



# Influence and analysis of Chaihu plus Longgu oyster decoction combined with five-elements music therapy on inflammatory factors and depression in patients with reflux cholangitis after cholangiocarcinoma surgery

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## Abstract

The purpose of this study is to investigate the influence and analysis of Chaihu plus Longgu oyster decoction combined with five-elements music therapy on inflammatory factors and depression in patients with postoperative reflux cholangitis of cholangiocarcinoma. 90 patients with reflux cholangitis and mild to moderate depression after cholangiocarcinoma surgery were selected and were randomly divided into control and treatment groups. Control group was treated with antibiotics and antidepressant drugs, and treatment group was given Chaihu plus Longgu oyster decoction plus five-elements music therapy based on antibiotics. After treatment, the improvement of the main clinical symptoms, the serum IL-6, IL-10, TNF- $\alpha$ , CRP levels, and Hamilton Depression Scale evaluation of depression were analyzed. Follow up for 12 months, analyze the recurrence of the two groups of patients. The levels of IL-6, IL-10, TNF- $\alpha$  and CRP in the treatment group were significantly lower than in the control group. The scores of the main clinical symptoms and the efficacy of relieving depression in the treatment group were better. Therefore, Chaihu plus Longgu oyster decoction combined with five-elements music therapy can reduce the release of serum IL-6, IL-10, TNF- $\alpha$  and CRP inflammatory factors, improve fever, jaundice, abdominal pain and other symptoms, and reduce the degree of depression and the recurrence after treatment.

**Keywords:** Chaihu plus Longgu oyster decoction; five-elements music therapy; reflux cholangitis; inflammatory transmitter; integrated traditional Chinese and Western medicine treatment.

**Practical Application:** Based on conventional treatment, the application of Bupleurum Chinese plus Ossa Draconis and oyster decoction with five-elements music therapy for the treatment of patients with reflux cholangitis with moderate to mild depression has certain advantages and practical significance, and is beneficial in terms of improving patients' symptoms, accelerating their recovery, reducing postoperative depression and improving quality of life.

## 1 Introduction

Reflux cholangitis, also known as ascending cholangitis, is most commonly caused by a retrograde bacterial infection in the intestinal tract and reflux of intestinal contents into the biliary system after choledochojejunostomy, and it can also occur after Oddi sphincterotomy and biliary stent implantation. The main clinical symptoms are abdominal pain, fever, chills and jaundice, and the condition is prone to recurrence. The current treatment principles are mainly anti-inflammatory and choleresis, and some patients need surgical treatment. Patients with malignant tumours are prone to depressive states, and the mechanism of 'obstructive cardinalate of liver and gallbladder' in TCM runs through the whole course of the post-tumour depressive state. Bupleurum Chinese plus Ossa Draconis and oyster decoction has the effect of catharsis and regulating Shaoyang, and it is also essential for the smooth passage of systemic qi. Five-elements

music therapy has received more attention and has been recognised by scholars as a marginal-discipline adjuvant therapy for the depressive state in recent years. We used modified Bupleurum Chinese plus Ossa Draconis and oyster decoction in combination with five-elements music therapy and Western medicine to treat patients with reflux cholangitis and mild to moderate depression after cholangiocarcinoma surgery and compared it with Western medicine treatment alone. The effect of the two treatment methods on the levels of inflammatory cytokines in patients with reflux cholangitis after cholangiocarcinoma surgery was analysed and compared, along with the recurrence rate within 12 months between the two groups, in order to provide a reference and basis for fast recovery and to improve the patients' quality of life.

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## 2 Information and methods

### 2.1 General information

A total of 90 patients diagnosed with cholangiocarcinoma at Tangshan Hospital of Traditional Chinese Medicine between June 2015 and January 2018 who underwent choledochoduodenostomy and were diagnosed with reflux cholangitis were analysed (Huang, 1998). Both groups were diagnosed with reflux cholangitis after clinical symptom examinations, laboratory tests and imaging examinations. According to treatment based on disease differentiation, both had liver qi stagnation syndrome and hepatobiliary damp-heat syndrome. The study was approved by the Ethics Committee of Kailuan General Hospital and followed throughout. Participants were randomly divided into the treatment and control groups, and the groups were comparable. See Table 1.

### 2.2 Inclusion criteria and exclusion criteria

#### Inclusion criteria

(1) Patients aged 42 to 70 years with a clear diagnosis of reflux cholangitis. (2) No special restrictions, such as educational/cultural-social background and occupation. (3) No radiotherapy, chemotherapy, targeted drugs, bioimmunotherapy or other antitumour therapy during treatment. (4) The surgical approach was clearly defined; all were choledochoduodenostomy.

#### Exclusion criteria

(1) Other definite diagnoses, such as recurrent or metastatic malignancy, viral hepatitis, pancreatitis and biliary stones.

(2) Severe liver and kidney function impairment affecting drug metabolism. (3) Have received other relevant TCM treatments that may affect the test indicators. (4) Special populations, such as patients with viral infections, autoimmune diseases, psycho-psychiatric disorders, pregnancy or lactation. (5) Patients treated with special surgical procedures, such as Roux-en-Y choledochojejunostomy, jejuno-pancreaticobiliary Y-anastomosis. (6) Disagreed with this clinical observation or refused to sign the informed consent.

### 2.3 Methods

#### Treatment methods

Western medicine treatment in both groups

The patients were hospitalised for two weeks over the course of treatment. According to their disease condition and individual situation, the patients were given the antibiotics cefmendoxate sodium (Hainan Lingkang Pharmaceutical Co. Ltd., Registration No. 5027H9022, 0.5 g/pc) with a dose of 1.5 g twice a day by intravenous infusion, or levofloxacin (Yangtze River Pharmaceutical Group, GYZZ H20060026, 0.1 g/pc) with a dose of 0.2 g twice a day by intravenous infusion, or omeprazole injection (AstraZeneca Pharmaceuticals Co. Ltd., Registration No. H20130633, 40 mg/pc) 40 mg once a day by intravenous infusion. Patients with obvious symptoms of high fever and chills were given 'aspirin DL-lysine' (Chongqing Yaoyou Pharmaceutical Ltd., GYZZ H50021319, 5 mL/pc) intramuscularly to reduce fever. Patients with severe pain were given 'bougurizine hydrochloride injection' (Tianjin Jinyao, GYZZ H12020966, 100 mg/pc) by intramuscular injection for

**Table 1.** Comparison of general data of both groups of patients.

		Treatment group (n = 42)	Control group (n=48)	$\chi^2/t$	P-value
M/F (example)		29/13	32/16	0.058	0.809
Age (years)		47.3 ± 11.7	46.5 ± 9.8	0.798	0.423
BMI (kg/m <sup>2</sup> )		24.8 ± 1.9	24.3 ± 2.1	0.951	0.314
NRS2002 rating		4.5 ± 1.5	4.7 ± 1.6	0.768	0.441
Post-operative time (months)		8.8 ± 2.6	8.1 ± 2.2	0.635	0.527
Liver Qi stagnation evidence		25	28	0.754	0.098
Hepatobiliary damp-heat syndrome		17	20		
Hyperbilirubinemia (cases)	yes	10	12	0.017	0.896
	no	32	36		
Chronic gastritis (cases)	yes	12	16	0.237	0.626
	no	30	32		
Pneumonia (cases)	be	11	13	0.009	0.924
	yes	31	35		
Bacteraemia (cases)	no	6	5	0.313	0.576
	deny	36	43		
Bacterial liver abscess (cases)	yes	6	5	0.313	0.576
	no	36	43		
Smoking history (cases)	yes	21	22	0.156	0.693
	no	21	26		
Alcohol history consumption (examples)	yes	20	22	0.029	0.865
	no	22	26		

pain relief. During treatment, electrolyte regulation, stomach protection, trace element supplementation and nutritional support therapy were given according to the condition.

#### Treatment of patients in the treatment group

The patients in the treatment group were additionally treated with Bupleurum Chinese plus Ossa Draconis oyster decoction based on Western medicine treatment, and the main prescriptions were: 10 g Bupleurum Chinese, 10 g Scutellaria baicalensis, 10 g Codonopsis pilosula, 10 g Pinellia ternata, 15 g Poria cocos, 30 g Ossa Draconis, 30 g oyster, 6 g Acorus calamus, 10 g Polygala tenuifolia, 30 g Poria with hostwood, 30 g Salvia miltiorrhiza, 10 g Curcumae Radix, 30 g Cortex Albiziae, 10 g turtle shell, 10 g tortoise plastron and 15 g Rhizoma Paridis. For those with spleen and stomach deficiency, 15 g Atractylodes macrocephala and 30 g Coix seed were added. For those with heat toxin, 40 g raw gypsum, 10 g Anemarrhena asphodeloides, 8 g Cortex Moutan, 10 g Rhizoma Coptidis and 10 g Fructus Forsythiae were added. For those with qi stagnation and blood stasis, 10 g Fructus Toosendan, 10 g Rhizoma Corydalis, 12 g Carthamus tinctorius and 10 g Rubia cordifolia were added. For those with liver and kidney yin deficiency, 15 g raw Rehmannia glutinosa, 10 g Schisandra, 10 g Eclipta alba and 10 g Ligustrum lucidum were added. For those with long-illness qi deficiency, 30 g Astragalus membranaceus and 10 g ginseng were added. For those with yin deficiency internal heat, 15 g Artemisia annua, 10 g Cortex Lycii Radicis, 20 g Radix Trichosanthis and 12 g Lophatherum gracile were added. For those with internal stagnation of water and dampness, 10 g Rhizoma Alismatis, 10 g Pericarpium Citri Reticulatae, 15 g Polyporus umbellatus and 15 g Atractylodes macrocephalae were added. A total of 400 mL of decoction was taken, 200 mL each in the morning and evening, for four weeks, with five-elements music therapy once daily. During hospitalisation, patients were treated with syndrome differentiation, and the formula was added or reduced according to the symptoms. If gastrointestinal symptoms were obvious, the dosage of herbs was adjusted according to the symptoms, and the dosage was adjusted to smaller and more frequent doses for those who were older or had difficulty taking oral medications.

#### Control group treatment

Patients in the control group were given escitalopram oxalate tablets (Danish Ling North Pharmaceuticals, registration number H20150163, 10 mg/tablet) 10 mg orally once daily for four weeks for antidepressant treatment.

#### Test methods and test indicators

Venous blood was drawn from patients in both groups before treatment (T1), 10 days after treatment (T2) and 20 days after treatment (T3) and stored for future use after anticoagulation and freezing. Among them, the levels of inflammatory cytokines, including serum IL-6, IL-10 and TNF- $\alpha$ , were determined by enzyme-linked immunosorbent assay (ELISA). Serum CRP was determined by latex-enhanced transmission immunoturbidimetric assay. The test kit was manufactured by Shanghai Yikosai Company,

and all operations were performed following the instructions on the kit and the laboratory requirements and specifications.

#### Clinical symptoms observation index and depression efficacy criteria

The patient's clinical symptoms included fever, jaundice and abdominal pain. The clinical symptom score was referenced to the Diagnostic and Therapeutic Criteria for TCM Diseases (State Administration of Traditional Chinese Medicine, 1994), which was statistically analysed according to the severity of the patient's symptoms, with 0 points for no symptoms, 1 point for mild symptoms, 2 points for moderate symptoms, and 3 points for severe symptoms. The reduction rate of the Hamilton Depression Scale (24 items) (HAM-D) score after treatment was used as the main efficacy determination criterion, which was formulated with reference to the 1984 Chinese Medical Association Depression Efficacy Criteria: ① cured: total HAM-D score  $\leq 7$  or a reduction rate of  $\geq 75\%$ ; ② significantly effective:  $\geq 50\%$ ; ③ effective:  $\geq 25\%$ ; ④ ineffective:  $< 25\%$ . Effective = cured + significantly effective + improved. HAM-D reduction rate = (score before drug administration - score after drug administration)/score before drug administration  $\times 100\%$ . The SDS standard score, total HAM-D score and the change of each factor were also used to evaluate the treatment efficacy of each group.

#### 2.4 Follow-up visits

Patients were followed up for 12 months after discharge. Follow-up visits were conducted every one to two weeks, with a cut-off date of 1 October 2020, by taking medical record information, arranging telephone appointments and interviews for outpatient follow-ups and recording whether the patient's condition recurred and whether they were still alive.

#### 2.5 Withdrawal or drop-out

There were no withdrawals or drop-outs among the enrolled patients during the clinical observation and study period.

#### 2.6 Statistical methods

SPSS 23.0 software was used for statistical analysis of the collected data. The measurement data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) and a t-test was used. Count data were tested using the chi-square ( $\chi^2$ ) test. Two different times were compared using the t-test.  $P < 0.05$  was defined as a statistically significant difference.

### 3 Results

#### 3.1 Comparison of inflammatory mediator levels before and after treatment in the two groups

Repeated measures of analysis of variance for the two overall factors in the groups showed statistically significant differences in the indicators of inflammatory mediator levels, time and interaction between the two groups ( $P < 0.05$ ). There were no statistically significant differences in the serum IL-6, IL-10, TNF- $\alpha$  and CRP levels between the two groups of patients before

treatment ( $P > 0.05$ ). Compared with levels before treatment, the serum levels at 10 and 20 days after treatment in the two groups were significantly different ( $P < 0.05$ ), with the serum levels in the treatment group lower than in the control group, as shown in Table 2 and Figure 1A-1B.

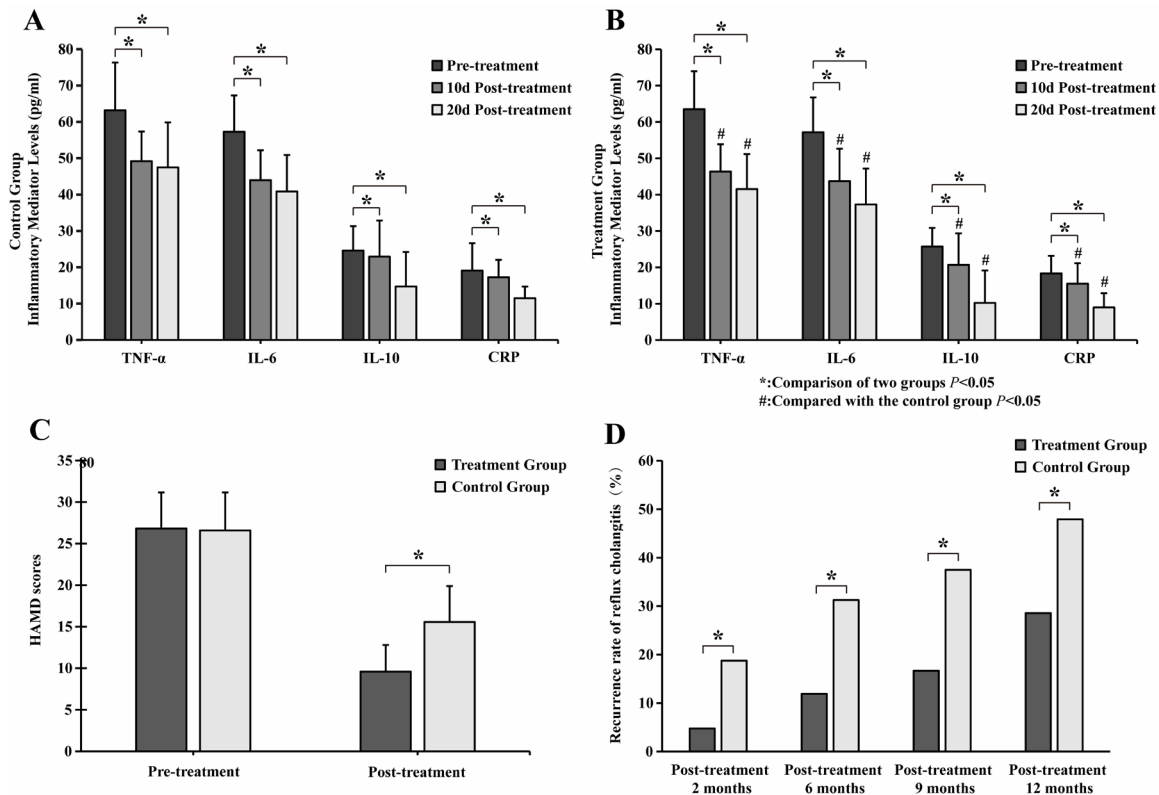
### 3.2 Comparison of clinical symptom scores between the two groups of patients

The clinical symptoms of patients in both groups before and after treatment included fever, jaundice and abdominal

**Table 2.** Comparison of IL-6, IL-10, TNF- $\alpha$  and CRP levels between the two groups.

Inflammatory indicators	Treatment group n = 42	Control group n = 48	High frequency modulus	Comparison between groups		Comparison of two points of time		Intra-group comparison	
				F	P	F	P	F	P
IL-6(pg/mL)			1.031	2.821	0.047	2.658	0.102	4.218	0.059
T1	57.17 $\pm$ 9.59	57.28 $\pm$ 10.01							
T2	43.73 $\pm$ 8.91*	43.96 $\pm$ 8.24*							
T3	37.32 $\pm$ 9.87*	40.85 $\pm$ 10.03*							
IL-10(pg/mL)			0.933	4.982	0.034	68.396	0.042	2.897	0.038
T1	25.72 $\pm$ 5.15	24.59 $\pm$ 6.72							
T2	20.68 $\pm$ 8.67*	22.92 $\pm$ 9.94*							
T3	10.21 $\pm$ 8.92*	14.71 $\pm$ 9.48*							
TNF- $\alpha$ (pg/mL)			1.001	3.198	0.047	1.632	0.055	4.172	0.042
T1	63.51 $\pm$ 10.44	63.18 $\pm$ 13.15							
T2	46.35 $\pm$ 7.51*	49.18 $\pm$ 8.17*							
T3	41.52 $\pm$ 9.63*	47.47 $\pm$ 12.39*							
CRP (mg/L)			1.006	4.121	0.032	2.217	0.032	3.089	0.023
T1	18.34 $\pm$ 4.83	19.09 $\pm$ 7.52							
T2	15.51 $\pm$ 5.62*	17.24 $\pm$ 4.81*							
T3	8.97 $\pm$ 3.94*	11.49 $\pm$ 3.19*							

\* $P < 0.05$  compared with pre-treatment. CRP = C-reactive protein; T1 = pre-treatment; T2 = 10 d post-treatment; T3 = 20 d post-treatment. F value is the statistical value of the F-test. The P value is the probability that (F test or T or any other test) is greater than the desired value.



**Figure 1.** (A) IL-6, IL-10, TNF- $\alpha$  and CRP levels of control group; (B) IL-6, IL-10, TNF- $\alpha$  and CRP levels of treatment group; (C) Comparison of HAMD scores in groups of two groups; (D) Recurrence rate of reflux cholangitis.

pain. For comparison of the clinical symptom scores, there was no difference between the two groups before treatment. There was also no statistically significant difference between the two groups after treatment ( $P > 0.05$ ), although the clinical symptom scores of the patients in the treatment group were lower than the control group. See Table 3.

### 3.3 Comparison of HAM-D scores (24 items) in the two groups

See Table 4 and Figure 1C.

### 3.4 Comparison of recurrence of reflux cholangitis in the two groups within 12 months after treatment

The recurrence of reflux cholangitis within two, six, nine and 12 months after treatment was 2/42, 5/42, 7/42 and 12/42 in the treatment group, and 9/48, 15/48, 18/48 and 23/48 in the control group, respectively, and there were statistically significant differences in the recurrence after treatment in the treatment group compared with the control group ( $P = 0.041, 0.038, 0.028, 0.042$ , respectively). See Figure 1D.

## 4 Discussion

Reflux cholangitis belongs to the categories of ‘jaundice’, ‘hypochondriac pain’ and ‘heat syndrome’ in TCM, and it is often characterised by the coexistence of ‘internal heat’ and ‘toxins’, liver qi stagnation and internal damp-heat. Depression is a kind of ‘Major Depressive Disorder’ in TCM, which refers to the illness caused by emotional discomfort and qi stagnation, and can be divided into deficiency and excess syndromes. In diagnosing and treating malignant tumours and their comorbidities, some patients have pathological emotional reactions and lose their normal mental state; this is tumour-related depression. Depression is the more significant problem among many emotional disorders. Some studies have shown that the incidence of cancer is positively correlated with a depressive state, and the diagnosis of cancer is the primary source of psychological and emotional stress. It has been found that a significant proportion of tumour patients have depressive symptoms with their illness (Walker et al., 2013), and the pathological mechanism of ‘obstructive cardinalate of liver and gallbladder’ occurs throughout the course of post-tumour depression. The treatment for the liver and the application of the method of dispersing stagnated liver qi for relieving depression play an indispensable role in tumour-related depression. As the

ancient saying goes, ‘when we see the disease of the liver, we know that liver transmits to spleen’, so we need to consider strengthening the spleen and replenishing qi. In the formula of Bupleurum Chinese plus Ossa Draconis and oyster decoction, Bupleurum Chinese reconciles superficial and interior and disperses stagnated liver qi. Scutellaria baicalensis clears heat and dampness, purges fire and removes toxins. Bupleurum Chinese and Scutellaria baicalensis combine to resolve Shaoyang, clear heat and benefit the gallbladder. Codonopsis pilosula invigorates and strengthens the spleen, replenishes qi and blood, and benefits the lungs. Pinellia ternata eliminates dampness, while Poria cocos permeates dampness and moves downward; both are used to strengthen the treatment of dampness and resolve fluid retention. Ossa Draconis and oysters calm the heart and mind, suppress yang and stop perspiration with astringents to promote the relative equilibrium of yin and yang. Acorus calamus is used in combination with Polygala tenuifolia to benefit the kidneys, strengthen the brain and intellect, enhance the power to open and close the orifice and calm the mind. In combination with Poria with hostwood it relieves mental stress and induces diuresis. Salvia miltiorrhiza promotes blood circulation to relieve pain, clear the mind and remove irritation and cool blood to eliminate carbuncles, while Curcumae Radix regulates qi to relieve stagnation, remove blood stasis and relieve pain, and treat jaundice. The combination of both drugs enhances blood circulation and relieves pain. Cortex Albiziae alleviates mental depression and promotes blood circulation to remove stagnancy, while the turtle shell and tortoise plastron are both salty and cold in nature and belong to the liver and kidney meridians, with the effect of nourishing yin and reducing yang. Rhizoma Paridis cools the liver, calms panic, relieves swelling and pain and clears heat and detoxification. Modern pharmacological experiments have proved that Scutellaria baicalensis, Curcumae Radix and Bupleurum Chinese have certain choleric, anti-inflammatory and hepatocyte-protective effects (Liu, 2007; Shi et al., 2022; Wang et al., 2022).

Music therapy is an adjuvant therapy based on the theory and methods of psychotherapy. It is designed to make patients achieve the purpose of eliminating psychological barriers while restoring physical and mental health through specially designed musical behaviours. According to Liao et al. (2019), the five elements of music therapy in TCM can alleviate the anxiety and depression of tumour patients and play a good therapeutic role in improving patients’ insomnia and reducing their pain. It can play an essential role in regulating the physical and mental

Table 3. Comparison of postoperative complications in groups of two groups ( $x \pm s$ , points).

Groups	n	Clinical symptom score					
		Fever		Jaundice (TCM)		Abdominal pain	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment	42	2.62 ± 0.34	1.59 ± 0.21	2.18 ± 0.39	1.59 ± 0.81	2.61 ± 0.43	0.78 ± 0.34
Control	48	2.59 ± 0.47	1.56 ± 0.32	2.32 ± 0.41	1.68 ± 0.48	2.73 ± 0.56	0.99 ± 0.16
<i>t</i>			3.765		1.547		4.291
<i>P</i>			0.051		0.069		0.051

TCM = Traditional Chinese medicine.

**Table 4.** Comparison of HAM-D scores in groups of two groups ( $\bar{x} \pm s$ , points).

Groups	n	HAM-D scores	
		Before treatment	After treatment
Treatment	42	26.82 ± 4.34	9.59 ± 3.21
Control	48	26.59 ± 4.57	15.56 ± 4.32
<i>t</i>		0.03	3.765
<i>P</i>		0.98	0.041

HAM-D: Hamilton depression scale.

health of tumour patients in China, thus providing some clinical diagnostic ideas for the preventive treatment of disease in TCM and establishing a chronic disease management model with TCM characteristics, which is a special treatment technology of TCM. Meng (2016) found that the five-elements music therapy not only improves the sleep quality and psychological state of patients but also aids in the treatment of depression, which further improves the quality of survival and prolongs patients' lives. Zhao et al. (2020) believed that music therapy has an important influence on people's emotional regulation, so it can have a more positive effect on relieving people's emotions effectively. In the treatment process, TCM five-elements music therapy takes the theory of Chinese medicine organs and meridians as the critical foundation, and the law of five elements as the basic principle, so that people can focus on the spirit, calm the mind and harmonise the yin and yang to better achieve the purpose of treating diseases. Therefore, TCM five-elements music therapy as an emerging means to treat post-tumour depression is used in modern clinical applications. According to Zhang (2017), TCM five-elements music therapy follows the principle of TCM diagnosis and treatment and selects the prescribed music track corresponding to the patient's disease type and specific situation, which represents a kind of traditional auxiliary clinical treatment with TCM characteristics. According to Zhang et al. (2018), music therapy can regulate the emotional effect, optimise the psychological state and finally achieve the effect of psychological intervention, making it a more effective psychological treatment method. Lin & Wu (2012) observed the effect of music therapy on the adverse emotions of postoperative lung cancer patients and found that TCM music therapy could greatly improve their anxiety and depression. Sun & Zhou (2015) found that the five-elements music therapy selected according to the patient's condition had a good effect on the negative emotions of lung cancer patients during chemotherapy, and the effect was better than conventional music intervention. Zhang et al. (2014) demonstrated that immunotherapy could not significantly improve the depression of patients, while the combination of TCM five-elements music therapy and immunotherapy had a better effect on improving the depression of cancer patients. Chen et al. (2019) believed that TCM five-elements music therapy is a kind of nursing intervention that can relieve the negative psychological emotions of tumour patients, thus effectively improving the negative emotions of anxiety and depression of patients, and finally achieve the effect of relieving symptoms and treating diseases. Therefore, it is worthwhile to do further research and promotion. Qu et al. (2020), through a large number of experimental studies, deeply explored the improvement effect of TCM five-elements music therapy combined with other Chinese medicine treatment for patients'

depression, and concluded that five-elements music therapy, as a characteristic treatment technique of TCM in China, has a good therapeutic effect on treating depressed tumour patients, and is widely used in clinical practice.

Currently, Roux-en-y anastomosis mainly includes choledochojunostomy and choledochoduodenostomy. Postoperative patients are prone to recurrent reflux cholangitis because the surgery changes the normal physiological structure of the body, which is closely related to the level of inflammatory mediators, and when the level of the inflammatory mediator is excessive, it will lead to the emergence and progression of inflammation. IL-6 is a glycoprotein factor that plays a vital role in the process of acute inflammatory response (Zhao et al., 2022). It is commonly used for the early diagnosis and prognosis evaluation of clinical infection. In excess, it can stimulate and increase the level of TNF- $\alpha$ . IL-10 is a cytokine belonging to chemokine, which is the primary inflammatory factor involved in the process of reperfusion injury and systemic inflammatory response, and its level can determine the diagnosis, differential diagnosis and prognosis of patients with inflammatory diseases. TNF- $\alpha$  can regulate the immune level of the body, and excessive amounts of TNF- $\alpha$  can destroy hepatocytes, leading to liver inflammation and hepatocyte necrosis and aggravating the degree of liver injury (Xiao et al., 2014; Doll et al., 2015; Dziedzic, 2015). Serum CRP is a non-characteristic inflammatory index of infection. The results of this study showed that the serum IL-6, IL-10, TNF- $\alpha$  and CRP levels decreased in both groups at 7 d and 14 d after surgery. These serum levels in the treatment group were significantly lower than in the control group at 7 d and 14 d after treatment ( $P < 0.05$ ), indicating that, for patients with reflux cholangitis, taking Bupleurum Chinese plus Ossa Draconis and oyster decoction together with TCM five-elements music therapy can reduce these serum levels, lower cellular inflammatory factor levels and reduce the risk of patients' disease progression to heavy biliary tract infection.

In addition, the results of this study showed that the clinical symptom scores of fever, jaundice and abdominal pain in the treatment group were significantly lower than the control group. The recurrence of reflux cholangitis in the treatment group was lower than the control group at three, six, nine and 12 months after treatment, which indicates that the treatment of patients taking Bupleurum Chinese plus Ossa Draconis and oyster decoction with five-elements music therapy helps to relieve the symptoms of fever, jaundice and abdominal pain, and can reduce the recurrence of reflux cholangitis. Furthermore, the degree of depression in patients with malignancy is fundamentally different from that of normal individuals for reasons that include unusual symptoms and strong biological aetiology (Smith, 2015), and many patients continue to experience depression with their disease, reducing the quality of life (Dunn et al., 2011). This study suggests that treatment with Bupleurum Chinese plus Ossa Draconis and oyster decoction with five-elements music therapy can reduce the degree of the depressive state and improve the quality of life of patients with reflux cholangitis, as well as helping to avoid the prolonged application of antibiotics leading to intestinal flora dysbiosis, multiple bacterial infections, increased drug resistance and high drug costs. The results obtained in this study need to be supported and validated by increasing the clinical sample

size, extending the duration of observation or herbal treatment and conducting multicentre case studies.

## 5 Conclusion

In conclusion, based on conventional treatment, the application of Bupleurum Chinese plus Ossa Draconis and oyster decoction with five-elements music therapy for the treatment of patients with reflux cholangitis with moderate to mild depression has certain advantages and practical significance, and is beneficial in terms of improving patients' symptoms, accelerating their recovery, reducing postoperative depression and improving quality of life. It is worthwhile to promote the modernisation of TCM, which has a reliable clinical basis and broad application prospects, in primary hospitals.

## Abbreviations

IL-6: interleukin-6. IL-10: interleukin-10. TNF- $\alpha$ : tumour necrosis factor- $\alpha$ . ELISA: enzyme-linked immunosorbent assay. HAM-D: Hamilton depression scale.

## Ethical approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Tangshan Hospital of traditional Chinese Medicine.

## Conflict of interest

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

## Availability of data and material

All data generated or analyzed during this study are included in this published article.

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## Author contributions

Conceptualization: Qingxian Wang. Funding acquisition: Qingxian Wang. Investigation: Ying Wang, Qingxian Wang, Chaoyong Zhang, Ying Xu. Supervision: Qingxian Wang. Writing—original draft: Ying Wang, Qingxian Wang. Writing—review and editing: Ying Liu, Zilin Liu, Luying Zhang, Zhenwei Zhou, Zheng Duan. Approval of the final manuscript: all authors.

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