中文摘要

原发性肝癌合并门静脉癌栓的临床特征分析

目的：

回顾性分析吉林大学第一医院内原发性肝癌合并门静脉癌栓患者的流行病学及临床特征，通过对其临床资料进行分析，提高对该疾病的认识，早期干预以改善预后，延长生存期。

方法：

收集 2020 年 01 月至 2022 年 12 月就诊于吉林大学第一医院肝胆胰内科的 HCC 合并 PVTT、HCC 患者的临床资料，根据纳入排除标准，确定 247 例 HCC 合并 PVTT 患者、138 例 HCC 患者为研究对象。分析 HCC 合并 PVTT 患者的总体特征，并根据性别进行分组，探讨不同性别 HCC 合并 PVTT 患者的人群特征。本研究共纳入 208 例 HBV 相关感染的 HCC 合并 PVTT 患者，对其人群总体特征进行了详细描述。将患者按有无癌栓进行分组比较，进一步探讨了 HCC 合并 PVTT 与单纯 HCC 患者之间的差异。最后，我们采用 Kaplan-Meier 曲线、Log-Rank 检验及多因素 Cox 回归模型对 HCC 合并 PVTT 人群进行生存分析。

结果：

（1）HCC 合并 PVTT 人口学特征：本研究纳入 HCC 合并 PVTT 患者共 247 例，其中男性 210 例，占比 85%，女性 37 例，占比 15%，男女比例约 6：1。年龄分布集中在 45-55、55-65 岁 2 个年龄段，最小年龄为 23 岁，年龄最大为 85 岁，平均年龄（58.27±10.173）岁。民族分布以汉族为主，占比 90.7%，少数民族包括朝鲜族、回族、满族、蒙古族，分别占比 1.6%、0.4%、10%、8%。腹胀 、乏力、腹痛是首发临床表现，占比分别为 81.4%、19%、18.6%。病因分析中，HBV 所占比例最高，84.2%（208 例），其次为 HCV（24 例，9.7%），酒精因素占 4.5%（11 例）。

（2）HCC 合并 PVTT 生物学标记物及影像学资料分析：AFP 阳性率为 84.3%（204/242），阴性率为 15.7%（38/242）。AFP 异质体阳性率为 89.6%（52/58），

阴性率为 10.4%（6/58）。根据影像学对所有患者癌栓部位进行分型，Ⅰ型为 12 例（4.9%），Ⅱ型共 78 例（31.6%），Ⅲ型 134 例（54.3%），Ⅳ型 23 例（9.3%）。对 HCC 合并 PVTT 患者进行肿瘤病灶部位及肿瘤数目分析，病灶位于右叶有 95 例，病灶位于左叶有 19 例，病灶位于左右肝叶有 133 例。单发肿瘤比例占 33.2%，双发肿瘤占 3.2%，多发病灶（≥3 个）占 63.6%。对所有患者进行 Child-Pugh 评分，B 级多见，总计 114 例，占 46.1%。

（3）将 HCC 合并 PVTT 人群按性别进行分组，比较不同性别组 HCC 合并 PVTT 患者人口学及临床资料发现，合并乙肝、吸烟史、饮酒史、冠心病史、年龄、ALB、HGB、PT、PTA、肿瘤大小两组间具有统计学差异（P＜0.05）。

（4）HBV 感染 HCC 合并 PVTT 患者共计 208 例，分析人口学特征：男性 182 例，占比 87.5%，女性 26 例，占比 12.5%。青年发病人数为 22 例，占比 10.6%，中年发病人数为 116 例，占比 55.8%，老年发病人数为 70 例，占比 33.7%。年龄分布集中在 45-60 这一年龄段，平均年龄（55.56±9.812）岁。

（5）HBV 感染的 HCC 合并 PVTT 人群中，共有 182 例完善乙肝病原学检验，119 例患者血清学标志物为“HBsAg（+）、HBeAb（+）、HBcAb（+）”，占比 65.3%，标志物为“HBsAg（+）、HBeAg（+）、HBcAb（+）”患者 36 例，占比 19.7%，标志物为“HBsAg（+）、HBeAg（+）、HBeAb（+）、HBcAb（+）”患者 9 例，占比 4.9%，标志物为“HBsAg（+）、HBcAb（+）”患者 18 例，占比 10.1%。分析抗病毒情况，共有 68 例患者规律抗病毒治疗（32.6%），33 例患者应用恩替卡韦进行治疗，占抗病毒总人数 42.8%，未抗病毒治疗患者有 132 例，占比 63.1%。此外，还有 9 例患者在抗病毒期间出现擅自停药现象（4.3%）。

（6）对 HBV 感染的 HCC 合并 PVTT 患者按年龄分为青年组、中年组、老年组，比较相关资料显示，肝癌家族史、高血压病史、糖尿病史、发生肝外转移三组总体差异有统计学意义（P＜0.05），而性别、合并肝硬化、吸烟史、饮酒史、冠心病史、抗病毒治疗、实验室指标、肿瘤部位、肿瘤大小、肿瘤数目、Child-Pugh 评分、MELD 评分三组间总体差异无统计学意义（P＞0.05）。

（7）分析不同程式分型与 HBV 感染相关因素之间的相关性发现，HBV-DNA 水平与合并肝硬化两组间具有统计学差异（P＜0.05），与程式分型 I/II 型相比，程式分型为 III/IV 型的 HBV-DNA 水平明显更高（86% vs 74.6%），合并肝硬化

的比例显著上升（99.3% vs 93.1%）。而 HBsAg、HBeAg、是否抗病毒治疗两组间无统计学差异（P＞0.05）。

（8）单纯 HCC 组与 HCC 合并 PVTT 组一般资料比较分析：合并乙肝、性别、年龄、合并肝硬化、吸烟史、饮酒史、AST、ALT、GGT、ALP、CHE、ALB、TBIL、TBA、AFP、WBC、NE%、LY%、NE#、LY#、PLT、APTT、PT、肿瘤部位、有无转移、肿瘤数目、肿瘤最大直径组间比较具有显著差异（P＜0.05），HCC 家族史、高血压史、糖尿病史、冠心病史、HGB 组间比较均无显著差异（P＞0.05）。Child-Pugh 评分具有显著差异（P＜0.05），而 MELD 评分无差异（P＞0.05）。

（9）HCC 合并 PVTT 患者生存分析：共计 146 例患者出现了阳性事件（死亡），中位随访时间为 8.0 个月，中位生存时间为 4.0 个月，HCC 合并 PVTT 患者在 6 个月、1 年及 2 年的生存率分别为 39.7%、29.7%、15.4%。

（10）对 HCC 合并 PVTT 患者相关因素进行单因素 Cox 回归分析，结果显示，合并乙肝、有无治疗、高血压病史、冠心病史、AST、ALT、GGT、白蛋白、TBiL、PT、PTA、MELD 评分、是否转移、PVTT 分型差异有统计学意义（P＜0.05）。将上述有统计学意义的指标纳入多因素 Cox 比例风险模型中，调整其他混杂因素后，结果显示合并乙肝、发生肝外转移、程式分型为III/Ⅳ型的患者预后生存更差，其风险比及 95%置信区间分别为：1.609（95%*CI*：1.027-2.521，P=0.038），1.706（95%*CI*：1.173-2.480，P=0.005），1.446（95%*CI*：1.061-1.972，P=0.020）。抗肿瘤治疗的预后生存较好，其风险比及 95%置信区间分别为：0.618（95%*CI*：0.402-0.952，P=0.029）。

（11）对不同程式分型及抗肿瘤治疗情况进行生存分析：程式分型为 III/IV 型及未行抗肿瘤治疗患者的预后更差。I/II 型患者中位生存时间为 8.0 个月，在 6 个月、1 年及 2 年的生存率分别为 52.0%、36.3%、22.0%；III/IV 型患者中位生存时间为 3.0 个月，在 6 个月、1 年及 2 年的生存率分别为 31.5%、25.2%、12.1%。抗肿瘤治疗患者的中位生存时间为 20.0 个月，在 6 个月、1 年及 2 年的生存率分别为 64.1%、50.9%、24.2%；未行抗肿瘤治疗患者的中位生存时间为 3.0 个月，在 6 个月、1 年及 2 年的生存率分别为 33.1%、22.5%、9.4%。

结论：

（1）研究人群中，男性多见，发病年龄集中在 45～65 年龄段，乙肝病史居

多，首发临床表现为腹胀 、乏力、腹痛， PVTT 分型以程氏分型Ⅱ型、Ⅲ型多见。

（2）HBV 感染的 HCC 合并 PVTT 患者乙肝病原学以“HBsAg（+）、HBeAb（+）、HBcAb（+）”多见。随着癌栓侵犯程度的增加，HBV-DNA 水平及合并肝硬化患者的比例显著上升。

（3）合并乙肝或肝硬化的 HCC 患者需密切复查，警惕癌栓形成。

（4）合并乙肝、未行抗肿瘤治疗、发生肝外转移、程式分型为Ⅲ/Ⅳ型的患者预后生存差。

关键词：

门静脉癌栓，原发性肝癌，临床特征，HBV 感染

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论文题目：原发性肝癌合并门静脉癌栓临床特征、危险因素及预后因素分析

作者签名：黄俐洁 指导教师签名：

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Abstract

Analysis of clinical features of hepatocellular carcinoma with portal vein tumor thrombosis

Objective:

We retrospectively analyze the clinical characteristics of patients with hepatocellular carcinoma combined with portal vein tumor thrombosis within the First Hospital of Jilin University.Through the analysis of their clinical data, to improve the understanding of the disease, early intervention to improve the prognosis and prolong the survival.

Methods:

Clinical data of patients with HCC combined with PVTT and HCC who visited the Department of Hepatobiliary and Pancreatic Medicine of the First Hospital of Jilin University from 01, 2020 to 12, 2022 were collected. According to the inclusion and exclusion criteria, 247 patients with HCC combined with PVTT and 138 patients with HCC were chosen as the study subjects. The study analyzed the overall characteristics of patients with HCC combined with PVTT, and stratified them by gender to explore population differences between male and female patients with HCC combined with PVTT associated with hepatitis B virus infection. A total of 208 patients were included in this study, and their general characteristics were described in detail. Further analysis was conducted by grouping the patients based on the presence or absence of cancer thrombus. The survival of patients with HCC combined with PVTT, was analyzed using Kaplan-Meier curve, Log-Rank test, and multifactorial Cox regression model.

Results:

(1) Clinical characteristics of HCC combined with PVTT: A total of 247 patients with HCC combined with PVTT were included in this study. Among them, 210 cases were male, accounting for 85%; 37 cases were female, accounting for 15%, with a male to female ratio of about 6:1. The age distribution was concentrated in 2 age groups, 45 to 55 and 55 to 65 years old, with the minimum age being 23 years old and the maximum age being 85 years old, with a mean age of (58.27 ± 10.173) years. Ethnic distribution was dominated by Han Chinese, accounting for 90.7%. Minorities included Korean,

Hui, Manchu, and Mongolian, accounting for 1.6%, 0.4%, 10%, and 8%, respectively. Abdominal distension, weakness, and abdominal pain were the first clinical manifestations, accounting for 81.4%, 19%, and 18.6%, respectively. In the etiological analysis, HBV accounted for the highest proportion, (84.2%; 208 cases), followed by HCV (24 cases; 9.7%), and alcohol factors accounted for 4.5% (11 cases).

(2) Analysis of biological markers and imaging data of HCC combined with PVTT: The positive rate of AFP was 84.3% (204/242) and the negative rate was 15.7% (38/242). The positive rate of AFP-L3 was 89.6% (52/58) and the negative rate was 10.4% (6/58).All patients were staged according to imaging for the site of cancer thrombosis; type I was 12 cases (4.9%), type II totaled 78 cases (31.6%), type III 134 cases (54.3%), and type IV 23 cases (9.3%). The site and number of tumor lesions in patients with HCC combined with PVTT were analyzed. Ninety-five lesions were located in the right lobe, 19 in the left lobe, and 133 in both hepatic lobes. Single tumors accounted for 33.2%, double tumors accounted for 3.2%, while multiple lesions （≥3） accounted for 63.6%. Child-Pugh scores were performed on all patients, with B grade being more prevalent at a total of 114 cases or accounting for 46.1%.

(3) Patients with HCC combined with PVTT were stratified by gender, and the demographic and clinical characteristics of these patients in different gender groups were compared. The results showed that there were significant differences between the two groups in terms of hepatitis B infection, smoking history, alcohol consumption history, coronary heart disease history, age, ALB level, HGB level, PT value, PTA value and tumor size ($P < 0.05$).

(4) A total of 208 patients diagnosed with HBV infection and PVTT were analyzed for demographic characteristics, revealing that males accounted for 87.5% (n=182) and females accounted for 12.5% (n=26). The age distribution was as follows: young patients comprised 10.6% (n=22), middle-aged patients comprised 55.8% (n=116), and elderly patients comprised 33.7%(n=70). The majority of cases fell within the age range of 45-60 years old, with an average age of (55.56±9.812) years.

(5) Among patients with HCC combined with PVTT and HBV infection, 182 cases completed hepatitis B aetiological testing. Of these, 119 cases had serological markers of "HBsAg (+), HBeAb (+), HBcAb (+)", accounting for 65.3%. Thirty-six patients were identified as "HBsAg (+), HBeAg (+), HBcAb (+)", accounting for 19.7%, while nine patients were identified as "HBsAg (+), HBeAg (+), HBeAb(+), HBcAb(+)",

accounting for 4.9%. There were also eighteen patients with both HBsAg(+) and HBcAb(+) markers, representing 10.1% of the total. Analysis of the antiviral situation revealed that 68 patients (32.6%) received regular antiviral treatment, while 33 patients (42.8% of all antiviral patients) were treated with Entecavir. Additionally, 132 patients (63.1%) did not receive any form of antiviral treatment, and there were nine cases (4.3%) of unauthorized drug withdrawal during the antiviral period.

(6) HBV-infected patients with HCC combined with PVTT were stratified into three age groups: young, middle-aged, and elderly. The comparison of relevant data revealed statistically significant differences among the groups in terms of family history of liver cancer, hypertension history, diabetes history, and occurrence of extrahepatic metastasis ($P < 0.05$). There were no significant differences observed in terms of gender, cirrhosis, smoking history, drinking history, coronary heart disease history, antiviral therapy, laboratory indexes, tumor site and size as well as Child-Pugh score and MELD score among the three groups ($P > 0.05$).

(7) Analysis of the correlation between different program types and factors related to HBV infection revealed a statistically significant difference in HBV-DNA levels between the two groups with cirrhosis ($P < 0.05$). Patients with program types III/IV had significantly higher HBV-DNA levels compared to those with program types I/II (86% vs 74.6%).The proportion of patients with cirrhosis exhibited a significant increase (99.3% vs 93.1%). No statistically significant differences were observed in terms of HBsAg, HBeAg or antiviral treatment between the two groups ($P > 0.05$).

(8) Comparative analysis of general data between HCC alone group and HCC combined with PVTT group: There were significant differences in the scores related to combined hepatitis B, gender, age, combined cirrhosis, history of smoking, history of alcohol consumption, AST, ALT, GGT, ALP, CHE, ALB, TBIL, TBA, AFP, WBC, NE%, LY%, NE#, LY#, PLT, APTT, PT, tumor site, presence of metastasis , number of tumors, and maximum tumor diameter had significantly different correlation scores ($P < 0.05$). There were no significant differences in the scores of family history of HCC, history of hypertension, history of diabetes, history of coronary heart disease, and HGB ($P > 0.05$). There was a significant difference in the scores of Child-Pugh ($P < 0.05$), while there was no difference in the scores of MELD ($P > 0.05$).

(9) Survival analysis of patients with HCC combined with PVTT revealed that out of 146 patients, positive events (death) occurred. The median follow-up time was 8.0

months and the median survival time was 4.0 months. The survival rates for HCC patients with PVTT at 6-months, 1-year and 2-years were found to be 39.7%, 29.7% and15.4%, respectively.

(10) Univariate Cox regression analysis was conducted to examine factors associated with patients with HCC combined with PVTT, revealing statistically significant differences in hepatitis B patients with or without treatment, history of hypertension and coronary heart disease, AST, ALT, GGT, albumin, TBiL, PT and PTA levels, MELD scores as well as metastasis and PVTT typing ($P < 0.05$). The aforementioned statistically significant indicators were integrated into the Cox proportional risk model. After adjusting for other confounding factors, the results indicated that patients with hepatitis B, extrahepatic metastasis, and program type III/IV had a poorer prognosis. The hazard ratio and 95% confidence interval were as follows: 1.609 (95%CI: 1.027-2.521, P=0.038), 1.706 (95%CI: 1.173-2.480, P=0.005), and 1.446 (95%CI: 1 .061-1 .972,P =0 .020). The antitumor therapy exhibited a favorable prognosis, with a hazard ratio of 0.618 (95%CI: 0.402-0.952, P=0.029).

(11) Survival analysis was performed for different program classification and antitumor therapy: patients with program classification III/IV and those without antitumor therapy had worse prognosis. The median survival time of type I/II patients was 8.0 months, and the 6-month, 1-year and 2-year survival rates were 52.0%, 36.3% and 22.0%, respectively. The median survival time of patients with type III/IV was 3.0 months, and the survival rates at 6 months, 1 year and 2 years were 31.5%, 25.2% and 12.1%, respectively. The median survival time of antitumor treatment was 20.0 months, and the survival rates at 6 months, 1 year and 2 years were 64.1%, 50.9% and 24.2% respectively. The median survival time of patients who did not receive antitumor therapy was 3.0 months, and the 6-month, 1-year and 2-year survival rates were 33.1%, 22.5% and 9.4%, respectively.

Conclusion:

(1) In the study population, there were more males than females. The age of onset was concentrated in the 45-65 age group, and a history of hepatitis B was predominant. The first clinical manifestations were often abdominal distension, weakness, abdominal pain. PVTT typing is more common with Cheng's typing type II and type III.

(2) "HBsAg (+), HBeAb (+), HBcAb (+) “were identified as the predominant etiologies of patients with HCC combined with PVTT. The level of HBV-DNA and the

proportion of cirrhotic patients significantly increased with the extent of cancer thrombus invasion.

(3) HCC patients with hepatitis B or cirrhosis should undergo close surveillance to prevent cancer embolism.

(4) Patients with hepatitis B, no antitumor therapy, extrahepatic metastasis and program type Ⅲ/Ⅳ had poor prognosis and survival.

Keywords：

Portal vein tumor thrombosis，Hepatocellular carcinoma，Clinical features，HBV infection

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