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# A retrospective cross-sectional study: comparison of the clinicopathological features of schistosomal and non-schistosomal colorectal cancer in Central China

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## Abstract

**Aim** To analyze the clinicopathological features of schistosomal and non-schistosomal colorectal cancer in Central China and compare them with other areas of the Yangtze River Basin.

**Method** The 501 cases of colorectal cancer (CRC) were retrospectively analyzed from 2020 to 2022. They were divided into two groups: 406 cases of colorectal cancer without schistosomiasis (CRC-NS) and 95 cases of colorectal cancer with schistosomiasis (CRC-S).The clinicopathological characteristics included the distribution of schistosomiasis eggs, patient age, sex, tumor differentiation, lymph node metastasis, and clinical stage. By retrieving the database, this study compared the clinicopathological differences of colorectal cancer with schistosomiasis in other areas of the Yangtze River basin.

**Results** The cases of colorectal cancer with schistosomiasis accounted for 18.9%(95/501) in the study. The patients of CRC-S were older than the patients of CRC-NS ($P=0.002$, $P<0.05$). There was a statistical difference in the location of occurrence ($P=0.000$, $P<0.05$) between the two groups. There were no significant differences between CRC-S and CRC-NS in other clinicopathological features, such as sex ($P=0.054$), Type($P=0.242$), histological type($P=0.654$), infiltrative depth($P=0.811$), differentiation($P=0.837$), lymph node metastasis($P=0.574$), intravascular tumor thrombus($P=0.698$), T stage($P=0.354$). In other areas of the Yangtze River Basin, there were statistical differences in the age of occurrence and T stage ($P<0.05$) between colorectal cancer with schistosomiasis and non-schistosomal colorectal cancer.

**Conclusion** In Central China, colorectal cancer with chronic schistosomiasis infection occurs more in the rectum and sigmoid colon. It is more common in individuals over 60 years old, consistent with the findings in the Yangtze River Basin. Additionally, schistosomal colorectal cancer had a higher T stage in the Yangtze River Basin. This may be related to the malignant biological behavior of colorectal cancer and could result in a relatively poor prognosis. Therefore,

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the elderly population in schistosomiasis endemic areas should pay more attention to early screening and tumor prevention.

**Keywords** Schistosomiasis, Colorectal cancer, Clinicopathological characteristics, Central China

## Introduction

Colorectal cancer ranks as the fourth most common cancer worldwide and stands as the second leading cause of death. The studies have shown that it is closely related to schistosomal infection [1, 2]. Human schistosomiasis includes three main types: S.haematobium, S.mansoni and S.japonicum [3, 4], mainly schistosomiasis japonica in China. It is a parasitic disease widely prevalent along the Yangtze River Basin. Since the mid-1980s, efforts to control schistosomiasis have evolved from population chemotherapy to infection source control, with notable progress observed post the completion of the Three Gorges Dam. In the past decade, the incidence of schistosomiasis has decreased by 88.46% from 2010 to 2021. As of the end of 2021 [5], among the 451 schistosomiasis endemic to counties (cities, districts) in China, 339 counties have achieved elimination standard, 100 counties have attained transmission-blocking standards, and 12 counties are in the stage of transmission control. Among these, the number of acute schistosomiasis cases has steeply declined [6, 7]. The existing patients primarily consist of advanced schistosomiasis cases (29,037 cases), chiefly concentrated in five provinces in the lake area(Hunan, Hubei, Jiangxi, Anhui, Jiangsu) [8].

Although the prevention and treatment of schistosomiasis has achieved remarkable results, the eggs still exert adverse effects on various organs after chronic schistosomiasis infection, particularly in the liver and intestine. Calcified schistosomiasis eggs are commonly observed in tissue sections of radical resection specimens from colorectal cancer patients in central China, it is also the evidence of chronic schistosomiasis infection. However, there are few reports regarding the clinicopathological characteristics of colorectal cancer patients with schistosoma infection in the central region, especially in comparison with other areas in the Yangtze River basin.

Therefore, the author collected samples from colorectal cancer patients in the Jingzhou area, analyzed their clinicopathological characteristics, and compared them to data from the broader Yangtze River Basin. This study aims to elucidate the impact of chronic schistosomiasis japonicum infection on the clinicopathological features of colorectal cancer in the Yangtze River Basin.

## Materials and methods

### Patients and samples

A retrospective analysis was conducted on clinicopathological data and HE(hematoxylin and eosin)stained slides of individuals diagnosed with schistosomal and non-schistosomal colorectal cancer from January 2020 to August 2022. Two expert pathologists reviewed HE-stained slides to determine the diagnosis and re-stage the cases according to the eighth edition of American Joint Committee on Cancer (AJCC).

Among the 501 patients with CRC, there were 95 schistosomal patients with CRC were comprised of 65 males and 30 females, with a ratio of 2:1. Ages ranging from 46 to 88 years and an average age of 66.03.In contrast, the non-schistosomal colorectal cancer group (CRC-NS) included 406 cases, consisting of 234 males and 172 females. The male-to-female ratio in this group was 1.5:1, with ages ranging from 26 to 92 years and an average age of 61.84. All patients had no history of preoperative chemoradiotherapy and related immunotherapy.

### Clinicopathological features analysis

The clinicopathological features of the collected cases were thoroughly analyzed, including the following characteristics: tumor growth pattern(ulcer type, uplift type, infiltration type), growth sites(transverse colon, ascending colon, sigmoid colon and rectum). The depth of infiltration was divided into mucosa / submucosa, superficial / deep muscle layer and serosa (fibrous membrane)/ outside. Histological type included adenocarcinoma (including tubular adenocarcinoma) and mucinous adenocarcinoma. The degree of differentiation was mainly divided into: low, moderate and high, according to the 2017 eighth edition of AJCC T stage. To enhance the comprehensiveness of the study, a comparative analysis was conducted with colorectal cancer featuring schistosomiasis infection reported in the literature in other parts of the Yangtze River Basin.

### Statistical analysis

The data were analyzed using SPSS software for Windows (version 25.0; IBM Corp). Enumeration data (%), the rate of comparison with chi-square test, test level $\alpha = 0.05$.

## Results

### Morphological characteristics of schistosomiasis eggs in tissue slides

Upon analyzing the pathological slides of 95 cases of CRC-S, the following characteristics were observed: schistosomiasis eggs were found in various parts of the intestinal wall, including the mucosal layer (84 / 95), submucosa (95 / 95), muscular layer (8 / 95), and outer membrane layer (3 / 95) (Figs. 1 and 2). Detailed data are shown in Table 1. Notably, schistosome eggs can be

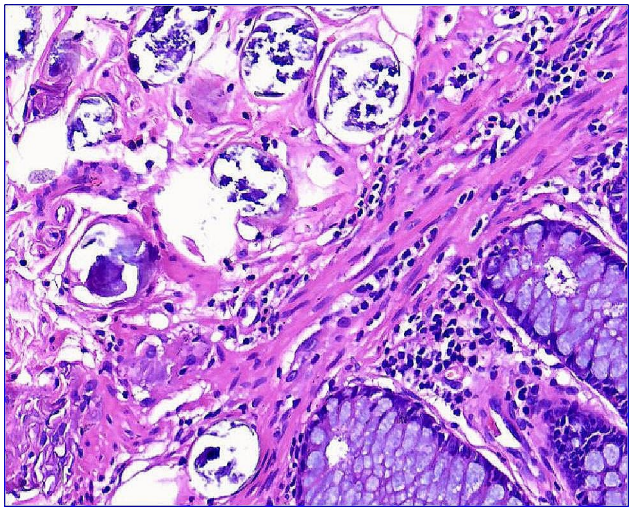

**Fig. 1** Schistosomal ova in submucosa: round or oval calcified schistosomal ova in the distal normal tissues after radical surgery of colorectal cancer, located in the submucosa.(HE×200)

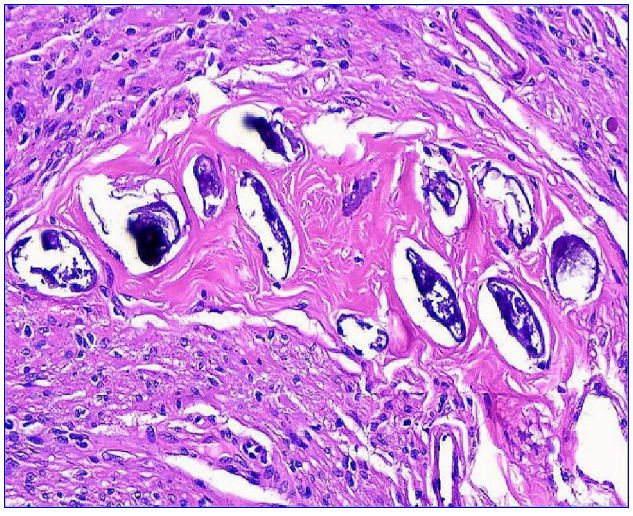

**Fig. 2** Schistosomal ova in muscle layer: schistosomal ova in the distal normal tissues after radical surgery of colorectal cancer, located in the muscle; in the slide, several schistosomal ova shaped cavity because of calcification.(HE×200)

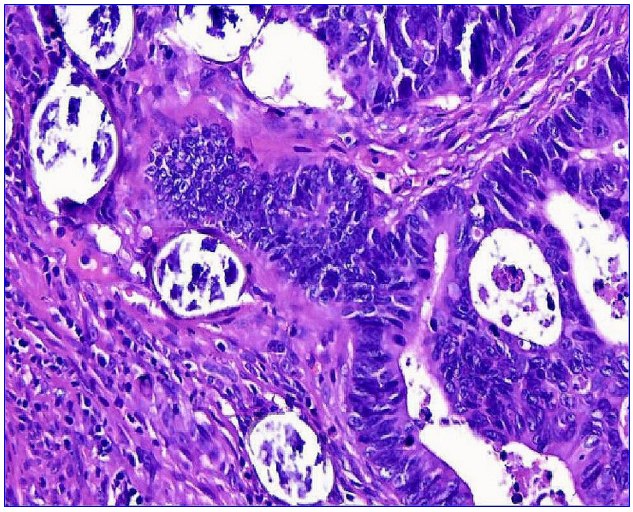

**Fig. 3** Schistosomal ova in highly differentiated tumors: In conventional paraffin sections of the highly differentiated colorectal cancer, showed old calcified schistosomal ova.(HE×200)

found in different layers of intestinal wall at the same time, and calcified schistosomiasis eggs were found in the submucosa of all lesions.

Most of the calcified schistosomiasis eggs were morphologically intact, showing a basophilic oval nodule. However, a few eggs were damaged during the preparation of tissue slides. Vascular proliferation and lymphocyte aggregation were observed around nearly all eggs, although interstitial reactions were not common. Interestingly, interstitial reactions were more easily observed in eggs deposited around tumor cells.

Microscopic examination revealed that different deposition sites of schistosomiasis eggs had diverse degrees of differentiation of tumors. The deeper the deposition site of schistosomiasis eggs, the lower the degree of differentiation(9/95); In some cases of CRC-S(5/95), tumors have different differentiation, and the degree of tumor differentiation is low where schistosome eggs exist.in the same specimen, diverse degrees of tumor differentiation can be observed in the presence or absence of schistosome egg deposition (5/95). (Figures 3 and 4: Calcified schistosomel egg deposition can be seen in adenocarcinoma slides with different degrees of differentiation)

**Table 1** The number and regional distribution of schistosome egg deposition in tumors with different degrees of differentiation

| Differentiation | Patients | ova in submucosa | ova in mucous layer | ova in muscle laye | ova in fibrous membrane/ outside |
|---|---|---|---|---|---|
| Well adenocarcinoma | 13 | 13 | 10 | | 3 |
| Moderate adenocarcinoma | 67 | 67 | 64 | 3 | |
| Poor adenocarcinoma | 9 | 9 | 9 | | |
| Mucinous carcinoma | 6 | | | | |
| All patients | 95 | 89 | 83 | 3 | 3 |

Annotation: a. There is no non-differentiated difference in mucinous carcinoma

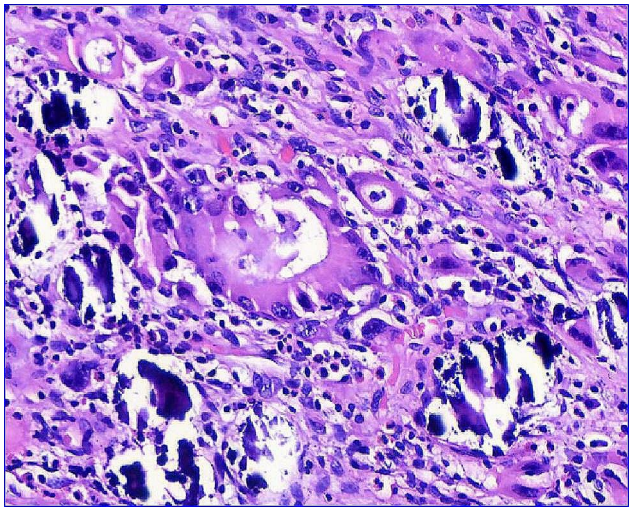

**Fig. 4** Schistosomal ova in poor differentiated tumors: In conventional paraffin sections of the poorly differentiated colorectal cancer, calcification schistosomal ova surrounded the tumor tissue, with promoting fibrous connective tissue reaction and inflammatory cell infiltration such as eosinophils.(HE×200)

### Clinicopathological features of colorectal cancer with schistosomiasis infection

The clinicopathological features of the cohort have been summarized in Table 2.

Colorectal cancer with schistosomiasis infection exhibited a higher prevalence in individuals older than 60 years, which was statistically significant compared with CRC-NS group($P$=0.002). In terms of tumor location($P$=0.000), there was a statistically significant difference between the two groups. However, there was no significant difference between the two groups in sex of tumor occurrence ($P$=0.054), tumor type($P$=0.242), histological type($P$=0.654),infiltrative depth($P$=0.811), degree of differentiation($P$=0.837), lymph node metastasis($P$=0.574), intravascular tumor thrombus($P$=0.698)and T stage($P$=0.354).

### Comparison of clinicopathological features of colorectal cancer with schistosomiasis infection in the Yangtze River Basin, China

A comprehensive review of relevant literature using the keywords "colorectal cancer," "colon cancer," "rectal cancer," "clinicopathological features," and "schistosomiasis" was conducted by searching the CNKI, Wanfang, and PubMed databases. It was observed that the majority of research data originated from the lower reaches of the Yangtze River, while research in the middle and upper reaches remains scarce. The results of the researches are some differences, they are generalized in Table 3.

In terms of the age of tumor occurrence, existing statistically differences between colorectal cancer with schistosomiasis and non-schistosomiasis, aligning with the conclusions drawn in this paper. Both of them had statistical significance in T stage. Most of the literature advanced that schistosomal are deposited in the rectum and sigmoid colon, and this is related to the fact that colorectal cancer with schistosomal occurs more frequently in the rectum and sigmoid colon in text.

## Discussions

### Clinical correlation analysis of schistosomiasis and colorectal cancer in the region

The research is located in central China. Relative data indicates that the CRC-S group exhibits a minimum patient age of 46 years, while the CRC-NS group shows a minimum age of only 26 years. This suggests that colorectal cancer with schistosomiasis infection is more likely to manifest in the elderly, consistent with Liu et al. [15]. A statistical distinction in the location of occurrence was observed between CRC-S and CRC-NS, with a higher likelihood of occurrence in the sigmoid colon and rectum, a trend consistent with the study conducted by Qin et al. [14]. It may be relevant to the location of schistosomiasis egg deposition. Wang et al. [16] brought to 7 studies by META analysis, indicating that there was no statistical difference between CRC-S and CRC-NS in type and Infiltrative depth, which was consistent with the experimental data in this paper. Both are mainly moderately differentiated adenocarcinoma. However, Almoghrabi [17] studies suggested a close association between schistosomiasis infection and the high pathological stage and early lymph node metastasis of colorectal cancer in the elderly, indicating a distinct correlation. This study manifested that there were no statistical differences in pathological stage, lymph node metastasis and whether exist intravascular tumor thrombus.

It is important to note that this study primarily focuses on the incidence of CRC-S patients in central China, thus there a certain geographical limitations.

### Clinicopathological features of colorectal cancer with S. japonicum infection in the Yangtze River Basin of China

Up to 2003, five provinces (municipalities and autonomous regions) including Guangdong, Shanghai, Fujian, Guangxi and Zhejiang have declared the elimination of schistosomiasis [5]. But in other provinces of China, more than half of counties(cities, districts)have reached the epidemic to block the spread, but there are still about 110 counties(cities, districts)are still in serious epidemic, accounting for 25.8% of the total [18], mainly distributed in the lake area of 5 provinces along the lake beach and Sichuan, Yunnan provinces of the mountain.

This paper integrates and summarizes relevant research on CRC-S in the Yangtze River Basin of China, incorporating findings from five selected articles. The majority of studies are concentrated in the lower reaches of the

**Table 2** Clinicopathological features of colorectal cancer with schistosome infection

| Clinicopathological features | All patients | CRC-NS(*N* = 406) *n* (%) | CRC-S(*N* = 95)n (%) | $\chi^2$-value | *p*-value |
|---|---|---|---|---|---|
| Age(year) | | | | | |
| < 60 | 203(40.5) | 178(43.8) | 25(26.3) | 9.912 | 0.002 |
| > 60 | 298(59.5) | 228(56.2) | 70(73.7) | | |
| Sex | | | | | |
| male | 299(59.7) | 234 (57.6) | 65 (68.4) | 3.722 | 0.054 |
| female | 202(40.3) | 172(42.4) | 30(31.6) | | |
| Location | | | | | |
| transverse colon | 48(9.6) | 34(8.4) | 14(14.7) | 28.109 | 0.000 |
| ascending colon | 122(24.4) | 114(28.1) | 8(8.4) | | |
| descending colon | 56(11.2) | 35(8.6) | 21(22.1) | | |
| sigmoid | 146(29.2) | 117(28.9) | 29(30.5) | | |
| rectum | 128(25.6) | 105(25.9) | 23(24.2) | | |
| Type | | | | | |
| elevated type | 206(41.1) | 174(42.8) | 32(33.7) | 2.834 | 0.242 |
| ulceration type | 263(52.5) | 206(51.1) | 57(60.0) | | |
| Infiltrating type | 32(6.4) | 26(6.5) | 6(6.3) | | |
| Histological type | | | | | |
| mucinous carcinoma | 37(7.4) | 31(7.6) | 6(6.3) | 0.196 | 0.654 |
| adenocarcinoma | 460(91.8) | 375(92.4) | 89(93.7) | | |
| Infiltrative depth | | | | | |
| mucosa / submucosa | 32(6.4) | 27(6.7) | 5(5.3) | 0.418 | 0.811 |
| superficial / deep muscle layer | 69(13.8) | 57(14.0) | 12(12.6) | | |
| fibrous membrane/ outside | 400(79.8) | 322(79.3) | 78(82.1) | | |
| Differentiation | | | | | |
| well | 59(11.8) | 46(11.3) | 13(13.7) | 0.355 | 0.837 |
| moderate | 357(71.3) | 290(71.4) | 67(70.5) | | |
| poor | 48(9.6) | 39(9.6) | 9(9.5) | | |
| Lymph node metastasis | 25(5.0) | 19(8.2) | 6(10.3) | 0.316 | 0.574 |
| Intravascular tumor thrombus | 209(41.7) | 174(42.9) | 38(40.4) | 0.150 | 0.698 |
| T stage | | | | | |
| I + II | 86(17.2) | 81(20.0) | 5(5.3) | 0.861 | 0.354 |
| III + IV | 415(82.8) | 325(80.0) | 90(94.7) | | |

Annotation: b. A case of colorectal cancer with non-schistosome infection in total colon; c. Since there is no non-differentiated difference, no differentiation degree statistics in mucinous carcinoma

Yangtze River, including one article in Jiading district and Qingpu district of Shanghai in the early years, as well as Wuhu area of Hubei Province representing the middle reaches of the Yangtze River. The area of Anhui Province is one of the most serious areas of schistosomiasis infection [8]. Therefore, most of the studies come from here.

Contrasting conclusions from various studies. Wang [10, 11] and other studies have shown that chronic schistosomiasis infection is not correlated with the growth pattern, histological type, depth of invasion, or differentiation of colorectal cancer. Instead, it is linked primarily to age, gender, and pathological stage. Liu's study [9] in Shanghai aligns with this, indicating a worse prognosis for colorectal cancer with schistosomiasis infection. Wang et al. [12] showed that CRC-S had early lymph node metastasis and higher pathological stage, while Liu et al. [9] also indicate that it. They all suggest poor prognosis; there are also different conclusions in the two literatures. Liu et al. [9] purported that CRC-S is more likely to occur in the elderly over 60 years old, and it is more likely to occur in the rectum and sigmoid colon. Adenocarcinoma is more common, but there is no difference in the growth pattern between CRC-NS and CRC-S, which is contrary to the conclusion of Wang et al. However, Zhou Weigen et al. [13] argue that schistosomiasis infection does not affect the pathological stage and lymph node metastasis of colorectal cancer but is associated with middle and low differentiation, which was different from the conclusions of previous studies.

The economic and social development of different regions affect the control effect of schistosomiasis, and regional differences between epidemic control areas and

**Table 3** Comparison of clinicopathological features of colorectal cancer with Schistosoma japonicum infection in the Yangtze River Basin of China

| Clinicopathological features | 2017Liu JL el [9] | | 2020Wang ZJ el [10, 11] | | 2020Wang el [12] | | 2021Zhou WG el [13] | | 2021Qin el [14] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | CRC-NS(*N* = 191) | CRC-S(*N* = 76) | CRC-NS(*N* = 3289) | CRC-S(*N* = 265) | CRC-NS(*N* = 214) | CRC-S(*N* = 137) | CRC-NS(*N* = 351) | CRC-S(*N* = 63) | CRC-NS(*N* = 992) | CRC-S(*N* = 248) |
| Place | Jiading, Shanghai | | Wuhu, Anhui | | Qingpu, Shanghai | | Wuhu, Anhui | | Wuhan, Hubei | |
| Age | | | | | | | | | | |
| < 60 | 42 | 0 | 1276 | 77 | 78 | 5 | 172 | 45 | NA | |
| ≥ 60 | 148 | 76 | 2013 | 188 | 136 | 132 | 179 | 18 | | |
| (*p*-value) | 0.000* | | 0.007* | | < 0.001* | | 0.001* | | | |
| Sex | | | | | | | | | | |
| male | 95 | 46 | 1946 | 185 | 126 | 86 | 199 | 47 | 732 | 183 |
| female | 93 | 30 | 1343 | 80 | 88 | 51 | 152 | 16 | 260 | 65 |
| (*p*-value) | 0.173 | | 0.0012* | | 0.467 | | 0.0077* | | 0.164 | |
| Type | | | | | | | | | | |
| elevated type | 30 | 13 | 365 | 10 | NA | | 247 | 20 | NA | |
| ulceration type | 45 | 18 | 2472 | 196 | | | 9 | 42 | | |
| Infiltrating type | 116 | 45 | 452 | 59 | | | 95 | 1 | | |
| (*p*-value) | 0.001* | | 0.003* | | | | 0.6917 | | | |
| Histological type | | | | | | | | | | |
| mucinous carcinoma | 19 | 20 | 107 | 37 | NA | | 34 | 52 | NA | |
| adenocarcinoma | 172 | 47 | 3182 | 228 | | | 317 | 11 | | |
| (*p*-value) | 0.000* | | 0.954 | | | | 0.0679 | | | |
| Differentiation | | | | | | | | | | |
| well | 13 | 6 | 722 | 7 | NA | | 226 | 1 | NA | |
| moderate | 127 | 45 | 2493 | 249 | | | 118 | 51 | | |
| poor | 51 | 25 | 74 | 9 | | | 7 | 11 | | |
| (*p*-value) | 0.530 | | 0.285 | | | | 0.0349* | | | |
| Lymph node metastasis | | | | | | | | | | |
| yes | 91 | 25 | NA | | 88 | 56 | NA | | NA | |
| (*p*-value) | 0.028* | | | | 0.883 | | | | | |
| T stage | | | | | | | | | | |
| I + II | 98 | 52 | 754 | 35 | 51 | 108 | 72 | 5 | NA | |
| III + IV | 93 | 24 | 2553 | 230 | 163 | 29 | 279 | 58 | | |
| (*p*-value) | 0.011* | | < 0.001* | | 0.562 | | 0.0603 | | | |

Annotation: d. *suggests statistically significant that the *p*-value is less than 0.05. e. NA meats that it cann't meet the inclusion criteria

epidemic blocking areas in the same region. Even the influence of geographical location and living habits factors.Finally, leading to differences in research results in various regions.

In the middle reaches of the Yangtze River region, only one literature. Qin et al. [14] studied the related intestinal lesions caused by schistosomiasis in Wuhan, Hubei Province, and finally concluded that female patients with schistosomiasis faced a higher risk of colorectal cancer. Across studies in the Yangtze River Basin, age consistently emerged as a crucial factor impacting colorectal cancer with schistosomiasis infection, aligning with the conclusions of this study.

Different conclusions in clinicopathological features across studies may be attributed to geographical location, the amount of sample data studied, and the effect of schistosomiasis prevention and treatment. For example, there are variances between the epidemic control area and the epidemic blocking area in Wuhu, Anhui Province. In the Yangtze River Basin, the results showed that colorectal cancer with schistosome infection was more likely to occur in elderly patients over 60 years old, which was consistent with the results of our study. However, it remains to be further studied whether chronic schistosomiasis infection is a high risk factor for lymph node metastasis and higher pathological stage of colorectal cancer, as well as a potential poor prognostic factor. Similar to trends in other countries, the incidence and mortality of CRC are rising in China [19–21]. Controlling related risk factors can reduce mortality. However, as an infectious parasitic disease with specific local

characteristics, the correlation between schistosomiasis and colorectal cancer is rarely studied [22, 23].

In the study, the clinicopathological features of CRC-NS and CRC-S were studied in Central China and compared they with other schistosomiasis endemic areas of the Yangtze River Basin. The findings indicate that colorectal cancer patients with schistosomiasis infection are more likely to be elderly, aged over 60, and more common in the rectum and sigmoid colon in Central China, which may be related to the deposition of schistosomiasis eggs in colorectal cancer. Moreover, the longer the duration of schistosomiasis infection, the deeper the deposition of schistosomiasis eggs, thereby increasing the possibility of diverse tumor differentiations. This leads to the conclusion that CRC-S may be associated with the malignant biological behavior of tumors. However, it is still unclear whether affects schistosomiasis infection survival and prognosis. Further research needs multicenter big data analysis.

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**Author contributions**
ZYT contributed to the data analysis, manuscript editing, and manuscript writing. GP contributed to the research design. RXS and RC contributed to the data supplement, data collection and performed the pathological examination. ZYT and WXX contributed to revising the manuscript and confirm the authenticity of all the raw data. ZYT and GP contributed to the article revision. All authors reviewed the manuscript.

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**Data availability**
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
Research performed on human subjects, materials or data must follow international and national regulations and be in agreement with the Declaration of Helsinki, or any other relevant set of ethical principles. This study was approved by the medical ethics committee of Jingzhou Hospital Affiliated to Yangtze University(ethical approval number 2023-106-01 ).

**Competing interests**
The authors declare no competing interests.

**Patient consent for publication**
Not applicable.

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