Prediction of the incidence of colorectal cancer by routine laboratory tests and anthropometric measurements about metabolism

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Abstract

Objective To investigate the relationship between metabolic disorders and the morbidity of colorectal cancer (CRC) compared with colorectal adenoma (CRA) and non-neoplastic inpatients, especially to investigate which anthropometric measures were better predictors of CRC.

Methods 80 patients with CRC, 80 patients with CRA and 80 non-neoplastic patients were selected from April 2017 to April 2019. The data of routine laboratory tests and anthropometric measurements about metabolism were analyzed retrospectively. Multinomial Logistic regression analysis was used to estimated odds ratio (OR) and 95% confidence interval (CI) for the risk of morbidity of CRC associated with potential risk factors.

Results Compared with CRA, OR of CRC was enhanced by weight loss self-reported, anemia and hypoproteinemia. Compared with non-neoplastic controls, diabetes, higher waist-neck ratio (WNR) and The Metabolic syndrome (MetS) identifified by the Chinese Diabetes Society was associated with significant increasing risk of all CRC patients. while in male subgroup, OR of CRC was enhanced by diabetes, higher hip circumference, waist-neck ratio (WNR)>2.42 (OR = 2.795, 95%CI: 1.169-6.680), waist-height ratio (WHtR)>0.550 (OR = 3.009, 95%CI: 1.260-7.185) and MetS. In female subgroup, only waist-hip ratio (WHR)>0.890 (multivariable-adjusted OR = 3.354, 95%CI: 1.011-11.129) was significantly associated with increased risk of CRC compared with colorectal adenoma and non-neoplastic controls. The risk factors for CRA were similar to CRC compared with non-neoplastic controls.

Conclusion Visceral adipose patients have a high incidence of CRC and CRA. For male, MetS, high level WNR and WHtR caused an increasing risk for CRC. For female, Only WHR is a high-risk factor. The patients with these high risk factors need to strengthen colorectal cancer screening, which is of great significance for the prevention and early detection of colorectal cancer.

Introduction

Colorectal cancer (CRC) is the third most common cancer in man and the second in woman worldwide. CRC causes more deaths (52%) and poor quality of life for survivors in less developed regions, reflecting poorer prognosis in these regions[1, 2]. The morbidity of CRC in China is increasing year by year due to economic development, dietary changes and longer life expectancy[3].

Metabolic diseases mainly include obesity, type 2 diabetes, non-alcoholic fatty liver disease, hyperlipidemia and cardiovascular disease which corporately constitute the greatest current threat to global human health and welfare[4, 5]. The main influences of metabolic disorders are genetic background, changes of diet, exercise, age and environmental factors (for example endocrine disrupting chemicals)[6, 7].

Metabolic disorders have been linked to an increased risk of cancer. The effects of metabolic disorders on the morbidity of colorectal cancer were not consistent, due to different sex, race, life style,

socioeconomic status, physical activity, diet and so on[8, 9]. Obesity is concerned most in multitudinous factors. Excess body fatness causes cancer of digestive organs such as gastric cardia, liver, gallbladder, pancreas, colon and rectum[10–12], due to a variety of biological mechanisms such as microenvironmental inflammation and immune mediated responses, hyperinsulinemia, insulin resistance, oxidative stress and insulin-like growth factors[13–15]. Prospective cohort studies found that obese participants had a statistically increased risk of multiple cancer mortality[16–18]. However some emerging studies found a decreased or equivocal morbidity and mortality risk among overweight CRC patients[19, 20]. A multicenter study in China found that participants with body mass index (BMI) as 25–27 kg/m2 have the lowest morbidity of digestive carcinoma. The risk of new onset digestive carcinoma in obesity group was not affected compared to normal BMI group[21]. A meta-analysis found that overweight patients had no increased risk for mortality of CRC. Both obese and underweight CRC patients have an increased risk of mortality, disease recurrence and disease-free survival compared to normal weight patients[22]. Some prospective studies found that there were no significant association between obesity and colorectal cancer in men[23, 24].

Compared with obesity defined by BMI, abdominal obesity is thought to be more important. The common markers of abdominal adiposity are waist circumference (WC) waist circumference-height ratio (WHtR), and waist-hip ratio (WHR). WC and WHR were increased risk factors for colorectal cancer proved by clinical trials[8, 25, 26].

Metabolic syndrome (MetS) is characterized by abdominal obesity, dyslipidemia, hypertension, and hyperglycemia. It covers laboratory tests and anthropometric measurements. MetS was used to stand for metabolic disorders in most clinical trials[27–30], due to MetS' representativeness, practicability and centrality. Other factors of metabolic disorders which are not included in MetS were rarely studied, but some of these plain indices may be good outcome predictors for CRC. To confirm this hypothesis, this study aimed to evaluate the association between metabolic disorders and the morbidity of colorectal cancer compared with colorectal adenoma(CRA) and Non-neoplastic inpatients, especially to investigate which anthropometric measures were better predictors of CRC.

Materials And Methods

Study population

This retrospective, case-control study enrolled patients belonging to one nursing unit from Tianjin 4th Center Hospital. 80 CRC patients from April 2017 to April 2019 were collected. During the same period, 80 CRA subjects were selected randomly. Every participant accepted colonoscopy and colorectal mass resection. All lesions were pathologically confirmed as adenomas or adenomatous polyps. In order to avoid biases, for each CRC case we selected one control who was matched on sex and age. These patients were hospitalized for other illnesses. Exclusive criteria were: a history of cancer; incomplete colonoscopy; inflammatory bowel disease; patients with familial adenomatous polyposis syndrome; evident edema; obvious seroperitoneum; incomplete data. The present study was approved by the Ethics

committee of Tianjin 4th Center Hospital and informed consent was obtained from every study participant.

Data collection

Baseline characteristics were abstracted from patients' electronic medical records. Subjects wear a light cotton hospital gown without shoes when anthropometrically measured. Height, weight and blood pressure were measured by trained nurses on the first day of hospitalization. Waist circumference was measured midway between the lower edge of the lowest rib and the upper edge of the iliac crest; hip circumference was measured at the level of the greater trochanter; neck circumference was measured in the midway of the neck just below the laryngeal prominence and perpendicularly to the long axis of the neck. These measurements were made at the end of a gentle expiration and in standing position.The waist-hip ratio, neck-waist ratio and neck-hip ratio were calculated separately[31-35]. BMI was calculated as kilograms per meter squared. Laboratory evaluation including hemoglobin, albumin, plasma glucose and lipid profile was measured by standard methods after overnight fasting.

Statistical analysis

Normally distributed data were expressed as mean±SD and comparisons among groups were analyzed by One way analysis of variance (ANOVA). Comparisons between each two groups were analyzed by least significant difference procedure (LSD) if equal variances were assumed, otherwise Dunnett's T3 was used. Data with non-normal distribution were expressed as median (range), and comparisons among groups were analyzed using Kruskal Wallis test. Enumeration data were described as case number and percentage, Chi-square test was performed for the intergroup comparison of rate.

The 2003 US National Heart, Lung, and Blood Institute guidelines were used to define hypertension: systolic pressure ≥140 mmHg/diastolic pressure ≥90 mmHg[36]. According to the definition of MetS recommended by Chinese Diabetes Society (CDS), we defined high fasting glucose as ≥6.1 mmol/L; a high TG as ≥1.7 mmol/L; a low HDL cholesterol level as <0.9 mmol/L for male and <1.0 mmol/L for female; and adiposity as BMI ≥25.0 kg/m^2[37]. Abdominal obesity was defined as WC >90 cm for male and >80 cm for female, as recommended by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[38]. High TC levels (≥5.2 mmol/L) and high levels of light density lipoprotein (LDL) cholesterol (≥3.1 mmol/L) were difined according to our laboratory reference value. Other anthropometric continuous variables were dichotomised. MetS was defined according to three different defifinitions: Chinese Diabetes Society(CDS), International Diabetes Federation (IDF) (Chinese) and NCEP-ATP-III (Asian)[37,38].

Multinomial Logistic regression analysis was used to estimated odds ratio (OR) and 95% confidence interval (CI) for the risk of morbidity of colorectal cancer associated with potential risk factors. All *P* values were two sided and considered statistically significant at *P* 0.05. Statistical analyses were performed by using SPSS version 20.0 (SPSS Inc, Chicago, IL).

Results

The baseline characteristics of CRC cases, CRA cases and non-neoplastic cases are summarized in table 1. Compared with non-neoplastic cases, a higher prevalence of diabetes mellitus was observed in total (*P*=0.016) and male (*P*=0.031) CRC cases. Compared with CRA cases and non-neoplastic cases separately, more CRC cases lost weight obviously, both for male and female. CRC cases did not differ significantly from CRA cases and non-neoplastic cases with regard to sex, age, hypertension, coronary heart disease, smoking status, drinking history and family cancer history.

Table 1. baseline characteristics of colorectal cancer cases, colorectal adenoma cases and non-neoplastic cases.

Characteristic	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	*F B or* X^2 value	*P* value
Sex(cases)				0.143	0.931
Male	51(63.8)	49(61.3)	51(63.8)		
Female	29(36.3)	31(38.8)	29(36.3)		
Age (years)	62.86±9.62	61.88±7.66	62.03±9.58	0.280	0.756
Male	62.84±8.19	60.59±8.46	62.51±8.64	1.032	0.359
Female	62.90±11.89	63.9±5.75	61.17±11.16	0.566 *B*	0.571
Hypertension(cases)	41 51.3	31 38.8	29 36.3	4.240	0.120
Male	26 51.0	23 46.9	18 35.3	2.736	0.255
Female	15 51.7	8 25.8	11 37.9	4.265	0.119
Coronary heart disease(cases)	18 22.5	8 10.0	11 13.8	5.049	0.080
Male	11 21.6	5 10.2	7 13.7	2.635	0.268
Female	7 24.1	3 9.7	4 13.8	2.425	0.289
Diabetes mellitus(cases)#	16 20.0	7 8.8	5 6.3	8.329	0.016
Male#	11 21.6	4 8.2	3 5.9	6.951	0.031
Female	5 17.2	3 9.7	2 6.9	1.623	0.444
Smoking status(cases)	36 45.0	22 27.5	25 31.3	6.004	0.050
Male	33 64.7	22 44.9	24 47.1	4.784	0.091
Female	3 10.3	0 0	1 3.4	4.646	0.098
Drinking history(cases)	7 8.8	10 12.5	14 17.5	2.741	0.254
Male	7 13.7	10 20.4	13 25.5	2.230	0.328
Female	0 0	0 0	1 3.4	1.534	0.215
Family cancer history (cases)	19 23.8	18 22.5	16 20.0	0.339	0.844
Male	10 19.6	6 12.2	8 15.7	1.016	0.602
Female	9 31.0	12 38.7	8 27.6	0.891	0.641
Weight	34 42.5	6 7.5	5 6.3	44.472	0.000

loss(cases)*#					
Male*#	21 41.2	3 6.1	3 5.9	28.463	0.000
Female*#	13 44.8	3 9.7	2 6.9	16.21	0.000

**P*<0.05 compared between CRC and CRA. #*P*<0.05 compared between CRC and Non-neoplastic controls.

Routine laboratory tests results were showed in table 2. In comparison with CRA cases and non-neoplastic cases, CRC cases had a lower prevalence of hemoglobin, particularly male CRC cases compared with CRA cases. In comparison with CRA cases and non-neoplastic cases, CRC cases had a lower prevalence of albumin and HDL, but there was no statistical difference for respective male and female cases.

Table 2. routine laboratory tests of colorectal cancer cases, colorectal adenoma cases and non-neoplastic cases.

Characteristic	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	*F B or* X^2 value	*P* value
Hemoglobin(g/L)*#	126.21±27.56	141.58±15.65	136.61±22.44	9.783 *B*	0.000
Male*	130.37±28.02	148.53±14.08	141.39±21.13	8.837 *B*	0.000
Female	118.90±25.57	130.58±11.12	128.21±22.55	2.609 *B*	0.081
Albumin(g/L)*#	41.18±4.44	42.78±3.18	42.44±4.20	3.573	0.030
Male	41.65±3.93	42.86±3.41	42.16±4.57	1.148	0.320
Female	40.36±5.19	42.65±2.84	42.94±3.46	3.688 *B*	0.030
Fasting plasma glucose (mmol/L)	5.27 2.05-12.45	5.23 3.64-9.30	5.16 3.29-12.19	1.525	0.467
Male	5.45 2.05-12.45	5.31 3.64-9.30	5.11 3.29-12.19	4.615	0.100
Female	5.33±1.08	5.35±0.82	5.57±1.24	0.443	0.644
TC(mmol/L)	4.69±1.10	4.89±1.18	4.67±1.00	0.977	0.378
Male	4.36±1.00	4.76±1.32	4.41±0.94	1.932	0.149
Female	5.28±1.02	5.11±0.92	5.13±0.94	0.282	0.755
TG(mmol/L)	1.40 0.48-4.95	1.43 0.50-8.61	1.30 0.49-6.40	4.915	0.086
Male	1.34 0.48-4.52	1.51 0.71-8.61	1.31 0.49-6.40	4.337	0.114
Female	1.43 0.56-4.95	1.29 0.50-7.28	1.17 0.62-6.17	1.955	0.376
LDL(mmol/L)	3.31±0.84	3.31±0.74	3.24±0.82	0.199	0.819
Male	13.06±0. 79	3.24±0.70	3.06±0.8	0.909	0.405
Female	3.75±0.75	3.43±0.80	3.57±0. 74	1.343	0.266
HDL(mmol/L)*#	1.17 0.67-4.37	1.24(0.66-4.79)	1.30(0.46-2.65)	7.49	0.024
Male	1.17±0.35	1.21±0.30	1.28±0.44	1.177 B	0.311
Female	1.36±0.67	1.52±0.70	1.48±0.34	0.540	0.585

**P*<0.05 compared between CRC and CRA. #*P*<0.05 compared between CRC and Non-neoplastic controls.

Table 3 showed the anthropometric measurements results. Compared with non-neoplastic patients, the patients with CRC and CRA had greater WC separately (*P*=0.036 and *P*=0.023), While CRA patients had

greater WHR only in female subgroup (*P*=0.003). In males, the weight of CRA patients was significantly greater than that of healthy control cases (P=0.005). When we added the lost weight self-reported to weight measured, we found that both CRC and CRA participators had greater weight than non-neoplastic participators. But those were not found in total and female populations. Compared in three groups, male, female and total patients did not have statistical difference in systolic blood pressure, diastolic blood pressure, neck circumference, hip circumference, height, neck-hip ratio, waist-neck ratio, waist-height ratio and BMI.

Table 3. anthropometric measurements of colorectal cancer cases, colorectal adenoma cases and non-neoplastic cases.

Characteristic	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	*F B or* X^2 value	*P* value
Systolic blood pressure (mmHg)	133.78±20.13	134.09±17.15	129.26±14.96	1.896 B	0.152
Male	135.08±21.02	133.37±16.75	128.47±13.58	1.982 B	0.142
Female	131.48±18.59	135.23±17.98	130.66±17.30	0.556	0.575
Diastolic blood pressure (mmHg)	80.00 55.0-116.0	80.00 65.0-110.0	80.00 53.0-110.0	2.330	0.312
Male	80.00 55.0-116.0	80.00 65.0-110.0	80.00 60.0-110.0	0.920	0.631
Female	79.55±12.22	82.52±10.75	77.93±11.53	1.232	0.297
Neck circumference (cm)	37.71±3.57	38.94±4.45	37.76±3.49	2.605	0.076
Male	39.43±3.39	40.17±3.60	38.92±3.33	1.671	0.192
Female	35.59±2.96	37.00±5.01	35.72±2.81	1.299	0.278
Waist circumference (cm)#$	95.11±11.30	95.40±10.68	91.70±8.55	3.230	0.041
Male	96.78±10.53	96.20±9.27	93.08±8.53	2.246	0.109
Female	92.17±12.19	94.13±12.65	89.28±8.15	1.414	0.249
Hip circumference (cm)	104.91±10.53	103.86±8.49	101.74±8.56	2.451	0.088
Male	104.94±9.60	104.71±7.41	101.37±8.74	2.709	0.070
Female	104.86±12.18	102.52±9.95	102.38±8.33	0.541	0.584
Height (cm)	167.28±8.14	167.18±9.13	165.45±7.42	1.234	0.293
Male	170 162-182	173 160-184	170 158-178	10.235	0.093
Female	158.72±4.77	157.87±4.46	157.59±4.92	0.459	0.633
Weight (kg)	68.30±11.99	70.71±12.61	66.46±10.35	2.651	0.073
Male$	72.41±11.14	75.67±11.17	69.39±10.54	4.110	0.018
Female	61.07±9.95	62.86±10.74	61.31±7.79	0.308	0.735
Neck-hip ratio (NHR)	0.364±0.031	0.376±0.036	0.373±0.041	2.054	0.130
Male	0.377±0.023	0.385±0.035	0.386±0.041	1.092	0.338
Female	0.343±0.032	0.361±0.034	0.350±0.030	2..506	0.088

Waist-neck ratio (WNR)	2.485 2.06-3.79	2.480 1.80-3.10	2.390 2.00-3.73	4.412	0.110
Male	2.46±0.20	2.40±0.23	2.40±0.26	0.961	0.385
Female	2.60±0.34	2.56±0.27	2.51±0.23	0.756	0.473
Waist-hip ratio (WHR)	0.907±0.065	0.917±0.056	0.903±0.060	1.210	0.300
Male	0.923±0.558	0.918±0.547	0.920±0.064	0.072	0.930
Female$	0.880±0.072	0.916±0.058	0.872±0.036	4.860 *B*	0.011
Waist-height ratio (WHtR)	0.569±0.065	0.573±0.070	0.555±0.052	1.795	0.168
Male	0.562±0.055	0.558±0.057	0.548±0.045	0.989	0.374
Female	0.581±0.080	0.597±0.082	0.568±0.060	1.103	0.336
Body mass index(BMI)	24.32±3.29	25.25±3.81	24.27±3.37	2.021	0.135
Male	24.38±3.11	25.29±3.70	24.01±3.41	1.849	0.161
Female	24.21±3.64	25.20±4.04	24.72±3.31	0.543	0.583
Weight-adjusted	69.99±12.26	71.02±12.51	66.85±10.42	2.723	0.068
Male#$	74.20±11.32	75.96±11.04	69.77±10.75	4.206	0.017
Female	62.59±10.30	63.21±10.70	61.72±7.60	0.178	0.837
BMI-adjusted	24.92±3.43	25.37±3.77	24.42±3.42	1.442	0.238
Male	24.99±3.24	25.38±3.63	24.15±3.52	1.664	0.193
Female	24.81±3.80	25.35±4.05	24.89±3.24	0.184	0.832

#*P*<0.05 compared between CRC and Non-neoplastic controls. $*P*<0.05 compared between CRA and Non-neoplastic controls. Weight-adjusted was equal to weight plus weight loss self-reported. BMI-adjusted was equal to weight-adjusted(kg)/height(m)^2.

Proportion of fasting plasma glucose, blood fat and anthropometric measurements was summarized in table 4-6 for total, male and female cases. As shown in Table 4, the proportion of high WNR in CRC and CRA patients was significantly greater than that in non-neoplastic patients. Significant higher proportion of high WHtR was observed in CRA cases compared with non-neoplastic cases. In male subgroup, we found a higher proportion of high hip circumference, WNR and WHtR in CRC patients compared with healthy controls. The proportion of high height, WNR and WHtR in CRA patients was significantly greater than that in non-neoplastic patients (Table 5). In female subgroup, the proportion of high WHR in both CRC and CRA patients was significantly greater than that in non-neoplastic patients (Table 6).

Table 4. Proportion of fasting plasma glucose, blood fat and anthropometric measurements for total cases.

Characteristic	definition	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	χ^2 value	*P* value
Fasting plasma glucose	≥6.1mmol/L	20 25.0	18 22.5	14 17.5	1.375	0.503
TC	≥ 5.2mmol/L	24(30.0)	29(36.3)	24(30.0)	0.956	0.620
TG	≥1.7mmol/L	29 36.3	30 37.5	18 22.5	5.086	0.079
LDL	≥3.1mmol/L	47(58.8)	45(56.3)	44(55.0)	0.238	0.888
HDL	<0.9mmol/L for male,<1.0 for female	14 17.5	11 13.8	9 11.3	1.302	0.521
Systolic blood pressure	≥140mmHg	26(32.5)	20(25.0)	15(18.8)	4.000	0.135
Diastolic blood pressure	≥90mmHg	11(13.8)	16(20.0)	11(13.8)	1.563	0.458
Neck-hip ratio	>0.370	34(42.5)	37(46.3)	40(50.0)	0.905	0.636
Waist-neck ratio#$	>2.45	44 55.0	46 57.5	29 36.3	8.634	0.013
Waist-hip ratio	>0.910	38(47.5)	44(55.0)	31(38.8)	4.248	0.120
Waist-height ratio$	>0.560	38(47.5)	45(56.3)	29(36.3)	6.462	0.040
BMI	≥25	33(41.3)	39(48.8)	33(41.3)	1.219	0.544

#*P*<0.05 compared between CRC and Non-neoplastic controls. $*P*<0.05 compared between CRA and Non-neoplastic controls.

Table 5. Proportion of fasting plasma glucose, blood fat and anthropometric measurements for male cases.

Characteristic	definition	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	χ^2 value	*P* value
Fasting plasma glucose	≥6.1mmol/L	15 29.4	13 26.5	6 11.8	5.222	0.073
TC	≥ 5.2mmol/L	7 13.7	15 30.6	8 15.7	5.322	0.070
TG	≥1.7mmol/L	20 39.2	20 40.8	12 23.5	4.086	0.130
LDL	≥3.1mmol/L	25 49.0	26 53.1	23 45.1	0.634	0.728
HDL	<0.9mmol/L	8 15.7	7 14.3	7 14.3	0.083	0.959
Systolic blood pressure	≥140mmHg	17(33.3)	12(24.5)	9 17.6	3.349	0.187
Diastolic blood pressure	≥90mmHg	7(13.7)	10(20.4)	8(15.7)	0.850	0.654
Neck circumference	>40cm	13(25.5)	18(36.7)	17(33.3)	1.542	0.463
Waist circumference	>90cm	38(74.5)	37(75.5)	33(64.7)	1.770	0.413
Hip circumference#	>103cm	31(60.8)	26(53.1)	18(35.3)	6.962	0.031
Height$	>170cm	24(47.1)	29(59.2)	17(33.3)	6.731	0.035
Weight	>72kg	24(47.1)	30(61.2)	19(37.3)	5.800	0.055
Neck-hip ratio	>0.38	18(35.3)	19(38.8)	26(51.0)	2.840	0.242
Waist-neck ratio#$	>2.42	30 58.8	28 57.1	18 35.3	6.994	0.030
Waist-hip ratio	>0.92	27(52.9)	24(49.0)	23(45.1)	0.628	0.731
Waist-height ratio#$	>0.55	29(56.9)	27(55.1)	17(33.3)	6.980	0.031
BMI	≥25	22(43.1)	25(51.0)	21(41.2)	1.090	0.580

#*P*<0.05 compared between CRC and Non-neoplastic controls. $*P*<0.05 compared between CRA and Non-neoplastic controls.

Table 6. Proportion of fasting plasma glucose, blood fat and anthropometric measurements for female cases.

Characteristic	definition	Colorectal cancer cases	Colorectal adenoma cases	Non-neoplastic cases	χ^2 value	*P* value
Fasting plasma glucose	≥6.1mmol/L	5(17.2)	5(16.1)	8(27.6)	1.456	0.483
TC	≥ 5.2mmol/L	17(58.6)	14(45.2)	16(55.2)	1.186	0.553
TG	≥1.7mmol/L	9(31.0)	10(32.3)	6(20.7)	1.177	0.555
LDL	≥3.1mmol/L	22(75.9)	19(61.3)	21(72.4)	1.659	0.436
HDL	<1.0mmol/L	6(20.7)	4(12.9)	2(6.9)	2.379	0.304
Systolic blood pressure	≥140mmHg	9(31.0)	8(25.8)	6(20.7)	0.810	0.667
Diastolic blood pressure	≥90mmHg	4(13.8)	6(19.4)	3(10.3)	0.998	0.607
Neck circumference	>35cm	16(55.2)	16(51.6)	12(41.4)	1.194	0.551
Waist circumference	>80cm	25(86.2)	27(87.1)	25(86.2)	0.014	0.993
Hip circumference	>103cm	14(48.3)	15(48.4)	13(44.8)	0.096	0.953
Height	>158cm	15(51.7)	12(38.7)	13(44.8)	1.026	0.599
Weight	>61kg	15(51.7)	15(48.4)	13(44.8)	0.276	0.871
Neck-hip ratio	>0.35	10(34.5)	15(48.4)	12(41.4)	1.193	0.551
Waist-neck ratio	>2.53	17 58.6	17 54.8	11 37.9	2.831	0.243
Waist-hip ratio#$	>0.89	15(51.7)	21(67.7)	7(24.1)	11.608	0.003
Waist-height ratio	>0.58	12(41.4)	19(61.3)	11(37.9)	3.864	0.145
BMI	≥25	11(37.9)	14(45.2)	12(41.4)	0.323	0.851

#*P*<0.05 compared between CRC and Non-neoplastic controls. $*P*<0.05 compared between CRA and Non-neoplastic controls.

We compared the proportion of patients with MetS among three groups according to three different popular definitions for Chinese populations (Table 7). In the total population, the patients with CRC had higher positive rate of MetS according to three definitions than non-neoplastic patients. The CRA patients

had higher positive rate of MetS only according to CDS criteria compared with non-neoplastic patients. In males, the proportion of MetS according to three different definitions respectively in CRC and CRA patients was significantly greater than that in control patients. But there were no statistically differences in the female population. Because the most differences were observed by CDS guideline, in addition, its Prevalence was closer to that reported in other literature[39], we calculated the odds ratios and 95%CI in the light of CDS criteria.

Table 7. Proportion of metabolic syndrome defined by three different criteria.

Characteristic		Colorectal cancer cases		Colorectal adenoma cases		Non-neoplastic cases		X^2 value	*P* value
Total									
CDS#$	Yes	25	31.3	24	30.0	8	10.0	12.563	0.002
	No	55	68.8	56	70.0	72	90.0		
IDF (Chinese)#	Yes	47	58.8	40	50.0	29	36.3	8.242	0.016
	No	33	41.3	40	50.0	51	63.8		
NCEPATP III (Asian)#	Yes	46	57.5	38	47.5	27	33.8	9.151	0.010
	No	34	42.5	42	52.5	53	66.3		
Male									
CDS#$	Yes	17	33.3	15	30.6	5	9.8	9.095	0.011
	No	34	66.7	34	69.4	46	90.2		
IDF (Chinese)#$	Yes	26	51.0	24	49.0	13	25.5	8.386	0.015
	No	25	49.0	25	51.0	38	74.5		
NCEPATP III (Asian)#$	Yes	25	49.0	23	46.9	10	19.6	11.555	0.003
	No	26	51.0	26	53.1	41	80.4		
Female									
CDS	Yes	8	27.6	9	29.0	3	10.3	3.649	0.161
	No	21	72.4	22	71.0	26	89.7		
IDF (Chinese)	Yes	21	72.4	16	51.6	16	55.2	3.034	0.219
	No	8	27.6	15	48.4	13	44.8		
NCEPATP III (Asian)	Yes	21	72.4	15	48.4	17	58.6	3.606	0.165
	No	8	27.6	16	51.6	12	41.4		

#*P*<0.05 compared between CRC and Non-neoplastic controls. $*P*<0.05 compared between CRA and Non-neoplastic controls.

Table 8-10 shows the univariate and multivariate analysis for association between potential factors and morbidity of CRC and CRA cases. Univariate analysis was adjusted by age and sex for total case, and adjusted by age for male and female cases. Smoking status, drinking history and family cancer history were added to adjusted factors for multivariate Logistic analysis. If the potential risk factors were unrelated to height, height was also added to adjusted factors. We performed Logistic analysis on the factors with statistical differences.

Table 8. Hazard ratios for colorectal cancer compared with colorectal adenoma.

Characteristic	Age and sex-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Hemoglobin	0.963(0.946-0.981)	0.000	0.960(0.942-0.979)	0.000
Albumin	0.902(0.828-0.983)	0.018	0.898(0.822-0.980)	0.016
Weight loss (yes vs. No)	9.140(3.552-23.516)	0.000	8.227(3.145-21.517)	0.000
HDL	0.609(0.280-1.324)	0.211	0.646(0.299-1.397)	0.267
Male	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Weight loss (yes vs. No)	10.574 2.884-38.770	0.000	8.405 2.218-31.850	0.002
Hemoglobin	0.959 0.937-0.983	0.001	0.956 0.932-0.980	0.000
Female	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Weight loss (yes vs. No)	7.773 1.904-31.733	0.004	8.460 1.989-35.984	0.004

Table 9. Hazard ratios for colorectal cancer compared with colorectal non-neoplastic cases.

Characteristic	Age and sex-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Hemoglobin	0.980(0.966-0.995)	0.009	0.979(0.963-0.995)	0.009
Albumin	0.925(0.852-1.005)	0.066	0.920(0.844-1.003)	0.059
Weight loss (yes vs. No)	11.072(4.035-30.381)	0.000	10.373(3.665-29.359)	0.000
HDL	0.537(0.249-1.156)	0.112	0.520(0.239-1.130)	0.099
Diabetes mellitus (yes vs. No)	3.693(1.278-10.675)	0.016	3.824(1.277-11.450)	0.017
Waist circumference	1.036(1.002-1.071)	0.037	1.031(0.995-1.067)	0.091
Waist-neck ratio (>2.45 vs. ≤2.45)	2.177(1.138-4.164)	0.019	2.426(1.221-4.822)	0.011
MetS (yes vs. No)	4.005(1.696-9.695)	0.002	3.778(1.539-9.277)	0.004
Male	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Weight loss (yes vs. No)	11.189 3.070-40.781	0.000	10.778 2.779-41.797	0.001
Diabetes mellitus (yes vs. No)	4.397 1.147-16.856	0.031	4.236 1.047-17.137	0.043
Hip circumference (>103cm vs. ≤103cm)	2.838 1.270-6.340	0.011	2.627 1.108-6.225	0.028
Waist-neck ratio (>2.42 vs. ≤2.42)	2.432(1.088-5.434)	0.030	2.795(1.169-6.680)	0.021
Waist-height ratio (>0.55 vs. ≤0.55)	2.651(1.179-5.963)	0.018	3.009(1.260-7.185)	0.013
CDS (yes vs. No)	4.598(1.544-13.693)	0.006	4.120(1.327-12.795)	0.014
Female	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Weight loss (yes vs. No)	10.869 2.163-54.625	0.004	10.710 2.067-55.504	0.005
Waist-hip ratio (>0.890 vs. ≤0.890)	3.294(1.048-10.348)	0.041	3.354(1.011-11.129)	0.048

Table 10. Hazard ratios for colorectal adenoma compared with colorectal non-neoplastic cases.

Characteristic	Age and sex-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Waist circumference	1.042(1.008-1.077)	0.015	1.034(0.999-1.071)	0.054
Waist-neck ratio (>2.45 vs. ≤2.45)	2.446(1.275-4.694)	0.007	2.540(1.299-4.968)	0.006
Waist-height ratio (>0.560 vs. ≤0.560)	2.354(1.220-4.542)	0.011	2.337(1.205-4.533)	0.012
MetS (yes vs. No)	3.909(1.629-9.381)	0.002	3.781(1.553-9.208)	0.003
Male	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Weight	1.053 1.014-1.094	0.008	1.035 0.991-1.079	0.118
Height (>170cm vs. ≤170cm)	2.782 1.224-6.324	0.015	3.134 1.335-7.360	0.009
Waist-neck ratio (>2.42 vs. ≤2.42)	2.802(1.232-6.371)	0.014	2.833(1.193-6.730)	0.018
Waist-height ratio (>0.550 vs. ≤0.550)	2.635(1.157-6.005)	0.021	2.780(1.183-6.535)	0.019
MetS (yes vs. No)	4.076(1.345-12.352)	0.013	3.764(1.204-11.769)	0.023
Female	Age-adjusted OR (95% CI)	*P* value	Multivariable adjusted OR (95% CI)	*P* value
Waist-hip ratio	1.142 1.032-1.264	0.010	1.156 1.037-1.289	0.009
Waist-hip ratio (>0.890 vs. ≤0.890)	6.348(1.989-20.265)	0.002	6.253(1.895-20.632)	0.003

We expressed the comparison of CRC and CRA first. In the total population, OR of CRC was reduced by continuous hemoglobin (multivariable-adjusted OR = 0.960, 95%CI: 0.942-0.979) and albumin (multivariable-adjusted OR = 0.898, 95%CI: 0.822-0.980). OR of CRC was enhanced by weight loss self-reported (multivariable-adjusted OR = 8.227, 95%CI: 3.145-21.517). In males, continuous hemoglobin was associated with decreased risk for CRC (multivariable-adjusted OR = 0.956, 95%CI: 0.932-0.980). Weight loss self-reported was correlated with increased risk for CRC (multivariable-adjusted OR = 8.405, 95%CI: 2.218-31.850). In females, OR of CRC was only enhanced by weight loss.

Then we expressed the comparison of CRC and colorectal non-neoplastic cases. Among the 240 patients, OR of CRC was reduced by continuous hemoglobin (multivariable-adjusted OR = 0.979, 95%CI: 0.963-0.995). OR of CRC was enhanced by diabetes (multivariable-adjusted OR = 8.227, 95%CI: 3.145-21.517), MetS by CDS (multivariable-adjusted OR = 3.778, 95%CI: 1.539-9.277), waist-hip ratio in the high half (multivariable-adjusted OR = 3.778, 95%CI: 1.539-9.277) and weight loss self-reported (multivariable-adjusted OR = 10.373, 95%CI: 3.665-29.359). In male patient subgroup, OR of CRC was also enhanced by

diabetes, MetS by CDS and weight loss self-reported. A significant increased risk for CRC was observed between the high and low halves of hip circumference (multivariable-adjusted OR = 2.627, 95%CI: 1.108-6.225), WNR (OR = 2.795, 95%CI: 1.169-6.680) and WHtR (OR = 3.009, 95%CI: 1.260-7.185). In female patient subgroup, OR of CRC was enhanced by WHR in the high half (multivariable-adjusted OR = 3.354, 95%CI: 1.011-11.129) and weight loss self-reported.

Because of the close relationship of CRC and CRA, the comparison of CRA and colorectal non-neoplastic cases was also important. MetS by CDS, WNR and WHtR from the high half were associated with increased risk for CRA cases compared with colorectal non-neoplastic cases. Male patients with MetS by CDS, WNR, WHtR and height from the high half had a greater risk than their counterparts from the low half. Both continuous and grouped WHR was correlated with increased risk for CRA in females.

Discussion

Metabolic disorders are a collective term for multiple metabolic risk factors. Metabolic disorders have been found to be modifiable risk factors for chronic diseases including hypertension, diabetes and dyslipidemia[40–42]. As recent studies from several centrals have shown, there is a linkage between metabolic disorders and the prevalence of many malignancies, including CRC[8–11, 25, 26]. During doctors' office visiting and regular medical examinations, patients with metabolic disorders undergo routine laboratory tests and anthropometric measurements, which have important value in predicting the incidence of CRC. Especially anthropometric indices have been widely used due to their low cost and ease of administration.

Patients with advanced gastrointestinal malignancies often have anemia and emaciation. Compared with patients with CRA, incidence of CRC was enhanced by anemia, hypoproteinemia, weight loss self-reported in this study. Other indicators showed no statistical difference by multivariable-adjusted analysis. These remind that there is no obvious change in the body during the transition from polyps to malignant tumors. If there are high-risk factors for colorectal masses or indications for colonoscopy, colonoscopy should be actively performed. If the patient is diagnosed with colorectal polyps, he should actively undergo endoscopic resection and confirm the diagnosis. After colorectal polypectomy, regular follow-up and reexamination of colonoscopy are necessary.

In comparison with CRA cases and non-neoplastic cases, CRC cases had a lower prevalence of HDL In the total population, which was consistent with literature[43]. But there was no statistical difference if multivariable-adjusted. It was still believed that there was a certain correlation between the reduction of HDL and the occurrence of malignant tumor. There was no statistical difference between CRA cases and non-neoplastic cases. It indicated that the reduction of HDL was of little significance in the occurrence of adenoma. When adenomas became malignant tumors or malignant tumors occurred, HDL dropped rapidly.

MetS is a cluster of metabolic abnormalities. Many clinical trials have confirmed that MetS is a risk factor for CRC[28, 29]. In our study, we found that the increased OR of total and male CRC and CRA patients with

MetS, but MetS has no effect on women. Choi et al found that the hazard ratio for CRC development in Korean patients with MetS was 1.22 and the association was more prominent in male than in female (HR 1.41 95% vs. HR 1.23 $P < 0.001$) [27]. This literature is similar to our conclusion. Type 2 diabetes, one element of MetS, has also been related to the morbidity of colorectal cancer [44, 45]. This confirmed association is biologically plausible. Hyperglycemia and glycated hemoglobin increase mitochondrial glucose oxidation which promotes DNA damage through oxidative stress[46]. we found that compared with non-neoplastic patients, OR of CRC was enhanced by diabetes in total and male patients. It indicates that diabetes plays a promoting role in the development of CRC.

We found that there were no significant differences in body weight and BMI between CRC patients and non-tumor patients. If the lost weight self-reported was added to weight measured, only male CRC and CRA participators had greater weight than non-neoplastic participators, but BMI was still no statistical difference. These suggest that male CRC patients were in a high weight state before weight loss, which is consistent with the high weight state of CRA patients. But weight is affected by the correction of height, which is proved by no difference in BMI. Previous literature have suggested that obesity is a high risk factor for CRC patients, but general obesity and BMI are not obvious[47]. Perhaps other anthropometric measures that better reflect abdominal obesity are superior predictors of CRC [48, 49].

Visceral adipose tissue as an active endocrine organ produces more pro-inflammatory factors than the subcutaneous tissue[50]. Several studies indicate that visceral obesity is positively associated with CRC risk, especially in men[8, 25, 26, 51]. The results of research for women are inconsistent, with some studies considering visceral obesity cause an increasing risk for CRC[52], but other studies considering no such association[53]. WC is used to measure total body and abdominal fat accumulation, which is correlated with visceral adipose tissues. Our study found that WC adjusted by sex and age caused an increasing risk for CRC, but there was no statistical difference if multivariable-adjusted. So we considered that WC was greatly affected by height, various ratios of WC would be of great significance. We studied a few ratios related to WC. Only greater WNR was significantly associated with increased risk of total colorectal cancer. Neck circumference is an indicator that was previously ignored, which has been considered to be important in assessing the risk of metabolic diseases and so on[54–56], then we should also pay attention to its role in tumor risk assessment. For male, WNR and WHtR were positively associated with CRC risk, but for female, only WHR caused an increasing risk for CRC. WC did not show its superiority in the stratified comparison. So we considered that abdominal fat is a bad body shape for CRC development. Continuous WC is relatively single, affected by height, body shape and other factors. The value and importance of WNR, WHtR and WHR were represented in different groups of patients, so the ratio of waist circumference was more significant in assessing CRC risk.

Adenoma is precursor of cancer. Some adenomas will progress to adenocarcinoma. Therefore, we hypothesized that the risk factors for adenoma and adenocarcinoma were similar, which was confirmed by our results. For the general population and male patients, WNR, WHtR and MetS were all high risk factors for adenoma, which were highly consistent with the risk factors for adenocarcinoma. The value of WNR and WHtR in the prediction of male colorectal tumor occurrence was verified once more. The height

of male patients was positively associated with CRA risk, but there was no significantly associated with CRC. Giovannucci and Edward found that height was associated with an elevated risk for colon cancer[25]. For female patients, higher WHR level caused an increasing risk for CRA, which was highly consistent with the risk factors for CRC. During routine laboratory tests and anthropometric measurements of female, we only need to focus on WHR. This reflects the difference of gender stratification.

This study also had some limitations. First, it was a retrospective study, maybe there was a selection bias. Second, the number of CRC patients was relatively small and was a single-center research, so the result needs to be further investigated in a multiple-center research with a large size of participants. Finally, only hospitalized individuals were included in this study, and the social normal population should be included in future studies.

In conclusion, visceral adipose patients have a high incidence of CRC and CRA. For male, MetS, high level WNR and WHtR caused an increasing risk for CRC. For female, Only WHR is a high-risk factor. Metabolic disorder might play an important role in the development of CRC. If metabolism-related routine laboratory tests and anthropometric measurements are fully utilized to screen the high risk groups of CRC, it will be of great help to the early detection and treatment of CRC.

Abbreviations

CR: Ccolorectal cancer

CR: Acolorectal adenoma

OR: odds ratio

CI: confidence interval

WNR: waist-neck ratio

MetS: Metabolic syndrome

WNR: waist-neck ratio

WHtR: waist-height ratio

WHR: waist-hip ratio

WC: waist circumference

BMI: body mass index

CDS: Chinese Diabetes Society

NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III

IDF: International Diabetes Federation

Declarations

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to personal privacy but are available from the corresponding author on reasonable request.

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Ethics statement

Ethics approval and consent to participate: This research project was approved by the Ethics Committee of Tianjin 4th Centre Hospital. Written consents were obtained from each patient.

Author contributions

Binglu Cheng, Xu Han and Hongjuan Wan analyzed and interpreted the patient data. Binglu Cheng and Zhijun Sun were major contributors in writing the manuscript. Weisheng Wang analyzed and interpreted and revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no competing interests.

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