Original Article

Traditional Chinese Medicine Syndromes Distribution in Colorectal Cancer and its Association with Western Medicine Treatment and Clinical Laboratory Indicators

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Abstract

Objective: The objective of the study is to explore the traditional Chinese medicine (TCM) syndrome distribution in colorectal cancer (CRC) and its correlation with treatment methods and clinical laboratory indicators. **Materials and Methods:** Using the CRC cases report form of TCM, 760 CRC patients with TCM four diagnosis information, western medicine treatment information and clinical laboratory indicators were collected, and TCM syndromes distribution in CRC were summarized. The correlation between TCM syndrome type and western medicine treatments, clinical laboratory indicators such as liver and kidney function, immune function, and tumor biomarkers was analyzed. **Results:** In 760 cases of CRC, Spleen deficiency syndrome (SDS, 25%), liver and kidney Yin deficiency syndrome (LKYDS, 13%), LKYDS-SDS, 12%, spleen deficient Qi stagnation syndrome (SDQSS, 10%), and damp heat syndrome (DHS, 9%) were more common TCM syndrome types. LKYDS, SDS, LKYDS-SDS, and SDQSS were significantly distributed under different treatment methods ($P < 0.001$). There was no statistically significant difference in the distribution of immune function and cytokine among the five TCM syndromes ($P > 0.05$), but there was statistically significant difference in the distribution of blood routine, liver and kidney function, and tumor biomarkers ($P < 0.05$). **Conclusion:** LKYDS, SDS, LKYDS-SDS, SDQSS, and DHS were the first five TCM syndromes in CRC. There were the significant correlations between the distribution of TCM syndrome and the clinical laboratory indicators, and the distribution of TCM syndromes was affected by surgery, radiotherapy, and chemotherapy.

Keywords: Clinical laboratory indicators, colorectal cancer, traditional Chinese medicine syndrome distribution, treatment methods

Introduction

Colorectal cancer (CRC) refers to malignant tumors that occur in the colon and rectum. As one of the most common malignant tumors of the digestive system in China, its morbidity and mortality increase gradually year-by-year with the improvement of people's living standards and lifestyle changes.[1] Traditional Western medicine treatments such as surgery,[2] chemotherapy,[3] and radiotherapy[4] present with the disadvantages of serious trauma, obvious side effects, high recurrence and metastasis rate, susceptible drug resistance, and poor quality of life. However, application of traditional Chinese medicine (TCM) treatment can improve the side effects due to surgery and chemotherapy,[5] inhibit multidrug resistance,[6] prevent recurrence and metastasis,[7] alleviate symptoms and signs, ameliorate quality of life and prolong survival period[8] in clinical practice.

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Under the guidance of TCM theory, clinical treatment for CRC displays its unique superiority characterized by syndrome differentiation and treatment. The syndrome is a summarization of the pathological essence of symptoms and signs at a certain stage.[9] TCM syndrome differentiation is a prerequisite for effective treatment. However, diversification of syndrome classification results in the diversity and complexity of the syndrome differentiation system, further absence of standardization, easy performance, and scientificity on applying TCM.[10] Previous studies show that CRC TCM syndrome patterns are related with clinical stage and disease development.[11] Based on the 760 CRC medical cases, we analyzed the distribution of CRC TCM syndromes, its relationship with different treatments, as well as the correlation between various syndrome patterns and Western medical laboratory indicators to uncover the internal rules, increase the accuracy of TCM syndrome differentiation, and provided a basis for better prediction and response to changes in posttreatment syndromes.

Materials and Methods

Source of clinical cases

The medical cases included in this study were all from the outpatient and inpatient CRC patients in Shuguang Hospital Affiliated to Shanghai University of TCM and Fudan University Shanghai Cancer Center. The diagnostic criteria are based on the Guiding Principles for Clinical Research on New Drugs in TCM (3rd edition).[12]

Inclusion criteria

The clinical diagnosis of CRC is confirmed by cytologic examinations or postoperative pathology. The clinical diagnostic criteria follow the Diagnosis and Treatment Regulations on CRC (2010 Edition) issued by the Ministry of Health of the People's Republic of China.[13] Specifically, (i) clinical stage being Stage I–IV; (ii) aged 18–80 years old; (iii) physical condition scoring[14] such as ECOG from 0 to 2 points, Karnofsky >60 points; (iv) expected survival period >3 months; (v) voluntary to participate in the study and in good compliance; and (vi) clear mind and expression, normal language performance and sensory response, capable of understanding this study and signing informed consent, and being followed up.

Exclusion criteria

Exclusion criteria were as follows: (i) those fail to meet the inclusion criteria; (ii) those with serious heart, kidney, hematopoietic disorders, and other factors affecting drug evaluation; (iii) those with mental disorders; those with digestive tract obstruction; (iv) those took medications beyond specified drugs in this study; and (v) those with poor compliance.

Investigation method

The demographic information, data from the four diagnostic methods including inspection, smelling, inquiry, and pulse-taking and palpation, and objective indexes were collected by TCM liver cancer and CRC case report form. To reduce selective and measurement bias, no judgment of TCM syndrome is given during data collection. In addition, we adopted two assessments: every case was pattern identified by three TCM oncologists in associated chief position; the collected data were assessed by Chi-square test for their consistency, and final judgment was made by a chief TCM oncologist.

Data input and processing

The collected data were entered into the Excel by a specific member or establish a specific database for sorting, screening, and statistics. Chi-square test was used to compare the syndromes distribution by different Western medical treatments. Nonparametric test was used to compare the objective indicators among syndrome patterns. $P < 0.05$ was considered statistically significant.

Results

Syndromes distribution of colorectal cancer

TCM syndrome is a summary of symptoms and signs reflecting the nature of the disease in the development and changes of the disease at a certain stage.[15] According to different composition and compound modes, the TCM syndrome is divided into a composite syndrome (also known as concomitant syndrome) and single syndrome. The composite syndrome refers to two or more disease locations or properties,[16] and the single syndrome also named the basic syndrome indicates only one disease location and property.

Distribution of total syndromes of colorectal cancer

Among 760 CRC cases, spleen deficiency syndrome (SDS) (n = 188, 25%), liver and kidney Yin deficiency syndrome (LKYDS) (n = 101, 13%), LKYDS-SDS (n = 93, 12%), spleen deficient Qi stagnation syndrome (SDQSS) (n = 76, 10%), damp-heat syndrome (DHS) (n = 67, 9%), and NS (n = 62, 8%) took the majority [Figure 1a]. Other single syndrome includes excess heat syndrome (n = 8) and YDS (n = 5, except LKYDS). For other concomitant syndromes, they can be divided into two categories of deficiency and excess types. In the former, they include spleen deficiency (SD) with DHS (n = 14), SD-YDS (n = 12), dual deficiency of Qi and Yin syndrome (n = 8). Besides, the SDS, LKYDS, spleen and kidney Yang deficiency syndrome (SKYDS), Yin deficiency, Qi and blood deficiency syndrome were all classified as deficiency syndromes. In the latter, DHS, excess heat syndrome, blood stasis syndrome, and dampness stagnation syndrome were classified as excess syndromes. The combination of deficiency and excess is called deficiency and excess complex syndrome. In calculation, the distribution laws of TCM syndromes in CRC were deficiency syndrome (n = 565, 74.34%) > excess syndrome (n = 81, 21.32%) > NS (n = 62, 8.16%) > deficiency and excess complex syndrome (n = 52, 6.84%), mainly manifested as deficiency in the spleen, liver, and kidney.

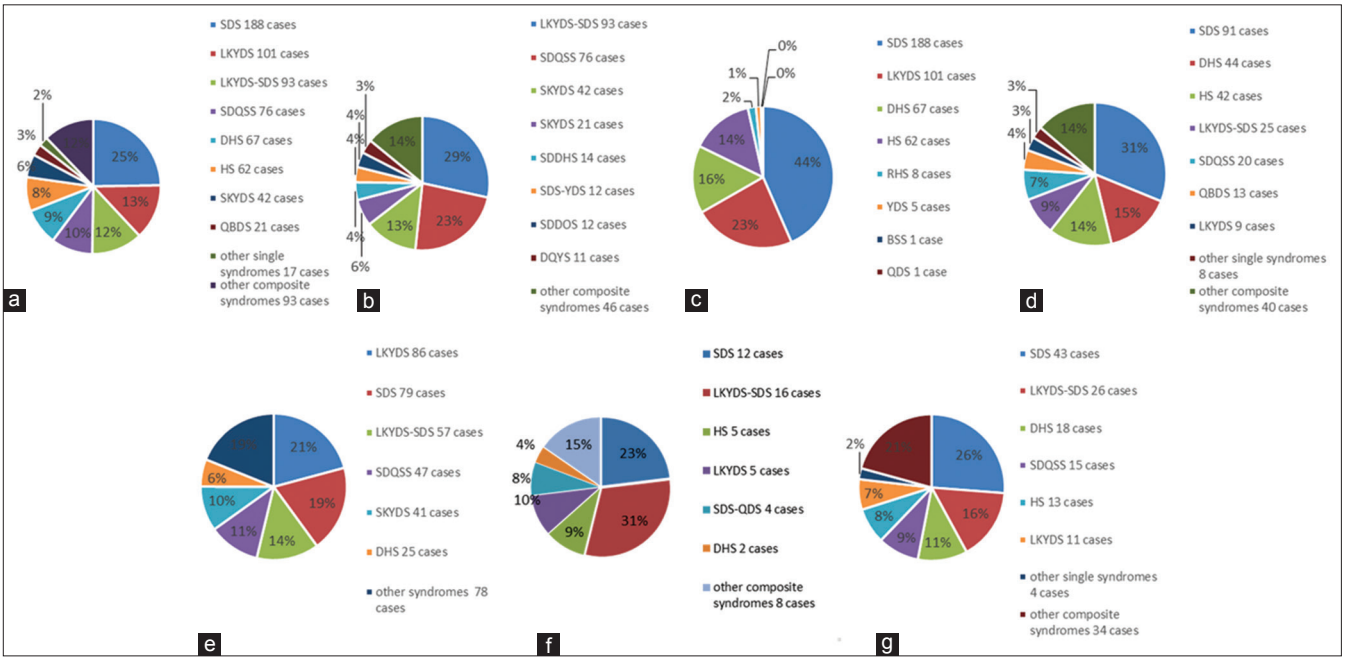

Figure 1: Traditional Chinese medicine syndromes distribution in colorectal cancer. (a) 760 cases of overall distribution; (b) 327 cases of composite syndromes; (c) 433 cases of single syndromes; (d) 292 cases with tumor metastases; (e) 413 cases without western medicine treatment; (f) 52 cases with surgery; (g) 164 cases with postoperative radiotherapy and chemotherapy. Hidden syndrome, Spleen and Kidney Yang deficiency syndrome, Qi and Blood deficiency syndrome, Spleen deficiency-damp heat syndrome, Spleen deficiency and Yin deficiency syndrome, Spleen deficiency and Damp obstruction syndrome, Deficiency of Qi and Yin syndrome, Real heat syndrome, Yin deficiency syndrome, Blood stasis syndrome, Qi deficiency syndrome, Spleen deficiency with Qi deficiency syndrome

Colorectal cancer composite syndrome distribution

Among 327 cases of composite syndromes (43.03%), LKYDS-SDS ($n = 93$, 29%), SD with Qi deficiency syndrome (QDS) ($n = 76$, 23%), SKYDS ($n = 42$, 13%), dual Qi and blood deficiency syndrome ($n = 21$, 6%), SD with DHS ($n = 14$, 4%) accounted for the top five [Figure 1b]. Other concomitant syndromes included liver constraint and SD, liver kidney Yin deficiency combined with damp-heat, and SD with damp-heat. Thus, it can be seen that CRC patients present with frequent SD in composite syndromes, so supplementation of the spleen and stomach, and Qi and blood should be paid great attention.

Colorectal cancer single syndrome distribution

Among 433 cases of single syndrome (56.97%), SDS ($n = 188$, 44%), LKYDS ($n = 110$, 23%), DHS ($n = 67$, 16%), invisible syndrome ($n = 62$, 14%) occupied the top four [Figure 1c], suggesting that the deficiency syndrome is mainly located in the spleen, liver, and kidney and Excess syndrome mostly manifested as DHS with the treatment principle of fortifying the spleen and draining dampness.

Distribution of syndrome patterns in patients with colorectal cancer metastasis

Among 292 CRC metastasis patients (38.42%), SDS ($n = 91$, 31%), DHS ($n = 44$, 15%), NS ($n = 42$, 14%), LKYDS-SDS ($n = 25$, 9%), and SD-QDS ($n = 20$, 7%) occupied the top five [Figure 1d]. Other syndromes include dual Qi and Yin deficiency, SD with damp-heat, and Yin deficiency. It is suggested that patients with advanced CRC metastasis mostly diagnosed as deficiency syndrome, mainly treated by supplementing the liver, spleen and kidney, assisted by dispelling and eliminating damp-heat to reinforce healthy Qi and dispel pathogen.

Characteristics of syndrome distribution after different treatments for colorectal cancer

Previous studies found that surgery,[17,18] chemotherapy[19,20] and other treatments all have impacts on the distribution of CRC syndromes. Here, we further analyzed the distribution of syndromes in CRC patients after different treatments, to detect the rules between syndrome pattern and treatment.

General data

Comparisons of the clinical characteristics of the five major syndromes including SDS, LKYDS, LKYDS-SDS, SDQSS, DHS, and Invisible syndrome (no obvious symptoms and signs, NS) were shown in Table 1. Chi-square test and nonparametric test results showed that there was no significant difference in gender, age, differentiated degree, or clinical stage of each syndrome pattern, which was comparable (all $P > 0.05$).

Syndrome distribution without Western medicine treatment

Among 413 CRC cases without Western medicine treatment, LKYDS ($n = 86$, 20.82%), SDS ($n = 79$, 19.13%), LKYDS-SDS ($n = 57$, 13.80%), SDQSS ($n = 47$, 11.38%), SKYDS ($n = 41$, 9.93%), and DHS ($n = 25$, 6.05%) accounted

Table 1: Comparison of clinical features in colorectal cancer with five major traditional Chinese medicine syndromes

Clinical features	Clinical classification	LKYDS	SDS	LKYDS-SDS	SDQSS	DHS	*P*
Number of cases		101	188	93	76	67	
Male/female (*n*)		69/32	124/64	63/30	51/25	51/16	0.658
Age (mean/year)		61.55±10.86	61.74±10.44	63.29±10	61.47±7.89	65.08±8.07	0.0531
Position	Transverse colon	5	2	3	1	2	0.776
	Lower colon	2	9	1	5	3	
	Ascending colon	16	29	17	10	9	
	Rectum	41	84	40	35	30	
	Sigmoid colon	19	33	16	15	13	
	Cecum	18	31	16	10	10	
Differentiation degree	Low	16	36	18	10	8	0.970
	Medium-low	8	10	8	2	7	
	Medium	55	74	51	55	32	
	High-medium	4	14	2	1	7	
	High	18	44	14	8	13	
Clinical stage	I	5	8	2	2	3	0.927
	II	42	85	41	38	24	
	III	50	90	47	34	36	
	IV	4	5	3	2	4	

LKYDS: Liver and kidney Yin deficiency syndrome, SDS: Spleen deficiency syndrome, SDQSS: Spleen deficient Qi stagnation syndrome, DHS: Damp heat syndrome

for a large proportion [Figure 1e]. Other syndromes include NS (n = 21), SD and dampness (n = 8), and dual deficiency of Qi and Yin (n = 2).

Distribution of postmortem syndrome

Of the 760 CRC patients, only 52 underwent surgery but without radiotherapy and chemotherapy, and their postoperative syndromes were summarized as follows: the SDS (n = 12, 23%), LKYDS-SDS (n = 16, 31%), NS (n = 5, 9%), and LKYDS (n = 5, 9%) took the majority [Figure 1f]. Other concomitant syndromes included SD and dampness, SD with Yin deficiency, SD and Qi stagnation.

Syndrome distribution after radiotherapy and chemotherapy after surgery

Among 164 CRC patients performed with radiotherapy and chemotherapy after surgery, those identified as SDS (n = 43, 26%), LKYDS-SDS (n = 26, 16%), DHS (n = 18, 11%), SD combined with QDS (n = 15, 9%), and NS (n = 13, 8%) occupied the top five [Figure 1g]. Other single syndromes included excess heat, Qi deficiency, and Yin deficiency. Moreover, other concomitant syndrome covered Qi and blood deficiency, dual Qi and Yin deficiency, and SD and damp-heat.

Influence of Western medicine treatment on syndrome distribution

Further, we explored the impact of Western medicine treatment on syndrome distribution. As shown in Table 2, significant differences were displayed in the overall distributions of CRC identified as LKYDS, SDS, LKYDS-SDS, SDQSS, and DHS after treatment without involvement of Western medicine, surgery, and radiotherapy/chemotherapy ($P < 0.001$). There were statistical differences in LKYDS, SDS, LKYDS-SDS, and DHS after different treatments in the two groups ($P < 0.001$).

Relationship between syndromes and clinical laboratory indicators of colorectal cancer

Next, we further explored the relationship between CRC identified as LKYDS, SDS, LKYDS-SDS, SDQSS, DHS, and common clinical indicators such as liver and kidney function, immunity, tumor markers, and cytokines [Table 3].

The blood routine indicators such as platelet (PLT) and hemoglobin (HB) were significantly different among the five syndrome patterns ($P < 0.05$). The PLT in DHS and SDQSS and HB in the DHS were all lower than those of the corresponding indicators in the LKYDS and LKYDS-SDS with statistical significance ($P < 0.05$).

Liver and kidney function indicators such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine (SCr), total bilirubin (TBIL), and alkaline phosphatase (ALP) displayed statistical differences in the overall distribution among the five syndrome patterns ($P < 0.05$). A significant difference was displayed in the overall distribution of gamma-glutamyl transpeptidase (GGT) among the five syndromes ($P < 0.001$). ALT was higher in SDQSS compared with that in the LKYDS and LKYDS-SDS while AST in the DHS was lower than that of the LKYDS and AST was higher in the SDQSS than that of the LKYDS, SDS, and LKYDS-SDS. The BUN was higher in the SDQSS compared with that in the LKYDS-SDS. The SCr distribution in the SDQSS was lower than that in the SDS. The TBIL distribution in the SDQSS was lower than that in the LKYDS, SDS, and LKYDS-SDS. The distributions of ALP and GGT in the SDQSS were both higher than those of the LKYDS and SDS with significant differences ($P < 0.05$). The GGT distribution was higher in the SDQSS than the LKYDS-SDS with significant difference ($P < 0.001$).

Table 2: Traditional Chinese medicine syndromes distribution in colorectal cancer after western medicine treatment

TCM syndrome	Cases number	No western medicine treatment (413 cases)	Surgery (52 cases)	Radiotherapy/chemotherapy (51 cases)	Surgery + radiotherapy/ chemotherapy/target therapy (146 cases)	≥3 treatment methods (98 cases)	*P*
LKYDS	101	86 (20.82)	5 (9.62)	4 (7.84	3 (2.05)	3 (3.06)	<0.001
SDS	188	79 (19.13)	12 (23.08)	6 (11.76)	59 (40.41)	32 (32.65)	<0.001
LKYDS-SDS	93	57 (13.80)	16 (30.77)	1 (1.96)	14 (9.58)	5 (5.10)	<0.001
SDQSS	76	47 (11.38)	4 (7.69)	2 (3.92)	17 (11.64)	6 (6.12)	0.253
DHS	67	25 (6.05)	2 (3.85)	2 (3.92)	25 (17.12)	13 (13.27)	<0.001

LKYDS: Liver and kidney Yin deficiency syndrome, SDS: Spleen deficiency syndrome, SDQSS: Spleen deficient Qi stagnation syndrome, DHS: Damp heat syndrome

Table 3: The correlation with traditional Chinese medicine syndromes distribution in colorectal cancer and clinical laboratory indicators ($\bar{x}\pm S$)

Clinical lab indicators	LKYDS	SDS	LKYDS-SDS	SDQSS	DHS	*P*
Blood routine (cases)	52	55	42	65	13	
WBC	7.58±9.04	8.4±5.54	8.48±10.3	10.85±9.17	10.41±8.88	0.104
RBC	4.31±0.64	4.31±1.04	4.18±0.53	4.41±1.3	4.08±0.74	0.581
PLT	203.97±284.76$^{\#,\S}$	155.33±69.83	171.37±80.45$^{\#,\S}$	132.93±73.36§,‡	119.4±62.19§,‡	0.012*
HB	120.71±31.84$^{\#\#}$	117.28±34.28	118.31±35.62$^{\#}$	89.05±54.9‡,§§	99.73±43.11	0.019*
Liver and kidney function (cases)	29	37	28	40	11	
ALT	21.82±12.4$^{\S,\#}$	21.79±15.53$^{\#}$	21.45±19.07	25.65±48.85†,§	12.51±11.91§	0.024*
AST	26±10.25$^{\#}$	25.72±10.93$^{\#}$	28.97±30.54$^{\#}$	72.93±170.27§,†,‡	26.27±13.49	0.001*
BUN	11.11±24.11	6.9±11.63	4.89±1.21‡	57.58±91.02$^{\#}$	29.33±43.72	0.018*
SCr	63.1±15.86	71.57±20.63$^{\#}$	61.13±12.8	59.15±40.5†	57.06±30.32	0.018*
TBIL	14.63±5.85$^{\#}$	14.97±8.03$^{\#}$	16.86±11.21$^{\#}$	11.31±7.02§,†,‡	11.64±5.96	0.035*
CB	3.9±3.66	4.62±3.96	5.21±4.62	4.07±2.58	3.98±2.05	0.526
ALB	42.26±7	41.34±7.11	40.55±6.75	47.73±17.79	41.88±18.3	0.298
ALP	91.28±26.19$^{\#}$	111.59±61.21$^{\#}$	93.1±31.36$^{\#}$	131.521.3621‡,§,†	96.73±44.64	0.027*
GGT	44.77±38.75$^{\#}$	49.96±60.84$^{\#}$	42.12±61.43$^{\#\#}$	89.49±61.43‡‡,§,†	58.62±56.12	<0.001**
UA	320.92±73.17	317.25±79.74	297.07±64.44	347.52±117.67	335.65±80.59	0.433
Immune function (cases)	41	40	37	52	12	
CD3	60.04±11.35	62.33±12.62	61.63±14.14	62.07±12.33	55.74±9.41	0.597
CD4	37.62±9.33	35.16±9.29	35.53±8.32	34.94±11.43	35.26±4.88	0.860
CD4/8	1.6±0.97	1.27±0.59	1.41±0.61	1.33±0.81	1.26±0.38	0.539
NK	19.52±7.81	20.03±11.05	20.47±12.82	19.27±10.32	23.1±8.91	0.738
Tumor biomarkers (cases)	48	42	42	86	11	
AFP	4.31±8.44$^{\#,\S\S}$	4.56±4.85§	2.96±1.32$^{\#,\S\S}$	17.24±90.9‡,§	18.75±24.69‡‡,§§,†	<0.001**
CEA	19.8±40.82	85.69±219.04	61.12±181.41	28.43±81.53	5.52±8.43	0.792
CA199	28.74±79.42	89.1±232.28	26.47±45.71	38.3±111.86	71.9±108.22	0.273
Cytokine (cases)	12	15	11	17	6	
IL-2	100.34±30.5	111.38±42.9	106.37±30.54	110.37±40.74	118.57±73.7	0.928
IL-10	8.16±10.94	7.83±5.6	5.29±0.95	9.49±12.58	5±0	0.502
IL-6	3.81±5.29†	8.03±8.93$	5.35±7.03	15.76±41.16	10.34±17.93	0.057
IL-8	11.74±9.72	24.34±19.89	105.48±282.14	41.65±72.03	37.7±37.01	0.135
TNF-α	12.22±9.35	12.47±6.07	10.16±4.26	14.27±10.67	10.6±1.81	0.632
VEGF	177.18±178.19	153.96±56.27	136.81±46.51	140.64±84.32	161.3±104.19	0.940

*Overall distribution, $P<0.05$, **Overall distribution, $P<0.001$, §Versus LKYDS, $P<0.05$, †Versus SDS, $P<0.05$, ‡Versus LKYDS-SDS, $P<0.05$, $^{\#}$Versus SDQSS, $P<0.05$, §Versus DHS, $P<0.05$, $^{\S\S,\dagger\dagger,\ddagger\ddagger,\#\#,\S\S}$Versus LKYDS, SDS, LKYDS-SDS, SDQSS and DHS respectively, $P<0.001$. LKYDS: Liver and kidney Yin deficiency syndrome, SDS: Spleen deficiency syndrome, SDQSS: Spleen deficient Qi stagnation syndrome, DHS: Damp heat syndrome, WBC: White blood cells, RBC: Right blood cells, PLT: Platelet, HB: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, SCr: Serum creatinine, TBIL: Total bilirubin, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transpeptidase, AFP: Alpha-fetoprotein, CEA: Carcinoembryonic antigen, IL: Interleukin, NK: Natural killer, CB: Conjugated bilirubins, ALB: Albumin, TNF: Tumor necrosis factor, VEGF: Vascular endothelial growth factor, UA: User agent

There was no significant difference in the overall distribution of tumor markers of carcinoembryonic antigen (CEA) and carbohydrate antigen among the five syndrome patterns (all $P > 0.05$), but interestingly, the distribution of

alpha-fetoprotein (AFP) was displayed a significant difference among the five syndromes in CRC ($P < 0.001$). Specifically, AFP in the SDQSS was higher than that of the LKYDS and LKYDS-SDS. The distribution of AFP in the DHS was higher than that of the SDS with a significant difference ($P < 0.05$). The distribution of AFP in the DHS was significantly higher than that of the LKYDS and LKYDS-SDS ($P < 0.001$).

There was no significant difference in the overall distribution of cytokines among the five syndrome patterns ($P > 0.05$), but after intergroup comparisons, the distribution of interleukin-6 (IL-6) in the LKYDS was less than that in the SDS ($P < 0.005$). The overall distributions of immune function indicators containing CD3, CD4, CD4/8 and natural killer among the five syndrome patterns were not displayed statistically ($P > 0.05$).

Discussion

To clarify the distribution of TCM syndromes in CRC, we analyzed the four diagnostic data from 760 recruited CRC patients' cases in the Shuguang Hospital Affiliated to Shanghai University of TCM and Fudan University Shanghai Cancer Center and found the SDS, LKYDS, LKYDS-SDS, SDQSS, and DHS are five common types in the clinic. The characteristics of the overall distribution of is deficiency syndrome > excess syndrome > invisible syndrome > deficiency and excess complex syndrome mainly manifested as liver, spleen and kidney deficiency. It is suggested that CRC treatment should focus on fortifying the spleen, supplementing the kidney, and enriching the liver, meanwhile, method to dispel dampness and clear heat should not be neglected due to common DHS. For those CRC patients with metastasis, the distribution of the SDS, DHS, OS, and LKYDS-SDS took the majority indicating LKYDS is occurred frequently in advanced CRC patients. Besides, the SD and damp-heat are also common pathogens, implicating the treatment principle of CRC should focus on supplementing, and pathogen dispelling acts as an assistance to avoid damaging the healthy Qi.

According to the statistical analysis of the distribution of five major syndrome patterns using different treatments, the distribution of LKYDS, SDS, and LKYDS-SDS differed significantly treatments ($P < 0.001$). The distribution of the above-mentioned three syndrome after surgery, or radiotherapy/chemotherapy was less than that of treatment without Western medicine, but the distribution of these syndromes in the surgery plus radiotherapy/chemotherapy increased compared with that of treatment without Western medicine, suggesting that surgery, or radiotherapy/chemotherapy can reduce the clinical manifestations of SDS or LKYDS in CRC patients, but postoperative radiotherapy/chemotherapy will damage the healthy Qi. Here, multicenter research is warranted to further increase the sample size to confirm the research results of this study, and to re-examine the significance of radiotherapy and chemotherapy in CRC patients, and may provide a novel evidence for TCM syndrome differentiation of CRC.

To date, the common acknowledgment of the syndrome patterns of CRC in the top five is internal accumulation of DHS, internal obstruction of stasis and toxins syndrome, Dual deficiency of Qi and blood syndrome, SKYDS, and LKYDS. In excess syndrome, damp-heat, stasis, toxins are the main pathogenic factors, while in deficiency syndrome, Qi and blood insufficiency, and liver, spleen, and kidney depletion are the main issues. After surgery and chemotherapy, excess syndrome reduced, while deficiency increased. Our results partially proved that DHS and LKYDS are in the top five and damp-heat and liver, spleen, and kidney deficiency are the main syndromes. Differences are the other three syndromes including internal obstruction of stasis and toxins, Dual deficiency of Qi and blood, and Spleen and kidney Yang deficiency in the former, while SDS, LKYDS-SDS, and SDQSS in our current study. Another great disparity is deficiency syndrome increase after surgery or chemotherapy in the former, while it is decreased in our study.[21]

In the current research, scholars have pointed out some correlations between clinical laboratory indicators such as liver and kidney function,[22] immune function,[23] tumor markers,[24] and cytokines[25] in CRC, and syndrome patterns, but the results are quite different due to region, culture, and lifestyle. No multicenter, large-scale research has been conducted. We explored the relationship between five typical syndrome types of CRC and the above-mentioned clinical laboratory indicators and found that the overall distribution of an immune function of CRC does not differ statistically among these five syndromes ($P > 0.05$). The distribution of PLT in the DHS and SDQSS, HB in the DHS, and TBIL in the SDQSS were all lower compared with those in the LKYDS and LKYDS-SDS. The distributions of TBIL and SCr in the SDQSS are lower than those of the SDS. The distributions of GGT, AST, and ALP in the SDQSS were more than those of the LKYDS and SDS. The distributions of ALT and AFP in the SDQSS were higher compared with those of the LKYDS and liver and LKYDS-SDS. The distributions of AST and BUN in the SDQSS were higher compared with those of the LKYDS-SDS. The distribution of ALT in the DHS is higher than that of the LKYDS. In the DHS, the distribution of AFP is higher than that of the SDS. The differences mentioned above all differ significantly ($P < 0.05$). The distribution of GGT in the SDQSS was higher than that of the LKYDS. The distribution of AFP in the DHS is more than that of the LKYDS and LKYDS-SDS with statistical significance ($P < 0.001$). There was no significant difference in the overall distribution of cytokines among the five syndrome patterns ($P > 0.05$), but the distribution of IL-6 in the LKYDS was less than that in SDS ($P < 0.005$). All of the above results suggest that clinical laboratory indicators may provide reference for TCM syndrome differentiation.

Conclusion

To sum up, our research found that the distributions of the SDS, LKYDS, LKYDS-SDS, SDQSS, and DHS were in the top five among these 760 CRC cases. These syndrome distributions were closely correlated with clinical laboratory indicators such

as blood routine, liver and kidney function, and tumor markers. However, it is not yet clear that the expression of a certain syndrome is the highest or lowest among all the TCM syndromes. We are not currently able to make syndrome differentiation based on only one clinical laboratory indicator. Perhaps TCM syndromes can be discriminated by a comprehensive analysis of several clinical laboratory indicators. Moreover, Western medicine surgery, radiotherapy/chemotherapy/targeted therapy can affect the distribution of CRC syndromes.

Prospects

Clarifying the TCM syndrome changes in CRC patients is beneficial for accurate selection of therapeutic mode and medication in clinical practice, and of great significance to improve the clinical efficacy of CRC. However, no standardized classification criteria for CRC syndromes have been issued, and the objectification of syndrome differentiation is quite urgent. In our study, we find a certain correlation between the TCM syndromes of CRC and the commonly used indicators in clinic, which can be further explored. In addition, the construction of scientific and objective quantitative indicators of CRC syndrome requires a new approach, such as omics related with syndromes using high-throughput biomarker screening technology to detect the syndrome biomarkers.[26] What's more, based on the large quantity of electronic medical records, select the appropriate data mining methods such as association rules, classification, and clustering[15,27] to carry out a broader, multi-center, multidisciplinary, large-sample phenotype research on TCM syndromes aiming at formulating a unified and standardized diagnostic criteria for CRC. Finally, we must further implement individualized precise diagnosis and precise treatment[28] to increase the overall therapeutic effectiveness rate, only then, we can achieve a breakthrough and new development in the field of TCM diagnosis and treatment on CRC.

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Conflicts of interest

There are no conflicts of interest.

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