

Report of the 16th follow-up survey of primary liver cancer

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Abstract

In the 16th nationwide follow-up survey of primary liver cancer, 19,920 patients were newly registered as patients with primary liver cancer at 795 medical institutions in Japan over a period of 2 years (from January 1, 2000 to December 31, 2001). Of these patients, 94.5% had hepatocellular carcinoma (HCC) and 3.6% had intrahepatic cholangiocarcinoma (ICC). In addition, 21,268 follow-up patients were registered, and a valid response rate of 75.6% was obtained in these follow-up patients. In this study, epidemiological and clinicopathological factors, diagnosis and treatment were investigated in patients who were newly registered in the 16th follow-up survey. As additional statistics, the cumulative survival rates of newly registered patients in the 11th to 16th follow-up surveys were calculated for each histological type (HCC, ICC and combined HCC and ICC) by background factor(s) and treatment, respectively. Furthermore, in patients with HCC, the cumulative survival rates were calculated for several types of treatment (hepatectomy, local ablation therapy and transcatheter arterial chemoembolization). It is anticipated that this follow-up survey will contribute to future research and medical practice for primary liver cancer.

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Keywords: Follow-up survey; Hepatocellular carcinoma; Intrahepatic cholangiocarcinoma; Combined hepatic carcinoma; Cumulative survival rate

1. Introduction

Since 1965, the Liver Cancer Study Group of Japan (LCSGJ) has conducted 15 nationwide follow-up surveys of primary liver cancer in patients in member hospitals and cooperative institutions in Japan, to promote research and medical practice in the treatment of liver cancer [1–9]. The 16th Nationwide Follow-up Survey of Primary Liver Cancer was conducted over a 2-year period (from January 1, 2000 to December 31, 2001), and 19,920 patients with primary liver cancer were newly registered from 795 institutions. Of these patients, 94.5% had hepatocellular carcinoma (HCC) and 3.6% had intrahepatic cholangiocarcinoma (ICC). In

addition, 21,268 follow-up patients were registered and a valid response rate of 75.6% was obtained in these follow-up patients. The newly registered patients were investigated using items related to epidemiological and clinicopathological factors, diagnosis and treatment. Furthermore, the cumulative survival rates of newly registered patients in the 11th to 16th follow-up surveys were calculated for histological type, background factors and treatment.

2. Materials and methods

2.1.1. Basic statistics

The subjects were 19,920 patients with primary liver cancer who underwent treatment or autopsy during a 2-year period (from January 1, 2000 to December 31, 2001) in 795 institutions in Japan. Doctors in the institutions completed a form developed by the Follow-up Survey Committee of

Abbreviations: HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; combined HCC and ICC, combined hepatocellular and cholangiocarcinoma; AFP, alpha-fetoprotein; PIVKA-II, protein induced by Vitamin K absence or antagonist-II

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Table 1
Classification of primary liver cancer

Diagnosis	Male (n = 14226)	Female (n = 5694)	Total (n = 19920)
HCC	13557	5270	18827 (94.51)
ICC	431	293	724 (3.63)
Combined	86	33	119 (0.60)
Cystadenocarcinoma	24	19	43 (0.22)
Hepatoblastoma	13	14	27 (0.14)
Sarcoma	6	5	11 (0.06)
Others	109	60	169 (0.85)

HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; combined: combined hepatocellular and cholangiocarcinoma. Values in parentheses are in percent.

the LCSGJ (Chairperson: Yoshio Yamaoka). Table 1 shows a breakdown of the cancer by histological type. When there was an inconsistency between the clinical, pathological and autopsy diagnoses, the autopsy diagnosis and the pathological diagnosis were given first and second priority, respectively. As far as possible, the data are shown as raw data prior to processing. The results in the tables are categorized into HCC, ICC and combined HCC and ICC, for which more than 100 new cases were registered in this follow-up survey. The abbreviations in the tables conform to the “The General Rules for the Clinical and Pathological Study of Primary Liver Cancer”, 2nd English ed. [10].

2.1.2. Additional statistics

The cumulative survival rates of newly registered patients in the 11th to 16th follow-up surveys whose final prognosis was determined to be survival or death (excluding patients with unknown outcomes) were calculated for each histological type (HCC, ICC and combined HCC and ICC) by background factors and treatment. Furthermore, the cumulative survival rates of patients with HCC were calculated for each treatment (hepatectomy, local ablation therapy and transcatheter arterial embolization).

3. Results

3.1.1. Causes of death during the study period

In patients with HCC, the death rate due to cancer was 57.2% and death rates due to hepatic failure, gastrointestinal bleeding and rupture of esophagogastric varices were 26.2, 2.7 and 4.9%, respectively. Of the patients who did not survive, 48 (1.6%) died within 30 days after surgery. These represented 0.9% of the 5374 patients who underwent surgery. In patients with ICC, the death rates due to cancer and hepatic failure were 84.7 and 11.3%, respectively. In patients with combined HCC and ICC, the death rate due to cancer was 75.0% (Table 2).

Table 2
Causes of death

	HCC	ICC	Combined
Alive	15256	422	69
Total deaths of between 2000 and 2001	3048	275	44
Cancer death	1744 (57.2)	233 (84.7)	33 (75.0)
Hepatic failure	798 (26.2)	31 (11.3)	9 (20.5)
Gastrointestinal bleeding	82 (2.7)	4 (1.5)	0 (0.0)
Rupture of esophageal varices	150 (4.9)	1 (0.4)	0 (0.0)
Rupture of tumor	226 (7.4)	2 (0.7)	2 (4.5)
Operative death	48 (1.6)	4 (1.5)	0 (0.0)
Other causes	311	17	3
Unknown	128	5	3

HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; combined: combined hepatocellular and cholangiocarcinoma. Values in parentheses are in percent.

3.1.2. Past history

Of the patients with HCC, 77.4 and 62.6% had a past history of chronic hepatitis and liver cirrhosis, respectively, while 19.0 and 9.9% of ICC patients and 58.3 and 29.9% of patients with combined HCC and ICC had this history, respectively. Of patients with HCC, 14.2% of patients with concomitant chronic hepatitis were treated with interferon therapy and 30.1 and 23.5% of the HCC patients had a past history of blood transfusion and habits of alcohol intake, respectively.

3.1.3. Clinical diagnosis

Clinical diagnosis of primary liver cancer in patients with HCC was made at an average age of 64.8 years in males and 68.5 years in females. For patients with ICC, the corresponding average ages were 65.2 years in males and 67.9 years in females. The average age has increased in every survey. The male to female ratios for the HCC and ICC patients were 2.84 and 1.50, respectively.

In patients with HCC, the level of liver injury at the time of diagnosis based on the liver damage classification of the LCSGJ was class A, B and C in 58.1, 32.9 and 9.0% of patients, respectively, whereas 69.3, 23.3 and 7.4% of HCC patients were in Child–Pugh Class A, B and C categories, respectively (Table 3). In this study, factors related to the criteria for LCSGJ liver damage classification and the Child–Pugh Score were included in the investigation items. The concordance rate for the LCSGJ liver damage classification reported from institutions and that estimated from the investigation items was 84.0% and the equivalent concordance rate for the Child–Pugh Class was 87.2%.

Of the HCC patients, 34.5, 36.7 and 28.8% had serum alpha-fetoprotein (AFP) levels of <15, 15–199 and 200 ng/mL or more, respectively, while 38.4, 14.1 and 47.5% of patients with HCC had a protein induced by Vitamin K absence or antagonist-II (PIVKA-II) level of <40, 40–99

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