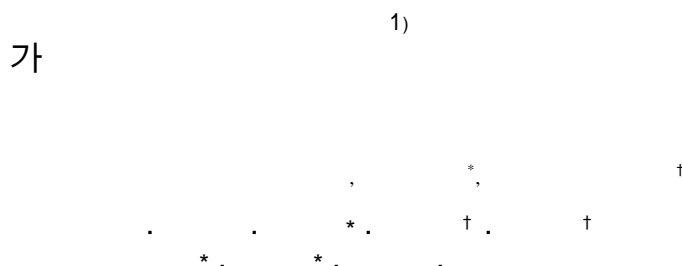


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Combined Transcatheter Arterial Chemoembolization and Local Radiotherapy for Unresectable Hepatocellular Carcinoma

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Purpose : The best prognosis for hepatocellular carcinoma can be achieved with surgical resection. However, the number of resected cases is limited due to the advanced lesion or associated liver disease. A trial of combined transcatheter arterial chemoembolization(TACE) and local radiotherapy(RT) for unresectable hepatocellular carcinoma(HCC) was prospectively conducted and its efficacy and toxicity were investigated.

Materials and Methods : From 1992 to 1994, 30 patients with unresectable HCC due either to advanced lesion or to associated cirrhosis were entered in the study. Exclusion criteria included the presence of extrahepatic metastasis, liver cirrhosis of Child' s class C, tumors occupying more than two-thirds of the whole liver, and an ECOG scale of more than 3. Patient characteristics were : mean tumor size $8.95 \pm 3.4\text{cm}$, serum AFP+ in all patients, portal vein thrombosis in 11 patients, liver cirrhosis in 22 patients, and UICC stage III and IVA in 10 and 20 patients, respectively. TACE was performed with the mixture of Lipiodol(5ml) and Adriamycin(50mg) and Gelfoam embolization. RT(mean dose $44.0 \pm 9.3\text{Gy}$) was followed within 7- 10 days with conventional fractionation.

Results : An objective response was observed in 19 patients(63.3%). Survival rates at 1, 2, and 3 years were 67%, 33.3% and 22.2%, respectively. Median survival was 17 months. There were 6 patients surviving more than 3 years. Distant metastasis occurred in 10 patients, with 8 in the lung only and 2 in both lung and bone. Toxicity included transient elevation of liver function test in all patients, fever in 20, thrombocytopenia in 4, and nausea and vomiting in 1. There was no treatment-related death.

Conclusion : Combined TACE and RT appear to produce a favorable response and survival results with minimal toxicity.

Key Words :Hepatocellular carcinoma, Transcatheter arterial chemoembolization, Radiotherapy

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Table 4. Toxicity of Combined TACE and Radiotherapy(N=30)

Type of toxicity	No. of Patients(%)
Transient elevation in LFT*	30(100)
Fever	20(66.7)
Thrombocytopenia †	4(13.2)
Nausea/vomiting	1(3.3)

*liver function test, †less than 50,000/mm³

30.6 Gy
 59.4 Gy
 44.0±9.3 Gy
 4-6

Table 2. CT Response of Unresectable HCC to Combined TACE and Radiotherapy (N=30)

Tumor response*	No. of Patients(%)
Complete response	0(0.0)
Partial response	19(63.3)
Stable disease	9(30.0)
Progressive disease	2(6.7)

*evaluated 4-6 weeks after treatment using CT scan; complete disappearance of the tumor as a complete response, decrease of more than 50% of the tumor size as a partial response, decrease of less than 50% of the tumor or no change as a stable disease, and progression as a progressive disease

50% (stable disease)
 (progressive disease)
 Kaplan-Meier
 27)
 4-6 가
 30 19
 63.3% (Table 2). 1, 2,

3 67, 33.3, 22.2% (Fig. 1), 19

Table 3 6) 50, 35 4

Adriamycin 5-Fu
 가 Table 3 6 3
 가
 가
 10 (33.3%) 가
 3-17 가
 4.5 10 가
 2 가

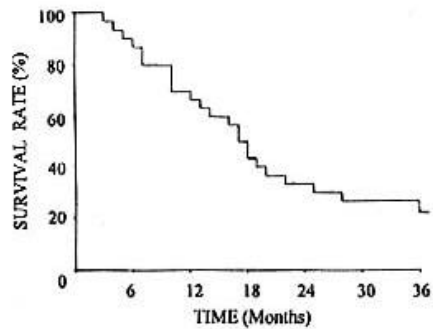


Fig. 1. Overall survival of 30 unresectable HCC patients who were treated with combined TACE and local radiotherapy.

Table 4
 TACE
 aspartate aminotransferase alanine
 aminotransferase 2/3
 가 1
 가 4, 1 1-2
 3
 2 1-3
 1 6 alkaline

phosphatase ³²⁾ 가

UICC , A 2/3 8.95 ±

TACE 3.4 cm 가 1, 2, 3 67, 33.3, 22.2%

가 가 가 17 가 가

TACE

¹¹⁻¹³⁾ 가 가 가

^{11-13, 28, 29)} TACE

¹¹⁻¹³⁾ 가 가 가 (Table

가 ^{14, 15)} 3 4). 가 가 가

가 3 cm 44% ³¹⁾ 가 가 가

TACE가

가 가

35

Gy ^{16, 17)} 가 가

4 (5-fluorouracil, cyclophosphamide, methotrexate, vincristine) ¹⁸⁾ 가 1-2

5-fluorouracil methotrexate ¹⁹⁾, cisplatin ^{16, 17)} 1

²⁰⁾ 26-36%

^{21, 22)} Stillwagon 2 , alkaline phosphatase

Adriamycin, 5-fluorouracil 15-24 Gy 1 가 가

46%

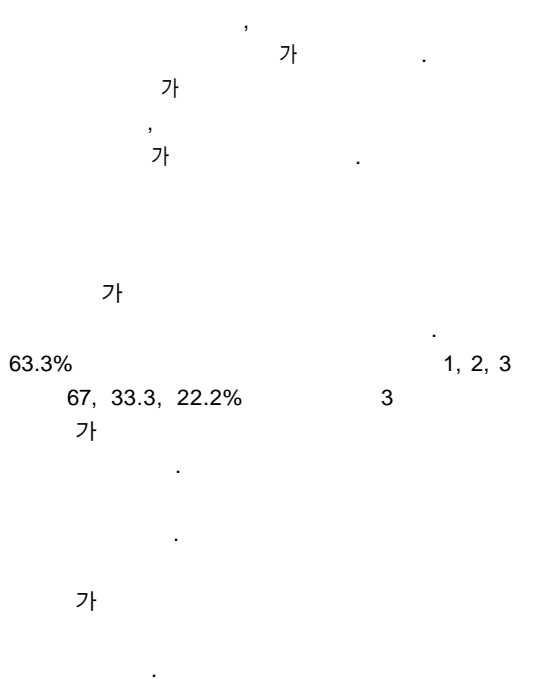
가 가 가

50-60 Gy 가 가 ^{25, 35)}

²²⁻²⁵⁾ 2 1 1.5 Gy 33% 66-72.6 Gy,

33-66% 48-52.8 Gy, 66% () 24-36 Gy

Adriamycin 44.0 ± 9.3 Gy 가



1. **Kew MC, Gedds EW.** Hepatocellular carcinoma in rural southern African blacks. *Medicine* 1965; 61: 98-108
2. **Kim IS, Kim HJ, Oh HC.** The cancer registry program in Kangwha county the first report. *Korean J Epidemiol* 1984; 6:100-105
3. **Li FP, Shiang EL.** Cancer mortality in China. *J Natl Cancer Inst* 1980; 65:217-221
4. **Dusheiko GM, Hobbs KE, Dick R, Burroughs AK.** Treatment of small hepatocellular carcinoma. *Lancet* 1992; 340:285-288
5. **Mori W.** Cirrhosis and primary cancer of the liver: Comparative study in Tokyo and Cincinnati. *Cancer* 1967; 55:627-631
6. **Venook AP.** Treatment of hepatocellular carcinoma: Too many options? *J Clin Oncol* 1994; 12:1323- 1334
7. **Lewis BJ, Friedman MA.** Current status of chemotherapy for hepatoma. In : Ogawa M, Editor.

Chemotherapy of hepatic tumors. Princeton, NJ : Excerpta Medica 1984:63-74

8. **Wellwood JM, Cady B, Oberfield RA.** Treatment of primary liver cancer: Response with regional chemotherapy. *J Clin Oncol* 1979; 5:25-31
9. **Atiq OT, Kemeny N, Niedzwiecki D, et al.** Treatment of unresectable primary liver cancer with intrahepatic fluorodeoxyuridine and mitomycin C through an implanted pump. *Cancer* 1992; 69:920- 924
10. **Patt YZ, Charnsangavej G, Lawrence D.** Hepatic arterial infusion of FUDR, leukovorin, Adriamycin, and platinol: eEffective palliation for nonresectable hepatocellular cancer. *Proc Am Soc Clin Oncol* 1992; 31:S89-S92
11. **Ikeda K, Kumada H, Saitoh S, et al.** Effect of repeated transcatheter arterial embolization on the survival time in patients with hepatocellular carcinoma. *Cancer* 1991; 68:2150-2154
12. **Lin DY, Liaw YF, Lee TY, et al.** Hepatic arterial embolization in patients with unresectable hepatocellular carcinoma : A randomized controlled trial. *Gastroenterology* 1988; 94:453-456
13. **Okuda K, Ohtsuki T, Obata H, et al.** Natural history of hepatocellular carcinoma and prognosis in relation to treatment. Study of 850 patients. *Cancer* 1985; 56:918-928
14. **Sakurai M, Okamura J, Kuroda C.** Transcatheter chemoembolization effective for treating hepatocellular carcinoma : A histopathologic study. *Cancer* 1984; 54:387-392
15. **Yu YQ, Xu DB, Zhou XD, et al.** Experience with liver resection after hepatic arterial chemoembolization for hepatocellular carcinoma. *Cancer* 1993; 71:62-65
16. **Ingold JA, Reed GB, Kaplan HS, et al.** Radiation hepatitis. *Am J Roentgenol* 1965; 93:200-208
17. **Wharton JT, Delclos L, Gallager S.** Radiation hepatitis induced by abdominal irradiation with the cobalt 60 moving strip technique. *Am J Roentgenol* 1973; 117:73-81
18. **Cochrane AMG, Murray-Lyon IM, Brinkley DM, et al.** Quadruple chemotherapy versus radiotherapy in treatment of primary hepatocellular carcinoma. *Cancer* 1977; 40:609-614
19. **Dhir V, Swaroop VS, Mohandas KM, et al.** Combination chemotherapy and radiation for palliation of hepatocellular carcinoma. *Am J Clin Oncol* 1992; 15:304-307

20. **Ebstein B, Ettinger D, Leichner PK, et al.** Multimodality cisplatin treatment in nonresectable alpha-fetoprotein-positive hepatoma. *Cancer* 1991; 67:896-900
21. **Friedman MA, Volberding PA, Cassidy MJ, et al.** Therapy for hepatocellular cancer with intrahepatic arterial adriamycin and 5-fluorouracil combined with whole-liver irradiation : A Northern California Oncology Group Study. *Cancer Treat Rep* 1979; 63:1885-1888
22. **Stillwagon GB, Order SE, Guse CG, et al.** 194 hepatocellular cancers treated by radiation and chemotherapy combinations: Toxicity and response: A Radiation Therapy Oncology Group(RTOG) study. *Int J Radiat Oncol Biol Phys* 1989; 17:1223-1229
23. **Nagashima T.** The study of radiotherapy for HCC. *Acta Radiol Jpn* 1989; 49:141-1151
24. **Tanaka N, Matsuzaki Y, Chuganzi Y, et al.** Proton irradiation for hepatocellular carcinoma. *Lancet* 1992; 340:1358
25. **Robertson JM, Lawrence TS, Dwarzanin LM et al.** Treatment of primary hepatobiliary cancers with conformal radiation therapy and regional chemotherapy. *J Clin Oncol* 1993; 11:1286-1293
26. **Robertson JM, McGinn CJ, Walker S, et al.** A phase I trial of hepatic arterial bromodeoxyuridine and conformal radiation therapy for patients with primary hepatobiliary cancers or colorectal liver metastasis. *Int J Radiat Oncol Biol Phys* 1997; 39; 1087-1092
27. **Kaplan E, Meier P.** Nonparametric estimations from incomplete observations. *Am Stat Assoc J* 1958; 53:457-481
28. **Okamura J, Horikawa S, Fujiyama T, et al.** An appraisal of transcatheter arterial embolization combined with transcatheter arterial infusion of chemotherapeutic agent for hepatic malignancies. *World J Surg* 1982; 6:352-357
29. **Sasaki Y, Imaoka S, Kasugai H, et al.** A new approach to chemoembolization therapy for hepatoma using ethiodized oil, cisplatin, and gelatin sponge. *Cancer* 1987; 60:1194-1203
30. **Kato T, Nemoto R, Mori H, et al.** Arterial chemoembolization with microencapsulated anticancer drug. An approach to selective cancer chemotherapy with sustained effects. *JAMA* 1981; 245: 1123-1127
31. **Higuchi T, Kikuchi M, Okazaki M.** Hepatocellular carcinoma after transcatheter hepatic arterial embolization. A histopathologic study of 84 resected cases. *Cancer* 1994; 73:2259-2263
32. **Byfield JE, Lynch M, Kulhanian F, et al.** Cellular effects of combined adriamycin and x-irradiation in human tumor cells. *Int J Cancer* 1997; 19:194-204
33. **Pechoux CL, Akine Y, Tokita N, et al.** Hepatocellular carcinoma diagnosed radiologically, treated by transcatheter arterial embolization and limited-field radiotherapy. *Br J Radiol* 1994; 67:591-595
34. **Tang Z, Yu Y, Zhou X, et al.** Cytoreduction and sequential resection for surgically verified unresectable hepatocellular carcinoma : Evaluation with analysis of 72 patients. *World J Surg* 1995; 19:784- 789
35. **Lawrence TS, Tesser RJ, Ten Haken RK.** An application of dose volume histograms to the treatment of intrahepatic malignancies with radiation therapy. *Int J Radiat Oncol Biol Phys* 1991; 20: 555-561

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: 1992 3 1994 8

가 30

가

. 가

가 Child's C

2/3

ECOG 3

8.95 ± 3.4

cm, UICC , A가 10 , 20 ,

22 ,

11 ,

alpha fetoprotein(AFP)

. TACE

5 ml

(Adriamycin 50mg)

(Gelfoam)

TACE 7-10

44.0 ± 9.3 Gy

: 30 19

63.3%

1, 2, 3

67, 33.3, 22.2%

17

19

6 3

가 4 , 1

1-2

: 가