

TNM Stage IVa

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Abstract

Treatment Outcome and Prognostic Factors in Patients with Advanced Hepatocellular Carcinoma (TNM Stage IVa) according to Anticancer drugs of Transhepatic Arterial Chemoinfusion

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Background/Aims: The study proposed to evaluate the efficacy of anticancer drugs of intraarterial chemoinfusion and investigate prognostic factors influencing survival. **Methods:** A total of 127 patients diagnosed as having advanced hepatocellular carcinoma(HCC) of same stage (TNM stage IVa) from 1996 to 1998 were examined. Two intraarterial infusion chemotherapeutic regimens were employed: Adriamycin(Group I) and Cisplatin(Group II). **Results:** Overall survival was significantly different(10.0 vs 5.7months) and favored Group I. By the univariate analysis, significant prognostic factors included: age, portal vein thrombosis(PVT), size(>5cm) and type of tumor, response rate (size & -fetoprotein) at 3 months after therapy, level of albumin, alkaline phosphatase, and total bilirubin. After repeated therapy, Group I showed better survival (14.0 vs 7.9 months), but there was no statistical difference in survival rate between two groups in the case of large size, PVT, and diffuse type. **Conclusion:** Group I showed better survival than Group II in advanced HCC of TNM stage IVa. But, considering prognostic factors, there was no significant difference in survival rate between two groups except small size or nodular type of HCC. TNM classification of stage IVa should be reconsidered to include prognostic factors influencing survival rate such as PVT, size and type of HCC..(Korean J Hepatol 2000 ;6:456-467)

Key Words : Neoplasm/Liver/Hepatocellular carcinoma, Treatment outcome, Prognostic factors, Intraarterial infusion, Neoplasm staging

◇ 2000 7 21 ; 2000 8 29 ; 2000 10 9
◇ Abbreviations: HCC, hepatocellular carcinoma; PVT, Portal vein thrombosis
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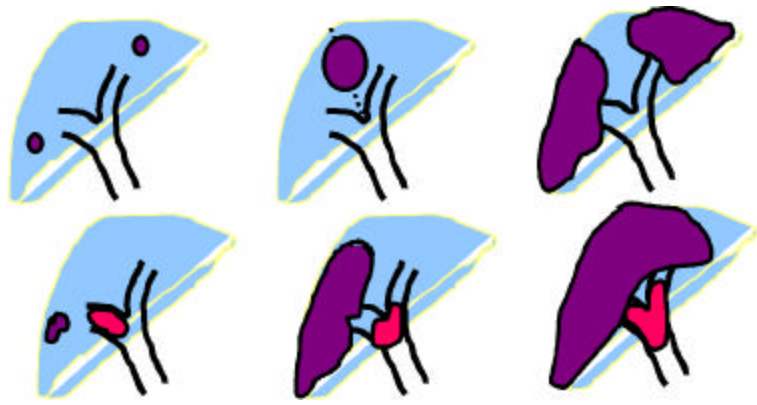
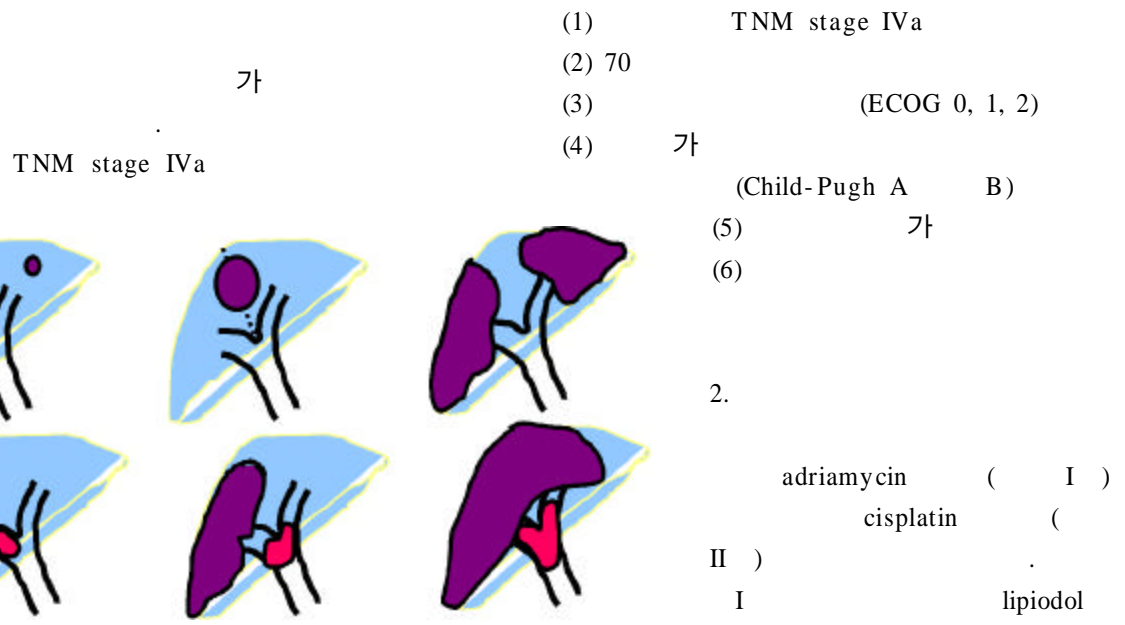


Figure 1. HCCs of TNM Stage IVa show different shape and vessel invasion of tumors.

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 (complete response, CR), 50%
 (partial response, PR), 50% 25%
 (minor response, MR), 25% 25%
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Figure 2. Cumulative survival curves of the Group I and Group II after repeated therapy.

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1. A 114 (89.8%), B 13 (10.2%)
 80 (63.0%),
 89 (70.1%)
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 B 87 (68.4%) 가 ,
 11 (8.7%), B (1).
 11 (8.7%), C 10 (7.9%), 8
 (6.3%) . 5cm 89 (70.1%), 2.
 5cm 38 (29.9%) . TNM Stage IVa
 56 (44.0%) 가 37
 (29.2%), 34 (26.8%) . Child-Pugh ,

Table 1. Demographic Findings of Total Subjects

	Group I N=71 (%)	Group II N=56 (%)	Total N=127 (%)	p- value
Sex (M:F)	59 : 12	48 : 8	107 : 20	NS
Age (Mean(SD))				NS
M:F	55 ± 8 : 59 ± 10	53 ± 9 : 55 ± 7	55 ± 9 : 55 ± 9	
Etiology				NS
Hepatitis B (HB)	52 (73.2)	35 (62.5)	87(68.4)	
Hepatitis C (HC)	8 (11.3)	2 (3.6)	10(7.9)	
Alcohol	4 (5.6)	7 (12.5)	11(8.7)	
HB+ Alcohol	4 (5.6)	7 (12.5)	11(8.7)	
Others	3 (4.2)	5 (8.9)	8(6.3)	
Child-Pugh class				NS
A	63 (88.7)	51 (91.1)	114(89.8)	
B	8 (11.3)	5 (8.9)	13(10.2)	
Tumor size				0.015*
5cm	43 (60.6)	46 (82.1)	89(70.1)	
< 5cm	28 (39.4)	10 (17.9)	38(29.9)	
Type of tumor				0.002*
Nodular	41 (57.7)	15 (26.8)	56(44.0)	
Massive	17 (23.9)	20 (35.7)	37(29.2)	
Diffuse	13 (18.3)	21 (37.5)	34(26.8)	
PVT	35 (49.3)	45 (80.4)	80(63.0)	0.000*
Bilobar involvement	52 (73.2)	37 (66.1)	89(70.1)	NS

*, <0.05, Group I; intraarterial adriamycin infusion, Group II; intraarterial cisplatin infusion

Table 2. Prognostic Factors influencing Survival

	Univariate	Multivariate	
	p-value	Exp(B)	(95% CI) p-value
Tumor size	0.000*	2.2	(1.28-3.90) 0.005*
Type of tumor	0.000*	1.9	(1.35-2.60) 0.000*
Albumin	0.005*	0.5	(0.33-0.70) 0.000*
Total bilirubin	0.018*	1.6	(1.15-2.29) 0.006*
Response at 3 months after therapy			
Size	0.000*	1.5	(1.11-1.93) 0.007*
FP	0.000*	1.4	(1.11-1.64) 0.002*
PVT	0.000*	1.2	(0.77-1.94) 0.385
Age	0.006*	1.0	(0.95-1.00) 0.070
ALP	0.002*	1.0	(0.99-1.00) 0.900
Bilobar involvement	0.902		

*, p<0.05

min), (ALP) (FP (albu- (bilirubin), alkaline phosphatase (1) 13.9 Stage IVa 6.3 TNM Stage 10.0 II 5.7 (p=0.000). I 14.0 II 7.9 (I, 3). I 가 (p=0.005) (p=0.000), albumin 가 5cm , (p=0.000), bilirubin (p=0.006), 3 , I II (FP (p=0.007, p=0.002) (2). II I 3. (3). I (20) 4.1 , II (30) 3.8 가 . 가 .

Table 3. The Survival Rate according to Prognostic Factors

	Group I		Group II		N
	N	Survival (mon)	N	Survival (mon)	
Total	51	14.0± 10.0	26	7.9±4.5	0.001*
Type of tumor					
Nodular	36	18.4± 11.1	11	9.0±5.8	0.029*
Massive	12	8.5± 7.2	9	7.2±2.7	0.226
Diffuse	3	11.0± 5.3	6	6.7±2.8	0.100
Tumor size					
5cm	27	10.8± 7.6	20	7.2±4.3	0.103
< 5cm	24	19.2± 11.3	6	8.0±5.9	0.018*
PVT	21	8.5± 11.7	18	7.1±4.1	0.051
PVT & Bilobe involvement	6	4.9± 4.2	11	7.0±4.5	0.512

*, P<0.05, Group I; intraarterial adriamycin infusion, Group II; intraarterial cisplatin infusion

(2) 3 (FP 가 I 7.8%, I II 가 5cm 25.5%, 62.8% II 6 I (4). 8.0%, 57.9% II 0%, 25.0% . 가 5cm 3 6 . FP I II 3 FP 4. I , , II , , I II . I II alanine aminotransferase 가 (ALT) (6). 5. 93 70 (75.3%), 11 (11.8%), 6 (6.5%), 6 (6.5%)가 (7). Group II 2 .

Table 4. The Response at 3 months after Therapy according to Tumor Size and FP

	Tumor size		FP	
	Group I	Group II	Group I	Group II
CR	4(7.8)	1(3.9)	6(11.8)	3(11.5)
PR	9(17.7)	1(3.9)	26(51.0)	8(30.8)
MR	3(5.9)	0(0)	0(0)	0(0)
NC	8(15.7)	6(23.0)	7(13.7)	4(15.4)
PD	27(52.9)	18(69.2)	12(23.5)	11(42.3)
Total (%)	51(100)	26(100)	51(100)	26(100)

Group I; intraarterial adriamycin infusion

Group II; intraarterial cisplatin infusion

Table 5. Characteristics and Therapeutic Response of Nodular typed HCC

	Group I N=36 (%)	Group II N=11 (%)	p -value
Sex (M:F)	31:5	11:0	0.322
Age (Mean(SD))	56 ± 8	54 ± 10	0.469
Child-Pugh class			0.578
A	33(91.7)	9(81.8)	
B	3(8.3)	2(18.2)	
Tumor size			
Maximal diameter	4.7 ± 2.2	5.2 ± 1.9	0.455
5cm	12(33.3)	6(54.5)	0.166
Albumin	3.9 ± 5.6	3.7 ± 0.5	0.359
Total bilirubin	1.1 ± 2.2	4.7 ± 2.2	0.657
ALT	44 ± 40	39 ± 23	0.729
ALP	110 ± 43	134 ± 78	0.197
PVT	10(27.8)	6(54.5)	0.101
Bilobar involvement	28(77.8)	9(81.8)	1.000
Response at 3 months after Therapy			
Size [CR : PR]	4:6(11.1:16.7)	0:1(0.9)	0.094
(FP [CR : PR])	6:18(16.7:50.0)	2:2(18.2)	0.264

Group I; intraarterial adriamycin infusion, Group II; intraarterial cisplatin infusion

Table 6. Side Effects of the Group I and Group II.

	Group I N=71(%)	Group II N=56(%)	Total N=127(%)
Anorexia	43(60.6)	46(83.6)	89(70.1)
Nausea	33(46.5)	38(67.9)	71(55.9)
Fever*	44(62.0)	19(33.9)	63(49.6)
Elevation of ALT* (more than 2 times)	40(56.3)	18(32.1)	58(45.7)
Abdominal pain*	40(56.3)	15(26.8)	55(43.3)
Vomiting	20(28.2)	25(44.6)	45(35.4)
Diarrhea	5(7.0)	4(7.1)	9(7.1)
Headache	5(7.0)	2(3.6)	7(5.5)
Cholecystitis	1(1.4)	1(1.8)	2(1.6)
Hiccup	1(1.4)	1(1.8)	2(1.6)

*, <0.05. between the group I and group II,
Group I; intraarterial adriamycin infusion,
Group II; intraarterial cisplatin infusion

Table 7. Causes of Death

	Group I N=49(%)	Group II N=44(%)	Total N=93(%)
Hepatic failure	36(73.5)	34(77.3)	70(75.3)
Renal failure	7(14.3)	4(9.1)	11(11.8)
Gastrointestinal bleeding	4(5.6)	2(4.5)	6(6.5)
HCC rupture	2(4.1)	4(9.1)	6(6.5)

Group I; intraarterial adriamycin infusion,
Group II; intraarterial cisplatin infusion

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(p=0.000)(8).

Table 8. Survival Rate and Prognostic factors of the Group I+II and Group III

	Group I N=127(%)	Group II N=26(%)	p - value
Survival (mon)	6.3±9.1	2.0±5.6	0.000*
Sex (M:F)	107:20	24:2NS	
Age (Mean(SD))	54±8	49±10	0.005*
Child-Pugh class			0.000*
A	114(89.8)	11(42.3)	
B	13(10.2)	15(57.7)	
Tumor size			
Maximal diameter	7.2±3.6	9.1±3.9	0.048*
5cm	87(68.5)	21(80.8)	NS
Type of tumor			0.050*
Nodular	56(44.1)	5(19.2)	
Massive	37(29.1)	11(42.3)	
Diffuse	34(26.8)	10(38.5)	
Albumin	3.8±0.5	3.4±0.6	0.006*
Total bilirubin	1.2±0.5	2.7±2.8	0.000*
ALT	51±54	94±110	0.003*
ALP	156±96	295±178	0.000*
PVT	80(63.0)	24(92.3)	0.003*
Bilobar involvement	89(70.1)	14(53.9)	0.108*

*, <0.05. between the group I+II and group III, Group I+II; intraarterial adriamycin or cisplatin infusion, Group III; No treatment

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