Efficacy and Prognostic Factors of TACECombined with Apatinib in the Treatment of BCLC stage C Hepatocellular Carcinomas

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INTRODUCTION

Apatinib is a small molecule targeting drug with independent intellectual property rights in China. It can selectively act on the ATP binding site of VEGF receptor in tumor cells, inhibit a variety of tyrosine kinases, block its downstream pathway, thus inhibit the migration and proliferation of vascular endothelial cells, reduce tumor neovascularization density, and inhibit residual tumor growth[1, 2]. A recent randomized controlled study showed that TACE combined with apatinib is safe and can significantly prolong the overall survival and progression-free survival of patients with advanced hepatocellular carcinoma[3] .Based on these findings, the clinical data of TACE combined with apatinib in the treatment of stage BCLC-C HCC were retrospectively evaluated

AIM

To explore the efficacy and prognostic factors of transarterial chemoembolization (TACE) combined with apatinib in the treatment of Barcelona clinic liver cancer

METHOD

Clinical data of 146 patients with BCLC stage C HCC in our hospital were collected and analyzed retrospectively, of which 76 cases were treated with TACE combined with apatinib(TACE-apatinib) and 70 cases were treated with TACE alone. The tumor response,survival time and adverse events of the two groups were compared, and the factors affecting the prognosis were analyzed

RESULTS

	CR	PR	SD	PD	ORR（%）	DCR（%）
TACE+ apatinib	4 (5.26%)	28 (36.84%)	32 (42.10%)	12 (15.78%)	32 (42.10%)	64 (84.21%)
TACE alone	3 (4.28%)	15 (21.42%)	21 (30.00%)	31 (44.28%)	18 (25.71%)	39 (55.71%)
X^2					4.34	14.24
P-value					0.03	0.001
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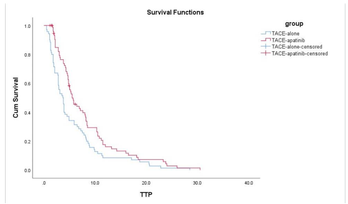
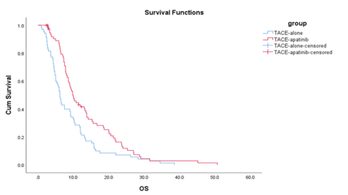
After one month of treatment, the rates of disease remission and stable disease in the TACE-apatinib group were 42.10% and 84.21%, respectively. Corresponding values in the TACE-alone group were 25.71% and 55.71%. The difference in local curative effect between the two groups was statistically significant (p < 0.05)

Variable	Number	HR	95%CI	P-value
PVTT		2.199	(1.549-3.122)	0.001
no	58			
yes	88			
Tumor size (cm)		1.749	(1.247-2.454)	0.001
< 10	71			
≥10	75			
Child-Pugh class		1.649	(1.162-2.340)	0.005
A	85			
B	61			
Treatments		0.652	(0.466-0.911)	0.012
TACE-alone	70			
TACE+apatinib	76			

Univariate analysis showed that portal vein tumor thrombus, tumor size, Child-Pugh grade, and treatment modality were all related to the prognosis of the patients (P<0.05)

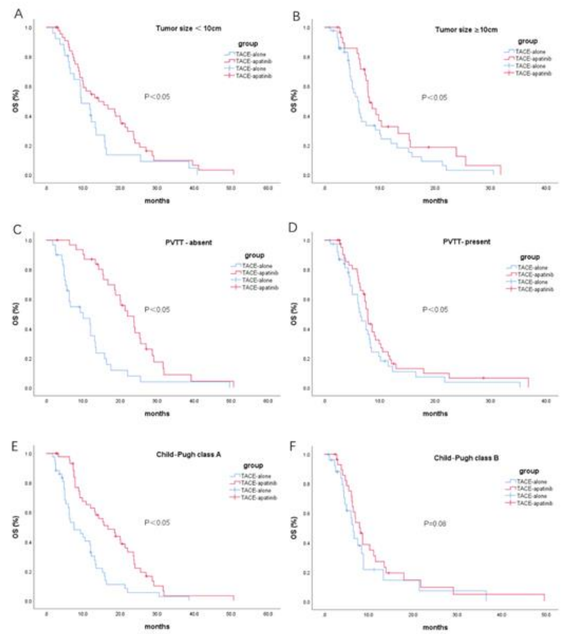




The median TTP was 5.5 months (95% CI: 4.0-6.9 months) in the TACE-apatinib group and 3.7 months (95% CI: 2.9-4.4 months) in the TACE-alone group, and this difference was statistically significant (P<0.02). The median OS was 10.0 months (95% CI: 8.2-11.7 months) in the TACE-apatinib group and 6.2 months (95% CI: 5.4-6.9 months) in the TACE-alone group and this difference was statistically significant (P<0.01).

Variable	HR	95%CI	P-value
PVTT	2.212	(1.547-3.164)	0.001
Tumor size	1.465	(1.026-2.092)	0.036
Child-Pugh class	1.542	(1.062-2.241)	0.023

Cox regression multivariate analysis showed that tumor thrombus, tumor size, Child-Pugh grade, and treatment modality were independent risk factors for prognosis (P<0.05)



In patients with stage BCLC-C, the median OS after TACE-apatinib was higher than after TACE alone in patients with Child-Pugh class A, any tumor size, and with or without portal vein tumor thrombus (P<0.05). There was no significant difference between TACE-apatinib and TACE-alone treatment in patients with Child-Pugh class B (P=0.08)

AEs	TACE+ apatinib (n=76)	TACE (n=70)	X^2	P-value
Nausea	27 (35.52%)	22 (31.42%)	0.27	0.6
Diarrhea	21 (27.63%)	21 (30.00%)	0.09	0.75
Leukopenia	17 (22.36%)	16 (22.85%)	0	0.94
Fever	36 (47.36%)	28 (40.00%)	0.8	0.37
Hepatic failure	25 (32.89%)	16 (22.85%)	1.81	0.17
Oral ulcer	9 (11.84%)	2 (2.85%)	4.04	0.04
Fatigue	17 (22.36%)	23 (32.85%)	2.01	0.15
Alopecia	12 (15.78%)	10 (14.28%)	0.06	0.79
Hand-foot syndrome	39 (51.31%)	1 (1.42%)	45.59	0.001
Hypertension	17 (22.36%)	2 (2.85%)	12.25	0.001

The most frequent adverse events in the TACE-apatinib group were nausea, fever, and hand-foot syndrome, and in the TACE-alone group, nausea, fever, and fatigue. The incidence of hand and foot syndrome, hypertension, and oral ulcer in the combined treatment group was higher than in the TACE-alone group, and the difference was statistically significant (P < 0.05). All these adverse events disappeared after symptomatic treatment.

CONCLUSIONS

TACE-apatinib is an effective and safe method for the treatment of BCLC stage C HCC. Tumor size, Child-Pugh class, and portal vein tumor thrombus affect survival time in HCC patients with BCLC stage C.

KEYS

primary hepatic carcinoma
TACE
Apatinib

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