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Research Article

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Evaluation of Some Quality Factors of Patients Chemoembolization of Hepatocellular Carcinoma with Doxorubicin

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Abstract Evaluation of the results of survival and analysis of some prognostic factors in patients with chemotherapy-treated hepatocellular carcinoma with Doxorubicin. Research describes in 76 patients were treated chemoembolization of hepatocellular carcinoma with doxorubicin. In this study, a total of 76 patients the average age was 51 years old. Male / female ratio 90.7% / 9.3%. The concentration of AFP has a median value of 1045.0 (25.15-125000.0) ng/ml. There are 88% of hepatitis B. Child - Push A / B classification 95.0% / 5.0%, average tumor size 6.5 cm. Clinical stage II; III; and IV respectively accounted for 42.1%; 40.8 and 17.1. The average follow-up time was 32.8 months, with an average life span of 33.4 months. Survival rate of 1 year, 3 years and 5 years of patients using hepatic angioplasty with Doxorubicin is 92.7%, 70.7% and 16.9%, respectively, with P (1 & 2) < 0.001; p (2 & 3) = 0.009. The average survival rate of patients with high serum GGT level> 200 U / L and low serum GGT level ≤ 200 U / L are 23 months and 28 months respectively, with p <0.001; high serum CRP (> 5.0 mg / L) and low (mg 5 mg / L) were 22.7 and 31.5 months (p <0.001) respectively and serum ALP concentration was 22.0 months and 29.4 months in the high group ALP and low group ALP, respectively (p <0.001). The current study showed that the primary hepatocellular carcinoma treated with hepatic vessels gives good results, lifetime of 1 year; 3 years and 5 years respectively 92.7%, 70.7% and 36.9%.

Keywords Liver cancer, Hepatocellular carcinoma, patients

1. Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer and is the second leading cause of cancer-related deaths worldwide, with up to 700,000 deaths annually [1]. According to the population cancer in Ho Chi Minh City, Hanoi and some provinces, the age-standardized rate of men is 22.6 / 100,000 people, the third most common, in women is 6, 3 / 100,000 people [2-5]. The HCC prognosis is very poor, most likely due to the diagnosis of late-stage disease and limited access to timely and standard treatments [1, 6]. About 80% to 90% of patients develop HCC when the diagnosis is considered ineligible for any radical treatment, especially liver removal or liver transplantation. Treatment is based on the stage of the disease, liver function and body condition. For advanced patients, treatments including percutaneous chemotherapy circuit (TACE) and sorafenib have been widely used. According to the classification approved by the American Society for Liver Disease Research (AASLD) / European Association for Liver Research (EASL), treatment guidelines for the progression of the nucleus are developed to achieve disease control and mitigation. Symptoms of using sorafenib, a kinase inhibitor, have been recommended as standard treatments for these patients [1]. However, the treatment effect of Sorafenib provides a modest lifetime for patients and expensive treatment. Therefore, the use of sorafenib as the first treatment for progressive HCC is uncommon in real life, a large number of patients diagnosed with advanced stage disease [7-8]. Instead of sorafenib, TACE and treatment for patients with this stage. This is the method of directing chemicals into the liver cancer, then using Lipiodol to block the peripheral

arteries, minimizing the development of tumour circulation and at the same time selective necrosis of the tumour. Liver cancer without serious necrosis of healthy liver parenchyma. Some research results in the world have shown that the results of the treatment of cutaneous chemotherapy with Doxorubicin give good results. However, no author has fully evaluated the results of Doxorubicin in the treatment of the percutaneous chemotherapy circuit for advanced liver cancer. To assess the treatment results in HCC patients who used TACE with Doxorubicin, therefore we have conducted the research with the main objectives of the study: Evaluating the results of survival and analysis of some prognostic factors in patients with chemotherapy-treated hepatocellular carcinoma with Doxorubicin.

Materials and Methods

Materials

A total of 76 patients diagnosed with advanced HCC initially treated with TACE at the Cancer Center of Thai Nguyen Central Hospital from January 2015 to December 2018.

Criteria for selecting patients: HCC patient with phase II; III and IVA; Liver function Child-Pugh A or B; HCC was not treated before. No vein thrombosis, Body status ECOG 0-2. Exclusion criteria: Complete condition ECOG 3-4 or no monitoring data.

Methods

Research design: Descriptive method with analysis

Sample size: Whole.

Research targets: General characteristics: age, gender. Clinical characteristics: ability, entity, body. Subclinical features: Ultrasound, X-ray, computerized tomography assessing tumor status: tumor position, tumor size, tumor properties, number of tumors, abdominal fluid (Acid). The indicators for assessing liver function: HbSAg; AFP; AST; ALT; GGT; LDH; ALP; CRP; TBIL; ALB; PT; Child-Pugh classification...

Diagnostic criteria for hepatocellular carcinoma: Diagnosis of HCC based on guidelines of the Ministry of Health with Have one of the following three criteria: (1) There is pathological anatomical evidence that primary liver cell cancer**;** (2) A typical CT scan of the abdominal scan with contrast or MRI of the abdominal cavity is prevented from + AFP> 400ng / ml; (3) A typical CT scan of the abdominal scan with contrast or MRI of the abdominal cavity with AFP is higher than normal (but less than 400ng / ml) + with hepatitis B virus infection; or C. A liver biopsy can be made for a definitive diagnosis if necessary (Decision 5250 / decision - Ministry of Health on December 28, 2012).

Implementation: TACE is carried out by the technical procedures specified by the Ministry of Health. Depending on the size, location and supply of the arteries to the tumor, the catheter tip is inserted into the arterial artery or artery that supports the specific tumor. The chemotherapy used is Doxorubicin mixed in 9 ml of water-soluble solvents and 1 ml of sterile water for injection. Pure lipiodol porous particles (500-1,000 m) are then injected into the arterial region to nourish the tumor causing embolism. The dose of anticancer agent Doxorubicin, lipiodol and the combined materials used for the percutaneous chemotherapy circuit is determined based on tumor size, tumor lesion and tumor blood supply.

Percutaneous chemotherapy circuit is repeated after 8-12 weeks after every node until one of the following endpoints as following: (1) Complete the tumour vascular elimination process; (2) There is no technical possibility for tumor remnants left over, for example, tumors are only provided by arteries outside the body; (3) Develop contraindications to TACE; or (4) completely remove or remove the tumor by subsequent surgery or local resection

Evaluate tumor response after TACE: The evaluation of response to TACE within three months (after the first or second TACE) was evaluated by the cancer and imaging diagnosis experts according to the Criteria for Evaluation of Solid Tumor Response (mRECIST) [9]. The patient has a complete response (CR); Partial

response (PR) is grouped as having an objective response to TACE. Complete response results, partial response; disease remains the same or progresses [9].

Monitoring of treatment results: patients were monitored by CT or MRI 4 weeks after treatment and then every 3-4 months. During each follow-up visit, all detailed results have been collected and a comprehensive check has been performed. Blood tests, including serum liver function tests and alpha fetoprotein (AFP) levels, are also performed.

The end of the study is the end date of data collection, calculated from the initial TACE treatment until all causes of death or until the last follow-up.

Data analysis

Data were entered and analyzed on SPSS 20.0 software. For continuous variables, the data were expressed as the mean value ± the standard error of the mean. The categorical variables were analyzed by Fisher's exact test and continuous variables are compared using the non-paired T - Student test. Patient survival was calculated by Kaplan-Meier method and analyzed by log-Rank test. Prognostic factors are evaluated by univariate and multivariate analyzes using the linear regression, Cox regression. $P < 0.05$ was considered statistically significant.

Ethics in research

This study was approved by the hospital's professional evaluation boards. The consent of all patients studied.

Results and Discussion

The characteristics of patients are related to overall survival

Progressive primary hepatocellular carcinoma has been studied by many authors on the treatment method to find the optimal method for high results in treatment. A French survey of current practices on treatments for primary hepatocellular carcinoma suggests that Doxorubicin is most frequently used for hepatic vascular nodes [8]. In 76 patients, we studied an average age of 51 years, the highest of 77 years, the lowest of 35 years. According to research by Kim et al [10], the average age is 60 years, the highest is 84, the lowest is 27 [10]. According to author Tim A. Labour and the average age of 69, the highest 74, the lowest 61 [11]. According to research by Yong et al [1] reported that the average age 50, highest 77, lowest 23 [1]. In this study, characteristics associated with general survival in patients with hepatocellular carcinoma (n = 76) as shown in Table 1. In univariate analysis, concentration of AFP, aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), C-reactive protein (CRP) and total bilirubin (TBIL) showed that related to overall survival (all p <0.05). In multivariate analysis, significant independent prognostic factors for overall survival were GGT (> 200 U / L), CRP (> 5.0 mg / L), ALP (> 130 U / L).

Table 1: The characteristics associated with general survival in patients with hepatocellular carcinoma

Features	Overall Survive		
	Analysis of the whole application	Multivariate analysis	
		HR (95% CI)	P value
Year (≥50 with <50)	0.914		> 0,05
Gender (male vs female)	0.708		> 0,05
HbsAg (Yes/ No)	0.683		> 0.05
AFP, ng/ml, (≥400 vs <400)	0.019		> 0.05
AST, UL, (>60 vs ≤60)	0.008		> 0.05
ALT, U/L, (>50 vs ≤50)	0.474		
GGT, U/L, (>200 vs ≤200)	<0.001	1.742 (1.333-2.276)	<0.001
LDH, U/L, (>250 vs ≤250)	0.054		
ALP, U/L, (>130 vs ≤130)	<0.001	1.323 (1.012-1.730)	0.041
CRP, mg/L, (>5.0 vs ≤5)	<0.001	1.526 (1.145-2.036)	0.004

TBIL, umol/L, (>25 vs ≤25)	0.022	> 0.05
ALB, g/L, (>35 vs ≤35)	0.715	> 0.05
PT, sec, (>14.0 vs ≤14.0)	0.275	> 0.05
Child-Pugh classified (B vs A)	0.821	> 0.05
Acid (Yes/ No)	0.061	> 0.05
Tumor size, cm,, (≥5.0 vs <5.0)	0.052	> 0.05
Number of tumours (>1 vs 1)	0.593	> 0.05

The relationship between pay factors and lifetime

The relationship between GGT and lifetime: The average survival rate of patients with high serum GGT level> 200 U / L and low serum GGT level ≤ 200 U / L are 23 months and 28 months respectively, with p <0.001 as shown in Figure 1.

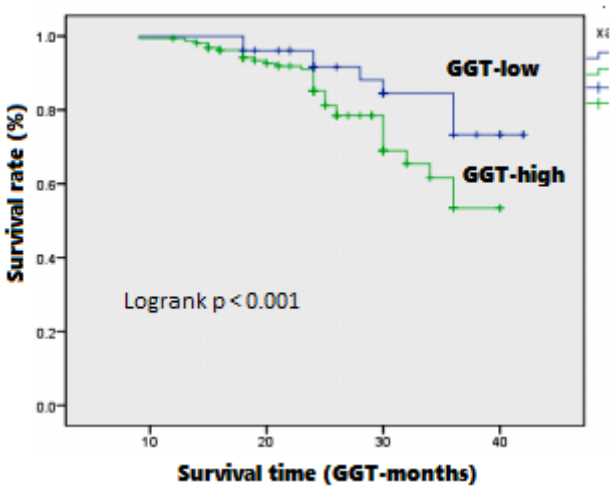

Figure 1: The relationship between GGT and the extra time

The average survival rate of patients with HCC has high serum CRP (> 5.0 mg / L) and low serum CRP concentration (≤ 5 mg / L) treated with TACE is 22, respectively. 7 and 31.5 months (p <0.001) as presented in Figure 2.

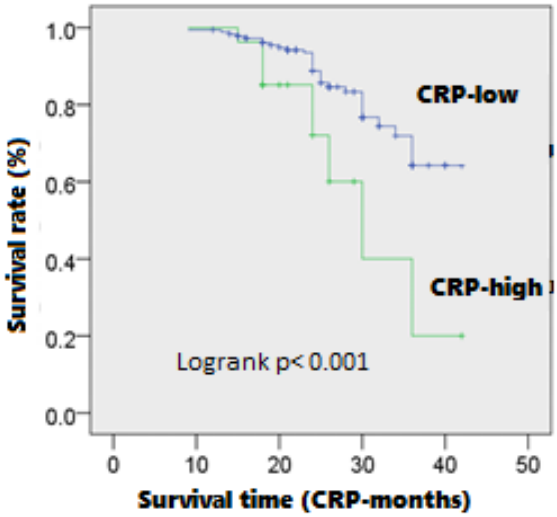

Figure 2: The relationship between CRP and lifetime

The relationship between ALP and lifetime

The average survival rate with serum ALP concentration was 22.0 months and 29.4 months in the high group ALP and the low group ALP, respectively (p <0.001) (Figure 3.3)

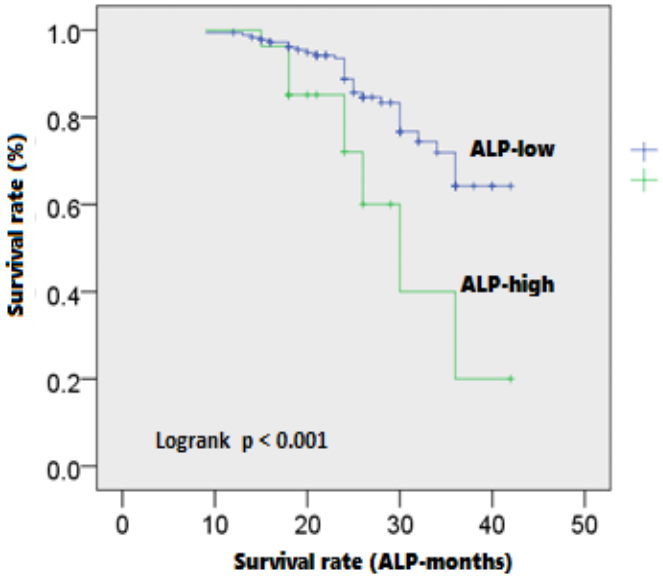

Figure 3: The relationship between ALP and lifetime

The relationship between the period of disease and lifetime

The survival rate after 1 year, 3 years and 5 years of patients using hepatic node method with Doxorubicin were 92.7%, 70.7% and 16.9%, respectively (P 1 & 2) <0.001; p (2 & 3) = 0.009 (Figure 4).

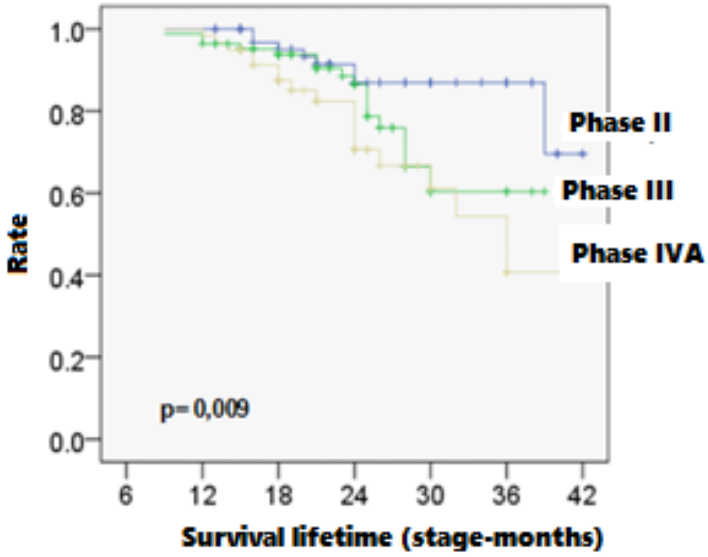

Figure 4: The relationship between the period of disease and lifetime

The proportion of males accounts for 90.7%, females 9.3%, according to Yong et al [9] and the proportion of males is 90.4%, females are 9.6%. The concentration of AFP is one of the criteria for the diagnosis of primary hepatocellular carcinoma, in our study the concentration of AFP in patients is quite high, the median value is 1045.0 (25.15-125000.0) ng/ml. It showed that the average age 50, highest 77, lowest 23 [9]. The proportion of males accounts for 90.7%, females 9.3%, according to Yong. Le and the proportion of males is 90.4%, females are 9.6% [9]. The concentration of AFP is one of the criteria for a diagnosis of primary hepatocellular carcinoma, in our study the concentration of AFP in patients is quite high, the median value is 1045.0 (25.15-125000.0) ng/ml. This index is 1145.0 (1.15-121000.0). Having hepatitis B 88% is similar to Yong's study of 88.1% [9]. ALT levels; AST slightly increased with an average value of 47.7 U / L; 65.0 U / L. In the study of Yong et al [9], there were 46.7 U / L and 62.0 U / L. The median value of ALP 140.0 U / L and CRP is 15.79

mg / L, 136.0 U / L and 13.79 mg / L. Child - Push category A / B 95.0% / 5.0%,, while, Yong et al [9] reported 94.7% and 5.3%, respectively. The average tumour size is 6.5 cm, the largest is 10.5 cm, the smallest is 2.1 cm. The number of tumours 1 block 80.5%; More than 1 block 19.2%, the results of Yong et al [9] showed that 38.9% and 61.1% were more than 1 block. The peritoneal fluid has 5 patients, accounting for 6.6% but the number is very small. According to the report of Kim et al [8], it is 13.6% having abdominal fluid. In our clinical phase II study; III; and IV respectively accounted for 42.1%; 40.8 and 17.1%. This result is similar to that of the study of Kim et al [8] and phase II; III; and IV respectively 41.6%; 41.0% and 17.4% [8]. In our study, 76 patients received hepatic vascular nodes according to tumour size, systemic status, liver function ... that Doctor calculated Doxorubicin dose accordingly, with the average dose used was 50 mg. mixed with Lipodol to circuit nodes, depending on the size of the tumour, the ability of the tumour to meet the number of times the vein ensures complete vascular embolization nourishing the tumour, the distance between each round of nodes from 4 - 8 weeks. Evaluation of tumour response after 3 months after the first or second vein node. Criteria for assessing tumour response according to solid tumour response criteria (RECIST). In our study, the study patients selected earlier and these patients did not have venous thrombosis. The average follow-up time was 32.8 months, with an average life span of 33.4 months. The survival rate of 1 year, 3 years and 5 years of patients using hepatic node method with Doxorubicin were 92.7%, 70.7% and 36.9%, respectively, with P (1 & 2) <0.001; p (2 & 3) = 0.009. According to Kim and colleagues, the average lifetime is 23.4 months, lifetime is 1 year; 3 years and 5 years respectively 92.7%; 70.7% and 52.4% [8]. The average survival rate of HCC patients with high serum CRP (> 5.0 mg / L) and low serum CRP levels (≤ 5 mg / L) treated with TACE were 22.7 and 31 respectively. , 5 months (p <0.001). The average survival rate of HCC patients with high serum CRP (> 5.0 mg / L) and low serum CRP levels (≤ 5 mg / L) treated with TACE were 22.7 and 31 respectively. , 5 months (p <0.001). The average survival rate with serum ALP concentration was 22.0 months and 29.4 months in the ALP group and the ALP low group, respectively (p <0.001). The survival rate of 1 year, 3 years and 5 years of patients using hepatic node method with Doxorubicin were 92.7%, 70.7% and 16.9% respectively, with P (1 & 2) <0.001; p (2 & 3) = 0.009.

Conclusion

Primary liver carcinoma treated with percutaneous chemotherapy circuit has good results, lifetime is 1 year; 3 years and 5 years respectively 92.7%, 70.7% and 36.9%.

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