# 중국 한의학에서 간암의 치료에 관한 연구

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# Study on Traditional Chinese Medicine against Liver Cancer

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간암은 전 세계적으로 발병률이 높은 암 중 하나이며 매년 5만 명이상이 간암에 의하여 사망하고 있으며, 특히 한국과 중국 그리고 아시아의 다른 국가들에서 매우 높은 사망률을 보이고 있다. 따라서 본 연구는 간암치료에 있어서 한·중간의 한의학적 교류와 이해를 도모하기 위해 병인(病因), 병기(病機), 변증논치(辨證論治), 다용처방, 민간요법, 한약의 적용, 침 보안요법, 간섭치료 등 최근 중국에서 시행되고 있는 다양한 임상적 치료방법을 고찰하였다.

Key words: liver cancer, oriental medicine, Traditional Chinese Medicine (TCM)

## Introduction

Liver cancer is one of the most common cancerous diseases especially in Asia, killing over five hundred thousand people throughout the world annually. In oriental medicine, liver cancer has been known from ancient time as written as "難經:肝之積,名曰肥氣.在左脅下,如覆杯,有頭足,久不愈,令人咳逆瘧". Liver cancer is a pathological state of deficient viscera-Qi and blood in interior, and damp-heat and stasis in exterior by oriental theory.

On the other hands, many aspects including race, living region and many kind of cultural characteristics are very similar between Korean and Chinese. Also, the morbidity of liver cancer present a high rate in these two countries. In China, liver cancer's mortality rate is 20.37/100,000 and is second just after gastric cancer [1]. About two hundred sixty thousand people die of liver cancer in China every year. It is mostly resulted from the fact that one hundred and twenty million Chinese are chronic HBV carriers because eighty percentages of primary liver cancer is arising from chronic B hepatitis. This medical issue is not much difference between Korean and China. WHO has recognized Korea and China as a high morbidity country of chronic B hepatitis.

Western medicine has a rapid progress in diagnosis and therapy technology in cancer treatments. However, early diagnosis determining the clinical outcome of liver cancer is still very difficult and its

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conventional therapeutic efficacy is still low. Therefore, alternative approaches including herbal drug treatments have been adapted worldwide.

Hereby, we reviewed and presented the approaches for oriental medicine-based liver cancer treatment in China, called as traditional Chinese medicine (TCM). It is expected that this article can provide the useful information to Korean oriental doctors or scientists in this fields.

## Survey study and discussion

Etiology and pathogenesis of liver cancer

As general concepts of other cancers, etiology and pathogenesis liver cancer is basically based on deficiency of healthy-Qi (正 氣), incontrollable state of viscera's vin-yang and Qi blood(臟腑陰陽氣血), exogenous pathogenic factors, and spleen-Qi (脾氣) deficiency and liver-Qi (肝氣) staginess. These conditions thereafter cause pathologic product such as phlegm, damp, bad Qi (邪 氣), and blood stasis, reasoning liver cancer. Liver cancer should be combining of "toxin" and "accumulate", so is pathologic state of interior asthenia and exterior sthenic (本虛標 實). Here, interior asthenia refers to deficient of Qi-blood and loss of healthy-Qi. Exterior asthenia refers to pathogenic factors of interior accumulation, blood stasis and virulent fire.

At the beginning of disease, usually depression of liver-Qi and asthenia of spleen-Qi, and Qi stagnation and blood stasis were observed. After a long time, Qi depression transforms into fire, and endogenous damp and heat cause interior accumulation of virulent damp heat, amenorrhea with blood

stasis, and obstruction. So many symptoms such as accumulation, jaundice and swell up were shown. At last, because of pathogenic factors caused asthenia of both Qi and blood, impairment of healthy Qi, and asthenia of hepatonephric Yin (肝腎陰虛), convulsion and bleeding signs were observed. [2]

Several experts for liver cancer present differently these etiologies and pathogenesis of TCM as summarized in table 1 [3-7].

Table 1 Main point of liver cancer etiology and pathogenesis of TCM [3-7]

	Author	Viewpoints
1	Qian BW (錢伯文)	Splenic asthenia and "hepatic stagnation" is the important pathogenesis in liver cancer [3]
2	Pan MQ (潘敏求)	The basic pathogenesis in live cancer is stasis, toxicity, and asthenia [4]
3	Wang QC (王慶才)	The asthenia of the healthy Qi, visceral dysfunction, cannot eliminate the pathogenic factors. Liver cancer damages more healthy Qi, and come into being interior asthenia and exterior sthenic (本虛標實) [5]
4	Wang P (王沛)	Qi stagnation, gathered toxicity, and Yin asthenia is the basic pathological changes. The main pathogenesis is a disease involving both liver and spleen; Wood restricting Earth (木克土) [6]
5	lv SJ (呂書勤)	Pathogenic dampness, exogenous factor, caused dysfunction of visceral Qi [7]

Summary of treatments for liver cancer in TCM

	Table 2 C	Clinical	Distribution	of	Basic	Syndrome	of	TCM	[8]
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Stage	Amount	Syndromes of Primary Liver Cancer of TCM		
The first stage	45	Blood-stasis and spleen-Qi deficiency		
The second stage	120	Blood-stasis, spleen-Qi deficiency, liver-bladder dampness-heat, and liver-Qi stagnation		
The third stage	102	Blood-stasis, spleen-Qi deficiency, liver-bladder dampness-heat, dampness retention, liver-Qi stagnation liver-yin deficiency and kidney-yin deficiency		
Remark		The six syndromes in third stage are the major syndromes of primary liver cancer		

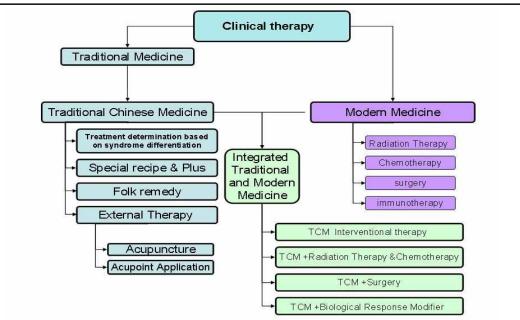


Figure 1. Clinical therapy system for liver cancer in China

Generally, there are typical three categories of liver treatment, such as conventional western therapy, traditional Chinese medicine, and combination therapy of these two treatments. This is summarized in figure 1. Among these, we will mainly describe the traditional Chinese medicines in present article.

Syndrome differentiation and treatment Treatment determination based on syndrome

differentiation (辨症論治) is an essential principle in TCM. It is different both from common "symptomatic treatment" or "treatment according to different disease" in western medicine. The different syndromes in one disease should be treated by different treatments; while different diseases, as long as they express the same syndrome, can be treated with the same treatment.

Table 3 Clinical Distribution of liver cancer and medication of TCM [6]

Types	Treatment	Medication		
Hepatic stagnation and splenic asthenia (肝鬱脾虛)	Regulate hepatic Qi, supplementing Qi and tonifying blood	逍遙散,異功散,參苓白朮散		
Qi and blood stagnation (氣血瘀滯)	Activate and eliminate blood-stasis, regulate Qi	血府逐瘀湯,桂枝茯苓丸		
Accumulation of dampheat (濕熱蘊 結)	Clearing away heat, removing toxin and draining dampness	茵陳蒿湯, 五苓散, 五皮飲		
Liver and kidney asthenia of Yin <u>(肝腎陰虚)</u>	Supplementing Qi and nourishing kidney Yin	一貫煎,大補陰丸,生脈散, 六 味地黃丸		

Table 4 Clinical Distribution of liver cancer and medication of TCM [9]

Types	Treatment	Medication	
Splenic asthenia and hepatic Stagnation (脾虛肝鬱)	Strengthening spleen and activating Qi, clearing the liver and relieves constraint	太子蔘、炒白術、薏苡仁、绞股蓝、猪苓、茯苓、白花蛇舌草、猫人蔘、 鬱金、八月扎、鶏內金、白豆蔻	
Damp heat and toxin stagnation濕熱瘀毒)	Clearing away heat and draining dampness, stasis- eliminates and removing toxin	茵陈、栀子、半枝莲、白花舌蛇草、 金银花、板藍根、山豆根、茜草根、 炒黄芩、三葉青、生大黄、澤瀉、車 前子、鶏內金、水牛角	
Liver and kidney asthenia of Yin (肝腎陰虛)	Nourishing Yin and clearing away heat	北沙蔘、生地黄、天冬、麥冬、石 斛、山茱萸、仙鶴草、乾蟾皮、茜 草、牡丹皮、生牡蛎、青蒿、蛇莓、 龍葵	

Table 5 Clinical Distribution of liver cancer and medication of TCM [10]

	Types	Medication
1	Splenic asthenia and stagnation of Qi (脾虛氣滯)	香砂六君子湯
2	Damp and heat stagnation (濕熱阻滯)	白朮散
3	Syndrome of edema due to splenic sthenia (脾虚水泛)	枳實導滯丸
4	The retention of blood stasis (瘀血内停)	厚樸三物湯 , 失笑散

Based on the syndrome and stages of disease with etiology and pathogenesis (病因病機), the procedure of TCM determines the principle of treatment and prescriptions. This method keeps the concept of wholism, one of the theories of TCM character. On the other

hands, the liver cancer's syndrome type and therapeutic principles are not identical but a little different depending on different physician in TCM. There are investigation for intrinsic laws of the major syndrome distribution of primary liver cancer from hundred sixty seven subjects. The analyzed data were divided into three stages as table 2 [8].

Experts's syndrome differentiations for liver cancer

According to clinical experts there are slightly different characteristics to determine syndrome differentiations. They differently categorized the types and treatment principles with main prescriptions for liver cancer. It was summarized as

followed experts: Wang P (王沛) as table 3 [6]; Wu LC (吳良村) as table 4 [9]; Zhang (張效霞) as table 5 [10] and Ling LF(湊勵峰) as table 6 [11]. Table 3 Clinical Distribution of liver cancer and medication of TCM [6]

Table 6 Four types in liver cancer of TCM [11]

Hepatic stagnation	Hepatobiliary		
and splenic asthenia	damp heat		
(肝鬱脾虚)	(肝膽濕熱)		
Blood stasis and Qi	Hepatonephric Yin		
stagnation	asthenia		
(氣滯血瘀)	(肝腎陰虛)		

Analysis for most frequently used treatments and herbs

Liu Q (劉慶) et al analyzed the frequencies

of treatments and medical plants of TCM in 978 pieces of papers concerning primary liver cancer as table 7. And, the top 50th frequently prescribed herbs of TCM for primary liver cancer, from 459 kinds of herbs in this data are as follows [12]: 茯苓 (236)、 黃芪(194)、白朮(186)、白花蛇舌草(185)、當歸 (174)、柴胡 (173)、黨參 (170)、丹蔘 (159)、半 支蓮 (153)、甘草 (143)、白芍 (142)、莪术 (14 1)、鱉甲 (139)、鬱金 (129)、陳皮 (115)、赤芍 (105)、茵陈 (99)、八月札 (85)、三棱 (84)、生地 黄 (82)、薏苡仁 (82)、栀子 (74)、大黄 (73)、枳 壳 (73)、香附 (70)、桃仁 (66)、半夏 (64)、澤瀉 (63)、延胡索 (61)、猪苓 (61)、丹皮 (60)、川楝子 (58)、山藥 (57)、厚樸 (55)、麥芽 (54)、黄芩 (53)、蜈蚣 (52)、人參 (51)、木香 (48)、女貞子 (48)、枸杞子(47)、紅花(47)、山甲片(47)、太子 參(47)、蚤休(47)、山楂(47)、鶏内金(46)、麥 冬 (44)、三七 (43)、牡蠣 (42)

Special recipes and clinical studies

During the course of treatment of liver cancer, all types of main symptom can be exist in the same time, or transform rapidly. So Prescription should be correctly and

Table 7 Therapeutic methods of TCM for PLC [12]

Therapeutic method	Frequency	Percentage (%)
Activating blood (活血)	217	23.98%
Invigorating Qi (補氣)	191	16.90%
Clearing away heat (清熱)	170	15.04%
Regulating Qi (理氣)	169	14.96%
Nourishing Yin (滋陰)	120	10.62%
Expelling dampness (祛濕)	92	8.14%
Nourishing blood (養血)	25	2.21%
Warming Yang (溫陽)	12	1.06%
Strengthening healthy Qi (扶正)	36	3.19%
Expelling pathogenic factors (祛邪)	27	2.39%
Relieving pain (止痛)	8	0.71%
Purgation (瀉下)	6	0.53%
Stopping bleeding (止血)	3	0.27%

flexibly modified according to the symptoms instead of a rigid recipe. Follows are some examples for its application and related clinical studies.

When the ascites appeared to patients with primary liver cancer, they show usually a bad prognosis, and life span of ninety percent of them is about two month. YGXST(養肝消水湯) (丹參30g, 赤芍30g, 地鳖虫10g, 鬱金10g, 車前 子30g, 澤瀉15g, 半邊蓮30g, 莪术10g) used as a main recipe to cure 24 cases of the ascites-bearing primary liver cancer. When Qi asthenia appears, added by 黨參10g, 白朮 10g, 灸黄芪10g; or added 生地10g, 女貞子10g, 知母10g, 淮山藥12g for Yin asthenia; 太子參 12g, 天麥冬10g, 炙黄芪10g for both Qi and Yin asthenia; likely, 茵陈30g, 大黃10g for jaundice. So, seventeen cases (70.8%) of 24 cases with ascites were cured, and 22 cases of 24 cases had been got availability (91.6%). After treatment with YGXST (養肝消水湯), the patient's life span was protracted from 1 month to 5 years, and survival rates for 6 month, 1 year and 5 year are 54%, 25% and 4% respectively [13].

RGT (軟肝湯; 柴胡 15 g, 枳實 15 g, 泽蘭 15 g, 鬱金 12 g, 厚樸 15 g, 土鳖蟲 10g, 龍葵 20g, 牛隻蓮 20g, 丹參 15g, 莪术 15g, 穿山甲 12g, 桃仁 10g, 黄芪0 g 3, 當歸 15 g, 薏苡仁 20 g) was treated to 530 cases of the diffuse liver cancer. RGT (軟肝湯) was modified according to symptoms as follows; when the ascites appeared, added by 猪苓、車前草; and 茵陈、金錢草 jaundice, plus; 延胡素、川楝子 for pain in liver area, 地骨皮、青蒿 low fever respectively. This medication showed, at last remission of 1 case, stabilization 22 cases, and exacerbating of 7 cases [14].

HYT (化岩湯; 黄芪 50 g, 丹參 20g, 白芍 15g 蚤休 20g, 土鱉蟲 10g, 桃仁 10g, 白花蛇舌草 30g, 茯苓 10g 炙鳖甲 10g, 黨參 15g. 白朮10 g, 枳壳 10g, 莪术 l0g, 薏苡仁 30g) was used to treat 60 cases of the primary liver cancer, with modification according to symptoms. And, 30 patients were treated with combined chemotherapy The as control group. assessment followed the clinical assessment standards for solid tumors. which classified as complete response (CR), partial response (PR), stable disease (SD) or no change (NC), and progressive disease (PD). There were 6 PR. 31 SD. and 23 PD in the 60 cases of TCM group comparing to 4PR. 8NC, 18 PD in the 30 cases of control group. There is significant difference compared with the two groups (p<0.05) [15].

SJHGD(三甲互肝湯;玳瑁 30g,鳖甲、龜板、太 子蔘、石斛 20g, 麥冬、丹蔘、茜草根 15g. 白花 蛇舌草 30g, 白藏 15g) was prescribed for patients the primary liver cancer. 90 cases of patients were randomly divided into two groups; 50 patients treated by supporting western treatment plus SJHGD, and the control group (40 patients) treated supporting western treatment alone. After treatment, the quality of life in the treated group was 54% self-helped, 16% half-selfhelped and 30% not self-helped, while those in the control group were 27%, 22% and 52% respectively. The quality of life in the former was superior to that in the latter (P<0.05). The average of lived time in the treated group significantly increased (p<0.01) as  $11.9\pm6.5$  to  $6.8\pm4.3$  months in control group. Comparing the changes of tumor's stable time, the mean of the treated group was increased (P<0.01) by  $8.9\pm6.5$  months  $(1.8\pm4.3)$  in control group) [16].

Folk remedy with single ingredient

Folk remedy with single ingredient has a centuries-old history in TCM. It has a characters of wide indication, simple method, rapid and reliable curative effect, safety and inexpensiveness. Chinaroot (菝葜) was used to terminal patients with primary liver cancer, for purpose of giving feel better to patients. In a clinical trial, survival time after taking this medicine was 2 years 8 month [17]. japonicum (田基黃) could Hypericum ameliorate the symptoms of 30 cases of the primary liver cancer patient except diarrhea [18]. Agkistrodon (蕲蛇) was reported that one case survived more than 14 years, one case survived with in 5 years, and the other 2 cases survived with in 2 years [19].

#### An external therapy of TCM

It is a method of treatment by applying drugs to certain part of the body. This therapy is effective and practical, and has a long history and wide indications. Especially, it has a good effect on curing the pain caused by liver cancer. The pain caused by liver cancer is most common among the advanced cases and is most difficult to control. However the external application was superior to the west medicine, and more conveniently as fewer side effects.

TGN (痛肝寧), waistband consists of 8 kinds of herbs including 半支蓮、莪术、黨參、當歸、白 朮、生地黃、丹參、陳皮. It was applied to 175 terminal stages of liver cancer patients for pain control. Curing group has a 77.4% good effective rate and 96.5% total effective rate, whereas the control group has a 33.3% good effective rate and 83.3% total effective rate. This external therapy shows a good effect on curing pain of liver cancer, and obviously enhanced and improved the living quality

[20].

GZG (肝癌止痛膏), a formula which consists of 白花蛇舌草30 g, 夏枯草20 g, 丹參20 g, 延胡索20 g, 龍葵15 g, 蚤休12 g, 三棱15g, 莪术15 g, 生乳没20g, 血竭5g, 生川乌5g, 冰片10g, 砒霜0.03g, 黄白蜡10g 米醋20ml, vaseline 10g was applied to 60 primary liver cancer patients, and compare with 60 patients applied cinobufacini. The GZG obviously eliminated the pain comparing to cinobufacini (P<0.05) [21].

SZG (麝冰止痛膏) was made from 麝香、延胡索、當歸、丹參、台乌药、冰片、地鳖虫、血竭、干蟾皮、大黄、朱砂、陳皮、蚤休、血竭、甘遂 etc. Twenty-six cases of primary liver cancer in middle and terminal stage were applied with this SZG, which showed a faster effect than tramcontin recommended by WHO on reducing pain [22].

#### Acupuncture therapy

Acupuncture is one of an important TCM technique for unblocking Qi by inserting needles or moxibustion at particular points on the body. Acupuncture can change the flow or quality of the life force and rebalancing body energies. There are many advantages such as wide application range, simple preparative method, working quickly, easy to generalize, security without toxic and side convenient medication, no addiction, improving body immunity, and so on. Acupuncture has been used to treat persistent pain, arthritis, asthma, infertility, and acute and chronic diseases. In cancer, it can alleviate the pain and functional disorders associated with the illness, though the Chinese are more likely to utilize herbal remedies to support immunity and control malignant growth. Acupuncture can also be helpful in stress reduction and the alleviation of pain following surgery. Principles of acupoints-selecting and manipulations are the most important on acupuncture complementary therapy. The principles of acupoints-selecting are "points along the meridian, remoteness first (尋經取穴, 遠隔當先)".

In clinic practice for liver cancer. acupuncture mainly affect three aspects. The first is regulation of the immune system indirectly restraining the tumor's progress [23]. Researches show that the material base for "strengthen the healthy Qi (扶正)" is to strengthen the immune system [24]. One hundred and nine cases of malignant tumor patients including liver cancer were treated with warm acupuncture. BL26 (矣元), ST36 (足三里), SP6 (三阴交) and SP10 (血海) were selected as main acu-points. The dynamic changes in tumor-related immune factors were observed. Worm acupuncture significantly elevated the level of IL-2, CD3, CD4 and NK cell and reduced the level of IL-2 receptor. It also inhibited the tumor growth; promote quality of life and prolong the survival of patients with malignant tumor [25].

The second is reduction of the toxic and side effect resulted from radio-chemotherapy. Two hundred cases of liver cancer were randomly divided into two groups; treated and control group. The treated group used the both of chemotherapy and acupuncture complementary therapy. 2 inch filiform-needle was penetrated into the PC6 (内异)、LR3 (太冲)、ST36 (足三里) point by even reinforcing-reducing (平補平寫) methods. The effective rate was significantly increased by 82 % (P<0.01) in treated group [26].

The third is to control and alleviate of carcinomatous pain. In accordance with the

principle "to tonify its mother in deficiency and to sedate its son in excess (虚则补其母, 实则為其子)". 43 cases with bellyache caused by primary liver cancer were treated with acupuncture at both sides of ST36 (足三里) points. The total effective rate showed 94.7% [27]. The "Qici" technique (齊刺法), puncturing a affected central region with a needle and two needling around was used for eighty patients with pain. The total effective rate showed by 96.2% [28].

#### Interventional therapy of TCM

Interventional therapy is a kind of new treatment since 1970s. Αt present, interventional therapy is a one of most effective appeasement therapy on intermediate and advanced liver cancer. It's become a general treatment on liver cancer in clinic. interventional therapy of chemoembolization is the first choice in treating [29]. unresectable hepatic carcinomas However there many side are effects including liver function damage and bone marrow restraints which may affect the patient's life expectancy and living quality in the long run [30]. The advancement of the combination of interventional treatment with traditional Chinese drugs is fast in China. Statistic analysis on the data of VIP information database of China, the common traditional Chinese drugs that be used on interventional therapy included Common Bletilla Tuber., Rhizoma Zedoariae Oil, Brucea Javanica Seed Oil, HCPT (hydroxy camptothecin), Elemene Emulsion, Radix Salviae Miltiorrhizae, Marsdenia tenacissima (Roxb.) Wight et Arn. Huachansu (華蟾素) and so on.

In one clinical study, 66 cases of primary

liver cancer were randomly divided into two groups (experiment group and control group). Experiment group included 36 cases treated with the suspensions of supermicro-bletiua striata powder plus hydroxyl camptothecinum (HCPT) and iodine oil, All the patients were subjected to TACE (transarterial chemoembolization) under DSA (Digital subtractive angiography). Experiment group decreased the ratio of tumor to short-term effects. and postoperative survival remarkably were increased. There were no significant differences in the adverse reactions of two groups [31].

The Oleum of Brucea javanica lipiodol compound (BJLC) was made by the mixed oleum of Brucea javanica and lipiodol, and injected through hepatic artery by catheter to 56 with treat patients hepato-cellular carcinoma. After treatment, the tumors were shrunk 33.8% averagely. 1, 2, 3 year survival rates were 87.5%, 48.2%, and 30.1% respectively. No bone marrow suppression caused by the treatment was found. The BJLC has a definite effect in treatment of hepatocellular carcinoma by transhepatic arterial embolization. As an oily anticancerous agent its conspicuous characteristic includes low toxicity, embolizability remain-ability in tumor tissue. So it has a great superiority to become a satisfactory embolic agent for the treatment of hepatocellular carcinoma [32].

## Conclusion

With through review for liver cancer treatment in TCM, we searched the general principle of syndrome differentiation and diversity of it depending on each expert or

oriental clinician. This is one of typical characteristics in oriental medicine including liver caner. In clinic, symptoms of liver cancer are very complex and changeable, and same patient may has different symptom and sign in different times so should be given by modified medicine. In china, there are three options for liver cancer treatments; conventional western traditional therapy, Chinese medicine, and combination therapy. developed Also. many herbal-derived therapeutics has been used in clinic. Many clinical studies evaluated traditional Chinese medicine and showed the medical benefits of it such as gain of survival time, improving life quality, relief pain or reducing side effects by western therapeutics.

Liver cancer is one of violent disease ranked in 2nd to 5th killing cancer patients in China and Korea; therefore, new drug or therapeutics has been necessarily waited in present. Accordingly worldwide investigation for it has been attended using oriental medical resource, and traditional Chinese medicine has performed somewhat tremendous works prior to Korea. So, we hope that this might provide some of useful information to Korea oriental doctors or scientist in this field.

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