

Clinical features and prognosis in colorectal cancer patients with different ethnicities in Northwest China

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Abstract

AIM: To compare the clinical factors and tumor characteristics that predict survival in colorectal cancer (CRC) patients with different ethnicities in Xin Jiang area.

METHODS: A total of 1421 histopathologically confirmed sporadic CRC patients who were either Han/Chinese or Uyghur were identified and enrolled from a database of both diagnoses and operative procedures from Xin Jiang Tumor Hospital, which is affiliated to Xin Jiang Medical University between 2000 and 2007. Patients with family histories of CRC, hereditary nonpolyposis CRC, familial adenomatous polyposis, inflammatory bowel disease, carcinoid, squamous carcinoma or melanoma were excluded. The two ethnic groups were compared with regard to clinical features, tumor characteristics, disease stage, overall survival rate, disease-free survival rate and cancer-specific survival rate. The factors predicting long-term survival were assessed *via*

both univariate and multivariate analysis.

RESULTS: Among the 1421 patients with CRC enrolled in this study, 1210 patients were Han/Chinese (mean age, 62.3 ± 4.5 years; range, 19-92 years), while 211 patients were Uyghur (mean age, 52.4 ± 15.6 years; range, 17-87 years). There were significant differences in proportions of gender, age, blood type, occupation and histopathological type between the Han/Chinese and Uyghur patients ($P < 0.05$). The median overall, disease-free and cancer-specific survival time were 45, 62 and 65 mo for the Han/Chinese patients and 42, 49 and 61 mo for the Uyghur patients ($P = 0.000$, $P = 0.005$, $P = 0.007$). The cumulative 5-year survival of the Uyghur patients was significantly worse than that of the Han patients ($P = 0.000$). A multivariate analysis showed that age, ethnicity, histopathological type, differentiation, T (Infiltration depth), N (Lymph node metastasis), staging, postoperative metastasis and metastatic site ($P < 0.05$) were found to be the prognostic factors.

CONCLUSION: The Uyghur CRC patients are associated with significantly younger age, more aggressive histopathologic characteristics and have significantly worse prognosis than the Han/Chinese patients.

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Key words: Colorectal cancer; Ethnicity; Clinicopathological factor; Survival

Core tip: Racial/ethnic differences in colorectal cancer (CRC) survival have been documented in the literatures. However, the reasons for these disparities are difficult to decipher. These disparities may be attributed to many factors, including differences in socioeconomic status, tumor biology, stage at diagnosis, treatment, post-treatment surveillance, physician characteristics and hospital factors. This is the first comparative study on the clinicopathological factors and survival of CRC

patients with different ethnicities in Xin Jiang. We found some marked differences and performed preliminary analysis for possible reasons.

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INTRODUCTION

The incidence and mortality rates of colorectal cancer (CRC) worldwide are continuously rising. There were approximately 1.2 million new cases and 630000 deaths world-wide in 2007, which is increased compared with that in 2000 (by 27% and 28%, separately). The average increases for these figures are 3.9% and 4.0% annually^[1,2]. With the development of the economy and the improvement of living conditions and eating habits, the incidence of CRC in China has been increasing continuously and has become the second most common malignancy^[3,4]. According to WHO reports, the death rate of CRC has increased by 70.7% in 2005 compared with that in 1991, annually increasing by 4.9%^[5].

Disproportionately high mortality rates are observed among African Americans for cancers of the lung, breast, prostate, colon and rectum, oral cavity and pharynx, cervix^[6], and esophagus^[7]. In addition, the 5-year survival rates for African Americans are lower than those for whites for all of the major cancer sites. Similarly, mortality rates for cancers of the cervix, liver, and stomach are higher among Asians/Pacific Islanders and Native Americans than among non-Hispanic whites. Overall breast cancer mortality rates for Native Hawaiians are the highest of all racial/ethnic groups^[8]. Colon cancer incidence and mortality vary markedly by race/ethnicity; specifically, African Americans have a higher incidence and mortality for colon cancer compared with other population groups^[9].

The Xinjiang Uyghur Autonomous Region is a part of the People's Republic of China located in the northwest of the country. This region is the home to a number of different ethnic groups, including Uyghur, Han/Chinese, Kazakh, Hui, Kyrgyz, and Mongols, accounting for the a majority of the population. The Uyghurs are a population with Eastern and Western Eurasian anthropometric and genetic traits and one of the many populations of Central Eurasia that can be considered to be genetically related to European and East Asian populations. Uyghur and Han/Chinese people are the two major ethnic groups in this area and have different origins, cultures, religions as well as living and eating habits. The purpose of this study was to determine whether racial disparities in clinicopathological features and survival exist among CRC patients in two ethnic groups in Xin Jiang.

MATERIALS AND METHODS

The Xin Jiang Tumor hospital is a unique hospital capable of comprehensive treatment for cancers in Xin Jiang that serves the patients from all parts of the Xin jiang Uyghur Autonomous Region and functions as a primary cancer registration unit. Thus, data from this hospital possess relative representativeness and reliability. Between 2000 and 2007, there were 1759 newly diagnosed cases of histopathologically confirmed colorectal malignancies at Xin Jiang Tumor Hospital affiliated to Xin Jiang Medical University. A total of 1421 patients who were either Uyghur or Han/Chinese were identified and enrolled using a computer-generated search from a database with information on both diagnoses and operative procedures. Patients with family histories of CRC, hereditary non-polyposis CRC, familial adenomatous polyposis, inflammatory bowel disease, carcinoid, squamous carcinoma or melanoma were excluded. The clinicopathological characteristics included age, gender, ethnicity, occupation, blood type, onset tumor location, tumor size, histopathological types, gross type, pathological staging, recurrence, metastasis, metastatic site and so on were retrospectively analyzed. The right colon included the cecum, ascending colon, hepatic flexure, and transverse colon, while the left colon included the splenic flexure, descending colon, and sigmoid colon. A surgical metachronous tumor was considered the presence of another tumor found away from the primary tumor, when detected at least 6 mo after the primary operation. Resection was considered radical when there was macroscopic resection of all malignant tissue and no microscopic evidence of surgical margin spread. The tumor, node and metastasis (TNM) staging system^[10] was used for tumor staging. Postoperatively, all patients were followed up at 3-mo intervals for the first year, 6-mo intervals from years 2 to 5, and annually thereafter. The end of follow-up was December 31, 2010. The two ethnic groups were compared in regard to clinical features, tumor characteristics, disease stage, overall survival rate, disease-free survival rate, and cancer-specific survival rate.

Statistical analysis

Differences in the distribution of baseline characteristics between ethnic groups were assessed using Students T test or χ^2 or Fisher's exact tests. The overall survival was calculated as the time from diagnosis to death due to any cause. Colon cancer-specific survival was calculated as the time from diagnosis to death due to colon cancer. Disease-free survival was calculated as the time from surgical resection of the tumor to recurrence due to colon cancer. The cumulative survival rates were calculated using the Kaplan-Meier method and compared with the log rank test. The Cox technique was used for univariate and multivariate survival analyses. Significance was established at $P < 0.05$. Statistical calculations were performed using Stata Statistical Software, version 15 (SPSS, Inc., Chicago, IL).

Table 1 Characteristics of colorectal cancer patients of different ethnicities *n* (%)

Characteristic	Han (<i>n</i> = 1210)	Uyghur (<i>n</i> = 211)	<i>P</i> value
Age (yr)			0.000
< 30	9 (0.7)	21 (10.0)	
30-50	230 (19.0)	71 (33.6)	
50-70	580 (47.9)	94 (44.5)	
≥ 70	391 (32.3)	25 (11.8)	
Gender			0.040
Male	694 (57.4)	105 (49.8)	
Female	516 (42.6)	106 (50.2)	
Occupation			0.000
Cadre (Office worker)	511 (42.2)	61 (28.9)	
Physical worker	337 (27.9)	30 (14.2)	
Farmer and herder	205 (16.9)	90 (42.7)	
Unemployed	157 (13.0)	30 (14.2)	
Blood type			0.013
A	378 (31.2)	44 (20.9)	
B	386 (31.9)	81 (38.4)	
AB	139 (11.5)	32 (15.2)	
O	307 (25.4)	54 (25.6)	
Tumor location			0.054
Rectum	704 (58.2)	141 (66.8)	
Left hemi colon	300 (24.8)	39 (18.5)	
Right hemi colon	206 (17.0)	31 (14.7)	
Tumor size			0.183
< 4	196 (16.2)	24 (11.4)	
4-8	838 (69.3)	157 (74.4)	
> 8	176 (14.5)	30 (14.2)	
Tumor differentiation			0.360
Poorly	203 (21.1)	42 (24.6)	
Moderate	606 (63.0)	108 (63.1)	
Well	153 (15.9)	21 (13.3)	
Histopathology			0.012
Adenocarcinoma	1031 (85.2)	175 (82.9)	
Mucinous cell	146 (12.1)	22 (10.4)	
Signet-ring cell	33 (2.7)	14 (6.6)	
Gross type			0.395
Invasive	153 (12.6)	20 (9.5)	
Ulcerous	576 (47.6)	101 (47.9)	
Fungus	481 (39.8)	90 (42.7)	
T			0.673
1	34 (2.8)	4 (1.9)	
2	249 (20.6)	40 (19.0)	
3	520 (43.0)	99 (46.9)	
4	407 (33.6)	68 (32.2)	
N			0.071
No	494 (40.8)	77 (36.5)	
≤ 4	538 (44.5)	111 (52.6)	
> 4	178 (14.7)	23 (10.9)	
M			0.692
No	1039 (85.9)	179 (84.8)	
Yes	171 (14.1)	32 (15.2)	
Staging			0.669
I	129 (10.7)	20 (9.5)	
II	362 (29.9)	56 (26.5)	
III	548 (45.3)	103 (48.8)	
IV	171 (14.1)	32 (15.2)	
CEA			0.992
≤ 3.4	301 (27.8)	52 (27.8)	
> 3.4	780 (72.2)	135 (72.2)	

T: Tumor infiltration depth; N: Number of lymph node; M: Metastasis at diagnosis; CEA: Carcinoembryonic antigen.

RESULTS

Patients and clinical data

A total of 1421 patients with sporadic colorectal adeno-

carcinoma were enrolled, of which 1210 patients were Han/Chinese (mean age, 62.3 ± 4.5 years; range, 19-92 years), while 211 patients were Uyghur (mean age, 52.4 ± 15.6 years; range, 17-87 years, Table 1). There were more patients who were over 50 years of age in the Han/Chinese group (80.2% *vs* 56.3%, $P = 0.000$) and more patients who were under 50 years of age in the Uyghur group (43.6% *vs* 26%, $P = 0.000$). The proportion of male patients in the Han/Chinese group was higher than that of the Uyghur group ($P < 0.05$). There were differences between occupational proportions in the two ethnic groups. Cadre (office workers) and physical workers were the most prevalent in the Han/Chinese group (70.1% *vs* 43.1%) and farmers and herders were more prevalent in the Uyghur group (42.7% *vs* 16.9%). There were more A blood type patients in the Han/Chinese group (31.2% *vs* 20.9%, $P < 0.05$), while there were more B blood type patients in the Uyghur (38.4% *vs* 31.9%, $P < 0.05$) group. Although there was no significant difference in tumor sites between the two ethnic groups, the most common sites for cancer occurrence were the sigmoid colon and the rectum in both groups (73.0% in the Han/Chinese group *vs* 79.1% in the Uyghur group, $P = 0.196$). There was no statistically significant difference in treatment including surgery, post-operative chemotherapy or radiotherapy between the two ethnic groups ($P > 0.05$, Table 2).

Tumor characteristics

The histopathologic differences between the two ethnic groups are summarized in Table 1. Compared with the Han/Chinese group, the Uyghur patients had a greater proportion of suffering from signet-ring cell type (6.6% *vs* 2.7%, $P < 0.05$). A comparison of the Han/Chinese and Uyghur patients revealed that they exhibited almost the same incidence of any stage, presence of metastasis at the initial diagnosis and recurrence rate after resection ($P > 0.05$). There were no significant differences in gross type, tumor size or carcinoembryonic antigen between the two groups, respectively.

Recurrence and survival

The median follow-up in all patients was 42 mo (range, 7-122 mo; mean, 48.73 mo in the Han/Chinese group and 42.37 mo in the Uyghur group). A total of 175 patients (12.3%) were lost to follow-up; in total, 543 patients (44.9%) in the Han/Chinese group and 104 in the Uyghur group (49.3%) developed either local or distant recurrence ($P = 0.235$, Table 2). The Han/Chinese group had respective 1-year, 3-year, and 5-year overall survival rates of 87.2%, 46.8%, and 29.2%, whereas the respective rates were 80.4%, 42.9%, and 10.1% in the Uyghur group. There was significant difference in median survival time between the two groups ($P = 0.000$). As shown in Figure 1, overall survival, disease-free survival and cancer-specific survival in the Uyghur group were significantly lower than the Han/Chinese group ($P = 0.000$, $P = 0.005$, $P = 0.007$, respectively). Using univariate Cox proportional-hazards regression analyses, the related factors of age, ethnicity, tumor site, histopathological type,

Table 2 Treatment, recurrence and survival *n* (%)

	Han (<i>n</i> = 1210)	Uyghur (<i>n</i> = 211)	<i>P</i> value
Chemotherapy			0.493
Yes	692 (57.2)	126 (59.7)	
No	518 (42.8)	85 (40.3)	
Radiotherapy			0.216
Yes	247 (20.4)	51 (24.2)	
No	963 (79.6)	160 (75.8)	
Surgery			0.872
Radical	1091 (90.2)	191 (90.5)	
Palliative	119 (9.8)	20 (9.5)	
Local recurrence			0.282
Yes	151 (12.5)	32 (15.2)	
No	1059 (87.5)	179 (84.8)	
Postoperative metastasis			0.535
Yes	620 (51.2)	113 (53.6)	
No	753 (48.8)	98 (46.4)	
Metastatic site			0.224
No	591 (48.8)	97 (46.0)	
Liver	394 (32.6)	81 (38.4)	
Non-liver	225 (18.6)	33 (15.6)	
Median overall survival	45	42	0.000
Median dis-free survival	62	49	0.005
Median tumor-specific survival	65	61	0.007

differentiation, tumor infiltration depth (T), numbers of lymph node metastasis (N), metastasis (M), TNM staging, postoperative metastasis and the metastatic site were found to be the prognostic factors ($P < 0.05$); multivariate analysis showed that age, ethnicity, histopathological type, differentiation, T, N, TNM staging, postoperative metastasis and the metastatic site were the prognostic factors ($P < 0.05$, Table 3).

DISCUSSION

Our results provide the first single center-based comparison of clinicopathological factors and hazard ratios regarding the survival of patients with CRC between the two ethnic groups in Xin Jiang. The ethnic distribution significantly differed in Xin Jiang; the majority of Uyghurs inhabited in the south of Xin Jiang and most of the Han/Chinese population resided in northern Xin Jiang. The economic development of southern and northern Xin Jiang is not consistent and thus is related to level of education. Northern Xin Jiang is undergoing more rapid economic and educational developments, while socioeconomic status and health care knowledge are higher than those in southern Xin Jiang. Additionally, the quality of health care services in northern Xin Jiang is superior to those in southern Xin Jiang. This circumstance may be able to explain the difference between occupational proportions in the two ethnic groups. Our study showed that the proportion of male patients in the Han/Chinese group was higher than that in the Uyghur group ($P < 0.05$). In a study by Brenner *et al.*^[11], gender is also shown to be a contributing factor to the development of CRC in young individuals. The risk of CRC in male patients is higher at an earlier age than in women; accordingly, their recommendation is that the optimal age for initiating

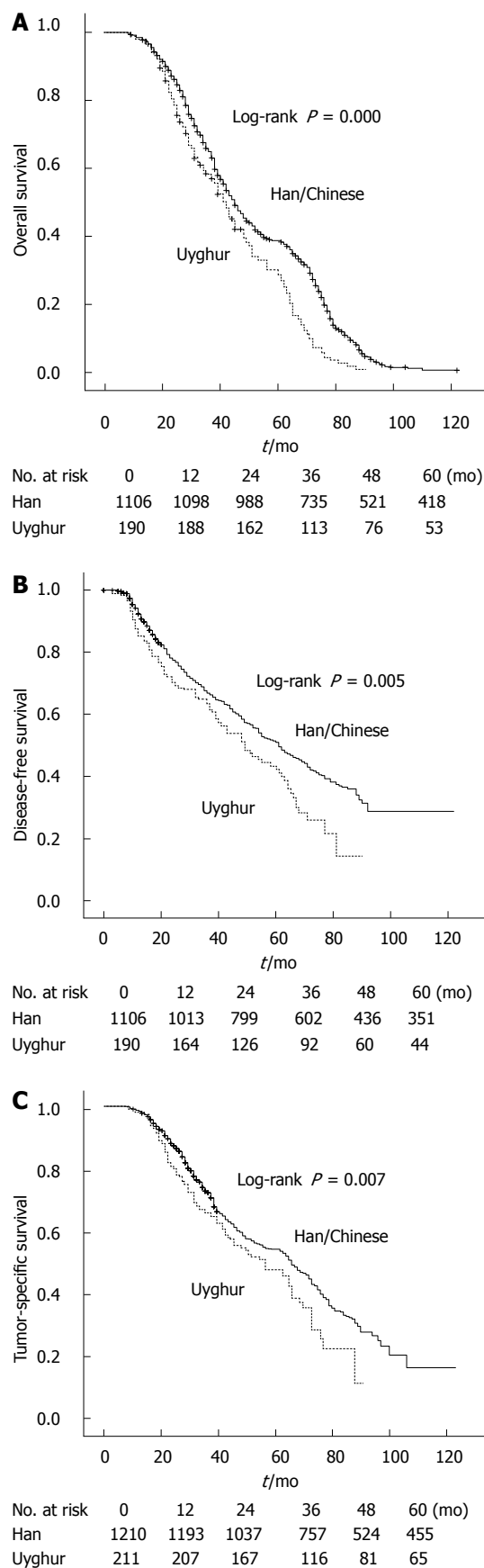


Figure 1 Kaplan-Meier estimates. A: Overall survival for different ethnic patients with colorectal cancer (CRC); B: Disease-free survival for different ethnic patients with CRC; C: Tumor-specific survival for different ethnic patients with CRC.

Table 3 Significant predictive factors for cancer-specific survival in a Cox proportional-hazard analysis

Prognostic factor	Univariate HR (95%CI)	P value	Multivariate HR (95%CI)	P value
Age	0.768 (0.706-0.836)	0.000	0.828 (0.751-0.913)	0.000
Ethnicity	1.494 (1.277-1.749)	0.000	1.316 (1.107-1.565)	0.002
Tumor site	0.918 (0.852-0.988)	0.023	0.972 (0.889-1.063)	0.531
Histopathological type	0.584 (0.537-0.634)	0.000	0.479 (0.307-0.748)	0.001
Tumor differentiation	1.201 (0.976-1.479)	0.028	1.421 (1.126-1.795)	0.003
T	1.475 (1.374-1.582)	0.000	1.378 (1.268-1.498)	0.000
N	1.684 (1.561-1.817)	0.000	1.169 (1.007-1.357)	0.040
M	3.829 (3.264-4.492)	0.000	1.179 (0.895-1.554)	0.243
Staging	2.009 (1.865-2.164)	0.000	1.579 (1.418-1.798)	0.000
Postoperative metastasis	2.538 (2.260-2.850)	0.000	2.329 (1.805-3.004)	0.000
Metastatic site	1.513 (1.416-1.617)	0.000	0.837 (0.716-0.978)	0.025

T: Tumor infiltration depth; N: Number of lymph node; M: Metastasis at diagnosis.

CRC screening in women is approximately 5 years older than that for men^[10,11]. In terms of dietary habit, Uyghurs primarily consume meats (roasted, fried and boiled) and pastas every day, while Hans (Chinese) primarily consume rice and vegetables. The incidence of CRC is generally higher in populations with a high intake of meat and a low intake of staple plant foods^[12]. A comprehensive review by the WCRF and the American Institute for Cancer Research concluded that “the evidence that red meat and processed meat are a cause of CRC is convincing”^[13]. The disparities regarding age, blood type and histological features may also suggest some biological or genetic differences between the two ethnic groups, which is the area of study of our future investigations. Because of this prominent bias, it was particularly important to take regional, social and conventional gaps into consideration during the analysis.

Ethnic disparities have been demonstrated at each step of the cancer care continuum. Although these disparities are multifactorial in nature, they have a profound impact on cancer-related survival. Increased mortality among African American colon cancer patients has been attributed to decreased screening, more advanced stage at diagnosis, the disproportional receipt of standard surgical therapy and the unequal receipt of adjuvant therapy and postoperative surveillance^[14,21]. Additionally, African American patients present at more advanced disease stages and are more likely to have an undetermined stage at presentation^[22]. In contrast, East Asian American patients had significantly better 5-year overall and colon cancer-specific survival than non-Hispanic white, Hispanic white, and African American patients, which persisted when separately analyzed in patients with stage II and stage III diseases^[23]. Several studies have suggested that there may be variations in CRC stage and survival between the Asian/Pacific Islander subgroups^[24].

In our study, the Uyghur patients had significantly worse prognosis than Han/Chinese patients given no significant differences in staging, recurrence or treatment. Numerous reports have suggested that socioeconomic status is a important factor in the poor prognosis of African American patients^[25,26]. However, Wudel *et al.*^[27] suggested that the marked reductions in survival of African

American patients did not appear to be related to variations in treatment but may have been due to biological factors or non-cancer-related health conditions. Uyghurs are more reluctant to screen with colonoscopy due to their traditional and religious beliefs and are more likely to live in a low-income community with limited access to gastroenterologists. Uyghurs also may have a lower incidence of insurance to cover a colonoscopy. In the present study, a poor prognosis in the Uyghur patients was consistently observed in overall survival, disease free survival and colon cancer-specific survival across nearly all stages. Therefore, it is likely that biological differences, socioeconomic status, disparities in health care service and ideology all contributed to the poor prognosis. A further epidemiological multicenter survey is needed to better quantify and determine whether dietary, regional, educational, socioeconomic status or genetic background could impact the incidence and mortality of CRC patients in these ethnic groups.

In a conclusion, Uyghur CRC patients are associated with a much younger age at disease onset, more aggressive histopathologic characteristics and a significantly worse prognosis than those in the Han/Chinese patients. Therefore, more attention should be paid to enhancing health care education and regular screening for the Uyghur population as well as promoting comprehensive treatment techniques in an effort to improve survival for both ethnic groups.

COMMENTS

Background

Cancer disparities between racial and ethnic groups are major public health concerns. It has been well established that the rates of cancer incidence and colorectal cancer (CRC)-related death are variable between patients from different racial and ethnic groups. Despite the great advances in medicine over recent decades, racial disparities in cancer-related mortality remain a challenging problem. The authors attempted to identify whether there are any differences that may contribute to survival between these ethnic groups.

Research frontiers

The survival of patients with colon cancer reportedly differs according to race/ethnicity in the United States. Several studies have shown that African Americans are more likely to be diagnosed with advanced stage CRC and to have poorer survival rates after diagnosis compared with Caucasians. Several factors

including lack of health insurance, inability to access medical care, poverty, and low education level, are attributable to such findings. There has been no formal research thus far regarding the disparities between CRC patients with different ethnicities in the Xin Jiang area. This is the first report on clinicopathological factors and survival of CRC patients with differing ethnicity in Xin Jiang.

Innovations and breakthroughs

This study has several strengths. First, the sample size was relatively large and the reliability and representativity of data were strong. Second, when the authors compared the survival rates of two different ethnic groups, the comparability between other confounding factors, such as staging, recurrence and treatment were guaranteed. Third, Uyghur CRC patients were found to be associated with significantly younger age, more aggressive histopathologic characteristics and significantly worse prognosis than Han/Chinese patients. These disparities may suggest that some biological or genetic differences exist between the two ethnic groups or that several factors, including a lack of health insurance, reluctance to access medical care, poverty, and low education level, in Uyghur patients contributed to such findings.

Applications

This article demonstrated that there were disparities between the two ethnic groups in regard to clinicopathological factors and survival. The possible reasons for poor survival were preliminarily analyzed. These findings are valuable for CRC detection and prevention in the Xin Jiang region.

Peer review

This is a retrospective study to assess clinical features and prognosis in CRC patients of different ethnicity in a medical center in Xinjiang province. The results provide valuable information for communities and public health programs.

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