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Special Report

Report of the 20th Nationwide follow-up survey of primary liver cancer in Japan

Masatoshi Kudo,[1,2] Namiki Izumi,[1,3] Shoji Kubo,[1,4] Norihiro Kokudo,[1,5] Michiie Sakamoto,[1,6] Shuichiro Shiina,[1,7] Ryosuke Tateishi,[1,8] Osamu Nakashima,[1,9] Takamichi Murakami,[1,10] Yutaka Matsuyama,[1,11] Arata Takahashi,[12,13] Hiroaki Miyata[12,13] and Tadatoshi Takayama[1,14]

[1]Follow-up Survey Committee, Liver Cancer Study Group of, [2]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka-Sayama, [3]Department of Gastroenterology, Musashino Red Cross Hospital, [5]National Center for Global Health and Medicine, [6]Department of Pathology, Keio University School of Medicine, [7]Department of Gastroenterology, Juntendo University School of Medicine, Departments of [8]Gastroenterology Graduate School of Medicine,, and [13]Healthcare Quality Assessment, Graduate School of Medicine, The University of Tokyo, [11]Department of Biostatistics, School of Public Health, University of Tokyo, [12]National Clinical Database, and [14]Department of Digestive Surgery, Nihon University School of Medicine, Tokyo, [4]Department of Hepato-Biliary-Pancreatic Surgery, Osaka City University Graduate School of Medicine, Osaka, [9]Department of Clinical Laboratory Medicine, Kurume University Hospital, Kurume, [10]Department of Diagnostic and Interventional Radiology, Kobe University Graduate School of Medicine, Kobe, Japan

In the 20th Nationwide Follow-up Survey of Primary Liver Cancer in Japan, data from 21 075 new patients and 40 769 previously followed patients were compiled from 544 institutions over a 2-year period from 1 January 2008 to 31 December 2009. Compared with the previous 19th survey, the population of patients with hepatocellular carcinoma (HCC) was older at the time of clinical diagnosis, included more female patients, included more patients with non-B non-C HCC, had smaller tumor diameters and more frequently received radiofrequency ablation as local ablation therapy. Cumulative survival rates were calculated for HCC, intrahepatic cholangiocarcinoma, and combined hepatocellular cholangiocarcinoma (combined HCC and intrahepatic cholangiocarcinoma) by treatment type and by background characteristics for patients newly registered between 1998 and 2009 whose final outcome was survival or death. Cumulative survival rates for HCC were calculated by dividing patients by combinations of background factors (number of tumors, tumor diameter, and Child–Pugh grade) and by treatment types (hepatectomy, local ablation therapy, and transcatheter arterial chemoembolization). Cumulative survival rates and median overall survival in patients treated by resection, transcatheter arterial chemoembolization, and local ablation therapy were calculated. The same values were also calculated by the registration date by dividing patients newly registered between 1978 and 2009 into four time period groups . The results of the analysis show that the prognosis of HCC is improving dramatically. It is expected that the data obtained from this nationwide follow-up survey will contribute to advancing clinical research, including the design of clinical trials, as well as the treatment strategy of primary liver cancer in the clinical practice setting.

Key words: combined hepatocellular cholangiocarcinoma, cumulative survival rate, hepatocellular carcinoma, intrahepatic cholangiocarcinoma, Liver Cancer Study Group of Japan, nationwide follow-up survey

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Correspondence: Professor Masatoshi Kudo, Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, 377-2 Ohno-Higashi, Osaka-Sayama, Osaka, Japan, *589-8511. Email:* m-kudo@med.kindai.ac.jp

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INTRODUCTION

THE LIVER CANCER Study Group of Japan has worked to advance the study and treatment of liver cancer since 1969, carrying out 19 national surveys on primary liver cancer with institutional members and collaborating institutions across Japan based on its General Rules for the Clinical and Pathological Study of Primary Liver Cancer,[1–11] and publishing the official results of those surveys[12–41] and original article using this database.[42–70] The group also reports on the Response Evaluation Criteria in Cancer of the Liver.[71–75]

This report presents the results of the 20th Nationwide Follow-up Survey of Primary Liver Cancer in Japan, with data obtained for 21 075 newly registered patients attending 544 institutions across Japan over the 2-year period from 1 January 2008 to 31 December 2009. The valid response rate for the 40 769 previously followed patients was 90.4%. Epidemiological, clinicopathological, diagnostic, and treatment-related data were compiled for newly registered patients. Cumulative survival rates by histological type, background characteristics, and treatments were also calculated for patients newly registered in the 15th to 20th surveys during 1978 to 2009. This special report is a concise version of the original full-version report published in Japanese.[41,76]

Table 1 Primary liver cancer diagnosed clinically or histopathologically

Histological type	Men $n = 14\,512$	Women $n = 6563$	Total n (%)
Hepatocellular carcinoma	13 626	6043	19 669 (93.33)
Intrahepatic cholangiocarcinoma	626	379	1005 (4.77)
Cholangiolocellular carcinoma	29	13	42 (0.20)
Biliary cystadenocarcinoma	14	12	26 (0.12)
Combined hepatocellular cholangiocarcinoma	113	42	155 (0.74)
Hepatoblastoma	6	6	12 (0.06)
Undifferentiated carcinoma	11	5	16 (0.08)
Other	87	63	150 (0.71)
Total			21 075

METHODS

Basic statistics

THE PARTICIPANTS OF this survey were patients who were hospitalized, underwent outpatient treatment, or underwent autopsy for primary liver cancer at each

Table 2 Prognosis

	Hepatocellular carcinoma n (%)	Intrahepatic cholangiocarcinoma n (%)	Combined hepatocellular cholangiocarcinoma n (%)
Surviving patients	14380	600	101
Deaths from all causes	3396	302	38
Cancer	2124 (62.5)	258 (85.4)	31(81.6)
Liver failure	544 (16.0)	13 (4.3)	4 (10.5)
Gastrointestinal hemorrhage	49 (1.4)	1 (0.3)	0 (0.0)
Rupture of esophageal/gastric varices	83 (2.4)	0 (0.0)	2 (5.3)
Intraperitoneal tumor rupture	89 (2.6)	0 (0.0)	0 (0.0)
Surgery	30 (0.9)	3 (1.0)	0 (0.0)
Other	477 (14.0)	27 (8.9)	1 (2.6)
Unknown	1893	103	16

Table 3 Past medical history

	Hepatocellular carcinoma n (%)	Intrahepatic cholangiocarcinoma n (%)	Combined hepatocellular cholangiocarcinoma n (%)
Chronic hepatitis	n=17945	n=899	n=133
No	2619 (14.6)	670 (74.5)	45 (33.8)
Suspected	947 (5.3)	28 (3.1)	7 (5.3)
Yes	14379 (80.1)	201 (22.4)	81 (60.9)
Liver biopsy findings (fibrosis)	n=2212	n=30	n=1
F0	115 (5.2)	5 (16.7)	0 (0.0)
F1	233 (10.5)	5 (16.7)	1 (10.0)
F2	411 (18.6)	5 (16.7)	1 (10.0)
F3	443 (20.0)	7 (23.3)	2 (20.0)
F4	1006 (45.5)	8 (26.7)	6 (60.0)
Other	4 (0.2)	0 (0.0)	0 (0.0)
Liver biopsy findings (activity)	n=1546	n=23	n=6
A0	108 (7.0)	3 (13.0)	0 (0.0)
A1	588 (38.0)	14 (60.9)	1 (16.7)
A2	763 (49.4)	6 (26.1)	4 (66.7)
A3	87 (5.6)	0 (0.0)	1 (16.7)
History of interferon therapy	n=11645	n=134	n=68
No	9072 (77.9)	111 (82.8)	55 (80.9)
Yes	2573 (22.1)	23 (17.2)	13 (19.1)
Response to interferon therapy	n=2056	n=20	n=10
No response	1152 (56.0)	7 (35.0)	3 (30.0)
Response (Biological Response)	197 (9.6]	4 k20.0)	3 (30.0)
Recurrence	233 (11.3)	2 (10.0)	1 (10.0)
Complete response (SVR)	474 (23.1)	7 (35.0)	3 (30.0)
Transfusion history	n=12404	n=663	n=92
No	9344 (75.3)	609 (91.9)	76 (82.6)
Yes	3060 (24.7)	54 (8.1)	16 (17.4)
Number of years unknown	934	19	6
0-9 years prior	171	7	5
10-19 years prior	102	3	0
20-29 years prior	248	5	1
30-39 years prior	420	6	2
40-49 years prior	706	8	2
≥ 50 years prior	479	6	0
Post-transfusion hepatitis	n=1344	n=29	n=8
No	718 (53.4)	21 (72.4)	6 (75.0)
Suspected	266 (19.8)	2 (6.9)	1 (12.5)
Yes	360 (26.8)	6 (20.7)	1 (12.5)
History of excessive alcohol use	n=15895	n=812	n=108
No	12143 (76.4)	688 (84.7)	75 (69.4)
Yes	3752 (23.6)	124 (15.3)	33 (30.6)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
F0, no fibrosis; F1, fibrous expansion of portal tract; F2, fibrous septa formation, usually incomplete; F3, bridging fibrous formation accompanying lobular distortion A0, no necroinflammatory reaction; A1, mild necroinflammatory reaction; A2, moderate necroinflammatory reaction; A3, severe necroinflammatory reaction; SVR; sustained viral response.

Table 4 Clinical diagnosis

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Evidence for diagnosis	*n* = 33 125	*n* = 1822	*n* = 255
CT	15 306	822	118
MRI	4666	324	38
Ultrasound	6889	342	46
Contrast ultrasound	822	23	4
Angiography	3984	90	25
Pathology	1213	165	22
Other	245	56	2
Percentages not calculated as multiple responses were allowed			
Performance status	*n* = 17 307	*n* = 887	*n* = 138
PS0	13 618 (78.7)	633 (71.4)	111 (80.4)
PS1	2685 (15.5)	185 (20.9)	16 (11.6)
PS2	616 (3.6)	42 (4.7)	9 (6.5)
PS3	274 (1.6)	19 (2.1)	2 (1.4)
PS4	114 (0.7)	8 (0.9)	0 (0.0)
Encephalopathy	*n* = 18 488	*n* = 913	*n* = 143
No	18 021 (97.5)	907 (99.3)	143 (100.0)
Mild	359 (1.9)	4 (0.4)	0 (0.0)
Moderate-to-severe	108 (0.6)	2 (0.2)	0 (0.0)
Ascites	*n* = 18 863	*n* = 947	*n* = 147
No	16 707 (88.6)	878 (92.7)	130 (88.4)
Responded to treatment	1434 (7.6)	31 (3.3)	8 (5.4)
Refractory to treatment	722 (3.8)	38 (4.0)	9 (6.1)
Serum bilirubin	*n* = 19 053	*n* = 949	*n* = 150
0.0–0.9	11 422 (59.9)	626 (66.0)	100 (66.7)
1.0–1.9	6097 (32.0)	214 (22.6)	42 (28.0)
2.0–3.0	983 (5.2)	26 (2.7)	3 (2.0)
≥3.1 mg/dL	551 (2.9)	83 (8.7)	5 (3.3)
Serum albumin	*n* = 18 997	*n* = 946	*n* = 148
<2.8	1438 (7.6)	52 (5.5)	4 (2.7)
2.8–2.9	878 (4.6)	27 (2.9)	5 (3.4)
3.0–3.5	5085 (26.8)	146 (15.4)	34 (23.0)
>3.5 g/dL	11 596 (61.0)	721 (76.2)	105 (70.9)
ICG R_{15}	*n* = 10 619	*n* = 622	*n* = 106
≤14	4508 (42.5)	466 (74.9)	65 (61.3)
15–24	3105 (29.2)	117 (18.8)	31 (29.2)
25–40	2021 (19.0)	35 (5.6)	7 (6.6)
>40%	985 (9.3)	4 (0.6)	3 (2.8)
Prothrombin activity	*n* = 18 174	*n* = 877	*n* = 148
< 40	287 (1.6)	25 (2.9)	2 (1.4)
40–49	296 (1.6)	14 (1.6)	2 (1.4)
50–70	3012 (16.6)	65 (7.4)	8 (5.4)
71–80	3641 (20.0)	108 (12.3)	28 (18.9)
> 80%	10 938 (60.2)	665 (75.8)	108 (73.0)
Prothrombin time (INR)	*n* = 9175	*n* = 436	*n* = 67
≤1.20	6840 (74.6)	363 (83.3)	59 (88.1)
1.21–1.30	1140 (12.4)	37 (8.5)	5 (7.5)

(*Continues*)

Table 4. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
1.31–1.50	826 (9.0)	19 (4.4)	2 (3.0)
1.51–1.80	253 (2.8)	11 (2.5)	1 (1.5)
≥1.81	116 (1.3)	6 (1.4)	0 (0.0)
Platelets	*n* = 18 875	*n* = 942	*n* = 150
<3.0	133 (0.7)	2 (0.2)	0 (0.0)
3.0–4.9	807 (4.3)	8 (0.8)	5 (3.3)
5.0–9.9	5541 (29.4)	54 (5.7)	20 (13.3)
10.0–14.9	5768 (30.6)	151 (16.0)	36 (24.0)
15.0–19.9	3513 (18.6)	236 (25.1)	42 (28.0)
20.0–99.9	2980 (15.8)	479 (50.8)	45 (30.0)
≥100 × 10^3/mm^3	133 (0.7)	12 (1.3)	2 (1.3)
Liver damage grade by LCSGJ	*n* = 15 137	*n* = 807	*n* = 128
A	10 388 (68.6)	700 (86.7)	96 (75.0)
B	4007 (26.5)	77 (9.5)	29 (22.7)
C	742 (4.9)	30 (3.7)	3 (2.3)
Child–Pugh grade	*n* = 18 314	*n* = 890	*n* = 145
A	14 068 (76.8)	775 (87.1)	122 (84.1)
B	3545 (19.4)	85 (9.6)	20 (13.8)
C	701 (3.8)	30 (3.4)	3 (2.1)
AFP	*n* = 18 438	*n* = 675	*n* = 143
<15	8551 (46.4)	571 (84.6)	57 (39.9)
≤199	5732 (31.1)	69 (10.2)	40 (28.0)
≤399	835 (4.5)	12 (1.8)	4 (2.8)
≤999	912 (4.9)	7 (1.0)	15 (10.5)
≤9999	1390 (7.5)	10 (1.5)	21 (14.7)
≤99 999	670 (3.6)	4 (0.6)	5 (3.5)
≥100 000 ng/mL	348 (1.9)	2 (0.3)	1 (0.7)
$AFPL_3$	*n* = 8619	*n* = 195	*n* = 81
Below detectable levels	3063 (35.5)	124 (63.6)	25 (30.9)
<5.0	2129 (24.7)	30 (15.4)	14 (17.3)
≤9.9	699 (8.1)	7 (3.6)	6 (7.4)
≤14.9	354 (4.1)	2 (1.0)	2 (2.5)
≤19.9	256 (3.0)	3 (1.5)	1 (1.2)
≥20.0%	2118 (24.6)	29 (14.9)	33 (40.7)
PIVKA-II	*n* = 17 540	*n* = 565	*n* = 137
<40	6927 (39.5)	449 (79.5)	61 (44.5)
≤99	2700 (15.4)	46 (8.1)	12 (8.8)
≤299	2303 (13.1)	26 (4.6)	17 (12.4)
≤499	823 (4.7)	4 (0.7)	5 (3.6)
≤999	919 (5.2)	4 (0.7)	6 (4.4)
≤2999	1237 (7.1)	14 (2.5)	16 (11.7)
≤9999	1036 (5.9)	7 (1.2)	8 (5.8)
≥10 000 mAU/mL	1595 (9.1)	15 (2.7)	12 (8.8)
CEA	*n* = 7294	*n* = 858	*n* = 117
<2.5	2803 (38.4)	295 (34.4)	53 (45.3)
≤4.9	2826 (38.7)	250 (29.1)	31 (26.5)
≤9.9	1351 (18.5)	127 (14.8)	17 (14.5)
≤19.9	215 (2.9)	60 (7.0)	5 (4.3)

(*Continues*)

Table 4. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
≤49.9	55 (0.8)	47 (5.5)	4 (3.4)
≤99.9	17 (0.2)	26 (3.0)	1 (0.9)
≥100 ng/mL	27 (0.4)	53 (6.2)	6 (5.1)
CA19–9	*n* = 6311	*n* = 837	*n* = 109
<37	4541 (72.0)	317 (37.9)	54 (49.5)
≤99	1303 (20.6)	111 (13.3)	24 (22.0)
≤299	338 (5.4)	110 (13.1)	11 (10.1)
≤999	78 (1.2)	80 (9.6)	7 (6.4)
≤2999	28 (0.4)	76 (9.1)	9 (8.3)
≤9999	8 (0.1)	59 (7.0)	2 (1.8)
≥10 000 U/mL	15 (0.2)	84 (10.0)	2 (1.8)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
AFP, α-fetoprotein; $AFPL_3$, lectin-reactive α-fetoprotein; CA 19–9, carbohydrate antigen 19–9; CEA, carcinoembryonic antigen; ICG R15, indocyanine green retention rate at 15 min; INR, international normalized ratio; LCSGJ, Liver Cancer Study Group of Japan; PIVKA-II, protein induced by vitamin K absence or antagonist-II.

of 544 collaborating institutions across Japan during the 2-year period from 1 January 2008 to 31 December 2009, and whose treating institutions had entered patient data for survey items created by the Follow-up Survey Committee of the Liver Cancer Study Group of Japan (Chair: Masatoshi Kudo) into the National Clinical Database. A total of 21 075 patients were newly registered during this period. When clinical diagnosis, histopathological diagnosis, and histopathological diagnosis determined by autopsy were not consistent, the autopsy result was given precedence when available, and the histopathological diagnosis otherwise. The histological type was hepatocellular carcinoma (HCC) in 94.3% of patients, intrahepatic cholangiocarcinoma (ICC) in 4.8%, and combined hepatocellular cholangiocarcinoma in 0.7% (Table 1). The results for patients newly registered in this survey were tabulated. Patients with unknown data for a given parameter were excluded from tabulation for that parameter. The abbreviations used in the table are based on the Fifth Revised Edition of the General Rules for the Clinical and Pathological Study of Primary Liver Cancer.[6]

Cumulative survival

Cumulative survival rates were calculated for HCC, ICC, and combined HCC and ICC by treatments and by background characteristics for patients newly registered between 1998 and 2009 whose final outcome was survival or death (excluding unknown). Cumulative survival rates for HCC were calculated by treatments (hepatectomy, local ablation therapy, and transcatheter arterial chemoembolization [TACE]). Cumulative survival rates were also calculated by the registration date by dividing patients newly registered between 1978 and 2009 into four time period groups. These cumulative survival rate calculations were made without censoring any deaths, including those in the "Other" category.

RESULTS

Basic statistics

Causes of death of newly enrolled patients during the survey period

The mortality rate during the survey period for newly enrolled patients with HCC was 17.2% (3396 patients). The cause of death was cancer for 62.5%, liver failure for 16.0%, gastrointestinal hemorrhage for 1.4%, and rupture of esophageal or gastric varices for 2.4%. The mortality rate from surgery among the patients who underwent surgery was 0.9% (30 patients). The mortality rate for newly enrolled patients with ICC was 30.0% (302 patients). The cause of death was cancer for 85.4% and liver failure for 4.3% (Table 2).

Table 5 Hepatitis B virus antigen/antibody and hepatitis C virus antibody

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
HBsAg	*n* = 18 219	*n* = 934	*n* = 147
Negative	15 449 (84.8)	857 (91.8)	123 (83.7)
Positive	2768 (15.2)	77 (8.2)	24 (16.3)
Equivocal	2 (0.0)	0 (0.0)	0 (0.0)
HBsAb	*n* = 5670	*n* = 251	*n* = 45
Negative	4362 (76.9)	190 (75.7)	34 (75.6)
Positive	1267 (22.3)	61 (24.3)	10 (22.2)
Equivocal	41 (0.7)	0 (0.0)	1 (2.2)
HBcAb	*n* = 6033	*n* = 229	*n* = 62
Negative	2850 (47.2)	129 (56.3)	33 (53.2)
Positive	3141 (52.1)	100 (43.7)	29 (46.8)
Equivocal	42 (0.7)	0 (0.0)	0 (0.0)
HBeAg	*n* = 4030	*n* = 152	*n* = 42
Negative	3456 (85.8)	141 (92.8)	39 (92.9)
Positive	569 (14.1)	11 (7.2)	3 (7.1)
Equivocal	5 (0.1)	0 (0.0)	0 (0.0)
HBeAb	*n* = 4006	*n* = 151	*n* = 46
Negative	2155 (53.8)	90 (59.6)	22 (47.8)
Positive	1837 (45.9)	61 (40.4)	24 (52.2)
Equivocal	14 (0.3)	0 (0.0)	0 (0.0)
HBV-DNA load	*n* = 1379	*n* = 20	*n* = 9
<3.7 LGE	65 (4.7)	0 (0.0)	0 (0.0)
3.7–3.9 LGE	24 (1.7)	0 (0.0)	0 (0.0
4.0–4.9 LGE	39 (2.8)	0 (0.0)	0 (0.0)
5.0–5.9 LGE	27 (2.0)	0 (0.0)	0 (0.0)
6.0–6.9 LGE	34 (2.5)	0 (0.0)	0 (0.0)
7.0–7.9 LGE	25 (1.8)	0 (0.0)	0 (0.0)
8.0–8.7 LGE	9 (0.7)	0 (0.0)	0 (0.0)
>8.7 LGE	2 (0.1)	0 (0.0)	0 (0.0)
<2.1 Logcopy	90 (6.5)	2 (10.0)	0 (0.0)
2.1–2.9 Logcopy	269 (19.5)	7 (35.0)	1 (11.1)
3.0–3.9 Logcopy	176 (12.8)	3 (15.0)	3 (33.3)
4.0–4.9 Logcopy	145 (10.5)	1 (5.0)	0 (0.0)
5.0–5.9 Logcopy	131 (9.5)	2 (10.0)	1 (11.1)
6.0–6.9 Logcopy	201 (14.6)	3 (15.0)	3 (33.3
7.0–7.9 Logcopy	114 (8.3)	2 (10.0)	1 (11.1)
8.0–8.8 Logcopy	26 (1.9)	0 (0.0)	0 (0.0)
>8.8 Logcopy	2 (0.1)	0 (0.0)	0 (0.0)
HCV-Ab	*n* = 18 097	*n* = 931	*n* = 13
Negative	7094 (39.2)	790 (84.9)	86 (64.7)
Positive	10 976 (60.7)	139 (14.9)	47 (35.3)
Equivocal	27 (0.1)	2 (0.2)	0 (0.0)
HCV-RNA	*n* = 3761	*n* = 69	*n* = 22
Negative	885 (23.5)	38 (55.1)	10 (45.5)

(*Continues*)

Table 5. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
<1.2	41 (1.1)	1 (1.4)	0 (0.0)
1.2–2.9	98 (2.6)	1 (1.4)	2 (9.1)
3.0–4.9	428 (11.4)	5 (7.2)	2 (9.1)
5.0–6.9	2006 (53.3)	18 (26.1)	6 (27.3)
7.0– logIU/mL	303 (8.1)	6 (8.7)	2 (9.1)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
HBcAb, antibody to hepatitis B core antigen; HBeAb, antibody to hepatitis B e antigen; HBeAg, hepatitis B e antigen; HBsAb, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

Past medical history

The proportion of patients with a history of chronic hepatitis and cirrhosis was 80.1% for HCC and 22.4% for ICC. The proportion for patients with HCC who had received interferon therapy for chronic hepatitis was 22.1%. For patients with a history of transfusion and excessive alcohol use, the figures were 24.7% and 23.6% for HCC, and 8.1% and 15.3% for ICC, respectively (Table 3).

Clinical diagnosis

Mean age of men and women at clinical diagnosis of primary liver cancer was 67.8 and 71.2 years for HCC, and 67.4 and 68.2 years for ICC, respectively. The ratio of male to female patients was 2.26:1 for HCC and 1.68:1 for ICC.

The Child–Pugh grade was A for 76.8%, B for 19.4%, and C for 3.8% of patients (Table 4). In HCC, serum α-fetoprotein was <15 ng/mL in 46.4%, 15–199 ng/mL in 31.1%, and≥200 ng/mL in 22.5% of patients. lectin-reactive α-fetoprotein was <10% in 68.3%, 10–14.9% in 4.1%, and≥15% in 27.6% of patients. Protein induced by vitamin K absence or antagonist-II was <40 mAU/mL in 39.5%, 40–99 mAU/mL in 15.4%, and ≥100 mAU/mL in 45.1% of patients. In ICC, CEA was <5.0 ng/mL in 63.5%, 5.0–9.9 ng/mL in 14.8%, and ≥10 ng/mL in 21.7% of patients. CA19–9 was <37 U/mL in 37.9%, 37–99 U/mL in 13.3%, and≥100 U/mL in 48.8% of patients (Table 4).

The hepatitis B surface antigen-positive rate was 15.2% for HCC, 8.2% for ICC, and 16.3% for combined HCC and ICC. The hepatitis C virus antibody-positive rate was 60.7% for HCC, 14.9% for ICC, and 35.3% for combined HCC and ICC (Table 5).

Tumor diameter on imaging at diagnosis was ≤2 cm in 34.4% and 2.1–5.0 cm in 43.7% of patients with HCC. For ICC, these figures were 13.7% and 47.2%. The proportion of patients with unifocal disease was 61.3% for HCC and 74.8% for ICC (Table 6). Tumor staining was observed in 93.1%, tumor rupture in 0.9%, and F2 or larger/red color sign (+) esophageal or gastric varices in 35.8% of patients.

Initial treatments

The initial treatment method for HCC was surgical intervention (resection or transplantation) in 37.7%, local ablation therapy in 28.4%, and TACE in 27.5% of patients. For ICC, these figures were 72.9% for surgery (resection only) and 16.6% for systemic chemotherapy, and for combined HCC and ICC, they were 71.8% for surgery (hepatectomy only) and 4.2% for systemic chemotherapy (Table 7). The distribution of Child–Pugh grades (A/B/C) was 78.4%/20.3%/1.3% for those who underwent surgery, 69.2%/27.4%/3.3% for those who underwent local ablation therapy, and 59.7%/35.8%/4.4% for those who underwent TACE.

Surgery

A total of 6940 patients with HCC underwent hepatectomy and 122 underwent liver transplantation. The most common macroscopic classification of resected specimens was simple nodular type for HCC at 59.9% and mass-forming type for ICC at 76.4% (Tables 8, 9).

Tumor diameter among patients who underwent hepatectomy for HCC was ≤2 cm in 20.0%, 2–5 cm in 52.0%, and 5–10 cm in 20.3%. The percentage with unifocal disease was 75.9%. Vascular invasion was observed in the portal vein in 16.1%, hepatic

Table 6 Imaging diagnosis

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Maximum diameter of primary tumor	*n* = 18 524	*n* = 901	*n* = 142
≤1 cm	995 (5.4)	22 (2.4)	1 (0.7)
>1 cm to ≤2 cm	5367 (29.0)	102 (11.3)	13 (9.2)
>2 cm to ≤3 cm	4354 (23.5)	179 (19.9)	27 (19.0)
>3 cm to ≤5 cm	3733 (20.2)	246 (27.3)	41 (28.9)
>5 cm to ≤10 cm	2841 (15.3)	279 (31.0)	42 (29.6)
>10 cm to ≤15 cm	898 (4.8)	60 (6.7)	14 (9.9)
>15 cm to ≤20 cm	232 (1.3)	12 (1.3)	4 (2.8)
>20 cm to ≤25 cm	73 (0.4)	1 (0.1)	0 (0.0)
>25 cm	31 (0.2)	0 (0.0)	0 (0.0)
No. tumors	*n* = 18 629	*n* = 923	*n* = 139
1	11 424 (61.3)	690 (74.8)	84 (60.4)
2	3150 (16.9)	69 (7.5)	20 (14.4)
3	1236 (6.6)	27 (2.9)	7 (5.0)
4	524 (2.8)	18 (2.0)	3 (2.2)
5	276 (1.5)	4 (0.4)	2 (1.4)
≥6	2019 (10.8)	115 (12.5)	23 (16.5)
Multifocal disease	*n* = 14 184	*n* = 669	*n* = 121
Single lobe	10 222 (72.1)	534 (79.8)	89 (73.6)
Both lobes	3962 (27.9)	135 (20.2)	32 (26.4)
Hepatocellular carcinoma	*n* = 17 276		
Morphological classification of primary tumor on imaging			
Nodular	15 307 (88.6)		
Massive	1308 (7.6)		
Diffuse	599 (3.5)		
Other	62 (0.4)		
Arterial phase enhancement	*n* = 17 642	*n* = 823	*n* = 135
No	1214 (6.9)	440 (53.5)	16 (11.9)
Yes	16 428 (93.1)	383 (46.5)	119 (88.1)
Venous phase washout	*n* = 16 180	*n* = 729	*n* = 113
No	1489 (9.2)	543 (74.5)	26 (23.0)
Yes	14 691 (90.8)	186 (25.5)	87 (77.0)
Internal component of tumor	*n* = 16 941	*n* = 761	*n* = 137
Solid	16 793 (99.1)	738 (97.0)	136 (99.3)
Cystic	148 (0.9)	23 (3.0)	1 (0.7)
Portal vein invasion by imaging	*n* = 17 855	*n* = 854	*n* = 137
Vp_0	15 669 (87.8)	580 (67.9)	97 (70.8)
Vp_1	579 (3.2)	61 (7.1)	10 (7.3)
Vp_2	463 (2.6)	78 (9.1)	9 (6.6)
Vp_3	616 (3.5)	102 (11.9)	15 (10.9)
Vp_4	528 (3.0)	33 (3.9)	6 (4.4)
Hepatic vein invasion by imaging	*n* = 17 263	*n* = 808	*n* = 133
Vv_0	16 401 (95.0)	683 (84.5)	119 (89.5)
Vv_1	305 (1.8)	45 (5.6)	6 (4.5)
Vv_2	295 (1.7)	60 (7.4)	4 (3.0)
Vv_3	262 (1.5)	20 (2.5)	4 (3.0)
Bile duct invasion by imaging	*n* = 17 039	*n* = 801	*n* = 133

(*Continues*)

Table 6. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
B_0	16 569 (97.2)	488 (60.9)	113 (85.0)
B_1	195 (1.1)	76 (9.5)	6 (4.5)
B_2	121 (0.7)	99 (12.4)	6 (4.5)
B_3	96 (0.6)	91 (11.4)	5 (3.8)
B_4	58 (0.3)	47 (5.9)	3 (2.3)
Tumor rupture	*n* = 18 337	*n* = 759	*n* = 144
No rupture	17 853 (97.4)	753 (99.2)	144 (100.0)
Suspected rupture	316 (1.7)	3 (0.4)	0 (0.0)
Rupture	168 (0.9)	3 (0.4)	0 (0.0)
Extrahepatic spread	*n* = 1091	*n* = 264	*n* = 41
Lung	319	48	6
Bone	204	22	2
Adrenal gland	67	6	2
Lymph node	410	148	27
Brain	11	1	0
Peritoneum	44	21	3
Other	36	18	1
Percentages not calculated as multiple sites were allowed			
Esophageal/gastric varices	*n* = 4195	*n* = 30	*n* = 15
≤F1, RC (−)	2428 (57.9)	21 (70.0)	9 (60.0)
≥F2, RC (+)	1503 (35.8)	8 (26.7)	5 (33.3)
Rupture	264 (6.3)	1 (3.3)	1 (6.7)
TNM Stage by LCSGJ	*n* = 18 207	*n* = 882	*n* = 138
Stage I	4583 (25.2)	78 (8.8)	24 (17.4)
Stage II	7280 (40.0)	268 (30.4)	36 (26.1)
Stage III	4162 (22.9)	206 (23.4)	32 (23.2)
Stage IVA	1504 (8.3)	118 (13.4)	21 (15.2)
Stage IVB	678 (3.7)	212 (24.0)	25 (18.1)

For all parameters, *n* is the total number of patients excluding those in the "unknown" category, and (%) is the percentage of *n*.
B_0, absence of invasion of the bile ducts; B_1, invasion of (or tumor thrombus in) the third order or more peripheral branches of the bile duct, but not of second order branches; B_2, invasion of (or tumor thrombus in) the second order branches of the bile duct; B_3, invasion of (or tumor thrombus in) the first order branches of the bile duct; B_4, invasion of (or tumor thrombus in) the common hepatic duct.; F1, small varices; F2, moderate varices; RC, red color sign; Vp0, absence of invasion of (or tumor thrombus in) the portal vein; Vp_1, invasion of (or tumor thrombus in) distal to the second order branches of the portal vein, but not of the second order branches; Vp_2, invasion of (or tumor thrombus in) second order branches of the portal vein; Vp_3, invasion of (or tumor thrombus in) first order branches of the portal vein; Vp_4, invasion of (or tumor thrombus in) the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe; Vv_0, absence of invasion of (or tumor thrombus in) the hepatic vein; Vv_1, invasion of (or tumor thrombus in) peripheral branches of the hepatic vein; Vv_2, invasion of (or tumor thrombus in) the right, middle, or left hepatic vein, the inferior right hepatic vein, or the short hepatic vein; Vv_3, invasion of (or tumor thrombus in) the inferior vena cava.

veins in 6.8%, and bile duct in 2.8% of patients. The non-cancerous part of the liver was normal in 10.6%, showed chronic hepatitis or fibrosis in 50.9%, and showed cirrhosis in 38.4% of patients. The type of surgery was Hr0 (limited resection) in 28.0%, HrS (1 subsegmentectomy) in 25.1%, Hr1 (1 segmentectomy) in 24.1%, Hr2 (2 segmentectomy) in 20.6%, and Hr3 (3 segmentectomy) in 2.2% of patients (Table 10).

Among patients with ICC, tumor diameter was ≤2 cm in 12.6%, 2–5 cm in 53.4%, and 5–10 cm in 28.1% of patients, and 84.9% had unifocal disease.

Table 7 Initial treatment

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
	n = 18 458	*n* = 872	*n* = 142
Surgery	6960 (37.7)	636 (72.9)	102 (71.8)
Local ablation therapy	5249 (28.4)	31 (3.6)	5 (3.5)
Transcatheter arterial chemoembolization	5083 (27.5)	15 (1.7)	16 (11.3)
Hepatic arterial infusion chemotherapy	829 (4.5)	25 (2.9)	11 (7.7)
Systemic chemotherapy	166 (0.9)	145 (16.6)	6 (4.2)
Other therapy	171 (0.9)	20 (2.3)	2 (1.4)
No therapy (BSC)	1099	118	11

BSC. best supportive care.

Table 8 Macroscopic classification of hepatocellular carcinoma

Macroscopic classification	Hepatocellular carcinoma				
	Hepatectomy		Liver transplantation		Total
	n = 4961		*n* = 71		5032
Small nodular type with indistinct margin	95	(1.9)	1	(1.4)	96
Simple nodular type	2970	(59.9)	55	(77.5)	3025
Simple nodular type with extranodular growth	1039	(20.9)	5	(7.0)	1044
Confluent multinodular type	793	(16.0)	10	(14.1)	803
Infiltrative type	64	(1.3)	0	(0.0)	64

Local ablation therapy

Local ablation therapy was performed in 6174 patients with HCC. Percutaneous ethanol injection therapy was performed in 7.4%, percutaneous microwave coagulation therapy in 3.2%, and radiofrequency ablation in 81.5% (Table 11). The treatment route was percutaneous for 88.8%. The percentage with unifocal disease was 89.2%. Tumor diameter was ≤2 cm in 64.6% and 2–3 cm in 26.2% of patients. The response assessed at

Table 9 Macroscopic classification of intrahepatic cholangiocarcinoma

Macroscopic classification	Intrahepatic cholangiocarcinoma	
	n = 521	
Mass-forming type	398	(76.4)
Periductal infiltrating type	23	(4.4)
Intraductal growth type	14	(2.7)
Mix of mass-forming type and periductal infiltrating type	71	(13.6)
Mix of periductal infiltrating type and intraductal growth type	6	(1.2)
Mix of mass-forming type and intraductal growth type	8	(1.5)
Other	1	(0.2)

Table 10 Macroscopic findings in resected specimen and surgery-related factors

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Maximum diameter of resected primary tumor	*n* = 6586	*n* = 597	*n* = 100
≤1 cm	169 (2.6)	6 (1.0)	1 (1.0)
>1 cm to ≤2 cm	1143 (17.4)	69 (11.6)	11 (11.0)
>2 cm to ≤3 cm	1619 (24.6)	125 (20.9)	25 (25.0)
>3 cm to ≤5 cm	1806 (27.4)	194 (32.5)	30 (30.0)
>5 cm to ≤10 cm	1339 (20.3)	168 (28.1)	27 (27.0)
>10 cm to ≤15 cm	380 (5.8)	30 (5.0)	5 (5.0)
>15 cm to ≤20 cm	98 (1.5)	5 (0.8)	1 (1.0)
>20 cm to ≤25 cm	24 (0.4)	0 (0.0)	0 (0.0)
>25 cm	8 (0.1)	0 (0.0)	0 (0.0)
No. tumors resected	*n* = 6616	*n* = 609	*n* = 98
1	5021 (75.9)	517 (84.9)	72 (73.5)
2	907 (13.7)	42 (6.9)	12 (12.2)
3	272 (4.1)	13 (2.1)	6 (6.1)
4	112 (1.7)	10 (1.6)	2 (2.0)
5	57 (0.9)	3 (0.5)	1 (1.0)
≥ 6	247 (3.7)	24 (3.9)	5 (5.1)
Tumor distribution[1]	*n* = 6456	*n* = 591	*n* = 97
H_S	2648 (41.0)	123 (20.8)	37 (38.1)
H_1	1877 (29.1)	182 (30.8)	23 (23.7)
H_2	1514 (23.5)	240 (40.6)	23 (23.7)
H_3	309 (4.8)	33 (5.6)	10 (10.3)
H_4	108 (1.7)	13 (2.2)	4 (4.1)
Tumor distribution[2]	*n* = 6383	*n* = 589	*n* = 96
Localized to one lobe	5582 (87.5)	517 (87.8)	78 (81.3)
Both lobes	801 (12.5)	72 (12.2)	18 (18.8)
Growth pattern	*n* = 6288	*n* = 536	*n* = 92
Eg	5843 (92.9)	267 (49.8)	67 (72.8)
Ig	445 (7.1)	269 (50.2)	25 (27.2)
Capsule formation	*n* = 6317	*n* = 540	*n* = 94
Fc (−)	1477 (23.4)	474 (87.8)	48 (51.1)
Fc (+)	4840 (76.6)	66 (12.2)	46 (48.9)
Capsule invasion	*n* = 4718	*n* = 66	*n* = 43
Fc-Inf (−)	2385 (50.6)	30 (45.5)	20 (46.5)
Fc-Inf (+)	2333 (49.4)	36 (54.5)	23 (53.5)
Septum formation	*n* = 6037	*n* = 530	*n* = 79
Sf (−)	2682 (44.4)	477 (90.0)	43 (54.4)
Sf (+)	3355 (55.6)	53 (10.0)	36 (45.6)
Serosal invasion	*n* = 6307	*n* = 552	*n* = 92
S_0 (no serosal invasion)	5398 (85.6)	363 (65.8)	68 (73.9)
S_1 (invasion +)	697 (11.1)	138 (25.0)	18 (19.6)
S_2 (invasion to adjacent organ)	110 (1.7)	47 (8.5)	4 (4.3)
S_3 (intraperitoneal rupture)	102 (1.6)	4 (0.7)	2 (2.2)
Lymph node metastasis	*n* = 6234	*n* = 581	*n* = 91
N_0	6172 (99.0)	434 (74.7)	81 (89.0)
N_1	62 (1.0)	147 (25.3)	10 (11.0)
Portal vein invasion	*n* = 6468	*n* = 586	*n* = 97

(*Continues*)

Table 10. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Vp_0	5429 (83.9)	378 (64.5)	68 (70.1)
Vp_1	618 (9.6)	90 (15.4)	16 (16.5)
Vp_2	188 (2.9)	58 (9.9)	8 (8.2)
Vp_3	158 (2.4)	51 (8.7)	5 (5.2)
Vp_4	75 (1.2)	9 (1.5)	0 (0.0)
Hepatic vein invasion	*n* = 6463	*n* = 580	*n* = 97
Vv_0	6022 (93.2)	457 (78.8)	88 (90.7)
Vv_1	289 (4.5)	72 (12.4)	7 (7.2)
Vv_2	96 (1.5)	42 (7.2)	2 (2.1)
Vv_3	56 (0.9)	9 (1.6)	0 (0.0)
Hepatic artery invasion	*n* = 6191	*n* = 543	n = 83
Va_0	6132 (99.0)	483 (89.0)	81 (97.6)
Va_1	46 (0.7)	28 (5.2)	2 (2.4)
Va_2	13 (0.2)	18 (3.3)	0 (0.0)
Va_3	0 (0.0)	14 (2.6)	0 (0.0)
Bile duct invasion	*n* = 6440	*n* = 567	*n* = 95
B_0	6258 (97.2)	296 (52.2)	87 (91.6)
B_1	89 (1.4)	83 (14.6)	5 (5.3)
B_2	40 (0.6)	78 (13.8)	1 (1.1)
B_3	38 (0.6)	74 (13.1)	1 (1.1)
B_4	15 (0.2)	36 (6.3)	1 (1.1)
Intrahepatic metastasis	*n* = 6228	*n* = 561	*n* = 93
IM_0 (no metastasis)	5375 (86.3)	483 (86.1)	76 (81.7)
IM_S (within subsegment)	167 (2.7)	14 (2.5)	3 (3.2)
IM_1 (within 1 segment)	314 (5.0)	31 (5.5)	7 (7.5)
IM_2 (within 2 segment)	249 (4.0)	23 (4.1)	2 (2.2)
IM_3 (within 3 segment)	123 (2.0)	10 (1.8)	5 (5.4)
Peritoneal metastasis	*n* = 6417	*n* = 597	*n* = 97
P_0 (no metastasis)	6382 (99.5)	584 (97.8)	97 (100.0)
P_1 (proximal peritoneum)	27 (0.4)	9 (1.5)	0 (0.0)
P_2 (distal peritoneum)	8 (0.1)	4 (0.7)	0 (0.0)
Invasion of surgical margin	*n* = 6298	*n* = 568	*n* = 93
SM (+) with exposure of cancer	298 (4.7)	51 (9.0)	9 (9.7)
SM (−) 0 mm	693 (11.0)	47 (8.3)	8 (8.6)
SM (−) ≤5 mm	1255 (19.9)	91 (16.0)	16 (17.2)
SM (−) ≤10 mm	676 (10.7)	53 (9.3)	9 (9.7)
SM (−) >10 mm	548 (8.7)	57 (10.0)	3 (3.2)
SM (−) distance unknown	2828 (44.9)	269 (47.4)	48 (51.6)
Findings in non-cancerous liver parenchyma	*n* = 6237	*n* = 549	*n* = 89
Normal liver	664 (10.6)	366 (66.7)	13 (14.6)
Chronic hepatitis, liver fibrosis	3177 (50.9)	132 (24.0)	48 (53.9)
Liver cirrhosis	2396 (38.4)	51 (9.3)	28 (31.5)
Hepatectomy	*n* = 6296	*n* = 594	*n* = 97
Hr0 (<subsegmentectomy)	1766 (28.0)	54 (9.1)	16 (16.5)
HrS (<1 segmentectomy)	1579 (25.1)	58 (9.8)	26 (26.8)
Hr1 (1segmentectomy)	1515 (24.1)	97 (16.3)	19 (19.6)

(*Continues*)

Table 10. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Hr2 (2 segmentectomy)	1297 (20.6)	338 (56.9)	28 (28.9)
Hr3 (3 segmentectomy)	138 (2.2)	46 (7.7)	8 (8.2)
Total hepatectomy	1 (0.0)	1 (0.2)	0 (0.0)
Lymph node dissection	*n* = 6116	*n* = 575	*n* = 89
D (−)	5983 (97.8)	285 (49.6)	76 (85.4)
D (+)	133 (2.2)	290 (50.4)	13 (14.6)
Residual cancer	*n* = 6277	*n* = 587	*n* = 93
No	6006 (95.7)	557 (94.9)	87 (93.5)
Yes	271 (4.3)	30 (5.1)	6 (6.5)
Extrahepatic metastasis	*n* = 6299	*n* = 605	*n* = 86
M_0	6227 (98.9)	583 (96.4)	84 (97.7)
M_1	72 (1.1)	22 (3.6)	2 (2.3)
TNM stage by LCSGJ	*n* = 6407	*n* = 590	*n* = 82
Stage I	945 (14.7)	33 (5.6)	8 (9.8)
Stage II	3294 (51.4)	197 (33.4)	30 (36.6)
Stage III	1534 (23.9)	171 (29.0)	30 (36.6)
Stage IVA	543 (8.5)	67 (11.4)	10 (12.2)
Stage IVB	91 (1.4)	122 (20.7)	4 (4.9)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
B_0, absence of invasion of the bile ducts; B_1, invasion of (or tumor thrombus in) the third order or more peripheral branches of the bile duct, but not of second order branches; B_2, invasion of (or tumor thrombus in) the second order branches of the bile duct; B_3, invasion of (or tumor thrombus in) the first order branches of the bile duct; B_4, invasion of (or tumor thrombus in) the common hepatic duct; Eg, expansive growth, well-demarcated border; Fc (−), absence of capsule formation; Fc (+), presence of capsule formation; Fc-Inf (−), absence of cancerous infiltration of the tumor capsule; Fc-Inf (+), presence of cancerous infiltration of the tumor capsule; H1, cancer limited to one segment; H2, cancer limited to two segments; H3, cancer limited to three segments; H4, cancer involving more than three segments; Hr0, resection of less than one subsegment (Couinaud's segment); HrS, resection of one subsegment (Couinaud's segment); Hr1, resection of one segment (anterior, posterior, medial, or left lateral segmentectomy); Hr2, resection of two segments (right or left bisegmentectomy or central bisegmentectomy); Hr3, resection of three segments (right or left trisegmentectomy); Hs, cancer limited to one subsegment, poorly demarcated border; Ig, infiltrative growth; IM_0, absence of intrahepatic metastasis; IM_1, intrahepatic metastasis within the subsegment in which the principal tumor is located; IM_2, intrahepatic metastasis in two segments; IM_3, intrahepatic metastasis to three or more segments; IM_s, intrahepatic metastasis within the subsegment in which the principal tumor is located; LCSGJ, Liver Cancer Study Group of Japan; S0, absence of invasion of the serosa; S1, tumor invasion of the serosa; S2, tumor invasion of adjacent organs; S3, tumor rupture with intraperitoneal bleeding; Sf (−), absence of formation of a fibrous septum within the tumor; Sf (+), presence of fibrous septum within the tumor; TNM, tumor–node–metastasis; Va_0, absence of invasion of the hepatic artery; Va_1, invasion distal to the second order branches of the hepatic artery, but not of the second order branches; Va_2, invasion to the second order branches of the hepatic artery; Va_3, invasion to the left or right hepatic artery, or the proper hepatic artery; Vp_0, absence of invasion of (or tumor thrombus in) the portal vein; Vp_1, invasion of (or tumor thrombus in) distal to the second order branches of the portal vein, but not of the second order branches; Vp_2, invasion of (or tumor thrombus in) second order branches of the portal vein; Vp_3, invasion of (or tumor thrombus in) first order branches of the portal vein; Vp_4, invasion of (or tumor thrombus in) the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe; Vv_0, absence of invasion of (or tumor thrombus in) the hepatic vein; Vv_1, invasion of (or tumor thrombus in) peripheral branches of the hepatic vein; Vv_2, invasion of (or tumor thrombus in) the right, middle, or left hepatic vein, the inferior right hepatic vein, or the short hepatic vein; Vv_3, invasion of (or tumor thrombus in) the inferior vena cava.

3 months after treatment initiation was complete response (CR) in 86.0%, partial response (PR) in 5.7%, stable disease (SD) in 3.6%, and progressive disease (PD) in 4.7% of patients. The corresponding response assessed at 6 months after treatment initiation was 83.0%, 5.0%, 2.7%, and 8.7%.

TACE

TACE was carried out in 8334 patients with HCC. Lipiodol alone was used in 16.0%, gelatin sponge alone in 2.2%, and lipiodol plus gelatin sponge particles in 78.7% of patients (Table 12). In addition, 93.6% of patients

Table 11 Local ablation therapy

	Hepatocellular carcinoma n (%)	Intrahepatic cholangiocarcinoma n (%)	Combined hepatocellular cholangiocarcinoma n (%)
Treatment	n=16970	n=773	n=130
Not performed	10796 (63.6)	725 (93.8)	123 (94.6)
Performed	6174 (36.4)	48 (6.2)	7 (5.4)
Percutaneous ethanol injection therapy	454 (7.4)	7 (14.6)	0 (0.0)
Percutaneous microwave coagulation therapy	198 (3.2)	1 (2.1)	0 (0.0)
Radiofrequency ablation	5505 (89.2)	39 (81.3)	7 (100.0)
Other	17 (0.3)	1 (2.1)	0 (0.0)
Purpose of treatment	n=5920	n=44	n=6
Curative	5593 (94.5)	39 (88.6)	6 (100.0)
Palliative	327 (5.5)	5 (11.4)	0 (0.0)
Treatment route	n=6061	n=43	n=7
Percutaneous	5478 (90.4)	34 (79.1)	6 (85.7)
Laparoscopic or thoracoscopic	179 (3.0)	2 (4.7)	0 (0.0)
Laparotomy or thoracotomy	383 (6.3)	6 (14.0)	1 (14.3)
Combination of percutaneous and laparotomy	18 (0.3)	0 (0.0)	0 (0.0)
Other	3 (0.0)	1 (2.3)	0 (0.0)
Number of tumors treated	n=5993	n=43	n=7
1	4533 (75.6)	34 (79.1)	6 (85.7)
2	1021 (17.0)	4 (9.3)	1 (14.3)
3	306 (5.1)	2 (4.7)	0 (0.0)
4	72 (1.2)	1 (2.3)	0 (0.0)
5	20 (0.3)	1 (2.3)	0 (0.0)
≥ 6	41 (0.7)	1 (2.3)	0 (0.0)
Maximum diameter of treated tumors	n=5842	n=40	n=7
≤ 1 cm	638 (10.9)	4 (10.0)	1 (14.3)
> 1 cm to ≤ 2 cm	3136 (53.7)	16 (40.0)	3 (42.9)
> 2 cm to ≤ 3 cm	1531 (26.2)	15 (37.5)	3 (42.9)
> 3 cm to ≤ 5 cm	464 (7.9)	5 (12.5)	0 (0.0)
> 5 cm to ≤ 10 cm	71 (1.2)	0 (0.0)	0 (0.0)
> 10 cm to ≤ 15 cm	1 (0.0)	0 (0.0)	0 (0.0)
> 15 cm to ≤ 20 cm	1 (0.0)	0 (0.0)	0 (0.0)
> 20 cm to ≤ 25 cm	0 (0.0)	0 (0.0)	0 (0.0)
> 25 cm	0 (0.0)	0 (0.0)	0 (0.0)
Combination with other treatment	n=5956	n=42	n=6
No	3725 (62.5)	30 (71.4)	3 (50.0)
Transcatheter arterial chemoembolization	2015 (33.8)	9 (21.4)	3 (50.0)
Other	216 (3.6)	3 (7.1)	0 (0.0)
Complications	n=185	n=1	n=0
Hemorrhage	33	0	0
Gastrointestinal perforation or penetration	2	0	0
Bile duct injury	12	0	0
Abscess	20	0	0
Extrahepatic dissemination	2	0	0
Hepatic infarction	14	0	0
Liver failure	16	0	0
Other	86	1	0
Percentages not calculated as multiple choices were allowed			
Direct response assessment	n=5138	n=33	n=6
TE4a	3915 (76.2)	22 (66.7)	6 (100.0)
TE4b	840 (16.3)	8 (24.2)	0 (0.0)
TE3	237 (4.6)	1 (3.0)	0 (0.0)
TE2	97 (1.9)	1 (3.0)	0 (0.0)
TE1	40 (0.8)	0 (0.0)	0 (0.0)
Overall response at 3 months	n=5067	n=35	n=6
CR	4360 (86.0)	27 (77.1)	5 (83.3)
PR	289 (5.7)	4 (11.4)	0 (0.0)
SD	181 (3.6)	0 (0.0)	1 (16.7)
PD	237 (4.7)	4 (11.4)	0 (0.0)
Overall response at 6 months	n=4845	n=34	n=6
CR	4021 (83.0)	21 (61.8)	4 (66.7)
PR	272 (5.6)	3 (8.8)	1 (16.7)
SD	129 (2.7)	1 (2.9)	0 (0.0)
PD	423 (8.7)	9 (26.5)	1 (16.7)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; TE2, treatment effect in target lesion (partial response); TE1, treatment effect in target lesion (progressive disease)TE3, treatment effect in target lesion (partial response); TE4a; treatment effect in target lesion (complete response with ablative margin); TE4b, treatment effect in target lesion (complete response without ablative margin).

Table 12 Transcatheter arterial chemoembolization

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Transarterial therapy	*n* = 16 920	*n* = 76	*n* = 115
Not performed	8586 (50.7)	697 (91.6)	74 (64.3)
Performed	8334 (49.3)	64 (8.4)	41 (35.7)
Transcatheter arterial chemoembolization	*n* = 8283	*n* = 63	*n* = 41
Not performed	729 (8.8)	24 (38.1)	11 (26.8)
Performed	7554 (91.2)	39 (61.9)	30 (73.2)
Therapy through implanted catheter system	*n* = 7102	*n* = 56	*n* = 41
Not performed	6488 (91.4)	42 (75.0)	32 (78.0)
Performed	614 (8.6)	14 (25.0)	9 (22.0)
Embolic agent	*n* = 7012	*n* = 33	*n* = 30
Lipiodol alone	1125 (16.0)	8 (24.2)	10 (33.3)
Gelatin sponge alone	157 (2.2)	1 (3.0)	2 (6.7)
Lipiodol + gelatin sponge	5518 (78.7)	22 (66.7)	17 (56.7)
Other	212 (3.0)	2 (6.1)	1 (3.3)
Lipiodol dose	*n* = 5250	*n* = 18	*n* = 20
Not used	2 (0.0)	0 (0.0)	0 (0.0)
0.1–1.0	440 (8.4)	0 (0.0)	1 (5.0)
1.1–3.0	2002 (38.1)	5 (27.8)	4 (20.0)
3.1–5.0	1439 (27.4)	7 (38.9)	10 (50.0)
5.1–7.0	559 (10.6)	3 (16.7)	2 (10.0)
7.1–10.0	662 (12.6)	3 (16.7)	3 (15.0)
>10	146 (2.8)	0 (0.0)	0 (0.0)
Combination with chemotherapy agents	*n* = 7804	*n* = 38	*n* = 30
Doxorubicin	399	2	0
Epirubicin	4281	16	19
Mitomycin	1008	4	3
Cisplatin	1416	10	6
SMANCS	203	3	1
Miriplatin	131	0	0
5FU	97	1	1
Interferon	17	1	0
Other	252	1	0
Percentages not calculated as multiple choices were allowed			
Area of embolization	*n* = 6385	*n* = 33	*n* = 24
<1 segment	2339 (36.6)	10 (30.3)	3 (12.5)
≥1 segment to <1 lobe	2574 (40.3)	12 (36.4)	10 (41.7)
≥1 lobe to < entire liver	1058 (16.6)	9 (27.3)	8 (33.3)
Entire liver	414 (6.5)	2 (6.1)	3 (12.5)
Complications	*n* = 241	*n* = 2	*n* = 0
Acute cholecystitis	26	1	0
Biloma	10	0	0
Hepatic abscess	27	0	0
Hepatic infarction	11	0	0
Liver failure	48	0	0
Tumor rupture	9	0	0
Gastrointestinal hemorrhage	10	0	0
Pulmonary infarction	0	0	0

(*Continues*)

Table 12. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Spinal cord injury	0	0	0
Other	100	1	0
Percentages not calculated as multiple choices were allowed			
Direct response assessment	*n* = 5602	*n* = 28	*n* = 22
TE4a	1134 (20.2)	5 (17.9)	1 (4.5)
TE4b	1494 (26.7)	3 (10.7)	4 (18.2)
TE3	1459 (26.0)	9 (32.1)	6 (27.3)
TE2	1053 (18.8)	6 (21.4	7 (31.8)
TE1	325 (5.8)	3 (10.7)	2 (9.1)
Overall response at 3 months	*n* = 5128	*n* = 23	*n* = 19
CR	2100 (41.0)	7 (30.4)	3 (15.8)
PR	1118 (21.8)	5 (21.7)	4 (21.1)
SD	803 (15.7)	5 (21.7)	6 (31.6)
PD	1107 (21.6)	6 (26.1)	6 (31.6)
Overall response at 6 months	*n* = 4505	*n* = 21	*n* = 16
CR	1806 (40.1)	5 (23.8)	2 (12.5)
PR	781 (17.3)	5 (23.8)	3 (18.8)
SD	545 (12.1)	2 (9.5)	3 (18.8)
PD	1373 (30.5)	9 (42.9)	8 (50.0)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
5FU, fluorouracil; CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SMANCS, styrene maleic acid neocarzinostatin; TE1, treatment effect in target lesion (progressive disease); TE2, treatment effect in target lesion (partial response); TE3, treatment effect in target lesion (partial response); TE4a; treatment effect in target lesion (complete response with ablative margin); TE4b, treatment effect in target lesion (complete response without ablative margin).

were also being treated together with anticancer cytotoxic agents. The scope of embolization was less than one segment for 36.6%, at least one segment but less than one lobe for 40.3%, one lobe or more for 16.6%, and the entire liver for 6.5%. The response assessed at 3 months after treatment initiation was CR in 41.0%, PR in 21.8%, SD in 15.7%, and PD in 21.6% of patients. The corresponding response assessed at 6 months after treatment initiation was 40.1%, 17.3%, 12.1%, and 30.5%.

Systemic chemotherapy

Systemic chemotherapy was carried out in 372 patients with HCC. The response assessed at 3 months after treatment initiation was CR in 3.3%, PR in 13.5%, SD in 21.4%, and PD in 61.9%. Systemic chemotherapy was carried out for 196 patients with ICC. The route of administration was intravenous for 80.6% and oral for 17.9%. The response assessed at 3 months after treatment initiation was CR in 4.2%, PR in 15.0%, SD in 30.8%, and PD in 50.0% of patients (Table 13).

Pathology

A pathological diagnosis was obtained for 44.7% of patients with HCC. Of these, 17.6% were made from a biopsy alone, 79.6% from a resected specimen alone, and 2.8% from a biopsy and resected specimen. In addition, 55.3% of patients had no pathological diagnosis, and the rate of diagnosis by biopsy had decreased since previous surveys, and the number of patients without a pathological diagnosis had increased. The histological grade of HCC was well differentiated in 24.9%, moderately differentiated in 62.8%, and poorly differentiated in 11.7% of patients (Table 14). ICC was well differentiated in 18.5%, moderately differentiated in 58.0%, and poorly differentiated in 20.3% of patients (Table 15). Table 16 shows

Table 13 Systemic chemotherapy

	Hepatocellular carcinoma n (%)	Intrahepatic cholangiocarcinoma n (%)	Combined hepatocellular cholangiocarcinoma n (%)
Route of administration	n=16543	n=779	n=130
Not performed	16171 (97.8)	583 (74.8)	118 (90.8)
Performed	372 (2.2)	196 (25.2)	12 (9.2)
Intravenous	92 (24.7)	158 (80.6)	4 (33.3)
Oral	262 (70.4)	35 (17.9)	8 (66.7)
Other	18 (4.8)	3 (1.5)	0 (0.0)
Type of chemotherapy agent	n=428	n=210	n=15
Doxorubicin	3	0	0
Epirubicin	8	0	0
Mitomycin	3	1	0
Cisplatin	47	18	3
5FU	98	17	4
Interferon	15	0	0
Sorafenib	124	4	0
Other	130	170	8
Percentages not calculated as multiple choices were allowed			
Direct response assessment	n=182	n=90	n=5
TE4a	6 (3.3)	3 (3.3)	0 (0.0)
TE4b	5 (2.7)	1 (1.1)	1 (20.0)
TE3	11 (6.0)	8 (8.9)	0 (0.0)
TE2	57 (31.3)	32 (35.6)	4 (80.0)
TE1	87 (47.8)	41 (45.6)	0 (0.0)
Overall response at 3 months	n=215	n=120	n=6
CR	7 (3.3)	5 (4.2)	1 (16.7)
PR	29 (13.5)	18 (15.0)	0 (0.0)
SD	46 (21.4)	37 (30.8)	4 (66.7)
PD	133 (61.9)	60 (50.0)	1 (16.7)
Overall response at 6 months	n=165	n=100	n=4
CR	5 (3.0)	6 (6.0)	1 (25.0)
PR	21 (12.7)	11 (11.0)	0 (0.0)
SD	29 (17.6)	24 (24.0)	3 (75.0)
PD	110 (66.7)	59 (59.0)	0 (0.0)

5FU, fluorouracil; CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SMANCS, styrene maleic acid neocarzinostatin; TE1, treatment effect in target lesion (progressive disease); TE2, treatment effect in target lesion (partial response); TE3, treatment effect in target lesion (partial response); TE4a; treatment effect in target lesion (complete response with ablative margin); TE4b, treatment effect in target lesion (complete response without ablative margin).

Table 14 Histological grade of hepatocellular carcinoma

	Well differentiated *n* (%)	Moderately differentiated *n* (%)	Poorly differentiated *n* (%)	Undifferentiated *n* (%)	Fibrolamellar carcinoma *n* (%)	Sarcomatous *n* (%)
n = 7620	1900 (24.9)	4787 (62.8)	890 (11.7)	34 (0.4)	3 (0.0)	6 (0.1)

Table 15 Histological grade of intrahepatic cholangiocarcinoma

	Well differentiated adenocarcinoma *n* (%)	Moderately differentiated adenocarcinoma *n* (%)	Poorly differentiated adenocarcinoma *n* (%)	Special type *n* (%)
n = 612	113 (18.5)	355 (58.0)	124 (20.3)	20 (3.3)

Table 16 Pathological findings from resected specimen or biopsy specimen

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Capsule formation	*n* = 6398	*n* = 553	*n* = 93
fc (−)	1640 (25.6)	512 (92.6)	54 (58.1)
fc (+)	4758 (74.4)	41 (7.4)	39 (41.9)
Capsule invasion	*n* = 4641	*n* = 40	*n* = 35
fc-inf (−)	1323 (28.5)	15 (37.5)	8 (22.9)
fc-inf (+)	3318 (71.5)	25 (62.5)	27 (77.1)
Septum formation	*n* = 6177	*n* = 525	*n* = 80
sf (−)	2174 (35.2)	463 (88.2)	29 (36.3)
sf (+)	4003 (64.8)	62 (11.8)	51 (63.8)
Serosal invasion	*n* = 6279	*n* = 554	*n* = 79
s_0	5509 (87.7)	373 (67.3)	63 (79.7)
s_1	605 (9.6)	133 (24.0)	13 (16.5)
s_2	84 (1.3)	44 (7.9)	2 (2.5)
s_3 (rupture)	81 (1.3)	4 (0.7)	1 (1.3)
Lymph node metastasis	*n* = 5441	*n* = 546	*n* = 84
n_0	5384 (99.0)	384 (70.3)	73 (86.9)
n_1	57 (1.0)	162 (29.7)	11 (13.1)
Portal vein invasion	*n* = 6560	*n* = 578	*n* = 95
vp_0	4795 (73.1)	307 (53.1)	54 (56.8)
vp_1	1341 (20.4)	169 (29.2)	28 (29.5)
vp_2	190 (2.9)	41 (7.1)	8 (8.4)
vp_3	168 (2.6)	50 (8.7)	5 (5.3)
vp_4	66 (1.0)	11 (1.9)	0 (0.0)
Hepatic vein invasion	*n* = 6560	*n* = 573	*n* = 94
vv_0	5812 (88.6)	406 (70.9)	76 (80.9)
vv_1	607 (9.3)	134 (23.4)	14 (14.9)
vv_2	88 (1.3)	25 (4.4)	4 (4.3)
vv_3	53 (0.8)	8 (1.4)	0 (0.0)
Hepatic artery invasion	*n* = 6474	*n* = 549	*n* = 81
va_0	6413 (99.1)	505 (92.0)	81 (100.0)
va_1	54 (0.8)	27 (4.9)	0 (0.0)
va_2	4 (0.1)	6 (1.1)	0 (0.0)

(*Continues*)

va_3	3 (0.0)		11 (2.0)		0 (0.0)			
Bile duct invasion	*n* = 6507		*n* = 550		*n* = 93			
b_0	6284 (96.6)		272 (49.5)		80 (86.0)			
b_1	137 (2.1)		107 (19.5)		8 (8.6)			
b_2	39 (0.6)		64 (11.6)		2 (2.2)			
b_3	33 (0.5)		76 (13.8)		2 (2.2)			
b_4	14 (0.2)		31 (5.6)		1 (1.1)			
Intrahepatic metastasis	*n* = 6265		*n* = 555		*n* = 88			
im_0 (no metastasis)	5394 (86.1)		465 (83.8)		69 (78.4)			
im_s (within subsegment)	170 (2.7)		14 (2.5)		3 (3.4)			
im_1 (within 1 segment)	394 (6.3)		41 (7.4)		8 (9.1)			
im_2 (within 2 segment)	205 (3.3)		23 (4.1)		5 (5.7)			
im_3 (within 3 segment)	102 (1.6)		12 (2.2)		3 3.4)			
Invasion of surgical margins	*n* = 6334						*n* = 570	*n* = 91
sm (+) with tumor exposure	467 (7.4)	93 (16.3)						14 (15.4)
sm (−) 0 mm	566 (8.9)	38 (6.7)						5 (5.5)
sm (−) ≤5 mm	1340 (21.2)	89 (15.6)						17 (18.7)
sm (−) ≤10 mm	565 (8.9)	44 (7.7)						5 (5.5)
sm (−) >10 mm	485 (7.7)	44 (7.7)						4 (4.4)
sm (−) distance unknown	2911 (46.0)	262 (46.0)						46 (50.5)
Findings in non-cancerous liver parenchyma	*n* = 6283						*n* = 531	*n* = 92
Normal	521 (8.3)	315 (59.3)						13 (14.1)
Chronic hepatitis, liver fibrosis	3106 (49.4)	167 (31.5)						49 (53.3)
Liver cirrhosis	2656 (42.3)	49 (9.2)						30 (32.6)
Fibrosis (new Inuyama classification)	*n* = 5020						*n* = 329	*n* = 70
F_0 (normal)	411 (8.2)	176 (53.5)						8 (11.4)
F_1	763 (15.2)	68 (20.7)						11 (15.7)
F_2	939 (18.7)	32 (9.7)						13 (18.6)
F_3	852 (17.0)	19 (5.8)						15 (21.4)
F_4 (liver cirrhosis)	2055 (40.9)	34 (10.3)						23 (32.9)
Activity (new Inuyama classification)	*n* = 3300						*n* = 231	*n* = 46
A_0	482 (14.6)	130 (56.3)						11 (23.9)
A_1	1585 (48.0)	74 (32.0)						20 (43.5)
A_2	1097 (33.2)	24 (10.4)						14 (30.4)
A_3	136 (4.1)	3 (1.3)						1 (2.2)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
A_0, no necroinflammatory reaction; A_1, mild necroinflammatory reaction; A_2, moderate necroinflammatory reaction; A_3, severe necroinflammatory reaction; proper hepatic artery; b_0, no invasion of bile duct, b1, branches of the bile duct, but not of second order branches; b_2, invasion of (or tumor thrombus in) the second order branches of the bile duct; b_3, invasion of (or tumor thrombus in) the first order branches of the bile duct; b_4, invasion of (or tumor thrombus in) the common hepatic duct; F_1, fibrous expansion of portal tract; F_2, fibrous septa formation, usually incomplete; F_3, bridging fibrous formation accompanying lobular distortion; fc (−), absence of capsule formation; fc (+), presence of capsule formation; b0, absence of invasion of the bile ducts; b1, invasion of (or tumor thrombus in) the third order or more peripheral; fc-inf (−), absence of cancerous infiltration of the tumor capsule; fc-inf (+), presence of cancerous infiltration of the tumor capsule; im_1, intrahepatic metastasis within the subsegment in which the principal tumor is located; im_2, intrahepatic metastasis in two segments; im_3, intrahepatic metastasis to three or more segments; im_s, intrahepatic metastasis within the subsegment in which the principal tumor is located; sf (−), absence of formation of a fibrous septum within the tumor; sf (+), presence of fibrous septum within the tumor; s_0, absence of invasion of the serosa; s_1, tumor invasion of the serosa; s_2, tumor invasion of adjacent organs; s_3, tumor rupture with intraperitoneal bleeding; va_0, absence of invasion of the hepatic artery; va_1, invasion distal to the second order branches of the hepatic artery, but not of the second order branches; va_2, invasion to the second order branches of the hepatic artery; va_3, invasion to the left or right hepatic artery, or the im_0, absence of intrahepatic metastasis; vp_0, absence of invasion of (or tumor thrombus in) the portal vein; vp_1, invasion of (or tumor thrombus in) distal to the second order branches of the portal vein, but not of the second order branches; vp_2, invasion of (or tumor thrombus in) second order branches of the portal vein; vp_3, invasion of (or tumor thrombus in) first order branches of the portal vein; vp_4, invasion of (or tumor thrombus in) the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe; vv_0, absence of invasion of (or tumor thrombus in) the hepatic vein; vv_1, invasion of (or tumor thrombus in) peripheral branches of the hepatic vein; vv_2, invasion of (or tumor thrombus in) the right, middle, or left hepatic vein, the inferior right hepatic vein, or the short hepatic vein; vv_3, invasion of (or tumor thrombus in) the inferior vena cava.

Table 17 Pathological findings on autopsy

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Autopsy	*n* = 2855	*n* = 248	*n* = 35
No	2770 (97.0)	242 (97.6)	35 (100.0)
Yes	85 (3.0)	6 (2.4)	0 (0.0)
Liver weight	*n* = 56	*n* = 5	*n* = 0
Not measured	7 (12.5)	2 (40.0)	0 (0.0)
400–499	0 (0.0)	0 (0.0)	0 (0.0)
≤599	1 (1.8)	0 (0.0)	0 (0.0)
≤699	2 (3.6)	1 (20.0)	0 (0.0)
≤799	4 (7.1)	0 (0.0)	0 (0.0)
≤899	5 (8.9)	0 (0.0)	0 (0.0)
≤999	6 (10.7)	0 (0.0)	0 (0.0)
≤1099	2 (3.6)	0 (0.0)	0 (0.0)
≤1199	1 (1.8)	0 (0.0)	0 (0.0)
≤1299	1 (1.8)	0 (0.0)	0 (0.0)
≤1399	7 (12.5)	0 (0.0)	0 (0.0)
≤1499	1 (1.8)	0 (0.0)	0 (0.0)
≤1599	4 (7.1)	0 (0.0)	0 (0.0)
≤1699	2 (3.6)	0 (0.0)	0 (0.0)
≤1799	1 (1.8)	0 (0.0)	0 (0.0)
≤1899	2 (3.6)	0 (0.0)	0 (0.0)
≤1999	3 (5.4)	0 (0.0)	0 (0.0)
≥2000	7 (12.5)	2 (40)	0 (0.0)
Maximum tumor diameter	n = 54	n = 3	n = 0
≤1 cm	2 (3.7)	0 (0.0)	0 (0.0)
≤2 cm	5 (9.3)	0 (0.0)	0 (0.0)
≤3 cm	5 (9.3)	0 (0.0)	0 (0.0)
≤5 cm	12 (22.2)	0 (0.0)	0 (0.0)
≤10 cm	18 (33.3)	1 (33.3)	0 (0.0)
≤15 cm	6 (11.1)	2 (66.7)	0 (0.0)
≤20 cm	5 (9.3)	0 (0.0)	0 (0.0)
≤25 cm	1 (1.9)	0 (0.0)	0 (0.0)
>25 cm	0 (0.0)	0 (0.0)	0 (0.0)
Capsule formation	*n* = 34	*n* = 2	*n* = 0
fc (−)	11 (32.4)	2 (100.0)	0 (0.0)
fc (+)	23 (67.6)	0 (0.0)	0 (0.0)
Portal vein invasion	*n* = 5	*n* = 3	*n* = 0
vp_0	25 (45.5)	3 (100.0)	0 (0.0)
vp_1	9 (16.4)	0 (0.0)	0 (0.0)
vp_2	4 (7.3)	0 (0.0)	0 (0.0)
vp_3	6 (10.9)	0 (0.0)	0 (0.0)
vp_4	11 (20.0)	0 (0.0)	0 (0.0)
Hepatic vein invasion	*n* = 52	*n* = 3	*n* = 0
vv_0	31 (59.6)	3 (100.0)	0 (0.0)
vv_1	6 (11.5)	0 (0.0)	0 (0.0)
vv_2	5 (9.6)	0 (0.0)	0 (0.0)
vv_3	10 (19.2)	0 (0.0)	0 (0.0)
Hepatic artery invasion	*n* = 42	*n* = 3	*n* = 0
va_0	38 (90.5)	3 (100.0)	0 (0.0)

(*Continues*)

Table 17. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
va_1	3 (7.1)	0 (0.0)	0 (0.0)
va_2	1 (2.4)	0 (0.0)	0 (0.0)
va_3	0 (0.0)	0 (0.0)	0 (0.0)
Bile duct invasion	*n* = 48	*n* = 3	*n* = 0
b_0	39 (81.3)	3 (100.0)	0 (0.0)
b_1	1 (2.1)	0 (0.0)	0 (0.0)
b_2	3 (6.3)	0 (0.0)	0 (0.0)
b_3	4 (8.3)	0 (0.0)	0 (0.0)
b_4	1 (2.1)	0 (0.0)	0 (0.0)
Intrahepatic metastasis	*n* = 54	*n* = 3	*n* = 0
im_0	22 (40.7)	1 (33.3)	0 (0.0)
im_s	0 (0.0)	0 (0.0)	0 (0.0)
im_1	5 (9.3)	1 (33.3)	0 (0.0)
im_2	8 (14.8)	0 (0.0)	0 (0.0)
im_3	19 (35.2)	1 (33.3)	0 (0.0)
Serosal invasion	*n* = 47	*n* = 3	*n* = 0
s_0	31 (66.0)	3 (100.0)	0 (0.0)
s_1	6 (12.8)	0 (0.0)	0 (0.0)
s_2	4 (8.5)	0 (0.0)	0 (0.0)
s_3 (rupture)	6 (12.8)	0 (0.0)	0 (0.0)
Peritoneal dissemination	*n* = 61	*n* = 4	*n* = 0
No	51 (83.6)	2 (50.0)	0 (0.0)
Yes	10 (16.4)	2 (50.0)	0 (0.0)
Ascites	*n* = 72	*n* = 4	*n* = 0
No	13 (18.1)	1 (25.0)	0 (0.0)
Yes	59 (81.9)	3 (75.0)	0 (0.0)
Findings in non-cancerous liver parenchyma	*n* = 65	*n* = 3	*n* = 0
Normal	3 (4.6)	2 (66.7)	0 (0.0)
Chronic hepatitis, liver fibrosis	20 (30.8)	1 (33.3)	0 (0.0)
Liver cirrhosis	42 (64.6)	0 (0.0)	0 (0.0)
Extrahepatic metastasis	*n* = 53	*n* = 6	*n* = 0
Lung	23 (43.4)	3 (50.0)	0 (0.0)
Bone	11 (20.8)	0 (0.0)	0 (0.0)
Brain	0 (0.0)	0 (0.0)	0 (0.0)
Intraperitoneal organs	7 (13.2)	3 (50.0)	0 (0.0)
Adrenal gland	6 (11.3)	0 (0.0)	0 (0.0)
Skin	0 (0.0)	0 (0.0)	0 (0.0)
Other	6 (11.3)	0 (0.0)	0 (0.0)
Lymph node metastasis	*n* = 63	*n* = 4	*n* = 0
n_0	51 (81.0)	1 (25.0)	0 (0.0)
n_1	12 (19.0)	3 (75.0)	0 (0.0)
Esophagus/gastric varices	*n* = 63	*n* = 4	*n* = 0
No	29 (46.0)	4 (100.0)	0 (0.0)
Yes	34 (54.0)	0 (0.0)	0 (0.0)

(*Continues*)

Table 17. (Continued)

	Hepatocellular carcinoma *n* (%)	Intrahepatic cholangiocarcinoma *n* (%)	Combined hepatocellular cholangiocarcinoma *n* (%)
Splenomegaly	*n* = 63	*n* = 4	*n* = 0
No	31 (49.2)	3 (75.0)	0 (0.0)
Yes	32 (50.8)	1 (25.0)	0 (0.0)

For all parameters, *n* is the total number of patients, excluding those in the "unknown" category, and (%) is the percentage of *n*.
b_0, no invasion of bile duct, b_1, branches of the bile duct, but not of second order branches; b_2, invasion of (or tumor thrombus in) the second order branches of the bile duct; b_3, invasion of (or tumor thrombus in) the first order branches of the bile duct; b_4, invasion of (or tumor thrombus in) the common hepatic duct; fc (−), absence of capsule formation; fc (+), presence of capsule formation; fc-inf (−), absence of cancerous infiltration of the tumor capsule; fc-inf (+), presence of cancerous infiltration of the tumor capsule; im_0, absence of intrahepatic metastasis; im_1, intrahepatic metastasis within the subsegment in which the principal tumor is located; im_2, intrahepatic metastasis in two segments; im_3, intrahepatic metastasis to three or more segments; im_s, intrahepatic metastasis within the subsegment in which the principal tumor is located; sf (−), absence of formation of a fibrous septum within the tumor; sf (+), presence of fibrous septum within the tumor; s_0, absence of invasion of the serosa; s_1, tumor invasion of the serosa; s_2, tumor invasion of adjacent organs; s_3,tumor rupture with intraperitoneal bleeding; va_0, absence of invasion of the hepatic artery; va_1, invasion distal to the second order branches of the hepatic artery, but not of the second order branches; va_2, invasion to the second order branches of the hepatic artery; va_3, invasion to the left or right hepatic artery, or the proper hepatic artery; vp_0, absence of invasion of (or tumor thrombus in) the portal vein; $_{vp1}$, invasion of (or tumor thrombus in) distal to the second order branches of the portal vein, but not of the second order branches; vp_2, invasion of (or tumor thrombus in) second order branches of the portal vein; vp_3, invasion of (or tumor thrombus in) first order branches of the portal vein; vp_4, invasion of (or tumor thrombus in) the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe; vv_0, absence of invasion of (or tumor thrombus in) the hepatic vein; vv_1, invasion of (or tumor thrombus in) peripheral branches of the hepatic vein; vv_2, invasion of (or tumor thrombus in) the right, middle, or left hepatic vein, the inferior right hepatic vein, or the short hepatic vein; vv_3, invasion of (or tumor thrombus in) the inferior vena cava.

Table 18 Cumulative overall survival rates in patients with hepatocellular carcinoma, who were registered between 1998 and 2009

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%) 1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
Fig. 1	All patients		100 394	53.95	82.8	71.5	61.9	53.6	46.6	40.7	35.7	31.3	27.9	24.7

details of pathological diagnosis. The non-cancerous part of the liver in patients with HCC was normal in 4.6%, showed chronic hepatitis or fibrosis in 30.8%, and showed cirrhosis in 64.6%; in patients with ICC, it was normal in 66.7%, showed chronic hepatitis or fibrosis in 33.8%, and showed cirrhosis in 0.0%.

Recurrence

Recurrence during the survey period (within 2 years of diagnosis) was reported in 34.3% of patients with HCC. The most frequently performed treatment for intrahepatic recurrence was TACE at 40.2%, followed by local ablation therapy at 24.9%. The most common sites of extrahepatic recurrence were the lungs, bone, and lymph nodes. The most frequently performed treatments

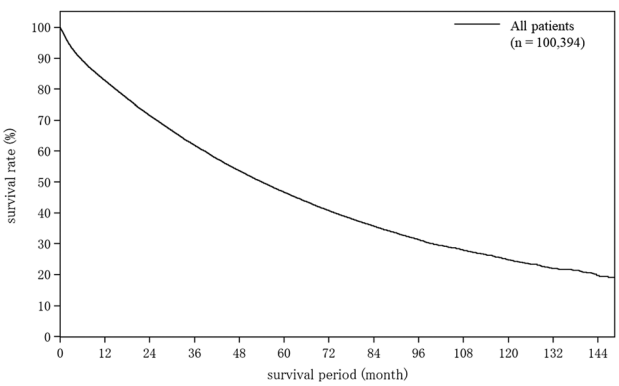

Figure 1 Overall survival among all 100 394 registered patients with hepatocellular carcinoma during 1998–2009. The median overall survival was 53.95 months, and 5- and 10-year survival rates were 46.6% and 24.7%.

Table 19 Cumulative survival rates for resected hepatocellular carcinoma (in patients registered between 1998 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%)									
					1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
	All patients		30 040	90.18	90.4	82.5	75.3	68.8	62.8	57.3	52.4	47.7	43.8	40.3
Fig. 2	Child–Pugh grade	Child–Pugh A	22 258	96.89	91.7	84.3	77.6	71.6	65.8	60.1	55.5	50.3	46.6	44.0
		Child–Pugh B	2136	60.19	81.6	72.7	62.4	55.0	50.0	42.7	36.4	33.7	23.2	–
		Child–Pugh C	74	39.26	67.4	53.3	51.1	46.5	43.1	43.1	32.4	24.3	24.3	24.3
Fig. 3	TNM stage by LCSGJ	Stage I	2810	124.42	97.2	94.6	90.0	84.9	79.3	74.9	69.3	64.3	59.5	51.0
		Stage II	13 859	106.91	94.9	89.0	82.5	76.3	70.5	64.2	59.1	53.6	49.6	47.4
		Stage III	6681	66.07	87.2	76.5	67.3	59.1	53.1	47.5	42.6	38.2	34.8	30.9
		Stage IVA	2186	28.45	70.5	53.6	43.8	37.8	32.2	28.3	25.7	23.0	20.3	18.9
		Stage IVB	333	15.34	57.1	40.5	31.7	30.2	25.8	23.7	19.3	19.3	19.3	19.3
	Maximum tumor diameter	≤2 cm	5478	118.05	96.1	92.4	87.0	80.8	74.3	69.2	64.0	58.3	54.5	47.5
		>2 cm to ≤3 cm	7247	99.48	94.9	88.9	82.0	75.7	69.5	63.2	57.1	51.9	46.2	42.1
		>3 cm to ≤5 cm	8253	87.23	92.1	84.2	76.2	69.1	62.9	56.6	51.6	47.3	44.4	41.7
		>5 cm to ≤10 cm	5858	68.37	85.2	73.9	65.3	58.6	53.2	48.2	45.1	40.4	37.7	36.1
		>10 cm	2352	32.79	70.6	56.2	48.5	42.7	39.2	35.8	32.8	29.8	27.1	26.4
	No. tumors	1	21 676	105.07	92.6	86.2	79.8	73.8	68.3	62.7	57.9	53.1	49.1	45.7
		2	4302	71.72	88.9	79.1	70.7	63.0	55.6	49.7	43.9	38.4	34.5	30.4
		≥3	3317	40.54	78.7	64.7	53.5	44.9	38.7	33.5	30.3	26.4	23.9	20.2
Fig. 4	Portal vein invasion	Vp_0	24 583	97.02	93.4	86.8	79.6	72.9	66.7	60.8	55.6	50.4	46.5	42.8
		Vp_1	2479	61.21	83.8	70.1	62.3	55.1	50.7	45.9	41.1	38.9	33.9	28.9
		Vp_2	918	25.86	67.3	51.5	41.2	38.5	33.1	29.6	28.2	25.4	21.8	21.8
		≥Vp_3	1101	15.70	56.8	40.0	33.1	28.6	24.9	22.4	22.0	21.5	19.9	19.9
Fig. 5	AFP (ng/mL)	≤20	14 319	114.43	95.2	89.6	83.5	77.3	71.5	65.9	60.9	55.8	51.9	48.1
		>20 to ≤200	7044	75.17	90.8	82.1	73.6	65.9	59.1	52.0	46.5	40.3	36.1	30.9
		>200 to ≤400	1425	72.71	87.8	76.8	68.1	61.4	55.9	50.6	44.8	41.0	36.3	33.5
		>400 to ≤1000	1647	65.02	85.7	75.5	65.3	58.7	52.8	47.1	43.8	40.3	35.9	34.4
		>1000 to ≤10,000	2663	62.23	81.0	71.5	62.6	55.8	50.5	47.2	44.4	41.2	38.8	36.9
		>10 000	1619	27.04	67.8	52.2	45.2	42.2	39.1	36.3	33.9	32.6	29.2	29.2

AFP, α-fetoprotein; LCSGJ, Liver Cancer Study Group of Japan; TNM, tumor–node–metastasis; Vp_0, absence of invasion of (or tumor thrombus in) the portal vein; Vp_1, invasion of (or tumor thrombus in) distal to the second order branches of the portal vein, but not of the second order branches; Vp_2, invasion of (or tumor thrombus in) second order branches of the portal vein; Vp_3, invasion of (or tumor thrombus in) first order branches of the portal vein; vp_4, invasion of (or tumor thrombus in) the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe.

for distant recurrence were systemic chemotherapy (total includes both cytotoxic chemotherapy agents and molecularly targeted agents), radiotherapy, and surgery, in that order.

Autopsy

Autopsies were carried out for a total of 91 patients with primary liver cancer. HCC was found in 85 patients. The rate of cirrhosis among autopsied patients with HCC was 64.6%, and rates of invasion of the portal vein, hepatic veins, and bile duct were 54.5%, 40.4%, and 18.7%, respectively. Extrahepatic spread was most frequently detected in the lungs (31.5%), lymph nodes (19.0%), and bone (16.7%). For ICC, the most common sites of extrahepatic spread were the intraperitoneal organs and the lungs, and the rate of lymph node metastasis was 75.0% (Table 17).

CUMULATIVE SURVIVAL RATES

Cumulative survival rates from the 15th to 20th surveys (1998–2009)

CUMULATIVE SURVIVAL RATES were calculated for patients with HCC, ICC, and combined HCC and

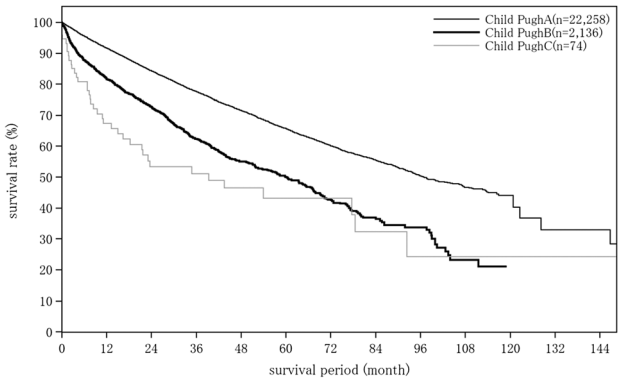

Figure 2 Overall survival by Child–Pugh grade in patients with hepatocellular carcinoma treated with resection (n = 30 040). The median overall survival for patients with a Child–Pugh grade A who underwent resection was 96.89 months, and 5- and 10-year survival rates were 65.8% and 44.0%.

ICC who were newly registered in the surveys from 1998 to 2009, and whose final outcome was survival or death (excluding unknown).

Cumulative survival rates for hepatocellular carcinoma

Table 18 shows cumulative survival rates among the 100 394 patients with HCC registered during 1998 and 2009. Median survival time was 53.95 months, and 5- and 10-year survival rates were 46.6% and 24.7% (Table 18; Fig. 1).

- Cumulative survival rates for resected HCC: median overall survival (OS) for all patients with a Child–Pugh grade A who underwent resection was 96.89 months, and 5- and 10-year survival rates were

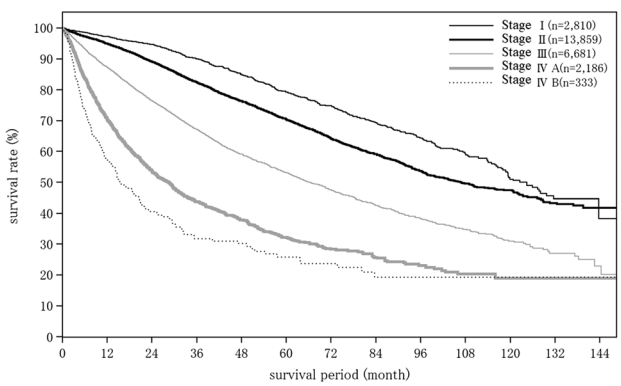

Figure 3 Overall survival in patients with hepatocellular carcinoma treated with resection according to the TNM stage by the Liver Cancer Study Group of Japan.

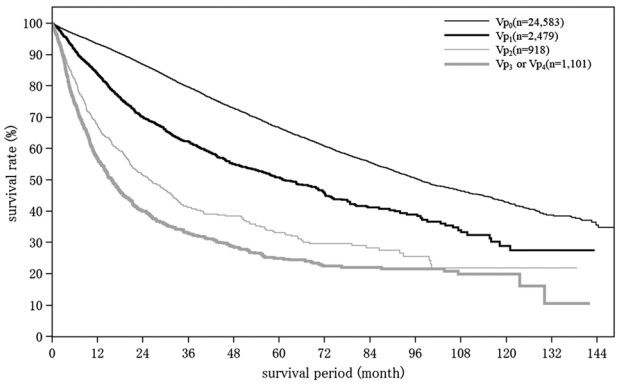

Figure 4 Overall survival according to portal vein invasion in patients with hepatocellular carcinoma treated with resection.

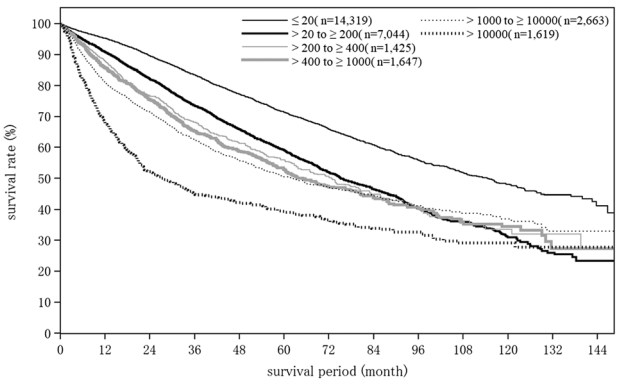

Figure 5 Overall survival by serum α-fetoprotein level in patients with hepatocellular carcinoma treated with resection.

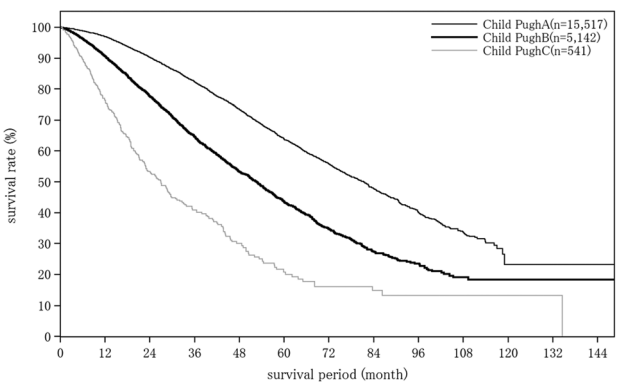

Figure 6 Overall survival by Child–Pugh grade in patients with hepatocellular carcinoma treated with local ablation therapy. The median overall survival for patients with a Child–Pugh grade A who underwent local ablation therapy was 81.41 months, and 5- and 10-year survival rates were 63.8% and 23.2%.

Table 20 Cumulative survival rates for hepatocellular carcinoma treated with local ablation therapy (in patients registered between 1998 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%)									
					1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
	All patients		27 181	67.19	94.3	85.2	75.0	64.6	55.0	47.1	39.8	33.8	28.9	24.3
Fig. 6	Child–Pugh grade	Child–Pugh A	15 517	81.41	97.0	90.2	82.3	73.5	63.8	55.8	47.8	40.0	33.5	23.2
		Child–Pugh B	5142	52.63	90.7	77.6	64.7	53.2	43.6	34.7	27.3	23.5	19.0	18.3
		Child–Pugh C	541	26.94	76.3	53.4	40.9	30.0	20.8	16.0	14.8	13.3	13.3	13.3
	No. tumors	1	17 986	74.68	95.3	87.2	78.2	68.6	59.6	51.7	44.0	38.8	33.4	28.2
		2	5309	60.12	93.4	83.5	72.5	61.0	50.1	42.2	35.5	28.3	22.8	19.9
		3	1986	51.48	92.8	80.8	66.8	53.0	43.3	35.0	28.4	21.6	18.7	15.1
		4	688	50.40	90.8	78.3	64.7	52.0	44.1	32.9	28.4	21.0	18.5	12.7
		≥5	818	40.80	87.4	69.8	54.9	44.8	33.1	27.0	23.1	17.8	17.0	15.0
	Maximum tumor diameter	≤1 cm	2034	86.67	96.8	90.8	82.6	75.2	65.9	57.5	51.6	44.5	38.2	29.9
		>1 cm to ≤2 cm	13 151	74.09	95.8	88.2	79.1	69.1	60.1	51.5	43.3	36.9	31.4	26.1
		>2 cm to ≤3 cm	7387	63.18	94.2	84.2	72.7	61.6	51.6	43.7	36.4	31.0	26.7	22.8
		>3 cm to ≤5 cm	2732	48.89	89.8	75.3	63.1	50.5	40.9	35.1	30.2	25.6	20.2	18.2
		>5 cm	572	46.39	83.4	68.5	57.8	48.9	38.5	30.3	27.9	21.6	20.7	14.3

OS, overall survival.

Table 21 Cumulative survival rates for hepatocellular carcinoma treated with transcatheter arterial chemoembolization (in patients registered between 1998 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%)									
					1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
	All patients		22 695	37.62	82.3	65.2	51.7	40.1	32.0	25.3	20.5	16.9	15.1	11.8
Fig. 7	Child–Pugh grade	Child–Pugh A	12 134	46.06	87.2	72.6	59.9	48.5	40.0	32.2	26.0	21.3	19.0	11.3
		Child–Pugh B	4803	27.83	77.0	55.8	39.2	26.2	19.2	14.5	10.4	8.9	7.5	–
		Child–Pugh C	686	16.16	59.6	35.5	23.8	16.6	12.2	9.2	7.0	7.0	7.0	–
Fig. 8	No. tumors	1	9406	47.34	87.1	73.6	61.4	49.4	41.1	33.4	27.6	23.5	20.6	15.3
		2	4347	41.07	86.3	69.5	55.5	41.7	31.3	24.0	18.6	13.5	12.4	10.4
		3	2541	33.48	84.6	64.5	47.4	34.4	26.1	20.3	14.9	13.4	12.4	11.0
		4	1232	31.47	84.5	61.5	42.9	32.3	24.2	17.6	14.0	9.3	9.3	8.0
		≥5	4565	21.19	68.1	46.1	32.8	23.8	18.2	14.7	12.6	10.3	8.6	6.6

OS, overall survival.

65.8% and 44.0% (Table 19; Fig. 2). The TNM stage was well correlated with survival (Table 19; Fig. 3). Maximum tumor diameter, number of tumors, and extent of portal invasion (Fig. 4), as well as α-fetoprotein (Fig. 5), were also well correlated with survival (Table 19).

- Cumulative survival rates for HCC treated with local ablation therapy: median OS for patients with a Child–Pugh grade A who underwent local ablation therapy was 81.41 months, and 5- and 10-year survival rates were 63.8% and 23.2% (Fig. 6). The number of tumors and tumor

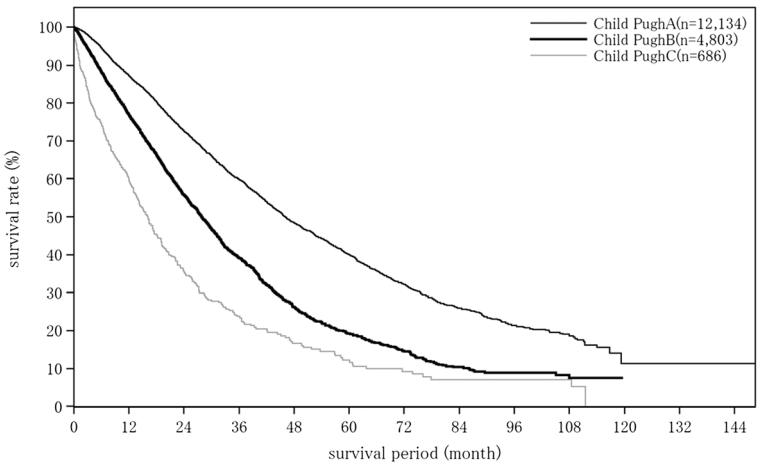

Figure 7 Overall survival by Child–Pugh grade in patients with hepatocellular carcinoma treated with transcatheter arterial chemoembolization. Cumulative survival rate by Child–Pugh score among patients with hepatocellular carcinoma treated with transcatheter arterial chemoembolization. The median overall survival for patients with a Child–Pugh grade A who underwent transcatheter arterial chemoembolization was 46.06 months, and 5- and 10-year survival rates were 40.0% and 11.3%.

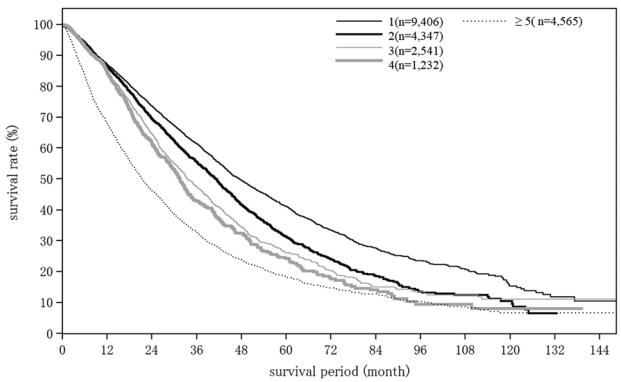

Figure 8 Overall survival by number of tumors in patients with hepatocellular carcinoma treated with transcatheter arterial chemoembolization.

diameter were well correlated with cumulative survival rate (Table 20).

- Cumulative survival rates for HCC treated with TACE: median OS for patients with a Child–Pugh grade A who underwent TACE was 46.06 months, and 5- and 10-year survival rates were 40.0% and 11.3% (Table 21; Fig. 7). The number of tumors was well correlated with survival rate after TACE (Table 21; Fig. 8).

Cumulative survival rates for intrahepatic cholangiocarcinoma and combined hepatocellular cholangiocarcinoma

Tables 22 and 23 show cumulative survival rates for patients with ICC (all patients and by patient factors) and combined HCC and ICC (all patients).

Changes in cumulative survival rate over time

Changes in survival over time for hepatocellular carcinoma

Cumulative survival rates were calculated by registration date for newly registered patients with HCC whose final outcome was survival or death (excluding unknown). Patients were grouped by 8-year periods into four time period groups. Period 1 consisted of those registered in the fifth to eighth surveys (1978–1985), period 2 of those registered in the ninth to 12th surveys (1986–1993), period 3 of those registered in the 13th to 16th surveys, and period 4 of those registered in the 17th to 20th surveys (2002–2009; Table 24; Fig. 9). Cumulative survival rates (5-year/10-year) and median OS were 11.9%/5.0% and 4.99 months for period 1 (1978–1985, $n = 5551$), 31.9%/10.1% and 25.63 months for period 2 (1986–1993), 39.7%/20.6% and 42.97 months for period 3 (1994–2001, $n = 53\,775$), and 50.4%/24.0% and 60.81 months for period 4 (2002–2009, $n = 65\,711$). The number of new registrations has been increasing over time, and the prognosis of HCC is improving dramatically (Table 24; Fig. 9).

Changes in survival over time for intrahepatic cholangiocarcinoma

Cumulative survival rate and median OS were calculated to determine how survival for ICC has changed over time. Median OS and survival rates (5-year/10-year) were 3.71 and 11.0%/8.2% for period 1 ($n = 338$), 7.56 months and 14.1%/7.7% for period 2 ($n = 1056$),

Table 22 Cumulative survival rates for intrahepatic cholangiocarcinoma (in patients registered between 1998 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%) 1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
	All patients		4436	18.14	59.6	43.4	37.4	32.9	28.9	26.2	24.2	21.8	20.2	18.2
	Hepatectomy	Yes	2412	43.27	78.5	61.0	53.8	47.5	41.9	38.8	35.9	32.9	30.7	28.6
		No	263	33.31	71.5	53.4	44.6	39.6	37.1	31.1	31.1	25.4	25.4	12.7
	Hepatectomy: maximum tumor diameter	≤2 cm	244	–	91.4	80.5	73.0	68.3	63.4	61.5	61.5	50.9	50.9	50.9
		>2 cm to ≤5 cm	1144	53.72	84.3	68.2	60.3	53.0	45.9	42.0	38.2	35.0	33.2	33.2
		>5 cm to ≤10 cm	739	22.67	68.1	47.4	40.4	34.9	30.7	27.7	25.9	25.9	23.9	20.5
		>10 cm	149	17.41	62.8	42.4	40.9	37.3	32.3	29.8	29.8	25.6	17.0	17.0
	Hepatectomy: No. tumors	1	1,925	54.28	81.8	66.0	59.3	52.9	46.8	43.4	40.9	36.9	35.1	32.2
		2	143	27.50	78.8	57.0	45.5	36.2	33.6	33.6	33.6	33.6	33.6	33.6
		≥3	241	14.00	56.1	26.9	19.4	13.7	11.1	9.7	7.3	7.3	3.6	–
	Hepatectomy: curability	Curability A or B	372	64.13	84.2	69.4	61.2	57.6	51.7	47.4	43.1	39.0	35.8	33.9
		Curability C	892	25.36	71.8	51.1	44.1	37.1	31.5	29.0	27.1	22.9	22.9	22.9
	Hepatectomy: lymph node metastasis	N_0	1612	64.26	85.6	70.2	62.7	56.0	51.0	48.3	45.4	41.4	40.4	40.4
		N_1	645	16.07	61.2	36.1	30.6	25.0	19.4	16.3	13.2	11.3	8.5	–

OS, overall survival.

Table 23 Cumulative survival rates for combined hepatocellular cholangiocarcinoma (in patients registered between 1998 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%) 1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
	All patients		708	19.78	60.8	44.8	37.9	34.0	30.2	28.4	24.9	22.4	20.7	17.7
	Hepatectomy	Yes	441	36.63	75.4	58.7	51.0	45.6	41.2	38.4	32.8	28.7	25.8	20.7
		No	108	17.91	60.5	34.2	28.3	25.1	16.8	16.8	16.8	16.8	16.8	16.8

OS, overall survival.

17.02 months and 22.6%/12.2% for period 3 ($n = 4552$), and 20.6 months and 30.9%/10.7% for period 4 ($n = 3184$). Survival has gradually improved over the years, although not as dramatically as for HCC (Table 24; Fig. 10).

Conclusion: Primary liver cancer is the fifth most common cause of cancer death in Japan after lung cancer, colorectal cancer, gastric cancer, and pancreatic cancer.[77] The number of deaths from HCC peaked at 34 510 in 2004, and has continued to decrease gradually every year since. Nevertheless, it is reported that >28 000 people still die from HCC each year. Approximately 37.5% of the patients with primary liver cancer registered in the 20th Nationwide Follow-up Survey of Primary Liver Cancer in Japan were newly registered.

Compared with the 19th survey, the population of patients with HCC in this survey was older at the time of clinical diagnosis, included more female patients, had smaller tumor diameters, and more frequently received radiofrequency ablation as local ablation therapy. Calculation of the median OS and cumulative survival rates for patients newly registered in the four time periods between 1978 and 2009 revealed marked improvement in survival rates for HCC, which can be attributed to advances in early diagnosis and treatment. The OS of HCC in Japan is number 1 in the world according to the comparison with the published data from other countries worldwide.[62,78] We

Table 24 Cumulative survival rates from the 5th to 20th surveys (patients registered between 1978 and 2009)

Fig. No.	Title	Category name	*n*	Median OS (months)	Survival rate (%)									
					1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years
Fig. 9	All patients with hepatocellular carcinoma	Registered in 1978–1985	5551	4.99	33.9	23.4	18.1	14.9	11.9	9.6	8.3	7.1	5.9	5.0
		Registered in 1986–1993	32 721	25.63	66.9	51.7	40.5	31.9	25.5	20.5	16.9	14.1	11.7	10.1
		Registered in 1994–2001	53 775	42.97	78.4	65.6	55.3	46.7	39.7	34.2	29.8	26.1	23.0	20.6
		Registered in 2002–2009	65 711	60.81	84.4	73.8	64.8	57.0	50.4	44.3	39.1	32.7	28.4	24.0
Fig. 10	All patients with intrahepatic cholangiocarcinoma	Registered in 1978–1985	338	3.71	21.2	14.9	11.5	11.5	11.0	9.1	9.1	9.1	8.2	8.2
		Registered in 1986–1993	1056	7.56	38.2	25.5	20.6	16.8	14.1	11.7	10.3	9.6	8.0	7.7
		Registered in 1994–2001	4552	17.02	57.7	41.4	33.0	27.1	22.6	19.6	17.4	15.2	13.4	12.2
		Registered in 2002–2009	3184	20.60	62.4	46.6	40.4	35.8	30.9	28.0	23.7	21.4	21.4	10.7
	All patients with combined hepatocellular cholangiocarcinoma	Registered in 1978–1985	69	2.86	15.5	7.7	7.7	6.2	6.2	3.1	3.1	3.1	3.1	3.1
		Registered in 1986–1993	126	19.55	61.9	35.8	29.0	23.7	22.6	21.4	18.7	17.3	17.3	17.3
		Registered in 1994–2001	330	16.82	55.5	39.6	29.8	25.1	23.2	21.7	18.8	16.9	15.5	12.9
		Registered in 2002–2009	501	24.02	65.5	50.1	43.0	39.2	33.6	31.0	28.8	–	–	–

OS, overall survival.

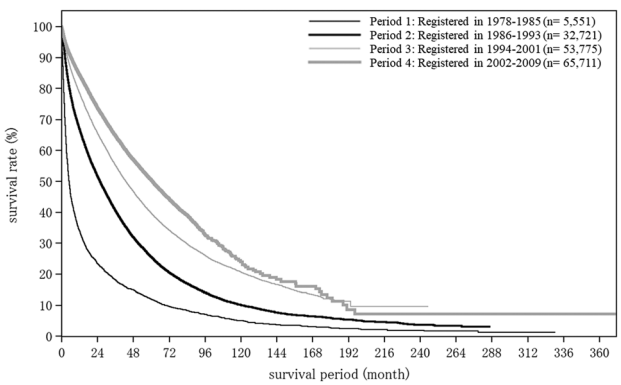

Figure 9 Improvement of overall survival among all patients with hepatocellular carcinoma according to the registration period. A comparison of cumulative overall survival among patients newly registered between 1978 and 2009 (n = 157 758) divided into four groups by registration date. The median overall survival and cumulative survival rates (5-year/10-year) were 4.99 months and 11.9%/5.0% for group 1 (1978–1985, n = 5551), 25.63 months and 31.9%/10.1% for group 2 (1986–1993), 42.97 months and 39.7%/20.6% for group 3 (1994–2001, n = 53 775), and 60.81 months and 50.4%/24.0% for group 4 (2002–2009, n = 65 711).

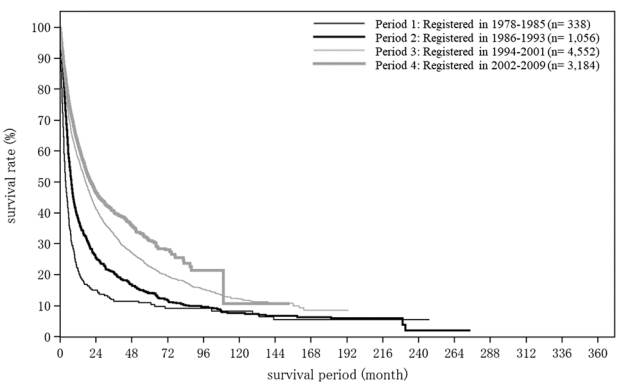

Figure 10 Improvement of overall survival among all patients with intrahepatic cholangiocarcinoma according to the registration period. A comparison of cumulative survival rates among patients newly registered between 1978 and 2009 (n = 9130). The median overall survival and survival rates (5-year/10-year) were 3.71 and 11.0%/8.2% for group 1 (n = 338), 7.56 months and 14.1%/7.7% for group 2 (n = 1056), 17.02 months and 22.6%/12.2% for group 3 (n = 4552), and 20.6 months and 30.9%/10.7% for group 4 (n = 3184).

believe that the large set of data from registered patients analyzed in this follow-up survey will advance the research and treatment outcome of primary liver cancer.

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