

• RAPID COMMUNICATION •

## Baseline characterization of patients aged 70 years and above with hepatocellular carcinoma

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### Abstract

**AIM:** To characterize the baseline profiles of patients aged 70 years and above with hepatocellular carcinoma (HCC).

**METHODS:** A series of 127 consecutive patients with HCC were enrolled between 2000 and 2004, and none of them had been diagnosed as having HCC previously. Baseline profiles, including parameters of hepatic function such as serum transaminase and prothrombin time [PT (% activity)] were compared between patients aged  $\geq 70$  and  $< 70$  years.

**RESULTS:** Patients  $\geq 70$  years old showed significantly lower levels of aspartate aminotransferase ( $P = 0.04$ ) and alanine aminotransferase ( $P = 0.01$ ), and significantly higher PTs ( $P = 0.04$ ) and platelet counts ( $P = 0.02$ ). Concomitantly, among  $\geq 70$ -year-old patients, HCC was more common in non-cirrhotics, whereas among patients  $< 70$  years old, HCC was more common in cirrhotics. There was no significant difference between the groups in the number or size of tumors.

**CONCLUSION:** Older HCC patients showed less inflammation and better preservation of hepatic function, indicating that not only cirrhotic patients but also non-cirrhotic patients should be considered as a high-risk group among the elderly.

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**Key words:** Hepatocellular carcinoma; Elderly patients; Baseline profile; Non-cirrhosis

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### INTRODUCTION

Hepatocellular carcinoma (HCC), one of the most common forms of tumors, is increasing in frequency worldwide<sup>[1-4]</sup>. The increase is attributable to the spread of hepatitis C virus (HCV) infection in the population. HCV-related HCC is more common among the elderly patients, whereas hepatitis B virus (HBV)-related HCC is more common among the younger patients<sup>[3,5]</sup>. In Japan, fatalities from HCC are higher among patients who are aged 70 years and above<sup>[3]</sup>. However, the baseline profiles of such patients, including various parameters of hepatic function, have not been thoroughly investigated. In this study, we have evaluated the baseline profiles, including parameters of hepatic function such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and prothrombin time [PT (% activity)] in HCC patients aged  $\geq 70$  and  $< 70$  years.

### MATERIALS AND METHODS

A total of 127 consecutive patients with HCC, who had not been diagnosed with HCC previously, were admitted to our department at Kyushu University Hospital between 2000 and 2004 (Table 1). HCC was diagnosed by computed tomography (CT), ultrasonography, angiography and tumor biopsy, and treated with transcatheter arterial chemoembolization (TACE), percutaneous ablation [percutaneous ethanol injection therapy (PEIT) or radio frequency ablation (RFA)], and/or hepatic resection. Liver cirrhosis (LC) was diagnosed based on liver biopsy, laboratory data, ultrasonography, and/or computed tomography. Variables were compared between patients aged  $\geq 70$  and  $< 70$  years, which included parameters of hepatic function (albumin, total bilirubin, AST, ALT, PT, and platelet number), serum levels of alpha-fetoprotein (AFP), tumor size and number (solitary or multiple), existence of liver cirrhosis, etiology [HBV, HCV, or non-HBV-non-HCV (NBNC)], and treatment.

Data were presented as mean  $\pm$  SE for quantitative variables. Differences in characteristics between patients aged  $\geq 70$  and  $< 70$  years were analyzed by Wilcoxon rank sum test and Fisher's exact test for qualitative variables.

### RESULTS

The number of older patients (aged  $\geq 70$  years) and younger patients (aged  $< 70$  years) with HCC was 49 and 78, respectively. There was no difference in the proportion

**Table 1** Comparison of baseline profiles between elderly patients and younger patients with HCC

Age (yr)	<70	≥70	P
n	78	49	
Male/female	56/22	34/15	0.772
Age (yr)	60.4±0.8	74.3±0.5	0.002
Platelet (mm <sup>3</sup> )	10.3±0.7	13.9±0.9	0.002
PT (%)	66.8±3.2	76.6±3.1	0.036
Albumin (g/dL)	3.6±0.1	3.8±0.1	0.146
TBil (mg/dL)	1.5±0.2	1.2±0.2	0.298
AST (U/L)	86.4±6.0	66.3±7.9	0.044
ALT (U/L)	79.6±7.1	53.0±6.1	0.010
AFP (ng/mL)	1 651±839	1 006±390	0.562
HBV/HCV/NBNC	11/69/5	2/42/3	0.629
Non-LC/LC	35/44	36/13	0.001
HCC: solitary/multi	61/17	39/10	0.868
HCC: size diameter (mm)	36.0±4.0	28.6±3.0	0.184

of males and females between the two groups (Table 1). The prevalence of HBV and HCV in older and younger patients was 4% and 86%, and 14% and 88%, respectively. A comparison of hepatic function parameters showed differences in the platelet counts, PT (%), and the levels of AST and ALT (Table 1). Platelet counts and PT were significantly higher in older patients ( $P = 0.016$  and  $P = 0.0355$ , respectively). The serum levels of AST and ALT were significantly lower in older patients ( $P = 0.0443$  and  $P = 0.0100$ , respectively). The incidence of HCC among older patients was higher in those without LC than in those with LC, whereas in the younger patients, HCC developed more frequently in those with LC than in those without LC. There was no difference between the age groups in tumor number (solitary or multiple), tumor size, or serum levels of AFP. Resection was performed in 14% of the patients aged  $\geq 70$  years and in 13% of those aged  $< 70$  years. There was no difference between the groups in the types of treatment received.

## DISCUSSION

This study demonstrated that older patients (aged  $\geq 70$  years) had higher PTs and platelet counts, and lower levels of AST and ALT as compared with younger patients (aged  $< 70$  years). The higher platelet counts and PTs indicate that liver function was better preserved, since platelet counts have been reported to correlate inversely with the degree of liver fibrosis<sup>[6]</sup>. In our study, 73% (36/49) of the older patients were diagnosed as having chronic hepatitis (non-LC), whereas only 45% (35/78) of the younger patients were diagnosed as having non-LC. Furthermore, the lower levels of AST and ALT indicate that hepatitis (inflammation) was less active. These results indicate that HCC in elderly patients tends to occur more frequently among those with non-LC and mild hepatic inflammation.

HCC is generally thought to be more common among LC patients, and the prevalence of cirrhosis in those with HCC is estimated. The EUROHEP group demonstrated that the 5-year risk of HCC was increased by 25% for a 60-year-old man with cirrhosis, mild elevation in total bilirubin (TBil) levels, and a low platelet count, whereas the risk was only increased by 3% for a 50-year-old man with cirrhosis,

normal TBil levels, and normal platelet counts<sup>[8]</sup>. Tarao *et al.* also reported that the incidence of HCC in LC patients with ALT  $\geq 80$  U/L was much higher than in those with ALT  $< 80$  (13%/year *vs* 3%/year)<sup>[9]</sup>. These results are similar to our observations in patients  $< 70$  years old. However, in contrast with the previous studies, we found that the development of HCC in older patients was not strongly associated with LC, ALT levels, or the duration of disease. Although the precise reasons for this difference remain unknown, aging itself might be an important factor, independent of the duration of disease, since older people generally have a higher risk of cancer, regardless of the type<sup>[10]</sup>. It is possible that the patients with cirrhosis and HCC have died before reaching the age of 70 and those survived patients had well preserved hepatic function. To clarify this point, a Kaplan-Meier survival analysis of the two groups over the 5-year period of observation is needed. Comparison of the two groups of patients ( $< 70$  and  $\geq 70$  years) with chronic viral liver disease without HCC is also needed to know whether our present findings are indeed unique for HCC patients or a common profile in all patients with chronic viral disease.

Recently, the importance of surveillance for HCC among older LC patients has been recognized<sup>[11]</sup>, due to the increasing life expectancy of cirrhotic patients as well as of the general population<sup>[11,12]</sup>, and because surveillance among the older subjects can facilitate early detection and more effective treatment<sup>[13-15]</sup>. Trevisani *et al.* reported that surveillance for HCC in elderly LC patients improves their survival by identifying certain cancers earlier when they are more amenable to the treatment<sup>[11]</sup>. Better preservation of hepatic function as well as an early diagnosis can allow for more effective treatment such as hepatic resection. In our study, 14% of older patients received hepatic resection, which was similar to the percentage among younger patients. Therefore, we suggest that elderly non-LC patients should also be included in the surveillance to facilitate both early diagnosis and effective treatment.

Another significant finding in our study is that most of the patients (86%) suffered from HCV infection. It was recently reported that interferon treatment lowered the incidence of HCC<sup>[16,17]</sup>, suggesting that interferon therapy would be advisable for preventing the development of HCC, even in elderly patients.

In conclusion, our study demonstrated that patients  $\geq 70$  years old with HCC had baseline clinical profiles that differed considerably from those of patients  $< 70$  years old; that is, HCC was more likely to develop among non-LC patients with well-preserved hepatic function and mild inflammation. Our results suggest that elderly non-LC patients, as well as LC patients, should be recognized as a high-risk group for HCC.

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