggest that combining multiple metabolic and organ dysfunction risk factors can help identify high-risk individuals for targeted cancer screening.

Several studies have shown that alcohol consumption increases the risk of GI and non-GI cancers with a dose-response relationship.[4,13,14] Our analyses revealed significant positive associations of alcohol consumption with gastric cancer and colon cancer, but not with esophageal cancer and rectal cancer. These findings may be attributed to the stronger effects of hyperlipidemia and diabetes mellitus in this group of patients, both of which are common comorbidities of hypertension. This contrasts with findings in the general population, where alcohol consumption has shown more consistent associations across different GI cancers, including esophageal and rectal cancers.[12,15,16] The interaction between metabolic conditions, such as hyperlipidemia and diabetes, and hypertension in our study population may have amplified the cancer risk from alcohol, particularly for gastric and colon cancers, suggesting that alcohol-related cancer risks may manifest differently in hypertensive patients compared to the general population.

Dietary patterns are important indicators of GI cancer risk. For instance, dietary fiber intake and fish consumption have been shown to decrease relative risk of colorectal cancer,[17,18] while high cholesterol intake and red meat consumption have been associated with increased risks of GI cancer.[19,20] However, in our study, we did not observe an increased risk for GI cancer among individuals who consumed a high-salt or high-fat diet. This could be due to the stronger influence of comorbid metabolic conditions, such as hyperlipidemia and diabetes, in hypertensive patients, which may overshadow the dietary effects observed in the general population. The interplay between hypertension, metabolic disorders, and dietary habits warrants further investigation, as these factors may behave differently in hypertensive individuals compared to the general population.

Previous evidence indicated that hyperlipidemia increased the overall risk of cancer, with some studies showing site-specific effects on GI cancer incidence and mortality.[21–23] In our study, hyperlipidemia was consistently associated with an increased risk of GI cancer, including all four types of cancers analyzed. While studies in the general population have shown mixed results regarding the relationship between cholesterol levels and gastric cancer risk,[24–26] our study revealed consistent positive associations between hyperlipidemia and overall GI cancer risk. This may be due to the cumulative

effect of vascular damage caused by both conditions, which is less prominent in non-hypertensive individuals. These findings highlight the need for targeted prevention strategies that address both hypertension and lipid metabolism in this high-risk population.

The relationship between diabetes and GI cancer risk has been extensively studied, but the results remain inconclusive.[27–32] Some meta-analyses have found a significant association between diabetes history and gastric cancer risk, while others have not.[8,33,34] In our case-control study, diabetes was a significant risk factor for GI cancer, with a stronger association than reported in previous studies. This may suggest that in hypertensive patients, diabetes has a more pronounced effect on cancer risk, possibly due to the synergistic impact of hypertension and metabolic dysregulation. This difference in risk profile compared to the general population indicates that hypertensive patients with diabetes require more careful monitoring for cancer development.

There are several limitations in this retrospective study. First, the study population consists of individuals with a history of primary hypertension, which may not be representative of the broader local population, limiting the generalizability of our findings. Second, key protective and risk factors for GI cancer, such as fruits and vegetables consumption, dietary fiber, fish intake, red meat and processed meat consumption, and physical activity, were not included due to their absence in medical records, potentially introducing confounding bias. Third, the sample sizes for some specific comorbidities, such as heart failure and chronic renal failure, were relatively small leading to wider confidence intervals for these subgroups. As such, these findings should be interpreted with caution, and larger sample sizes in future studies are warranted to confirm these results. Fourthly, using overall cases of esophageal, gastric, colon, and rectal cancers as the primary response variable may reduce the ability to identify significant risk factors for a specific type of GI cancer. Lastly, our study primarily relied on traditional clinical and metabolic data and did not incorporate newer diagnostic technologies, such as metabolic fingerprinting and plasma-based biomarkers,[35,36] which have shown promise in improving early detection and risk stratification for GI cancers. Future studies could benefit from integrating these advanced tools to provide a more comprehensive risk assessment for hypertensive patients. Despite these limitations, our study provided new information on the associations of severe comorbid conditions and the consumption of several fermented acidic foods with the risk of GI cancer.

Conclusions

Findings from this case-control study suggest that metabolic comorbid conditions, such as hyperlipidemia, diabetes, and more severe hypertension, as well as organ dysfunctions such as heart failure and chronic renal failure may be indicators of increased risk of GI cancer. These patients may benefit from screening procedures such as colonoscopy and upper endoscopy to prevent GI cancer.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Ethics Approval

This study was approved by the Medical Ethics Committee of Zibo Central Hospital.

Informed Consent Statement

All participants provided written informed consent prior to participation in the study, in accordance with the Declaration of Helsinki.

Author Contributions

Both authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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