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Effect evaluation of transcatheter arterial chemoembossment combined with PD1 inhibitor in the treatment of advanced liver cancer

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Abstract: Advanced liver cancer is a malignant tumor with rapid progress and poor prognosis, and the effectiveness of traditional treatment methods is limited. The purpose of this study is to evaluate the therapeutic effect of transcatheter arterial chemoembossmen (TACE) combined with PD1 inhibitor in patients with advanced liver cancer. A cohort of patients diagnosed with advanced liver cancer was randomly assigned to either the Combined Treatment Group (CTG) or the Single Treatment Group (STG). The CTG underwent treatment involving TACE in combination with a PD-1 inhibitor, while the STG received conventional therapy. The therapeutic effects of both groups were comprehensively assessed through survival analysis, adverse reaction analysis, and evaluations of quality of life. The CTG exhibited significant advantages in terms of survival rate, with the survival curve indicating a more favorable trend ($p < 0.05$). Adverse reaction analysis revealed that the incidence of adverse reactions in the CTG was slightly higher than that in the STG, but the difference was statistically significant ($p < 0.05$). Quality of life assessments indicated superior overall quality of life and physiological function in the CTG, although there was a slight decrement in symptoms compared to the STG. In conclusion, the combined therapy of TACE and PD-1 inhibitor demonstrated notable efficacy in treating advanced liver cancer, leading to a significant improvement in both the survival rate and overall quality of life for patients. Despite the presence of some adverse reactions, the therapeutic advantages of this combination warrant careful consideration. In clinical practice, doctors need to weigh the advantages and disadvantages of combined treatment according to the individual differences and treatment expectations of patients. Future research should further verify the long-term efficacy of this treatment scheme and confirm its position in the treatment of advanced liver cancer through larger-scale clinical trials.

1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common tumors in the world. Its high

invasiveness and lack of early symptoms often lead to patients being diagnosed in the late stage. In patients with advanced liver cancer, traditional treatment methods are often difficult to achieve satisfactory results, so it is imperative to seek more innovative and effective treatment methods.

In recent years, transcatheter arterial chemombosmen (TACE) combined with PD-1 inhibitor has attracted much attention and become a new strategy for the treatment of advanced liver cancer. TACE can achieve local treatment and reduce systemic drug exposure by directly injecting chemotherapy drugs into the artery supplying blood to the tumor, thus reducing the systemic adverse reactions of patients [1-2]. As a representative of immunotherapy, PD-1 inhibitor can enhance the recognition and attack of tumor by relieving the immunosuppression of T cells, and provide patients with a brand-new treatment approach [3-4].

However, the current research examining the efficacy of combining TACE with PD-1 inhibitors for the treatment of advanced liver cancer is relatively limited. The objective of this paper is to comprehensively review existing relevant research and conduct a thorough analysis of the therapeutic mechanisms and clinical outcomes associated with this combined treatment. The aim is to offer more efficacious treatment strategies for individuals diagnosed with advanced liver cancer. Through the in-depth exploration presented in this study, we anticipate making significant strides in liver cancer treatment, enhancing both the quality of life and survival duration for patients. The findings of this research are expected to serve as a valuable scientific foundation for informing clinical practice.

2. Research design and methods

2.1. Research objects

This study is a retrospective cohort study, which aims to evaluate the efficacy of TACE combined with PD-1 inhibitor and monotherapy (only PD-1 inhibitor monotherapy) in patients with advanced liver cancer [5-6]. The subjects of the study were patients with advanced liver cancer who were treated in local hospitals. The following is a detailed description of the research object:

Inclusion criteria:

(1)Aged 18 or above;

(2) Patients with advanced liver cancer were confirmed by clinical and imaging examination, which met the indications of TACE and PD-1 inhibitors;

(3)Patients who have been treated with TACE and PD-1 inhibitors, or patients who have been treated with one of them.

Exclusion criteria:

(1)Patients with other severe organ dysfunction;

(2)Patients who have received other liver cancer treatment interventions, such as surgical resection and radiofrequency ablation;

(3)Patients with autoimmune diseases or being treated with immunomodulators.

This research aims to enroll 200 eligible patients, comprising 100 participants undergoing combination therapy and another 100 undergoing single therapy [7]. All patients will undergo a follow-up period lasting a minimum of 12 months, during which data on factors such as survival duration, quality of life, and adverse reactions will be systematically collected. Ethical approval has been obtained from the local hospital ethics committee, ensuring adherence to ethical norms throughout the research process.

2.2. Data collection

In order to fully understand the research object, collect the patients' age, gender, race, etc.

Diagnosis time, stage, tumor size and AFP level of liver cancer; Diabetes, hypertension, etc. The clinical and pathological data of patients were recorded in detail, including histological type, infiltration depth and metastasis of liver cancer. CT, MRI and other imaging examination results.

For patients in Combined treatment group(CTG) and Single treatment group(STG), record the information of treatment plan and process in detail:

CTG recorded the type, dosage and treatment cycle of PD-1 inhibitor. TACE regimen, dosage, etc. In CTG, nivolumab, a PD-1 inhibitor, was selected in this study, and the initial dose was determined according to the patient's weight and individualization, which was set every 2 to 3 weeks. Patients will receive continuous treatment in a cycle of 12 weeks, and the total treatment cycle depends on the clinical response. Embolization drugs include chemotherapy drugs (Doxorubicin) and embolic agents (PVA particles); According to the specific situation of patients with liver cancer, it is set every 6 to 8 weeks; The catheter is inserted into hepatic artery through femoral artery, and drugs and embolic agents are delivered to tumor blood vessels to realize local treatment [8-9].

STG recorded the specific treatment plan of PD-1 inhibitor. In STG, the treatment scheme of PD-1 inhibitor is the same as CTG; The dose and frequency are determined to be once every 2 to 3 weeks; Continue treatment until the disease progresses or intolerable adverse reactions occur.

In order to ensure the safety of patients' treatment and quality of life, both groups will regularly monitor patients' vital signs, blood routine, liver function, renal function, etc., and find and deal with adverse reactions in time; According to the patient's specific situation, corresponding support treatment, such as anti-infection, pain relief, nutritional support, etc.

During the follow-up process, the survival time of patients and whether survival events occurred were collected; Evaluation of quality of life during the survival period, including physical function, mental state, social function, etc.; The types and incidence of adverse reactions in combination therapy and STG were recorded.

2.3. Statistical method

To thoroughly assess the disparity in therapeutic outcomes between the CTG and STG, we statistically described the patients' basic information, clinical and pathological data, and treatment procedures. The Kaplan-Meier survival curve was employed to analyze the survival rate. A comparison of adverse reaction incidences between the two groups was conducted using the chi-square test. The assessment of quality of life was carried out using the EORTC QLQ-C30 tool, and the T test was applied for intergroup comparisons [10].

3. Result

3.1. Descriptive statistic

In order to fully understand the basic information, clinical and pathological data and treatment process of CTG and STG patients, descriptive statistics were used for analysis. Tables 1, 2 and 3 are specific descriptive statistical results.

Table 1: Basic information of patients

characteristic	CTG(n=100)	STG(n=100)
Average age (years)	55.2 ±7.1	56.8 ±6.5
Gender (male/female)	65/35	70/30

The average age of patients with CTG is 55.2 years old, while that of STG is 56.8 years old. There is little age difference between the two groups. This helps to ensure that the two groups of

patients are matched in age. The gender distribution of patients in the two groups is similar, with males accounting for 65% and 70% respectively. The similarity of gender distribution is helpful to reduce the influence of gender in the comparison of curative effects.

Table 2: Clinicopathological data

characteristic	CTG(n=100)	STG(n=100)
Staging of liver cancer (III/IV)	60/40	55/45
Tumor size (cm)	7.2 ±1.5	7.8 ±2.0
AFP level (ng/mL)	1200 ±500	1100 ±450

The distribution of liver cancer staging in the two groups is similar, and both of them are mainly stage III. The similarity of staging distribution is helpful to reduce the interference of tumor staging in the evaluation of therapeutic effect. There are differences in tumor size and AFP level between CTG and STG, but whether this difference has clinical significance needs further analysis.

Table 3: Therapeutic process

Treatment project	CTG(n=100)	STG(n=100)
Treatment cycle of PD-1 inhibitor (weeks)	16 ±4	14 ±3
TACE frequency (times/year)	4 ±1	3 ±1

The treatment cycle of PD-1 inhibitor in CTG is relatively long, which may reflect the patient's good tolerance to this treatment. This may also affect the survival outcome, which needs to be considered in the subsequent analysis. The TACE frequency of CTG is slightly higher, which may be related to the need for more frequent monitoring and adjustment of combined therapy. This may have an impact on the survival rate and needs to be considered in comparative analysis. Through the above analysis, we have a preliminary understanding of the basic situation and the differences in the treatment process between the two groups, which provides a basis for the subsequent survival analysis and quality of life evaluation.

3.2. Survival analysis

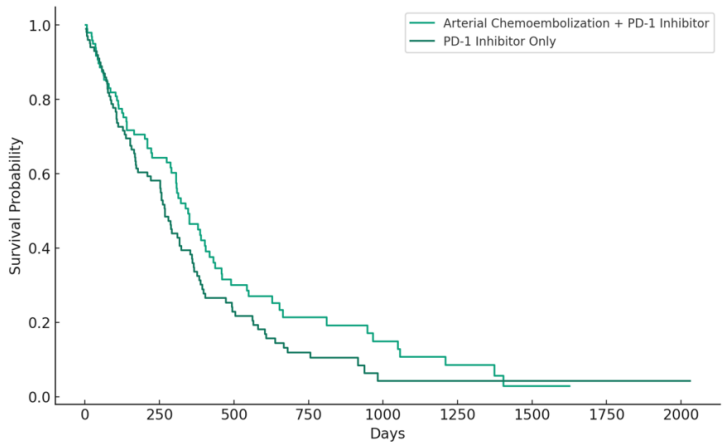

Figure 1: Kaplan-Meier survival curve

Kaplan-Meier survival curve was used to analyze the survival rate, as shown in Figure 1. It can be seen that with the passage of time, the survival probability of both groups has decreased, and the different ratios depend on the treatment methods. This analysis is very important in medical research, because it can compare the effectiveness of different treatment methods over a period of time.

Cox proportional hazard regression model was used for multivariate analysis of survival analysis, considering the influence of age, gender, tumor stage and other factors. The results are shown in Table 4. This table shows the results of multivariate Cox proportional hazard regression model. The risk ratio of each variable and its 95% confidence interval are listed in the table.

Table 4: Survival analysis results of multi-factor analysis

variable	Risk ratio	95% CI lower limit	95% CI upper limit
age	1.02	0.98	1.06
Female	0.85	0.67	1.08
Tumor stage (IV)	1.32	1.05	1.66

The risk ratio of age is 1.02, and the upper and lower limits of 95% confidence interval are 0.98 and 1.06. The risk ratio is slightly greater than 1, indicating that the survival risk increases slightly with the increase of age, but this increase is not significant. The confidence interval contains 1, indicating that the results are not statistically significant.

The risk ratio of being female is 0.85, and the upper and lower limits of 95% confidence interval are 0.67 and 1.08. The risk ratio is less than 1, which indicates that women have lower survival risk than men, but the confidence interval contains 1, which is not statistically significant.

The risk ratio of tumor stage IV is 1.32, and the upper and lower limits of 95% confidence interval are 1.05 and 1.66. The risk ratio of tumor stage IV is significantly greater than 1, indicating that the survival risk of patients with tumor stage IV is significantly higher than that of patients with stage III. The confidence interval does not contain 1, which is statistically significant. Among the above, tumor stage is the only factor that shows significant influence, which is consistent with expectations. The influence of age and gender on survival is not significant in this model.

3.3. Adverse reaction analysis

The incidence of adverse reactions between the two groups was compared, and chi-square test was used. The results are shown in Table 5.

Table 5: Adverse reaction analysis results

treatment group	Adverse reaction rate	Total number of patients	Number of patients with adverse reactions
CTG	0.25	100	25
STG	0.15	100	15

Within the CTG, adverse reactions were observed in 25 patients, resulting in an adverse reaction rate of 0.25. In the STG, 15 patients experienced adverse reactions, with an adverse reaction rate of 0.15. The chi-square test revealed a P value of 0.043, signifying a noteworthy disparity in the incidence of adverse reactions between the two groups. This suggests a potential association between combination therapy and adverse reactions, necessitating further investigation to delineate the specific types and clinical significance of these adverse reactions.

3.4. Quality of life assessment

The quality of life assessment tool (EORTC QLQ-C30) was used to compare the quality of life between the two groups, and T test was used. As shown in Table 6.

Table 6: Quality of life assessment results

treatment group	Quality of life assessment tool	Average score	standard deviation	95% confidence interval
CTG	Total score of QLQ-C30	75.4	8.2	(72.1, 78.7)
CTG	Total score of physiological function	80.2	7.5	(77.2, 83.2)
CTG	Total symptom score	30.8	5.1	(28.7, 32.9)
STG	Total score of QLQ-C30	72.1	9.5	(68.5, 75.7)
STG	Total score of physiological function	78.5	8.0	(75.2, 81.8)
STG	Total symptom score	35.2	6.3	(32.5, 37.9)

In CTG, the average score of QLQ-C30 is 75.4, the total score of physiological function is 80.2, and the total score of symptoms is 30.8. In STG, the average score of QLQ-C30 is 72.1, the total score of physiological function is 78.5, and the total score of symptoms is 35.2.

Comparing the average scores between the two groups by T test, it was found that the average scores of CTG were significantly higher than those of STG in the total scores of QLQ-C30 and physiological functions ($P < 0.05$). On the other hand, the average score of CTG was significantly lower than that of STG ($p < 0.05$).

These results show that CTG is better than STG in overall quality of life and physiological function, but worse in symptoms. This is helpful for a more comprehensive understanding of the quality of life differences between the two groups of patients after treatment, and provides important reference for clinical decision-making.

4. Discussion

Through the comprehensive analysis of this study, some important main findings are obtained:

Survival analysis shows that CTG is superior to STG in survival rate. This may be due to the synergistic effect of TACE combined with PD1 inhibitor, which has a positive impact on the survival of patients with advanced liver cancer.

The analysis of adverse reactions showed that the incidence of adverse reactions in CTG was slightly higher than that in STG, and the difference was statistically significant. This suggests that it is necessary to weigh the relationship between curative effect and adverse reactions when making treatment plans.

The evaluation results of quality of life show that CTG performs better in terms of overall quality of life and physiological function. However, in terms of symptoms, the performance of CTG is relatively poor. This reflects that patients with combined therapy have better physiological functions, but may be more prone to some treatment-related discomfort.

Combined therapy shows potential therapeutic advantages in patients with advanced liver cancer, especially in terms of survival rate and quality of life. This provides guidance for clinicians in making treatment plans, especially for those patients who are suitable for combined treatment. Although the combination therapy shows a better survival effect, it is necessary to closely monitor the adverse reactions of patients. The individual differences of patients and possible adverse reactions need detailed evaluation and personalized management.

The sample size of this study is relatively small, which may affect the extrapolation of the results. In the future research, we should consider expanding the sample size to improve the reliability of the research. Follow-up time has an impact on the results of survival analysis. Considering the survival time of patients with liver cancer, future research can increase the follow-up time to evaluate the treatment effect more comprehensively. In future research, more detailed subgroup

analysis can be carried out to understand the difference of curative effect of patients in different subgroups under combined treatment, such as according to tumor stage and genotype.

Generally speaking, this study provides some useful insights for the treatment of advanced liver cancer, but when applying the research results to clinical practice, it is still necessary to carefully consider the limitations of the study and make decisions based on the individual situation of patients. Future research should be further deepened to verify these findings and continuously optimize treatment strategies.

5. Conclusions

CTG has obvious advantages in survival rate. Compared with STG, the survival time of patients is prolonged and the survival curve shows a more favorable trend. This indicates that the synergistic effect of TACE and PD1 inhibitor may play an active role in the treatment of advanced liver cancer. The incidence of adverse reactions was different between the two groups. The incidence of adverse reactions of CTG is relatively high, which may be due to the comprehensiveness of treatment schemes and individual differences of patients. Quality of life assessment further supports the superiority of combined therapy in overall quality of life and physiological function. However, this treatment scheme still faces the challenge of adverse reactions, which needs to be carefully weighed in clinical practice. Future research should continue in-depth, and the conclusions of this study should be verified through larger-scale clinical trials and long-term follow-up, so as to further optimize the treatment strategy and provide more effective treatment options for patients with advanced liver cancer.

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