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Study on the dialectical criterion of liver cirrhosis and liver cancer syndrome of spleen deficiency dampness and stagnation based on cohort study and double frequency weight scissors algorithm

Yizhe Tong[1,a,*]

[1]*Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712000, China*
[a]*947799323@qq.com*
[*]*Corresponding author*

Abstract: *In order to analyze the syndrome elements characteristics of spleen deficiency dampness stagnation syndrome in liver cirrhosis and liver cancer, and establish the syndrome differentiation standard of spleen deficiency dampness stagnation syndrome in liver cirrhosis and liver cancer. We enrolled a total of 1263 inpatients with hepatitis B cirrhosis and liver cancer from 8 hospitals including Shaanxi Traditional Chinese Medicine Hospital. TCM syndrome types were identified by syndrome differentiation and double-level frequency weight scissors algorithm, and the characteristic syndromes of spleen deficiency dampness and stagnation syndrome were calculated by logistic regression analysis. According to the inclusion criteria and exclusion criteria, the syndromes of spleen-deficiency and dampness-stagnation syndrome in 1263 medical records were extracted and analyzed one by one, and the characteristic syndromes were obtained: dizziness (OR=4.903), insomnia (OR=4.035); Characteristics of spleen deficiency and dampness in decompensated liver cirrhosis: yellow and white coat on tongue (OR=74.51), pulse number (OR=11.809), epigastric discomfort (OR=2.530); Characteristics of spleen deficiency dampness and stagnation syndrome of liver cancer: delayed pulse (OR=307.305), mobile dullness (OR=38.781), oliguria (OR=29.425), ascites (OR=4.533), splenomegasis (OR=2.112), (P<0.05). Resultly, it is thus clear that double frequency weight scissors algorithm and Logistic regression analysis have good diagnostic efficacy for the study of syndrome differentiation standard of spleen deficiency dampness and stagnation syndrome of liver cirrhosis and liver cancer.*

Keywords: *hepatitis B cirrhosis; Cancer of the liver; Syndrome of dampness and stagnation of spleen deficiency; Logistic regression analysis; Syndrome differentiation standard*

1. Introduction

There is a close relationship between chronic viral hepatitis B, post-hepatitis B cirrhosis and primary hepatocellular carcinoma, and in a certain sense, it has been recognized as a different stage of development of a disease, that is, the three steps of hepatitis B [1]. However, there are few studies on the differentiation standards of spleen deficiency and moisture retardation at different stages, and there are different differentiation methods among doctors, and it is difficult to avoid the influence of subjective factors in the differentiation process [2]. Therefore, based on cohort research, double-layer frequency weight scissor algorithm and logistic regression analysis, relevant work has been carried out, and the report is as follows, please correct any inappropriateness.

2. Information and methodology

2.1. Data sources

In 2013~2020, 634 hospitalized cases of hepatitis B cirrhosis (117 cases in compensated period and 517 cases in decompensation stage), 629 hospitalized cases of primary liver cancer, a total of 1263 cases were selected for study, including the First Affiliated Hospital of the Fourth Military Medical University, the First Affiliated Hospital of Shaanxi Military Medical University, the Department of

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Gastroenterology and Oncology of the Fourth Military Medical University, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Shaanxi Provincial Hospital of Traditional Chinese Medicine, and 629 hospitalized cases of primary liver cancer.

2.2. Diagnostic criteria for the study subject

Diagnostic criteria for patients with hepatitis B cirrhosis: Chronic hepatitis B meets the "Guidelines for the Prevention and Treatment of Chronic Hepatitis B" formulated by the Hepatology Branch and the Infectious Diseases Branch of the Chinese Medical Association in 2015 [2], and patients with hepatitis B cirrhosis meet the diagnostic criteria in the 2014 Expert Consensus on the Diagnosis and Treatment of Hepatitis B Cirrhosis [3].

Diagnostic criteria for patients with primary liver cancer: (1) The patient was diagnosed with primary liver cancer by clinical imaging and cytopathology; (2) Patients admitted with primary liver cancer as the first diagnosis.

Diagnostic criteria of TCM evidence: Refer to Professor Zhu Wenfeng's "Dialectics of Evidence" [4]. According to the basic characteristics of the evidence and clinical practice, the evidence is divided into 50 items. Among them, there were 13 pathological elements and 37 pathological elements, and the morphemes were identified after weighted summation floating threshold operation.

2.3. Inclusion and exclusion criteria for study participants

Inclusion Criteria: All patients meet the diagnostic criteria described above in the Guidelines for the Prevention and Treatment of Chronic Hepatitis B, have pathology or imaging confirmation of cirrhosis or liver cancer, and are admitted to hospital with hepatitis B cirrhosis or liver cancer as the first diagnosis.

Exclusion Criteria: (1) Those who do not meet the above criteria; (2) Other causes such as HCV infection, alcohol, drugs, autoimmune diseases, schistosomiasis, metabolic diseases, etc.; (3) Other malignant tumors metastasized to the liver; (4) Lack of four diagnostic information and more important biological index information; (5) Exclude patients with related heart, lung, kidney, and other important organ dysfunctions; (6) People with mental illness.

2.4. Develop a questionnaire

Table 1: The main study variables

	items
Psychiatric symptoms	Delirium, five upset, insomnia, forgetfulness, emotional depression, irritability
The main symptoms of the site of the disease	Shortness of breath, cough, chest tightness, polydipsia, abdominal pain, bloating, dull stomach pain
Taste and texture	Loss of appetite, dry mouth, bitter mouth, sticky mouth, hiccups, vomiting, nausea
Head, eyes, officials, limb symptoms	Dizziness, dry eyes, chills, cold limbs, and heavy head and body
Constitutional symptoms	Fever, self-sweating, night sweats, poor spirits
Toilet	Low urination, yellow urine, frequent nocturia, constipation, loose stools, melena, blood in the stool
Signs	Chest tightness, lack of concentration, yellow complexion, pale complexion, liver disease appearance, weight loss, yellow sclera, pale tarsal conjunctiva, enlarged liver, enlarged spleen, abdominal tenderness, abdominal mass, abdominal distension, varicose veins of the abdominal wall, subxiphoid tenderness, mobile dullness, lower extremity edema, palmar erythema, spider angiomas, pale nails
Tongue diagnosis	Petechiae can be seen on the surface of the tongue, fat tongue, thin tongue, twisted sublingual veins, total tongue obscurity, light tongue, red tongue, white tongue, yellow tongue, yellow and white tongue, tongue peeling
Pulse diagnosis	Floating, sinking, late, counting, string, fine, solid, large, tight, virtual, slippery, flood
Lab metrics	Liver function(ALT,AST,ALP,GGT,ALB,TBIL,DBIL,IBIL);Blood routine(WBC,RBC,HGB,PLT);Coagulation function(PT,APTT,FIB,DD);Tumor markers(AFP,CEA,CA125,CA199)
Imaging tests	CT,MRI,B-scan

Case selection in accordance with inclusion and exclusion criteria, using the empirical scale compilation method, the symptom indicators for inclusion were selected, combined with relevant TCM literature, through on-site investigations of 574 hospitalized cases, determine the pool of TCM four

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diagnosis information entries, using this as background information to conduct the Delphi Law questionnaire, and include relevant laboratory indicators and imaging data, design and formulate case information collection forms for patients with hepatitis B cirrhosis and liver cancer. (Table 1)

2.5. Data entry and reconciliation

The recovered questionnaire was established in Excel, and the data was entered in double copies, and the inconsistent items after entry were checked and corrected; classify and assign their symptoms and signs by reference to the Quality of Life Scale, and divide them into none, mild, moderate, and severe (assigned as 0, 1, 2, 3); In addition, tongue image, pulse image, and imaging results are indicated by 0 and 1, respectively, and the laboratory indicators are subject to specific values. SPSS26.0 software was used to classify the data, and 10% of the cases were randomly selected in the later stage, and the four diagnosis indicators of some Chinese medicine were repeatedly investigated.

2.6. Double-layer frequency weight scissor algorithm

Establish SPSS.26 data files, classify data, process data according to the requirements of double-layer frequency weight scissor algorithm and quantitatively assign value. Severe or severe symptoms with a weight × 1.5; moderate symptoms with a weight × 1.0; mild symptoms with a weight × 0.7. Generally, 14 is used as the general threshold, that is, the sum of the contribution of each symptom to each factor reaches or exceeds 14, and these factors can be diagnosed, that is, the diagnosis of the factor is established. And according to the sum of the weights, distinguish the weight of the testimony, That is, if the total weight is < 14, the diagnosis of the factor cannot be established; The total weight is 14~20, and the certificate belongs to I. (first-class, lighter); The total weight is 21~30, and the certificate belongs to II. (secondary, obvious); If the total weight is greater than 30, the element belongs to III. (grade III, severe).

2.7. Statistical analysis

SPSS26.0 software was used to statistically analyze the basic information of patients by chi-square test; Using binary logistic regression analysis (Forward LR), taking the symptom type as the dependent variable, and taking the symptoms, signs, tongue, pulse and laboratory tests that constitute the symptom type as independent variables (the dichotomous variable with "asymptomatic" as the dumb variable), logistic regression analysis was carried out, and the relevant laboratory indicators affecting spleen deficiency and hygrosis were calculated. GraphPad was used to plot the forest to compare the characteristic syndrome OR values of spleen deficiency hysteresis at different stages.

3. Results

3.1. Distribution of splenic deficiency by gender and age

After the collection of 1263 patients were treated by double-layer frequency weight scissor algorithm, 6 patients (5.1%) were obtained with spleen deficiency and hysteresis in the compensated stage of liver cirrhosis, 10 cases (1.9%) in the decompensated stage, and 25 cases (4%) in liver cancer, as shown in Table 2.

Table 2: Distribution of spleen deficiency hygrosis in general data (cases)

		Compensated stage of cirrhosis (6 cases)	Decompensated cirrhosis (10 cases)	Liver Cancer (25 cases)
gender	male	6	8	16
	Female	0	2	9
Average age	$\bar{\chi}\pm s$	45.67±7.03	50.50±8.73	52.12±10.36

3.2. The incidence of spleen deficiency and its relationship with age and gender

According to the chi-square test, there was no significant significance in the sex distribution of spleen deficiency hysteresis (P>0.05), as shown in Table 3.

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Table 3: Gender distribution (cases)

	Spleen deficiency and hygrosis (Yes/No)	Male	Female	P	χ^2
Compensatory phase of cirrhosis	Yes	6	0	.324	.974
	No	82	30		
Decompensation of cirrhosis	Yes	8	2	.581	.305
	No	337	169		
Hepatocellular carcinoma	Yes	16	9	.224	1.480
	No	452	152		

After the 2×C chi-square test, there was no significant significance in the age distribution of spleen deficiency hygrosis (P>0.05), as shown in Table 4.

Table 4: Distribution of age groups (cases)

		Compensatory phase of cirrhosis		Decompensation of cirrhosis		Hepatocellular carcinoma	
	Spleen deficiency and hygrosis	Yes(8)	No(109)	Yes(52)	No(465)	Yes(79)	No(550)
Age	< 41 years old	1	23	1	61	3	53
	41-50 years old	4	44	3	159	8	129
	51-60 years old	1	27	5	155	9	188
	61-70 years old	0	15	1	103	4	176
	>70 years old	0	3	0	28	1	58
	Test statistics	$\chi2$=2.189 P=0.701		$\chi2$=2.302 P=0.680		$\chi2$=3.962 P=0.411	

3.3. Characteristic symptoms of spleen deficiency and hygrosis

3.3.1. Spleen deficiency and hygrosis in compensated stage of cirrhosis

There was no significant difference between the basic conditions of spleen deficiency and non-spleen deficiency in the compensated stage of liver cirrhosis, and the characteristic symptoms of the two groups were analyzed by binary logistic regression analysis. The results showed that the incidence of dizziness (OR=4.035, 95% CI: (1.141, 14.266), P=0.030) and insomnia (OR=4.903, 95% CI: (1.419, 16.945), P=0.012) in the spleen deficiency hysteresis group was higher than that in the non-splenic deficiency hysteresis group, and the difference was statistically significant. (Table 5)

Table 5: Logistic regression analysis of spleen deficiency and hysteresis in the compensatory period

	B	S.E.	Wald	df	Sig	Exp(B)	EXP(B) 95%C.I.	
							Lower	Upper
Insomnia	1.590	.633	6.314	1	.012	4.903	1.419	16.945
Dizziness	1.395	.644	4.687	1	.030	4.035	1.141	14.266

3.3.2. Decompensated spleen deficiency in cirrhosis

There was no significant difference between the basic conditions of spleen deficiency and non-spleen deficiency and hygrosis in the decompensated stage of liver cirrhosis, and the characteristic symptoms of the two groups were analyzed by binary logistic regression analysis. The results showed that the incidence of gastric discomfort (OR=2.530, 95% CI: (1.210, 5.289), P=0.014), yellow and white tongue (OR=74.510, 95% CI) and yellow and white tongue (OR=74.510, 95% CI) in the spleen deficiency hysteresis group was higher than that in the non-splenic deficiency hysteresis group. The difference was statistically significant. (Table 6)

Table 6: Logistic regression analysis of spleen deficiency and hysteresis in the compensatory period

	B	S.E.	Wald	df	Sig	Exp(B)	EXP(B) 95%C.I.	
							Lower	Upper
Upset stomach	.928	.376	6.088	1	.014	2.530	1.210	5.289
The tongue is yellowish and white	4.311	1.479	8.499	1	.004	74.51	4.107	1351.758
Fast pulse rate	2.469	.776	10.126	1	.001	11.809	2.581	54.008

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3.3.3. Liver cancer, spleen deficiency and stagnation

There was no significant difference in the basic conditions of spleen deficiency and non-spleen deficiency and hygrosis in liver cancer, and the characteristic symptoms of the two groups were analyzed by binary logistic regression analysis. Results showed that splenic deficiency hygrosis group had oliguuria (OR=29.425, 95% CI: (5.817, 148.854), P<0.001), splenomegaly (OR=2.112, 95% CI: (1.009, 4.419), P=0.047), mobile dullness (OR=38.781, 95% CI: (6.957, 216.168), P<0.001), and delayed pulse rate (OR=307.305, 95% CI: (6.084,15523.066), P=0.004), ascites (OR=4.533, 95% CI: (2.021, 10.170), P<0.001) were higher than those in the non-splenic deficiency hysteresis group, and the difference was statistically significant. (Table 7)

Table 7: Logistic regression analysis of spleen deficiency and hysteresis in the compensatory period

	B	S.E.	Wald	df	Sig	Exp(B)	EXP(B) 95%C.I.	
							Lower	Upper
Low urine output	3.382	.827	16.718	1	.000	29.425	5.817	148.854
Enlarged spleen	.747	.377	3.936	1	.047	2.112	1.009	4.419
Mobility dullness	3.658	.877	17.412	1	.000	38.781	6.957	216.168
Slow pulse rate	5.728	2.001	8.192	1	.004	307.305	6.084	15523.066
Ascites	1.511	.412	13.443	1	.000	4.533	2.021	10.170

4. Discussion

4.1. Characteristic symptoms of spleen deficiency and hygrosis

In this study, 41 patients with spleen deficiency and hygrosis in 1263 patients, accounting for 3.2%, 6 patients (5.1%) with splenic deficiency and hygrosis in the compensated stage of liver cirrhosis, 10 cases (1.9%) in the decompensated stage, and 25 cases (4%) with liver cancer, and the incidence of age, sex and spleen deficiency and hygrosis in different advanced stages was not statistically significant (P>0.05). The Digestive System Diseases Professional Committee of the Chinese Association of Integrative Medicine [5] identified cirrhosis as evidence of liver qi depression, internal obstruction of water and humidity, evidence of humid heat inclusion, evidence of liver and kidney yin deficiency, spleen and kidney yang deficiency, and blood stasis obstruction. "Internal Medicine of Traditional Chinese Medicine" (9th Edition) [6] divides liver cancer into three types: qi stasis and blood obstruction, blood stasis internal evidence, and positive deficiency stasis syndrome. Professor Ling Changquan [7] identified the evidence types as Qi stagnation, blood stasis, heat, wetness, qi deficiency, blood deficiency, yin deficiency, and yang deficiency through literature collation, clinical investigation, and expert discussion. However, in the process of clinical differentiation and the evolution of the disease, there will be various concurrent evidence and variations, such as the spleen deficiency and hygrosis evidence studied in this paper. With the assistance of the dialectical system, the nature of the disease can be reflected more objectively, accurately and scientifically, so as to show the true characteristics of the disease, so as to improve the accuracy of clinical differentiation and treatment and strengthen the clinical treatment effect [4].

The characteristics of spleen deficiency and hygrosis in the compensatory period were insomnia (OR=4.903) and dizziness (OR=4.035). There are about five reasons why "Medical Sect Must Read" is not sleepy: one is qi deficiency, one is yin deficiency, one is phlegm stagnation, one is water stop, one is stomach discord, water stops wet and stagnant, qi machine is not smooth, yin and yang are not in harmony, so insomnia; Wet evil is yin evil, its sex is heavy turbidity, indwelling in the medium focus to inhibit qi, meridian qi is unfavorable, yang qi is lost, then the head is heavy and drowsy, about vertigo history has the view of "no void and no vertigo", or yin deficiency or qi and blood deficiency, spleen is the source of qi and blood biochemistry, now spleen deficiency qi and blood biochemical lack of source, so see dizziness. Zhou Yang [8] and others believe that although there is still the evil of humid heat in the early stage of liver cirrhosis, the main contradiction is the damage of righteous qi, which is in the stage of the conflict between good and evil, manifested as fatigue, dry mouth, backache, and yellow urine. Reports [9] mention that compensated cirrhosis has no obvious manifestations of liver failure, but may have mild fatigue, decreased appetite, or abdominal distention. Although the main clinical manifestations are different, it is a consensus that the compensated stage of cirrhosis is mild

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and the symptoms are not obvious, so the spleen deficiency and dampness in the early stage of the disease are only seen in insomnia and dizziness.

The characteristics of spleen deficiency and hysteresis in the decompensated stage were yellow and white tongue (OR=74.51), pulse number (OR=11.809), and stomach discomfort (OR=2.530). The yellow and white tongue images and veins indicate that in the process of disease development, wet evil and heat fight together, resulting in the manifestation of moist heat internal resistance in the case of spleen mobilization dysfunction, and humid heat internal resistance is also an important reason for long-term inability to heal liver cirrhosis [10]. The study [8] showed that the decompensated stage of cirrhosis is similar to the compensatory period, and the high-frequency symptoms and signs obtained by cluster analysis include fatigue, dry mouth, dreaminess, backache, knee weakness, blurred vision, and yellow urine, suggesting that substantial damage to organs at this stage leads to dysfunction, so the gasification of Sanjiao is unfavorable, the operation of qi and blood is not smooth, resulting in water not moisturizing, aggregating into water, spleen deficiency and dampness are aggravated than before, and the incidence of ascites in patients with cirrhosis at this stage is also higher than before. Professor Chen Jianjie [11] believes that this disease is mostly caused by external evil injury to the liver, which will affect the spleen over time, and the spleen deficiency cannot be transported, the moisture stops agglomerating in the medium focus, the water and liquid distribution are abnormal, and the spleen deficiency and moisture stagnant evidence are most, and in the decompensation period, the characteristic symptoms are seen with humid heat residence and digestive tract symptoms. Combined with the research and statistics of various doctors, it is not difficult to conclude that at this time, wet evil is prone to heat image, and the symptoms are more severe than in the previous stage, which is consistent with the clinical reality of hepatitis B cirrhosis in the process of progression from compensatory to decompensated stage, complications increase and the condition tends to be complex.

Liver cancer spleen deficiency and hygrosis were characterized by slow pulse rate (OR=307.305), mobile dullness (OR=38.781), low urine output (OR=29.425), ascites (OR=4.533), and spleen enlargement (OR=2.112). "Lingshu Water Expansion" chapter Yun, "The belly is big, and its water has become complete." Press your hand on its abdomen, and rise up with it, like a wrapped in water. ” Mobile dullness and ascites are typical manifestations of wet internal arrest, "Edema due to spleen deficiency can not make water, water stains act rashly", its essence is spleen deficiency. The small urine output and slow pulse rate are due to the internal stop of the wet evil, the weak movement of the qi machine, the imbalance of the three-focal movement, the inability to promote the operation of qi and blood and liquid, the water stop collecting in the abdomen, and it cannot run downward, so the urine output is small, and the blood cannot fill the blood vessels, and the pulse rate is slow. Hydration is a relatively specific pathological factor in liver cancer patients [12], Due to the different constitutions of patients, dampness may become humid heat, abdominal distention, golden skin sclera, fever and thirst, short urine and redness and other humid heat; Or it may become cold and wet, see the whole body swelling, skin sclera is dark yellow, dark complexion, fatigue, cold intolerance and other cold and wet symptoms, which is often manifested in end-stage patients. Wu Tongyu believes that the symptoms of wet internal obstruction in primary liver cancer [13] are mostly manifested as: physical fatigue, sticky mouth, yellow skin, yellow urine, abdominal distention, etc. At the same time, those with cancerous ascites and spleen deficiency and water wetness [14] in addition to feeling obvious abdominal distention, and may have symptoms such as shortness of breath, loss of appetite, fullness, nausea, vomiting, and edema. With the aggravation of the disease, the wet manifestations become more and more obvious, so the characteristic manifestations of liver cancer patients are mainly wet internal arrest, that is, the clinical manifestations are often mobile dullness or ascites, accompanied by less urine output, more often slow pulse rate, and there may be spleen enlargement. In the three steps of hepatitis B, there is spleen deficiency and stagnation, and the spleen is wet and forms a hub [15], so the treatment is mainly to strengthen the spleen.

5. Summary

In summary, from the perspective of dialectics, the double-layer frequency weight scissor algorithm makes the dialectical classification more scientific and standardized, and is conducive to guiding clinical application. Due to the small number of samples confirmed by spleen deficiency and hygrosis in this study, the characteristic laboratory indicators could not be successfully obtained, and the next step is to expand the sample size in order to better reflect the clinical characteristic symptoms and laboratory indicators and imaging manifestations of hepatitis B cirrhosis and liver cancer in various TCM symptom types.

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