2175 Reappraisal of Radiotherapeutic Parameters in Terms of Predicting Liver Complication

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Purpose/Objective(s): In radiotherapy of liver cancer, determination of the optimal radiotherapeutic parameters is still under investigation. The purpose of this study is to identify the radiotherapeutic parameters associated with liver complication.

Materials/Methods: From 2001 to 2003, a total of 132 patients with hepatocellular carcinoma received 3D-CRT(3-dimensional conformal radiotherapy). The median dose of 45±16.5 Gy was delivered in daily 1.5–2.5 Gy fraction. The patients received combined treatment of radiotherapy with either transcather arterial chemoembolization, transcatheter arterial chemoinfusion or systemic chemotherapy. RILD was defined as either anicteric elevation of alkaline phophatase level of at least twofold and nonmalignant ascites, or elevated transaminases of at least five fold the normal or of pretreatment levels. CMILD was defined as RILD criteria plus abnormal elevation of bilirubin level. Three published guidelines were evaluated. In Cheng's guideline, radiation dose is determined based on the ICG-R15(indocyanin green retention rate at 15 min) and the non-tumorous liver volumes. In Michigan Univ. guideline, $V_{50\%}$(the fraction of normal liver treated to ≥50% of the isocenter dose) is divided in 3 intervals (<33%, 33–66%, and >66%). In Seong's guideline, radiation dose is determined by $V_{50\%}$, which is divided in 4 intervals (<25%, 25–49%, 50–75%, >75%).

Results: The overall survival rates at 1, 3 years were 47 and 14.4%, respectively, with a median survival of 12 months. Among the patients with liver complication, six patients (4.5%) developed RILD, and seven (5.3%) occurred CMILD. By Cheng's guideline, neither non-tumorous liver volume nor ICG-R15 was correlated to liver complication. In Seong's guideline, the observed hepatic toxicity incidence was 14.3%, 14%, and 10.9%, respectively, for $V_{50\%}$ of <25%, 25–49%, and 50–75%. For Michigan Univ. guideline, the incidence was 13.6%, 11.3%, and 20%, respectively, for $V_{50\%}$ of < 33%, 33–66%, and > 66%. Combination of $V_{50\%}$ and ICG R-15 criteria could not predict liver complication. However, liver complication was well predicted in the case using a combination of $V_{50\%}$ and Child-Pugh class; the incidence of liver complication was one in eight patients in the group of $V_{50\%}$ less than 25% and class A, higher for Child-Pugh class B (60%) than class A (7.5%) in the group of $V_{50\%}$ is 25–49%, and 14.3% for class B and 9.8% for class A in the group of $V_{50\%}$ is 50–75% (Table).

Conclusions: When we use the DVH and dosimetric parameters, caution should be taken as they have liver cirrhosis. We suggest the $V_{50\%}$ and Child-Pugh class may be simple and useful indicators for predicting liver disease as a radiation treatment guideline.

Table. The distribution of patients with liver complication by Seong's DVH criteria and Child-Pugh class

$V_{50\%}$	Child-Pugh class A	Child-Pugh class B	Recommended total dose	*p* value
< 25	1/8 (12.5%)	0/2	59.4 Gy or more	
25-49	4/53(7.5%)	3/5 (60%)	45-54 Gy	
50-75	4/41(9.8%)	1/7(14.3%)	30.6-41.4 Gy	
> 75	-	-	No treatment	
	9 /102(8.8%)	4 / 14 (28.6%)		0.03

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2176 Radiation-Induced Hepatic Toxicity in Radiotherapy Combined With Chemotherapy for Hepatocellular Carcinoma

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Purpose/Objective(s): Radiation-induced hepatic toxicity has been traditionally noted as a radiation induced liver disease (RILD). Currently, radiotherapy for hepatocellular carcinoma (HCC) is not done alone but combined with various form of chemotherapy, hence liver disease by combined modality therapy (CMILD) needs to be better understood. The purpose of this study is to analyze hepatic toxicity by radiotherapy combined with chemotherapy in HCC.

Materials/Methods: From 2001 to 2003, a total of 132 patients with HCC received 3D conformal radiation therapy (3D-CRT) combined with chemotherapy at our institution. The median dose 45 ± 16.5 Gy in daily 1.5–2.5 Gy was delivered with 6–10 MV linear accelerator. Patients were evaluated for any toxicity by biochemical parametmeters prior to, during and until 12 months after the 3D-CRT. Biochemical parameters included; albumin, total bilirubin (T. Bil), aspartate aminotransferase (AST), alanine aminotransferese (ALT), and alkaline phosphatase (ALP). RILD was defined as either anicteric elevation of ALP level of at least twofold and nonmalignant ascites, or elevated transaminases of at least five fold the upper limit of normal or of pretreatment levels. CMILD was defined as RILD criteria plus abnormal elevation of T. Bil level. According to the distribution of the chemotherapeutic drug, patients were divided into 2 groups; in transcatheter arterial chemoembolization (TACE) group, adriamycin 50 mg was administered via hepatic artery followed by gelfoam. In non-TACE group, patients were treated with either transcatheter arterial chemoinfusion of adriamycin (50 mg) or intraarterial infusion of 5-FU (500 mg/m^2) or cisplatinum (400 mg/m^2) via chemoport.

Results: TACE group and non-TACE group involved 53 patients 79 patients, respectively. In TACE group, 3 patients developed RILD (5.6%) and none for CMILD. In non-TACE group, 3 patients (3.7%) developed RILD and 7 patients (8.8%) developed CMILD. Three patients with CMILD expired 1 month after radiotherapy because of hepatic failure.

Conclusions: In TACE group, chemotherapeutic drugs are rather localized within the tumor. However in non-TACE group, the drugs diffusely spread over the whole liver. This difference results in heterogeneous features of radiation-induced hepatic toxicity. Considering a variety of liver-directed chemotherapy combined with radiotherapy, reappraisal of hepatic toxicity including CMILD is warranted.

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