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POOR PROGNOSTIC FACTORS AFTER RESECTION OF HUGE HEPATOCELLULAR CARCINOMA (≥10 CM)

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Abstract

Purpose: Huge hepatocellular carcinoma (H-HCC) is highly associated with vascular invasion and considered to have a poor prognosis. Transarterial chemoembolization (TACE) alone or in combination with drug therapy for H-HCC has a certain effect, but long-term control is difficult. Therefore, surgical resection is selected for patients with good liver function. We will analyzed the prognosis of resected H-HCC patients and verify the validity of surgical treatment.
Method: Among 2203 patients who underwent liver resection (LR) for HCC between 2001 and 2019, 119 patients (6.3%) with H-HCC ≥10 cm were included, and death within 1 year was defined as poor prognosis. A comparison was made between 37 patients who died less than 1 year and 82 patients who survived for more than a year.
Results: Nine patients (9.7%) had positive surgical margins. Preoperative major portal vein invasion (mVP) occurred in 20 cases (21.7%) and histological vascular invasion in 64 cases (69.5%).Univariate analysis revealed three prognostic factors : mVP (Odds ratio(OR): 3.90 [1.52-10.0], p = 0.005), poorly differentiation (OR: 3.43 [1.28-9.22], p = 0.049), vascular invasion (OR: 2.83 [95%CI; 1.06-7.57], p = 0.049). Multivariate analysis revealed that only one factor : mVP (OR: 3.12 [1.08-9.02], p = 0.035). The median survival time (MST) for resected H-HCC was 33.7 months, and the 5-year survival rate was 25.4%. The MST for mVP cases in H-HCC was 6.5 months, while the MST for TACE cases including combination with drug therapy was 5.5 months.
Conclusion: Although mVP is a poor prognostic factor, LR appears to be reasonable treatment compared with TACE.

Conclusion

LR is the first choice for treatment of H-HCC, alternative treatment should also be considered for mVP cases that can be diagnosed before surgery.

Introduction

- ✓ H-HCC has a high rate of vascular invasion and early recurrence.
  There are no established standards for treatment.
- ✓ However, the initial treatment for H-HCC varies depending on the institution, such as surgical resection, TACE, molecular-targeted drugs, or immune checkpoint inhibitors.
- ✓ In this study, we retrospectively analyzed the long-term outcome for the patients with H-HCC following surgical resection or TACE, and also evaluated the prognostic factors after liver resection.

Materials and methods

Among 2203 patients who underwent liver resection for HCC between 2001 and 2019, 119 patients (6.3%) with H-HCC ≥10 cm were included, and death within 1 year was defined as poor prognosis.
A comparison was made between 37 patients who died less than 1 year and 82 patients who survived for more than a year.

Results

Baseline characteristics of patients with liver resection

			LR (n=119)
Age		(years)	68 (59-75)
Gender		n (%)	
	Male		99 (83.2)
	Female		20 (16.8)
Viral hepatitis		n (%)	45 (37.8)
Child-Pugh score	A/B/C	n	110/9/0
mALBI	1/2a/b/3	n	55/42/22/0
Tumor diameter		n (%)	
	10 - 14.9 cm		88 (73.9)
	15 - 19.9 cm		28 (23.5)
	≥ 20 cm		3 (2.6)
Multiple tumor		n (%)	25 (21.1)
mVP		n (%)	23 (19.3)
Serum bilirubin		(IU/L)	0.63 (0.49-0.80)
Serum albumin		(IU/L)	3.8 (3.6-4.1)
Platelets		($x10^4/mm^3$)	23 (18-30)
Prothrombin time (INR)			1.0 (0.96-1.08)
ICG-R15		%	11 (2-31)
Serum AFP		(IU/L)	80 (5-3320)
Serum PIVKA		(IU/L)	4023 (656-25973)
Cirrhosis		n (%)	13 (10.9)
Presence of diabetes		n (%)	42 (35.3)

Surgical outcomes

			LR (n=119)
Surgery		n, (%)	
	Major hepatectomy		75 (63)
	Partial hepatectomy		44 (37)
Operation time		(min)	434 (369-500)
Blood loss		(g)	820 (498-1268)
Tumor differentiation		n, (%)	
	Well differentiated		9 (7.6)
	Moderate differentiated		90 (75.6)
	Poor differentiated		20 (16.8)
Margin		n, (%)	
	Positive		11 (9.2)
	Negative		108 (90.8)
Satelite lesion		n, (%)	
	yes		34 (28.6)
	no		85 (71.4)
Vascular invasion		n, (%)	84 (70.6)
Cirrhosis		n, (%)	13 (11)
Capsule exposure		n, (%)	44 (36.9)
Capsular invasion		n, (%)	90 (75.6)
Postoperative hospital stay		(day)	16 (8-51)
Morbidity (Clavien-Dindo clasification >III)		n, (%)	32 (26.9)
Mortality (30 days)		n, (%)	1 (0.8)

Prognostic factors

	Univariate analysis			Multivariate analysis		
Viriables	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age (>70yr)	1.34	0.61-2.92	0.550			
Viral hepatitis	0.77	0.32-1.85	0.560			
mALBI (2b/3)	0.43	0.13-1.38	0.204			
AFP (>400ng/ml)	1.64	0.72-3.65	0.300			
PIVKA-II (>1000mUA/ml)	1.09	0.47-2.55	0.892			
Blood loss (>800ml)	2.24	1.01-5.01	0.051			
Tumor size(>150mm)	1.42	0.58-3.49	0.480			
Multiple tumors	0.83	0.31-2.19	0.811			
Capsule exposure	2.04	0.92-4.52	0.101			
Vascular invasion	2.83	1.06-7.57	0.049	1.57	0.53-4.67	0.418
mVP	3.9	1.52-10.0	0.005	3.12	1.08-9.02	0.035
Poorly differentiation	3.43	1.28-9.22	0.017	2.52	0.87-7.30	0.089
Surgical margin	2.98	0.85-10.5	0.094			

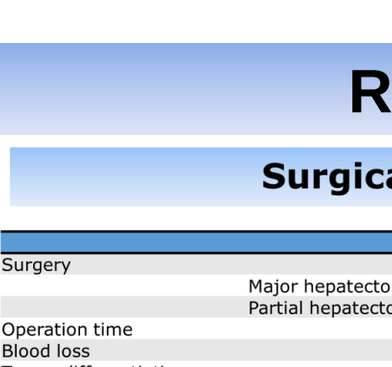
Patients characteristic after PSM

			LR (n=42)	TACE (n=42)	P value
Age		(years)	69 (62-76)	68 (63-74)	0.936
Gender		n (%)			1.000
	Male		35 (83.3)	35 (83.3)	
	Female		7 (16.7)	7 (16.7)	
Viral hepatitis		n (%)	24 (57.1)	23 (54.8)	1.000
Child-Pugh score	A/B/C	n	36 / 6 / 0	1932/9/1	0.399
mALBI	1/2a/b/3	n	12 / 15 / 15 / 0	13 / 13 / 14 / 2	0.291
Tumor diameter		n (%)			0.88
	10 - 14.9		32	29	
	15 - 19.9		9	13	
	≥ 20		1	0	
Multiple tumor		(%)	14	16	0.82
mVP		n (%)	10 (23.8)	16 (38.1)	0.159
Serum bilirubin		(IU/L)	0.68 (0.5-0.83)	0.64 (0.49-0.97)	0.608
Serum albumin		(IU/L)	3.6 (3.4-3.9)	3.7 (3.1-4.0)	0.332
Platelets		($x10^4/mm^3$)	21.4 (15.2-28.8)	22.4 (17.2-29.5)	0.855
Prothrombin time (INR)			1.03 (0.99-1.09)	1.02 (0.96-1.12)	0.728
Serum AFP		(IU/L)	63 (6-865)	1716 (67-9662)	0.382
Serum PIVKA		(IU/L)	3658 (649-23757)	8668 (798-18454)	0.68
Cirrhosis		n (%)	7 (16.7)	5 (11.9)	0.757
Presence of diabetes		n (%)	7 (16.7)	10 (23.8)	0.791

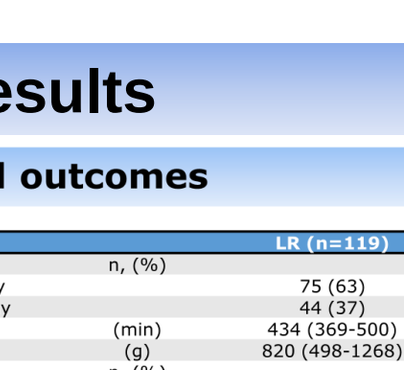
LR vs TACE

H-HCC 119 vs TACE 108

Propensity score matching (PSM)
H-HCC 42 vs TACE 42



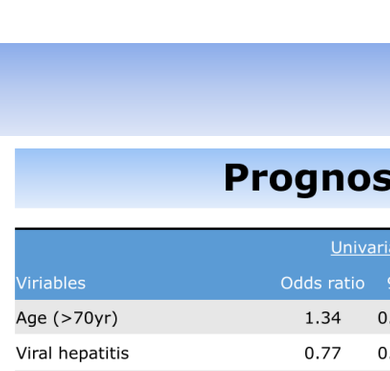
LR: MST 31.5m 5YOS 29.4%
TACE : MST 7.3m 5YOS 15.7%



LR: MST 29.7m 5YOS 29.3%
TACE: MST 8.1m 5YOS 18.5%

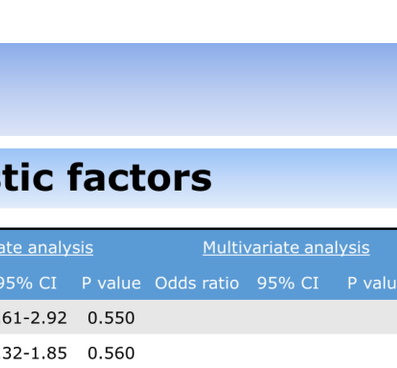
Limited mVp LR vs TACE

Before PSM



LR: MST 9.2m 5YOS 18.7%
TACE: MST 7.3m 5YOS 15.7%

After PSM



LR: MST 9.3m 5YOS 18.6%
TACE: MST 10.2m 5YOS 17.6%

Discussion

- ✓ The OS of liver resection for H-HCC at our department was 29.4%, which was a good result with a significant difference from the TACE group.
- ✓ mVP was a prognostic factor and there were no significant difference from the TACE group
- ✓ Surgical resection may be considered as the first choice even for H-HCC.
- ✓ However, in patients with clear VP on preoperative images, it is necessary to select a treatment method considering the patient's condition such as age and PS.