The Relationship between Golgi Protein 73, Alpha-Fetoprotein, Liver Function Indicators, and Traditional Chinese Medicine Syndrome Types of Primary Liver Cancer

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Abstract

Objective Our objective was to analyze the correlation between Golgi protein 73 (GP73), alpha-fetoprotein (AFP), liver function indicators, and traditional Chinese medicine (TCM) syndrome types of primary liver cancer (hereinafter referred to as “liver cancer”).

Methods In total, 156 liver cancer patients (liver cancer group) and 52 healthy individuals (health group) were selected as the research subjects to detect their GP73, AFP expression, and liver function-related indicators. The obtained data were statistically analyzed using SPSS 21.0 software.

Results (1) The positive expression rate of GP73 in the liver cancer group was 50%; the positive expression rates of qi stagnation and blood stasis syndrome, heat toxin in liver and gallbladder syndrome, and yin deficiency of liver and kidney syndrome were 37.9, 54.3, and 59.6%, respectively. There was no statistically significant difference between the groups ($p > 0.05$). The positive expression rate of AFP was 50%. The positive expression rates of qi stagnation and blood stasis syndrome, heat-toxin in liver and gallbladder syndrome, and yin deficiency of liver and kidney syndrome were 41.7, 54.3, and 59.6%, respectively. There was a statistically significant difference between the groups ($p < 0.05$). (2) The GP73 levels of patients with different syndrome types in the liver cancer group were ranked from high to low as yin deficiency of liver and kidney syndrome, heat toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome. There was no statistically significant difference between the groups ($p > 0.05$). (3) The AFP levels of patients with different syndrome types in the liver cancer group were ranked from high to low as heat toxin in liver and gallbladder syndrome, yin deficiency of liver and kidney syndrome, and qi stagnation and blood stasis syndrome. Analysis of liver function indicators in the liver cancer group: the alanine transaminase (ALT) levels of patients with different syndrome types were in descending order from

Keywords
► primary liver cancer
► Golgi protein 73
► alpha-fetoprotein
► liver function
► TCM syndrome types

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high to low, including yin deficiency of liver and kidney syndrome, heat toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome. The differences between groups were statistically significant ($p < 0.05$). The aspartate aminotransferase (AST) levels of patients with different syndrome types were ranked from high to low as follows: heat toxin in liver and gallbladder syndrome, yin deficiency of liver and kidney syndrome, and qi stagnation and blood stasis syndrome. The difference between groups was statistically significant ($p < 0.05$). The levels of albumin (ALB) in patients with different syndrome types were ranked from high to low, including heat toxin in liver and gallbladder syndrome, qi stagnation and blood stasis syndrome, and yin deficiency of liver and kidney syndrome. The differences between groups were statistically significant ($p < 0.05$).

**Conclusion** GP73 and indicators such as ALT, AST, and ALB are of great significance in the diagnosis of TCM syndrome differentiation and classification of liver cancer patients.

### Introduction

Primary liver cancer (hereinafter referred to as “liver cancer”) is one of the most common malignant tumors in China. Its onset is hidden, the early diagnosis rate is low, the mortality rate is high, and it seriously threatens people’s health. The main causes of liver cancer include viral infection, genetic metabolism, dietary factors, and water pollution. China is a major country with chronic hepatitis, and chronic hepatitis B virus infection is the main cause of liver cancer. Western medicine mainly treats this disease through surgery, chemotherapy, targeted treatment, etc., which has certain advantages in the short term. However, it has characteristics such as easy recurrence and large adverse reactions, and the long-term efficacy is not ideal.

Traditional Chinese medicine (TCM) takes a holistic approach and dialectical treatment as its core, while according to three categories of etiologic factors to develop personalized diagnosis and treatment plans. It has certain advantages in improving patient symptoms and improving the quality of life. At present, the integration of traditional Chinese and Western medicine in the treatment of liver cancer is a trend, and improving the level of syndrome differentiation and treatment of this disease is crucial. Currently, the TCM syndrome differentiation and classification of this disease have not been unified. On the one hand, it is susceptible to the subjective influence of clinical doctors. On the other hand, when patients have multiple or atypical clinical symptoms, there may be situations where there is no evidence to distinguish. Biochemical indicators and imaging examinations play an important role in disease diagnosis, disease changes, disease prognosis, and other aspects. Objective indicator detection is necessary for the determination of TCM syndrome types. Alpha-fetoprotein (AFP) is a classic indicator for diagnosing liver cancer and can be used as a diagnostic indicator for TCM syndrome differentiation, providing an objective basis for TCM syndrome differentiation and classification. Studies have shown that 20 to 30% of patients have insignificant or negative AFP elevation. In recent years, with the rapid development of technology and the continuous deepening of research, Golgi protein 73 (GP73) has been confirmed to have abnormal expression in various diseases, but it is more closely related to liver diseases, especially liver cancer. The sensitivity and specificity of GP73 in diagnosing liver cancer are higher than those of AFP, and it is mostly hepatocellular carcinoma. Therefore, this study chose GP73 as the main indicator for research, in order to provide more ideas for the objectification of TCM syndrome diagnosis of liver cancer.

### Materials and Methods

#### General Information

In total, 156 patients were included in the liver cancer group, who were admitted to Henan Cancer Hospital and Henan Province Hospital of TCM from January 2019 to December 2019 and were initially diagnosed with liver cancer. Fifty-two healthy individuals were selected from the medical examination personnel of Henan Province Hospital of TCM during the same period.

#### Diagnostic Criteria

**Western Medicine Diagnostic Criteria**

*Interpretation of the Diagnosis and Treatment Standards for Primary Liver Cancer (2017 Edition)* was referenced.

**Traditional Chinese Medicine Diagnostic Criteria and Criteria for Syndrome Differentiation and Classification**

They have been formulated with reference to the *Internal Medicine of Traditional Chinese Medicine*. According to the main symptoms, secondary symptoms, tongue, and pulse, liver cancer can be divided into three syndrome types: qi stagnation and blood stasis syndrome, heat-toxin in liver and gallbladder syndrome, and yin deficiency of liver and kidney syndrome.
Case Inclusion Criteria

Liver Cancer Group
Patients were included if they met the diagnostic criteria of traditional Chinese and Western medicine for liver cancer, ranged in the age group of 18 to 80 years, had the expected survival period of more than 3 months, and signed informed consent form.

Health Group
Patients in this group were included if they did not take liver injury medication since the past few months, ranged in the age group of 18 to 80 years, were nonhepatitis virus carriers, had no other serious systemic diseases, and signed an informed consent form.

Case Exclusion Criteria
Patients were excluded if they were pregnant and lactating women; individuals with severe other systemic diseases, such as circulatory, neurological, respiratory, and urinary system diseases; had severe mental and psychological disorders; had metastatic liver cancer or combined with other malignant tumors; and did not sign the informed consent form.

Case Termination Criteria
The case was terminated if, during the trial, the patients’ conditions deteriorated and their lives endangered and if they were unwilling to continue and could not continue, and requested the termination of the clinical trial.

Observation Indicator
Golgi Protein 73 From the elbow vein, 5 mL of blood was extracted on an empty stomach and the sample was allowed to stand for 2 hours. Then, it was centrifuged at 4,000 rpm for 20 minutes and stored the centrifuged serum sample (back-up) at −80°C.

Other Indicators
AFP and liver function-related indicators were tested by the receiving hospital as required after the patient’s admission.

Test Instruments and Reagent Kits
A model 0412-1 centrifuge was provided by Shanghai Surgical Instrument Factory; RT-3100 fully automatic plate washing machine was provided by Shanghai Yuejin Medical Equipment; S-HHW21-600S digital display three-purpose electric constant temperature water temperature box was provided by Shanghai Yuejin Medical Equipment Company; MultiskanFC type enzyme labeling instrument was provided by Thermo Fisher Instruments Co., Ltd. GP73 quantitative detection kit was purchased by Jianglai Biological Company, batch numbers JH19421 and JH19422, with the detection method operated according to the kit manual.

Quality Control
Two attending physicians or more professionals conducted TCM syndrome differentiation on patients, and if the results of the two diagnoses were consistent, their syndrome types would be determined. Unqualified serum samples (hemolytic samples) were removed before testing; GP73 testing was conducted uniformly by the technician in charge of the Laboratory of Henan Province Hospital of TCM.

Statistical Methods
The data collected in this study were statistically described and inferred using SPSS21.0 software. The measurement data that followed a normal distribution were represented by the mean ± standard deviation (x̄ ± s). Comparison between two completely random groups were as follows: two independent sample t-tests were used for homogeneous variances, and corrected t-tests were used for heterogeneous variances. Single-factor analysis was used to compare the three groups in a completely randomized design. The least significant difference (LSD) method was used for pairwise comparison between groups. The counting data were represented by the constituent ratio (%), and the comparison between groups was performed using the Pearson's chi-square test. This study adopted a bilateral test, with inspection level α = 0.05. p < 0.05 indicates a statistically significant difference.

Result

Comparison of Baseline Data between the Liver Cancer Group and the Health Group
There was no statistically significant difference in age and gender composition between the two groups of study subjects (p > 0.05), indicating comparability, as shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age/Year</th>
<th>Gender</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Liver cancer group</td>
<td>156</td>
<td>55.31 ± 11.14</td>
<td>120 (76.9)</td>
<td>36 (69.2)</td>
<td></td>
</tr>
<tr>
<td>Health group</td>
<td>52</td>
<td>57.33 ± 12.72</td>
<td>36 (23.1)</td>
<td>16 (30.8)</td>
<td></td>
</tr>
<tr>
<td>T value/χ² value</td>
<td></td>
<td>−1.088</td>
<td>1.231</td>
<td>0.267</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.278</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 Comparison of baseline data between the liver cancer group and the health group (x̄ ± s).
Comparison of Golgi Protein 73 Levels between the Liver Cancer Group and the Health Group

The GP73 levels in the liver cancer group were 155.73 ± 21.33 ng/mL, while those in the health group were 15.65 ± 4.74 ng/mL. The difference in GP73 levels between the two groups was statistically significant (t = 76.538, p < 0.001).

Distribution of Traditional Chinese Medicine Syndrome Types in the Liver Cancer Group

The TCM syndrome types of liver cancer patients mainly include qi stagnation and blood stasis syndrome, heat-toxin in liver and gallbladder syndrome, and yin deficiency of liver and kidney syndrome. There was no statistically significant difference in the distribution of the three TCM syndrome types (p > 0.05), as shown in Table 2.

Table 2: Distribution of TCM syndrome types in the liver cancer group

<table>
<thead>
<tr>
<th>Syndrome types</th>
<th>n</th>
<th>Constituent ratio /%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi stagnation and blood stasis syndrome</td>
<td>58</td>
<td>37.2</td>
</tr>
<tr>
<td>Heat toxin in liver and gallbladder syndrome</td>
<td>46</td>
<td>29.5</td>
</tr>
<tr>
<td>Yin deficiency of liver and kidney syndrome</td>
<td>52</td>
<td>33.3</td>
</tr>
</tbody>
</table>

Comparison of Golgi Protein 73- and Alpha-Fetoprotein-Positive Rates in the Liver Cancer Group

The comparison of GP73 and AFP positive rates in the liver cancer group is shown in Table 3.

Table 3: Comparison of GP73- and AFP-positive rates in the liver cancer group

<table>
<thead>
<tr>
<th>Indicators</th>
<th>n</th>
<th>Number of positive cases</th>
<th>Positivity rate/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP73 (ng/mL)</td>
<td>156</td>
<td>78</td>
<td>50.0</td>
</tr>
<tr>
<td>AFP (ng/mL)</td>
<td>156</td>
<td>65</td>
<td>41.7</td>
</tr>
</tbody>
</table>

Comparison of GP73 and Alpha-Fetoprotein Levels in Different Syndrome Types

There was a statistically significant difference in GP73 levels among the three types of syndromes (p < 0.05). After pairwise comparison using the LSD method, there was a statistically significant difference (p < 0.05) between the qi stagnation and blood stasis syndrome and the yin deficiency of liver and kidney syndrome, and the yin deficiency of liver and kidney syndrome was greater than the qi stagnation and blood stasis syndrome. There was no statistically significant difference in AFP levels among the three syndrome types (p > 0.05), as shown in Table 4.

Table 4: Comparison of GP73 and AFP levels among different syndrome types

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Qi stagnation and blood stasis syndrome (n = 58)</th>
<th>Heat toxin in liver and gallbladder syndrome (n = 46)</th>
<th>Yin deficiency of liver and kidney syndrome (n = 52)</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP73 (ng/mL)</td>
<td>148.32 ± 14.88</td>
<td>155.88 ± 16.91</td>
<td>163.86 ± 27.45</td>
<td>7.928</td>
<td>0.001</td>
</tr>
<tr>
<td>AFP (ng/mL)</td>
<td>387.67 ± 141.68</td>
<td>416.91 ± 160.37</td>
<td>410.20 ± 167.22</td>
<td>0.516</td>
<td>0.598</td>
</tr>
</tbody>
</table>

Notes: Comparing with qi stagnation and blood stasis syndrome, *p < 0.05.

Comparison of Positive Expression Rates of Golgi Protein 73 and Alpha-Fetoprotein in Different Syndrome Types

There was no statistically significant difference among the three types of syndromes (p > 0.05), as shown in Table 5.

Table 5: Comparison of GP73-positive rates among different syndrome types

<table>
<thead>
<tr>
<th>Syndrome types</th>
<th>n</th>
<th>Positive</th>
<th>Positive rate /%</th>
<th>χ² value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi stagnation and blood stasis syndrome</td>
<td>58</td>
<td>22</td>
<td>37.9</td>
<td>5.650</td>
<td>0.059</td>
</tr>
<tr>
<td>Heat toxin in liver and gallbladder syndrome</td>
<td>46</td>
<td>25</td>
<td>54.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yin deficiency of liver and kidney syndrome</td>
<td>52</td>
<td>31</td>
<td>59.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: GP73 > 150 ng/mL is considered positive.
Comparison of Alpha-Fetoprotein-Positive Rates among Different Syndrome Types

There was no statistically significant difference among the three types of syndromes \( (p > 0.05) \), as shown in Table 6.

<table>
<thead>
<tr>
<th>Syndrome types</th>
<th>n</th>
<th>Positive</th>
<th>Positive rate/%</th>
<th>( \chi^2 ) value</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi stagnation and blood stasis syndrome</td>
<td>58</td>
<td>19</td>
<td>32.8</td>
<td>4.147</td>
<td>0.126</td>
</tr>
<tr>
<td>Heat toxin in liver and gallbladder syndrome</td>
<td>46</td>
<td>19</td>
<td>41.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yin deficiency of liver and kidney syndrome</td>
<td>52</td>
<td>31</td>
<td>51.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: AFP, alpha-fetoprotein.
Notes: AFP \( > 400 \text{ ng/mL} \) is considered positive.

Comparison of Liver Function among Different Syndrome Types

There was no statistically significant difference between TBil and GLO among the three syndrome types \( (p > 0.05) \). There was a statistically significant difference in alanine transaminase (ALT), aspartate aminotransferase (AST), and albumin (ALB) among the three syndrome types \( (p < 0.05) \), as shown in Table 7.

Table 6 Comparison of AFP-positive rates among different syndrome types

<table>
<thead>
<tr>
<th>Syndrome types</th>
<th>n</th>
<th>Positive</th>
<th>Positive rate/%</th>
<th>( \chi^2 ) value</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi stagnation and blood stasis syndrome</td>
<td>58</td>
<td>19</td>
<td>32.8</td>
<td>4.147</td>
<td>0.126</td>
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<td>19</td>
<td>41.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yin deficiency of liver and kidney syndrome</td>
<td>52</td>
<td>31</td>
<td>51.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Analysis of Golgi Protein 73 Levels in the Liver Cancer Group and the Health Group

Research has shown that GP73 \( > 150 \text{ ng/mL} \) is feasible as a diagnostic standard for liver cancer. The average GP73 level in liver cancer patients is 122 to 289.64 ng/mL, while in healthy individuals it is 25.12 to 62 ng/mL. The average GP73 level in liver cancer patients in this study was 163.14 ng/mL, while the health group was 15.66 ng/mL. This result is to some extent consistent with relevant reports.

Distribution of Traditional Chinese Medicine Syndrome Types for Liver Cancer

As the pace of life accelerates and work pressure increases, the number of people suffering from depression and emotional disorders is on the rise. Research has shown that the risk of developing liver cancer in depressed individuals is 1.2 times higher than that in nondepressed individuals. Depression can be classified as an emotional disease in TCM and is most closely related to the liver. If the liver loses its function of conveyance and dispersion, the qi movement in the human body will stagnate and the blood flow will slow down, which can lead to blood stasis. Blood stasis is often accumulated gradually, and liver cancer is one of the accumulated diseases. Huang Di Nei Jing Ling Shu (The Yellow Emperor’s Inner Classic: The Spiritual Pivot) says: “If internal injury is caused by worry or anger, then the qi will go upward counterflowing...Blood stasis accumulates but does not disperse, and body fluid is stagnant and does not flow, which can lead to diseases.” Liu et al found in their research on depression in patients with tumors of different systems that liver cancer patients have more severe depression in the early and middle stages. When patients learn about their condition, they find it difficult to accept it psychologically and develop fear of the disease, leading to anxiety and insomnia. Sleep is mainly closely related to the liver. Huang Di Nei Jing Su Wen (The Yellow Emperor’s Inner Classic: Basic Questions) says: “When a person lies down, blood returns to the liver.” Bing Wang annotated: “The liver stores blood, the heart circulates blood. When a person moves, blood is transported to the various meridians, and when a person is still, blood returns to the liver.” If anxiety and insomnia occur, on the one hand, it can reduce the blood flow back to the liver, prevent the cultivation of liver qi, and cause liver qi stagnation; On the other hand, it undermines liver blood, leading to liver blood deficiency and inability to nourish various organs, resulting in dysfunction of the organs and promoting the deterioration of the disease. Therefore, qi stagnation and blood stasis syndrome occupy an increasing proportion in Table 7 Comparison of liver function among different syndrome types \( (\bar{x} \pm s) \)

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Qi stagnation and blood stasis syndrome ( (n = 58) )</th>
<th>Heat toxin in liver and gallbladder syndrome ( (n = 46) )</th>
<th>Yin deficiency of liver and kidney syndrome ( (n = 52) )</th>
<th>( F ) value</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (U/L)</td>
<td>54.07 ( \pm ) 15.90</td>
<td>64.41 ( \pm ) 19.08\textsuperscript{a}</td>
<td>89.98 ( \pm ) 20.41\textsuperscript{ab}</td>
<td>54.074</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>41.31 ( \pm ) 12.09</td>
<td>78.85 ( \pm ) 15.02\textsuperscript{a}</td>
<td>62.79 ( \pm ) 15.68\textsuperscript{ab}</td>
<td>91.193</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>TBil (( \mu )mol/L)</td>
<td>31.51 ( \pm ) 7.42</td>
<td>33.42 ( \pm ) 7.84</td>
<td>35.16 ( \pm ) 9.20</td>
<td>2.739</td>
<td>0.068</td>
</tr>
<tr>
<td>ALB (g/L)</td>
<td>36.62 ( \pm ) 4.86</td>
<td>41.96 ( \pm ) 5.28\textsuperscript{a}</td>
<td>28.58 ( \pm ) 4.56\textsuperscript{ab}</td>
<td>93.579</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>GLO (g/L)</td>
<td>32.09 ( \pm ) 3.29</td>
<td>33.59 ( \pm ) 2.54</td>
<td>31.69 ( \pm ) 5.57</td>
<td>2.969</td>
<td>0.054</td>
</tr>
</tbody>
</table>

Abbreviations: ALB, albumin; ALT, alanine transaminase; AST, aspartate aminotransferase; GLO, globulin.
Notes: Comparing with qi stagnation and blood stasis syndrome, \( ^{a} p < 0.05 \); comparing with heat toxin in liver and gallbladder syndrome, \( ^{b} p < 0.05 \).
the early and middle stages of the disease. Over time, liver depression transforms into heat, combined with the invasion of pathogenic toxins, forming the heat toxin in liver and gallbladder syndrome. Therefore, the heat toxin in liver and gallbladder syndrome is mostly in the middle and late stages of the disease. Over time, liver depression transforms into heat, or liver and gallbladder heat become excessive, which undermines liver yin and damages kidney yin over time, forming yin deficiency of liver and kidney syndrome, often in the later stages of the disease.

**Analysis of Golgi Protein 73 and Alpha-Fetoprotein Levels among Different Syndrome Types**

In this study, patients with yin deficiency of liver and kidney syndrome had the highest GP73 level, followed by heat toxin in liver and gallbladder syndrome, and patients with qi stagnation and blood stasis syndrome had the lowest GP73 level. The difference between qi stagnation and blood stasis syndrome and yin deficiency of liver and kidney syndrome was statistically significant (p < 0.05). AFP is most significantly elevated in liver and heat-toxin in liver and gallbladder syndrome, followed by yin deficiency of liver and kidney syndrome, and the lowest in qi stagnation and blood stasis syndrome. However, there is no statistically significant difference among the three syndrome types (p > 0.05). Both GP73 and AFP exhibit low levels in the syndrome of qi stagnation and blood stasis.

Ou et al showed that AFP is the lowest in the syndrome of qi stagnation and blood stasis, and the highest in the syndrome of excessive dampness and heat toxin and yin deficiency of liver and kidney. Qiao et al showed that GP73 is expressed at a low level in liver qi stagnation syndrome and blood stasis syndrome. Some studies suggest that the dampness heat accumulation syndrome is closely related to AFP, and the increase is most significant in the dampness heat accumulation syndrome. Fang et al found through a study of 2,060 liver cancer patients that tumor markers were positively correlated with heat symptoms such as high fever, yellow staining of the sclera, thick and greasy tongue coating, and yellow urine, while negatively correlated with cold symptoms. The results of this study are basically consistent with the above research conclusions.

Based on literature reports and the results of this study, it has been found that from the perspective of the cold and heat attributes, the heat toxin in liver and gallbladder syndrome, the syndrome of excessive dampness and heat toxin, and the dampness heat accumulation syndrome all have heat characteristics. These syndrome types may have high sensitivity to tumor markers, often manifested at a high level. However, combining the analysis of the stage of the disease is more appropriate. Qi stagnation and blood stasis syndrome are most common in the early and middle stages of the disease, with heat toxin in liver and gallbladder syndrome, the syndrome of excessive dampness and heat toxin, and dampness heat accumulation syndrome being mostly in the middle stage of the disease, and liver and kidney yin deficiency syndrome being mostly in the late stage of the disease. Therefore, in the early stage of liver cancer without thermal imaging, it is mostly insensitive to tumor markers and has low expression levels. Syndrome types have the characteristic of heat or are more sensitive to tumor markers in the middle and late stages of the disease, often manifested at high levels. The above is only speculation, and its rationality still needs further verification.

**Analysis of Golgi Protein 73- and Alpha-Fetoprotein-Positive Expression Rates among Different Syndrome Types**

The results of this study showed that the positive expression rates of GP73 and AFP in liver cancer ranged from high to low, followed by yin deficiency of liver and kidney syndrome, heat toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome. There was no statistically significant difference between syndrome types (p < 0.05). The study by Liu et al showed that the positive rate of AFP was ranked from high to low as liver depression and spleen deficiency syndrome, dampness heat accumulation syndrome, yin deficiency of liver and kidney syndrome, and qi stagnation and blood stasis syndrome. There was no statistically significant difference between each type of syndrome. Xu believes that the AFP-positive detection rate is the highest in yin deficiency of liver and kidney syndrome, followed by the dampness heat internal accumulation syndrome and qi stagnation and blood stasis syndrome, while the liver stagnation and spleen deficiency syndrome and qi stagnation and blood stasis syndrome are the lowest. Most studies have shown that AFP has the lowest detection rate in qi stagnation and blood stasis syndrome, but its mechanism is not yet clear. Due to the limited research on this topic, it is difficult to unify the conclusions drawn, making it difficult to form a final conclusion.

**Analysis of Liver Function among Different Syndrome Types**

This study shows that patients with yin deficiency of liver and kidney syndrome have the highest ALT level, followed by heat-toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome have the lowest, and the difference is statistically significant (p < 0.05). The AST level is the highest in patients with heat toxin in liver and gallbladder syndrome, followed by yin deficiency of liver and kidney syndrome, and the lowest in qi stagnation and blood stasis syndrome, with a statistically significant difference (p < 0.05). The ALB level in patients with heat-toxin in liver and gallbladder syndrome is the highest, followed by qi stagnation and blood stasis syndrome, and the yin deficiency of liver and kidney syndrome is the lowest, with a statistically significant difference (p < 0.05). The TBil level in patients with yin deficiency of liver and kidney syndrome is the highest, followed by heat toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome is the lowest, but the difference is not statistically significant (p > 0.05). The above indicates that patients with qi stagnation and blood stasis syndrome have relatively mild liver function damage, while those with yin deficiency of liver and kidney syndrome have the most severe damage. From the analysis of the evolution of diseases in TCM, in the early stage of the disease, liver function is abnormal, losing its function of
conveyance and dispersion, qi movement is stagnant, blood flow is delayed, and blood stasis occurs. Qi stagnation and blood stasis are mostly in the early or middle stages of the disease, with strong positive qi and shallow pathogenic qi. The body has strong resistance to pathogen and the damage is relatively mild. Blood stasis transforms into heat over time, combined with the invasion of pathogenic toxin, resulting in heat-toxin in liver and gallbladder syndrome. The syndrome is mostly in the middle stage of the disease, where the disease and pathogen go deep, and the competition between the positive and pathogen is intense, consuming the positive qi and further exacerbating the damage. Yin deficiency of liver and kidney syndrome is often in the late stage of the disease, often accompanied by changes such as jaundice, bloating, and blood syndrome. Prolonged illness often leads to deficiency, and in the later stages of the disease, visceral dysfunction is often accompanied by deficiency syndromes such as qi, blood, and body fluids. At this time, the pathogenic qi is hyperactive, the vital qi dissipates, and the ability to resist pathogen is weak, so the damage is the most severe.

Conclusion

GP73 can be used as a sensitive indicator for TCM syndrome differentiation and classification of liver cancer patients. Its expression in three types of liver cancer syndrome types is in descending order: yin deficiency of liver and kidney syndrome, heat toxin in liver and gallbladder syndrome, and qi stagnation and blood stasis syndrome. The expression of ALT in three types of liver cancer syndrome patients is consistent with the expression of GP73, and the levels of AST and ALB are the highest in patients with heat toxin in liver and gallbladder syndrome. Therefore, ALT, AST, and ALB can also serve as auxiliary indicators for TCM syndrome differentiation and classification of liver cancer patients.

Authors’ Contribution

B.L. was responsible for conceptualization, methodology, project administration, and writing-original draft. J.R. was responsible for formal analysis, investigation, validation, and writing-original draft. H.L. was responsible for funding acquisition, supervision, Writing-review & editing.

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Conflict of Interest

The authors declare no conflict of interest.

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