

RAPID COMMUNICATION

Radiotherapy for 65 patients with advanced unresectable hepatocellular carcinoma

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Abstract

AIM: To evaluate the efficacy of radiotherapy (RT) in patients with advanced unresectable hepatocellular carcinoma (HCC).

METHODS: A total of 65 patients were treated with RT in the Korea University Medical Center. The median age of the patients was 60 years, and 86.2% were men. 18.5% and 81.5% of the patients were diagnosed as TNM stage III and IV-A, respectively. Treatment response was assessed 4 mo after initiation of RT. Tumor regression rate 1 mo after initiation of RT (TRR_{1m}) was also assessed. Duration of survival was calculated from the initiation of RT.

RESULTS: The objective treatment response was 56.9%. The 12 mo survival rate was 34.7%. Predictive factors for survival were Child-Pugh grade, α -fetoprotein level and treatment response. An objective response was achieved more frequently in patients with TRR_{1m} \geq 20% than in those with TRR_{1m} < 20% ($P < 0.001$).

CONCLUSION: RT is effective in treating advanced HCC with a tumor response rate of 56.9%.

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Key words: Hepatocellular carcinoma; Radiotherapy; Treatment response; Survival

INTRODUCTION

In Korea, hepatocellular carcinoma (HCC) accounts for 83% of primary liver cancer, which is the third most common cancer and the third leading cause of cancer-related death^[1,2]. Although surgical resection is considered to be the treatment of choice for long-term control of HCC, this treatment is considered at diagnosis in less than 20% of HCC patients due to disease extent or a hepatic function that is inadequate for resection^[3-5].

Although percutaneous ablation therapy, such as percutaneous ethanol injection or radiofrequency ablation, could be the best treatment in patients who are not suitable for resection, this treatment is limited to early-stage HCC^[6]. Transarterial chemoembolization (TACE) is used for patients with unresectable HCC who are also ineligible for percutaneous ablation^[6]. However, because complete tumor necrosis is rare with TACE, repeated treatments are often needed. Additionally, TACE-induced vascular injury can limit further TACE^[7-10]. Finally, patients with portal vein thrombosis or extensive tumor burden are poor candidates for TACE, because their tumors are frequently associated with arterio-portal shunts and TACE-related liver damage. For these advanced HCCs, hepatic arterial infusion of chemotherapy (HAI) has yielded promising results in several recent studies^[11-13], but the benefit of HAI is still controversial.

Radiotherapy (RT) for the treatment of HCC has been attempted over the last four decades, but the results have been unsatisfactory because the doses were too low to be adequately tumoricidal^[14-16]. Recently, however, several studies have suggested local, high-dose RT is well tolerated and leads to a favorable treatment response in patients

with unresectable HCC^[17-20]. Therefore, this study was performed to evaluate the treatment responses of RT and survival in patients who underwent RT for unresectable HCC.

MATERIALS AND METHODS

Patients

This study was performed with patients who underwent RT for unresectable advanced HCC without distant metastases. Between July 2003 and June 2006, 80 patients with unresectable HCC underwent local RT to the liver at the Korea University Medical Center. Fifteen of these patients were excluded due to the presence of distant metastases prior to RT.

Diagnosis of HCC was based on either the identification of hypervascular masses by two imaging studies or by one imaging study combined with a serum alpha-fetoprotein (AFP) level > 400 ng/mL. If the vascular profile by dynamic imaging was not characteristic of HCC and the AFP was less than 400 ng/mL a biopsy was performed^[21]. Unresectability was determined using accepted surgical criteria^[3].

The baseline characteristics of the 65 patients are presented in Table 1. Fifty-six patients (86.2%) were male and 9 were female. The median age was 60 years (range, 42-83) years. Underlying liver diseases included chronic Hepatitis B virus (HBV) infection in 49 patients (75.4%), alcoholic liver cirrhosis in 13 patients (20%) and chronic Hepatitis C virus (HCV) infection in two patients (3.1%). In one patient (1.5%), co-infection with HBV and HCV was noted. Liver cirrhosis was present in 50 patients (76.9%). According to the Child-Pugh classification, 43 patients (66.2%) were classified as grade A and 22 patients (33.8%) were classified as grade B. Patients in class C were not included. Baseline tumor size was 10.8 ± 4.7 cm (median, 9.9 cm). In 31 patients (47.7%), the tumor size was larger than 10 cm. Based on the types of HCC described by Egge^[22], the most frequent tumor type was massive (58.5%), followed by multinodular (36.9%) and single nodular (4.6%). Prior to RT, portal vein thrombosis was observed in 45 patients (69.2%); this was confirmed by CT and/or angiogram. Among these 45 patients, thrombosis was observed in the main portal vein in 20 patients (30.8%), at the first branch level in 23 (35.4%), and at the second branch level in 2 (3.1%). The hepatic vein and bile duct were involved in 8 and 6 patients, respectively. No patients showed evidence of extrahepatic metastasis prior to RT. According to the TNM staging system of the Liver Cancer Study Group of Japan^[23], 53 patients (81.5%) fell into stage IV-A, and 12 (18.5%) fell into stage III.

Treatment

RT was performed as a primary treatment in 40 of the 65 patients (61.5%) due to an overly large tumor size in 20 patients (30.8%), portal vein thrombosis in 12 patients (18.5%), IVC thrombosis in 3 patients (4.6%), bile duct invasion in 3 patients (4.6%), and a massive portosystemic shunt around the tumor in 2 patients (3.1%). In the remaining 25 patients (38.5%), RT was performed as

Table 1 Baseline characteristics of the 65 patients who underwent radiotherapy for unresectable hepatocellular carcinoma

Characteristics	Number of patients (%)
Age (yr)	60 (42-83) ¹
< 60/≥ 60	35 (53.8)/30 (46.2)
Gender (Male/Female)	56 (86.2)/9 (13.8)
Underlying liver disease (viral/alcohol)	52 (80.0)/13 (20.0)
Liver cirrhosis	50 (76.9)
Ascites	24 (36.9)
Child-Pugh class (A/B)	43 (66.2)/22 (33.8)
Albumin (g/dL) ²	3.4 ± 0.5
Bilirubin (mg/dL) ²	1.2 ± 0.9
Alkaline phosphatase (IU/L) ²	151.8 ± 79.3
Platelet (10 ³ /mL) ²	156.3 ± 66.2
Prothrombin time (INR) ²	1.2 ± 0.2
Sodium (mEq/L) ²	137.7 ± 3.7
Creatinine (mg/dL) ²	1.0 ± 0.9
Tumor size (cm) ²	10.8 ± 4.7
< 10/≥ 10	34 (52.3)/31 (47.7)
Tumor type (SN/MN/massive)	3 (4.6)/24 (36.9)/38 (58.5)
Portal vein thrombosis	45 (69.2)
UICC stage (III/IV-A)	12 (18.5)/53 (81.5)
α-fetoprotein (IU/mL) ²	17454 ± 66005
> 400/≤ 400	28 (43.1)/37 (56.9)
Radiotherapy aim (primary/salvage)	40 (61.5)/25 (38.5)

¹Median (range); ²mean ± SD; INR: International normalized ratio; SN: Single nodular; MN: Multinodular.

a salvage treatment after ineffective TACE (21 patients, 32.3%) or vascular inaccessibility to the feeding vessel of the HCC (4 patients, 6.2%). External beam RT at a target dose of 61 Gy/34 fractions was planned, using 10 MV of X-rays. The RT strategy was devised using a CT-based 2-D planning system (CT Port, Toshiba, Tokyo, Japan). To account for respiratory-based liver motion, a 1-1.5 cm margin was added in the craniocaudal direction. The full 61-Gy irradiation dose was feasible in 55 of the 65 patients (84.6%).

During and after RT, TACE was also employed in 57 patients (87.7%; 2.9 ± 1.8 sessions; median, three sessions; range, 1-8 sessions). TACE was performed with an emulsion of doxorubicin at a dose of 10-30 mg and 4-12 mL of mixed solution of lipiodol and contrast agent. TACE was usually combined with embolization using gelfoam particles, except in cases with significant portal vein thrombosis. In 16 patients with portal vein invasion (24.6%), HAI with cisplatin and 5-FU was combined with or without TACE (3.3 ± 2.4 cycles; median, 2.5 cycles; range, 1-8 cycles).

Evaluation of treatment response

Tumor size was measured by computed tomography (CT) and was calculated as the longest diameter multiplied by the longest perpendicular diameter. CT scans were obtained before RT, 1 and 4 mo after the initiation of RT, and then every 2-3 mo. If a patient had multiple nodules, the extent of the tumor was determined by the sum of the extent of all tumors > 2 cm in diameter.

Treatment response was assessed at four months after initiation of RT. A complete response was defined as the complete disappearance of all clinical and radiographic tu-

mor evidence. A partial response was defined as more than a 50% decrease in tumor size from baseline. Stable disease was defined as less than a 50% decrease or a 25% increase in tumor size. The objective treatment response was calculated based on the complete and partial responses. Progressive disease was defined as a greater than 25% increase in extent of the tumor from the nadir extent of the tumor.

To evaluate the efficacy of using the early tumor response to predict the treatment response, the tumor regression rate at one month after initiation of RT (TRR_{1m}) was assessed using the following equation: TRR_{1m} = [(baseline tumor extent - tumor extent at one month after RT)/baseline tumor extent] × 100.

Adverse events were evaluated weekly during RT and one month following the treatment. Adverse hematologic events were evaluated by measuring hemoglobin, white blood cell (WBC) and platelet counts, while hepatic adverse events were evaluated by measuring serum bilirubin, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels. Gastrointestinal (GI) bleeding included any bleeding from the esophagus, stomach, duodenum, or liver. All adverse events were graded according to Common Terminology Criteria for Adverse Events V3.0.

Statistical analysis

All calculations were performed using SPSS 10.0 software for Windows (SPSS, Chicago, IL). Quantitative variables were expressed as mean ± SD or medians. Differences in quantitative and qualitative variables were assessed using the Student's *t*-test and chi-square test, respectively. Logistic regression analysis was performed to evaluate predictive factors for tumor response. Survival and progression-free survival were assessed from the initiation of RT according to the Kaplan-Meier method. Differences between variables were assessed using the log-rank test. The Cox regression model was used to detect associations between survival and AFP status, tumor type, the location of tumor thrombi, stage and therapeutic models. For multivariate analysis, variables with *P* < 0.2 at univariate analysis were entered. Differences with *P* < 0.05 were considered to be statistically significant.

RESULTS

Tumor response

Fifty-five of 65 patients (84.6%) completed the RT schedule. Ten patients (15.4%) could not complete RT due to HCC aggravation or deterioration of liver function after RT. Interruption of RT was more frequent in Child-Pugh class B patients (7 of 20 patients, 35%) than in class A patients (3 of 45, 6.7%; *P* = 0.003). Among the 55 patients who completed RT, treatment response was evaluated 4 mo after the initiation of RT. None of our patients had completely responded at this point in the response evaluation, but 37 patients (67.3%) had partially responded. Seventeen patients (30.9%) had stable disease, and 1 (1.8%) had progressive disease. Therefore, the objective treatment response at four months was 67.3%.

Table 2 Baseline characteristics of the 65 patients, according to treatment response

	Pts without OTR (<i>n</i> = 28)	Pts with OTR (<i>n</i> = 37)	<i>P</i> value
Age (yr)	61 ± 10	58 ± 8	0.271
Gender (M:F)	22:6	34:3	0.124
Hepatitis B	21 (75%)	28 (75.7%)	0.950
Hepatitis C	2 (7.1%)	1 (2.7%)	0.573
Alcohol abuse	5 (17.9%)	8 (21.6%)	0.707
WBC (/mm ³)	5450 ± 1671	6079 ± 2229	0.216
Hemoglobin (g/dL)	11.4 ± 2.2	12.0 ± 1.8	0.207
Platelet (× 10 ³ /mm ³)	160 ± 738	154 ± 608	0.733
AST (IU/L)	111 ± 93	71 ± 53	0.032
ALT (IU/L)	62 ± 51	69 ± 90	0.686
ALP (IU/L)	175 ± 89	134 ± 67	0.038
Bilirubin (mg/dL)	1.47 ± 1.27	0.91 ± 0.49	0.035
Albumin (g/dL)	3.3 ± 0.4	3.5 ± 0.5	0.103
Prothrombin time, INR	1.16 ± 0.22	1.15 ± 0.14	0.796
Creatinine (mg/dL)	1.17 ± 1.31	0.92 ± 0.25	0.329
Liver cirrhosis	21 (75%)	29 (78.4%)	0.749
Child-Pugh grade A	14 (50%)	31 (83.8%)	0.003
Alpha-fetoprotein (ng/dL)	31474 ± 98160	6844 ± 15814	0.199
≥ 400 ng/dL	15 (53.6%)	22 (59.5%)	0.635
Tumor size (mm)	118 ± 37	99 ± 52	0.112
≥ 10 cm	18 (64.3%)	14 (37.8%)	0.035
Multiple tumor	24 (85.7%)	30 (81.1%)	0.622
Massive type	18 (64.3%)	20 (54.1%)	0.407
Main portal vein thrombosis	10 (35.7%)	10 (27%)	0.452
Tumor stage IV	23 (82.1%)	30 (81.1%)	0.913

OTR: Objective treatment response; WBC: White blood cell; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; INR: International normalized ratio; Tumor stage: According to the TNM staging system of Liver Cancer Study Group of Japan.

However, if we label the 10 patients who did not complete RT as non-responders, then the partial response and stable disease rates decreased to 56.9% (37 of 65 patients) and 26.2% (17 of 65 patients), respectively.

Table 2 presents baseline characteristics according to treatment response. Logistic regression analysis was performed to evaluate predictive factors for an objective treatment response. Child-Pugh grade was the only independent predictive factor for an objective treatment response (Child-Pugh grade A *vs* B; OR, 5.167; 95% CI, 1.643-16.250; *P* = 0.005). Among the 45 patients with Child-Pugh grade A, 31 patients (68.9%) showed a partial response, as did 6 of the 20 grade B patients (30%, *P* = 0.003).

Time to progressive disease

During follow-up, 4 of the 37 patients showing a partial response (10.8%) and 3 of the 25 patients showing stable disease (12%) had progressive disease after a median of 6 (range, 3-9) mo. Among the 65 patients, time to progressive disease was 5 ± 3 mo after initiation of RT (median, 4 mo). Duration without progressive disease was longer in patients who met the objective treatment response (14.8 ± 1.4 mo) than in patients who did not (4.6 ± 0.4 mo, *P* < 0.001; Figure 1).

Survival

All enrolled patients were followed for 8 ± 6 (median,

6; range, 1-30) mo. During this period, 37 patients died. Fourteen patients died of hepatic failure, 13 died of HCC aggravation, 5 died of gastrointestinal bleeding, 2 died of tumor rupture, and 2 died of sepsis. The cumulative survival rates at 6, 12 and 18 mo were 61.5%, 34.7% and 27.0%, respectively. Patients who showed an objective treatment response (median survival, 346 d) survived longer than those who did not (median survival, 212 d; $P = 0.032$; Figure 2).

When multivariate Cox-regression analysis was performed with baseline characteristics, large tumor size (≥ 10 cm *vs* < 10 cm; OR, 2.416; 95% CI, 1.213-4.811; $P = 0.012$), Child-Pugh grade B *vs* A (OR, 4.094; 95% CI, 1.977-8.480; $P < 0.001$) and the presence of tumor thrombi in the main portal vein (OR, 2.315; 95% CI, 1.156-4.634; $P = 0.018$) were independent predictive factors for mortality. However, when multivariate analysis was performed after inclusion of the objective treatment response, Child-Pugh grade B *vs* A (OR, 3.706; 95% CI, 1.718-7.996; $P = 0.001$), high serum AFP level (OR, 2.459; 95% CI, 1.187-5.094; $P = 0.015$) and a failure to meet the objective treatment response (OR, 5.619; 95% CI, 2.475-12.760; $P < 0.001$) were independent prognostic factors for mortality (Table 3).

Tumor regression rate at 1 mo after RT initiation

TRR_{1m} was assessed in all 65 patients. TRR_{1m} was more than 20% in 41 patients (63.1%). Of the 41 patients with a TRR_{1m} $\geq 20\%$, 35 patients (85.4%) showed a partial response, while only 2 (8.3%) of the 24 patients with TRR_{1m} $< 20\%$ showed a partial response ($P < 0.001$; Figure 3). When logistic regression analysis was performed after inclusion of TRR_{1m} among the variables used to predict objective treatment response, Child-Pugh grade A (OR, 0.121; 95% CI, 0.019-0.784; $P = 0.027$) and TRR_{1m} $\geq 20\%$ (OR, 158.302; 95% CI, 14.032-1785.827; $P < 0.001$) were independent predictive factors.

Adverse events

Adverse events during and one month after RT are summarized in Table 4. Adverse hematologic events were identified in 78.5% of patients. Although most of them were mild and transient, grade 3 or 4 adverse events were noted in six patients (9.2%). Grade 3 or 4 hematologic adverse events were more frequent in patients who underwent RT combined with HAI (4 of 16 patients, 25%) than in patients with RT alone (2 of 49, 4.1%; $P = 0.012$). Adverse hepatic events were identified in 51.8% of the patients; the most common were hypoalbuminemia (33.8%) and hyperbilirubinemia (24.6%). Grade 3/4 adverse hepatic events developed in four patients (6.2%), with hyperbilirubinemia or elevation of AST in 1 (1.5%). Grade 3/4 adverse hepatic events were more frequent in patients with TRR_{1m} $< 20\%$ (4 of 24 patients, 16.7%) than in those with TRR_{1m} $\geq 20\%$ (1 of 41, 2.4%; $P = 0.038$). GI bleeding developed in five patients. The status of two patients with peptic ulcer disease and one patient with variceal bleeding was improved with medical or endoscopic treatment. However, two patients with hemobilia or HCC rupture expired after these events.

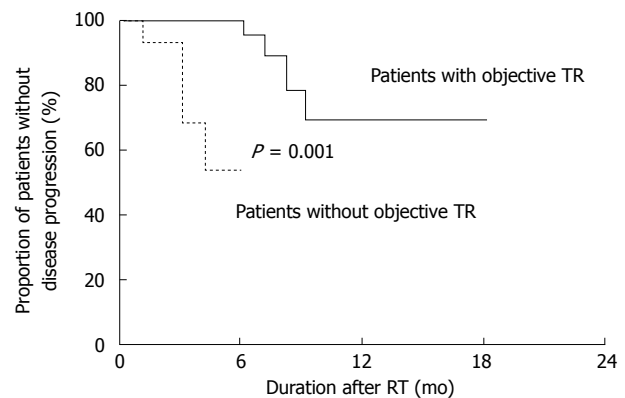


Figure 1 Duration without disease progression, according to treatment response. TR: Treatment response; RT: Radiotherapy.

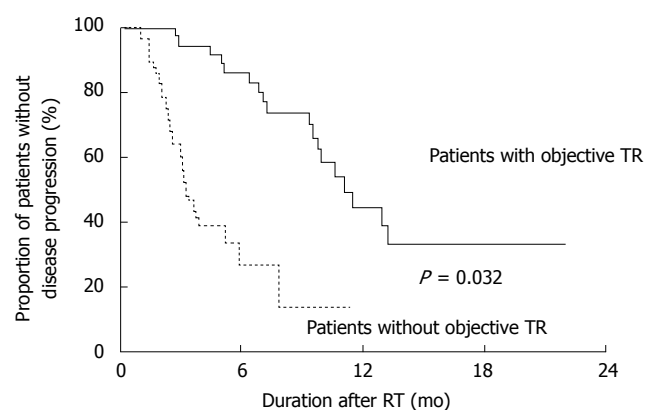


Figure 2 Overall survival of the 65 patients who underwent radiotherapy for advanced hepatocellular carcinoma according to treatment response. Patients with objective treatment responses (median survival, 346 d) survived longer than those without objective treatment responses (median survival, 212 d; $P = 0.032$). RT: Radiotherapy; TR: Treatment response.

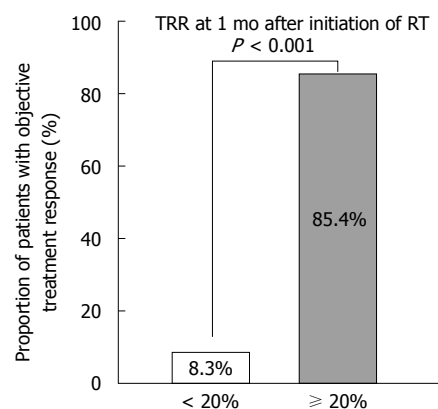


Figure 3 Proportion of patients who achieved an objective treatment response according to the tumor regression rate at one month after the initiation of radiotherapy. RT: Radiotherapy.

DISCUSSION

Recently, a number of reports have documented the effect of local RT on HCC^[17-20]. Although fractionation schemes were not identical to each other, local, high-dose RT alone or in combination with another modality such as

Table 3 Multivariate analysis of the mortality of patients who underwent radiotherapy for advanced hepatocellular carcinoma

		<i>P</i> value	β	Odds ratio	95% CI
Tumor size	0 ≤ 10 cm; 1 ≥ 10 cm	0.012	0.954	2.597	1.232-5.473
Child-Pugh grade	0 = Grade A; 1 = Grade B	0.001	1.336	3.802	1.687-8.568
Combined with TACE	0 = Yes; 1 = No	0.001	1.671	5.315	2.015-14.018
Objective treatment response	0 = Yes; 1 = No	0.006	1.194	3.300	1.414-7.699

Table 4 Adverse events in the 65 patients who underwent radiotherapy for unresectable hepatocellular carcinoma *n* (%)

	Grade					
	0	1	2	3	4	5
Hematologic	14 (21.5)	33 (50.8)	12 (18.5)	5 (7.7)	1 (1.5)	-
Hepatic	32 (49.2)	20 (30.8)	8 (12.3)	4 (6.2)	1 (1.5)	-
GI hemorrhage			1 (1.5)	2 (3.1)		2 (3.1)

TACE^[19,24], systemic chemotherapy^[25] or intra-arterial chemotherapy^[26,27] has achieved a substantial objective response. In this study, RT was performed with or without other treatment modalities and the objective response rate was 56.9%, which was somewhat lower than previous reported^[24,28-30]. However, when 10 patients (15.4%) who did not complete the whole RT schedule were excluded, the objective treatment response rate increased to 67.3%. We have no idea how the patients who could not complete RT were treated during these previous studies, because this was not reported. It is possible that all patients completed RT in the previous studies. However, a significant proportion of patients could not complete the RT schedule in the present study. Therefore, selection of appropriate patients for RT may be very important before RT initiation.

Child-Pugh grade was the only significant predictive factor for treatment response. This seems to be associated with the higher proportion of Child-Pugh grade B patients (35%) who could not complete the RT schedule compared with those with grade A (6.7%; *P* = 0.003). This speculation is supported by the fact that no variable was significantly associated with treatment response when the logistic analysis was performed on the 55 patients who completed RT (data was not shown). These results suggest that a circumspective decision was required in considering RT for patients with Child-Pugh grade B. Previously, tumor size was the one significant factor affecting treatment response^[29]. Similarly, a treatment response was more frequently seen in patients with a smaller HCC (23 of 32 patients, 69.7%) than in patients with a larger HCC (14 of 32 patients, 43.8%; *P* = 0.035). However, when multivariate analysis was performed, the significance disappeared.

Our results suggest RT may improve prognosis in patients who achieved an objective treatment response. RT appears to be associated with prolonged survival as well as prolonged suppression of HCC progression in patients who show an objective treatment response.

After the effects of other prognostic factors were corrected for, patients who achieved objective treatment responses survived longer than those who did not, as determined by multivariate analysis. In addition, time to progression was significantly longer in patients who met the objective treatment response than in patients who did not. However, several limitations should be discussed. First, 10 patients who could not complete the RT schedule were included in this analysis. However, even though these 10 patients were later excluded, patient survival still differed according to treatment response (*P* = 0.002; data not shown). Second, most patients were treated with not only radiotherapy, but also with TACE or HAI, and these combined treatments may affect patients' survival. To ideally assess the effect of RT on patient prognosis, RT should be the only treatment modality. However, considering the limitations of dose and field of RT, it seems unwise to use RT as the only treatment modality for advanced HCC.

In this study, the one-year survival rate was 34.7%, which was lower than in previous studies^[24,28-31]. It may be the patients enrolled in this study had more advanced disease than those in previous studies^[24,28-31]. In the present study, tumors were larger than 10 cm in 47.7% of patients, 69.2% of the cases had thrombi in portal vein, and 81.5% of the patients had stage IV-A disease. In addition, 10 patients (15.4%) who could not complete RT schedule were included in this study; none of these patients survived more than four months after initiation of RT. By contrast, most of the previous studies included patients who completed the RT schedule^[24,28-31], which may have led to the observed discrepancies with the present study.

In recent studies, PVT was the one prognostic factor for survival^[30,32]. Similarly, in this study, the presence of tumor thrombi in main portal vein as well as Child-Pugh grade and tumor size were independent prognostic factors for survival when multivariate analysis was performed with variables of baseline characteristics. However, when treatment response was included in the analysis, Child-Pugh grade, AFP level and treatment response were associated with survival. This result suggests that even if tumor thrombi are present in main portal vein before RT, RT may still improve survival when an objective treatment response is achieved.

In all of our patients, CT was performed at one month after initiation of RT. Tumor response at one month after initiation of RT was a useful predictor for RT response. In addition, grade 3 or 4 adverse hepatic events were more frequent in patients with TRR_{1m} < 20%. These results suggest if the mass does not decrease to 20% from baseline after one month of RT, interruption of RT can be considered due to the likelihood of a low objective treatment response rate and a high rate of severe adverse hepatic events.

In conclusion, RT was effective for the treatment of HCC with an objective tumor response rate of 56.9%; moreover, patients who met the objective treatment response survived longer than those who did not. Tumor regression at one month after the initiation of RT may be a useful predictor for RT response as well as severe adverse hepatic events.

COMMENTS

Background

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer-related death in the world, especially in Asia. In a large proportion of patients, HCC is diagnosed at an advanced stage and, in this stage, widely performed treatment modalities including surgical resection, local ablation therapy and transarterial chemoembolization are not indicated. Recently, several reports have suggested high-dose radiotherapy (RT) could be an effective treatment option for advanced HCC.

Research frontiers

Most previous studies have included only patients who completed the RT schedule. However, according to our experience, some proportion of patients could not complete the whole RT schedule and their prognosis was usually very poor. Therefore, this might lead to a selection bias when analyzing the treatment response and survival of patients. In this study, all patients with HCC who were treated with RT for more than 1 mo during the study period were included. In addition, we evaluated the prognostic significance of early tumor response by follow-up CT at 1 month after the initiation of RT.

Innovations and breakthroughs

RT was effective in patients with advanced HCC with an objective tumor response rate of 56.9%. Early tumor response rate at 1 month after the initiation of RT was shown to be a good prognostic indicator for RT response. In addition, severe adverse events were more frequent in patients with poor early tumor response rates.

Applications

RT could be considered as a treatment option for patients with advanced HCC. If the tumor does not decrease to 20% from baseline after one month of RT, interruption of RT can be considered due to the likelihood of a low objective treatment response rate and a high rate of severe adverse hepatic events.

Peer review

This is an interesting article, which may offer new insights in the treatment of advanced unresectable HCC. The paper is well organized and the results are clearly described and commented.

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