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Original article

**Prognoses and clinicopathological characteristics for hepatocellular carcinoma
originating from the caudate lobe after surgery**

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1 Abstract

2 **Background:** The aims were to evaluate the prognoses, and clinicopathological characteristics of
3 solitary hepatocellular carcinoma (HCC) originating from the caudate lobe (HCC-CL).

4 **Methods:** We analyzed 584 patients with a solitary tumor < 10 cm from January 1990 to November
5 2014. Patients were classified into a caudate lobe group (CL; n = 39) and a non-caudate lobe group
6 (NCL; n = 545). We investigated the prognoses and clinicopathological characteristics of solitary
7 HCC-CL. We compared the surgical procedures performed in these cases.

8 **Results:** HCC-CL had a similar rate of portal venous invasion (PVI) as HCC-NCL (21% vs. 19%);
9 however, the frequency of tumor thrombus at the first branch of the portal vein (PV) or extension to
10 the trunk or the opposite side of the PV was significantly higher in HCC-CL (8% vs. 2%). HCC-CL
11 had similar OS rates compared to HCC-NCL; however, HCC-CL showed significantly poorer RFS.
12 Although there were not significant differences among the three surgical procedure, blood loss and
13 complication rates tended to be higher in cases underwent an isolated caudate lobectomy. Tumor size
14 ≥ 5 cm, PVI, and liver fibrosis or cirrhosis (LF or LC) were independent unfavorable factors for both
15 OS and RFS. PIVKA-II ≥ 120 mAU/ml was an independent unfavorable factor for RFS.

16 **Conclusion:** HCC-CL presented a poorer RFS rate. Patients with a tumor size ≥ 5 cm, PIVKA-II ≥ 120
17 mAU/ml, portal venous invasion, and LF or LC should be diligently followed-up as these cases have
18 a high risk of recurrence.

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1 **Text**

2 **Background**

3 The hepatic caudate lobe is the smallest hepatic segment and is located deep between the
4 inferior vena cava (IVC) and the hilus hepatis. Therefore, resection for hepatocellular carcinoma
5 (HCC) originating from the caudate lobe is hard [1].

6 The caudate lobe was classified into two parts by Healy and Schroy: segment I right and
7 segment I left [2], while Couinaud used the terms segment IX and segment I [3]. Subsequently, the
8 caudate lobe was classified into three parts by Kumon, as the paracaval portion, caudate process, and
9 Spiegel lobe [4], which are the terms widely referred to these days. The Spiegel lobe is the portion
10 under the left side of the IVC and the lesser omentum. The paracaval portion is located in front of the
11 IVC and the caudate process is located behind of the portal trunk. The superior border of the
12 paracaval portion is at the dorsal aspect of the middle and right hepatic veins, and the inferior border
13 is the hilus hepatis [4].

14 The caudate lobe has the following anatomical specificities: 1) Caudate branches
15 of the portal vein directly emanate from the left and right branches of the portal vein (PV); and 2) the
16 hepatic vein flows directly into the IVC. Some reports have stated that HCC originating in the
17 caudate lobe (HCC-CL) have poorer prognoses than HCC in non-caudate lobes (HCC-NCL) [5, 6];
18 however, this stance remains controversial [7].

19 We evaluated the prognostic factors and clinicopathological characteristics of solitary HCC-
20 CL compared with HCC-NCL. We also investigated surgical procedures applied in such cases.

Patients and Methods

We investigated 996 patients with resected HCC at the Gastroenterological Surgery I Unit of Hokkaido University Hospital in Sapporo, Japan from January 1990 to November 2014. Those with a solitary tumor < 10 cm analyzed as part of our study totaled 584.

The patients were classified into a caudate lobe group (CL; n=39, 6.7%) or a non-caudate lobe group (NCL; n=545, 93.3%) based upon tumor location. Indications for hepatectomy and operative procedure type were typically determined according to liver function reserve, i.e., the indocyanine green retention test at 15 min (ICGR15) [8]. We selected anatomical resection for patients in whom the ICGR15 was < 25% [9]. Nonanatomical partial resection was selected in other cases. NCL showed that many major (≥ 3 segments) resections were 3 cases, and minor (< 3 segments) resections were 542 cases. All surgery showed surgical margin were histologically or macroscopically free. Follow-up studies were performed at 3-month intervals and included physical, radiological and serological studies [9]. The median follow-up period in this study was 61 months (range, 0.2-289 months).

According to the classification by Clavien–Dindo [10], postoperative morbidity was evaluated. We defined the postoperative complications above Clavien–Dindo IIIa. This study was performed according to the Declaration of Helsinki and the guidelines of our institution's ethics committee.

Statistical analyses

Univariate analyses were performed using the Mann-Whitney U test for continuous

variables and the chi-square test for non-continuous variables between two groups. The Kruskal-Wallis test for continuous variables and the Cochran-Armitage trend test for noncontinuous variables were used among three groups. Logistic regression model analyses were performed for multivariate analyses. Overall survival (OS) and relapse-free survival (RFS) were analysed by using the Kaplan-Meier method with the log-rank test or Cox proportional hazard model. JMP Pro 12.0.1 for Windows (SAS Institute, Cary, NC) was used for statistical analyses.

Results

Clinicopathological characteristics and operative variables

Among all 996 cases, HCC in the caudate lobe (CL) were 51 cases and HCC in the non-caudate lobe were 945 cases (NCL). CL of which size more than 10 cm in diameter were 3 cases (5.8%), however, NCL more than 10 cm were 140 cases (14.8%) ($p < 0.01$). We previously reported that huge HCC (≥ 10 cm) is an independent risk factor due to a high risk for initial extra-hepatic recurrence [11]. CL showed significantly lower cases with multiple tumors (12/51, 23.5%) than NCL (335/945, 35.4%) ($p < 0.01$). Therefore, we selected patients with single and tumor size less than 10 cm.

Median survival time (MST) and five-year OS rates of our 584 study patients were 125 months and 71%. The median RFS time was 36 months. Cardiac and pulmonary complications were 1.6%. Venous thrombosis complications were 0.7%. Reoperation rates were 3.1%. The rates of percutaneous drainage of a fluid collection were 8.6%. Median staying time at hospital was 19 (3-

1 128) days.

2 The univariate analysis showed that Albumin [Alb] < 4.0 g/dl and tumor thrombus in the first
3 branch of the PV (vp3) / tumor thrombus extension to the trunk or the opposite side of the PV (vp4)
4 were significantly higher in the CL group (Table 1). Three patients had vp3/vp4 in the CL group, two
5 patients were diagnosed preoperatively, one patient was not diagnosed preoperatively. These three
6 patients were performed total caudate lobectomy (two patients were performed isolated total caudate
7 lobectomy, one patient was performed total caudate lobectomy combined left lobe). The rate of portal
8 venous invasion (vp) was almost same between the two groups. According to multivariate analysis,
9 the rates of vp3/vp4 was significantly higher in the CL group.

10 Table 2a showed surgical outcome of caudate lobe and non-caudate lobe. These were no
11 significant differences. The rate of postoperative liver failure was 0% in the CL groups, that of the
12 NCL groups was 0.9%. The procedures for CL patients consisted of the following: 6 total caudate
13 lobectomies using a high dorsal resection technique, 21 partial caudate lobectomies, and 12 other
14 combined with hemi-hepatectomy. Table 2b displays the blood loss, operative time, mortality, and
15 morbidity. Significantly differences were not found.

16 **Causes of death and recurrence**

17 There were 235/584 (40.2%) deaths. Cancer-related deaths were 202/235 (86%). Liver failure-
18 related deaths with controlled HCC were 5/235 (2%). Deaths related to the operative procedure were
19 5/235 (2%). The cause of death were 4 posthepatectomy liver failure, 1 abdominal abscess. Other
20 disease-related deaths were 23/235 (10%). Regarding recurrence, 29 CL patients experienced a

recurrence (74.4%) with a median recurrence time of 13 months (0.9-115). Of the NCL patients, 340 experienced a recurrence (62.4%). Median recurrence time of the NCL patients was 20 months (0.4-255). Initial recurrence sites were not significant (Table 3).

Patient survival and recurrence-free survival

The five-year OS rates of the CL group was 59% and that of the NCL group was 72% ($p = 0.43$). The median RFS time of the CL and NCL groups were 16 months and 38 months, respectively. Although OS was not significantly different, RFS was significantly poorer in the CL than that in the NCL group ($p = 0.03$) (Fig. 1).

Furthermore, the five-year OS rates of the CL group with vp was 21% and that of the NCL group with vp was 53% ($p = 0.17$). The median RFS time of the CL and the NCL groups with vp were 13 months and 31 months, respectively ($p = 0.04$). Although OS was not significantly different, the RFS was significantly poorer in the CL group with vp than that in the NCL group with vp. Regarding the RFS of HCC without vp, there were not significant difference between the groups ($p = 0.39$).

Besides, we performed multivariate analyses for the factors including location of the tumor (caudate lobe vs. other segments) among 584 patients. Alb, serum alpha-fetoprotein [AFP], serum protein induced by vitamin K absence-II [PIVKA-II], tumor size, location, vp, and poorly differentiation were significantly independent factors for relapse-free survival (Table 4).

Prognostic factors of HCC originating from the caudate lobe

Table 5 presents the factors related to the OS and RFS in the CL group. Multivariate analysis

indicated that T-bil ≥ 1.5 mg/dl, tumor size ≥ 5 cm, vp, and liver fibrosis [LF] or liver cirrhosis [LC] were unfavorable factors for OS and that PIVKA-II ≥ 120 mAU/ml, tumor size ≥ 5 cm, vp, and LF or LC were unfavorable factors for RFS among the patients with caudate lobe HCC.

Discussion

Our present study indicated that HCC-CL had a similar rate of portal venous invasion as HCC-NCL; however, the frequency of vp3 or vp4 was significantly higher. Patients with HCC-CL showed similar OS compared to those with HCC-NCL; however, they had significantly poorer RFS rates. Regarding prognostic factors for HCC-CL, we found tumor size ≥ 5 cm, vp, and LF or LC to be independently unfavorable factors for both OS and RFS. T-bil ≥ 1.5 mg/dl was an independent unfavorable factor for OS, and PIVKA-II ≥ 120 mAU/ml was an independent unfavorable factor for RFS.

Previous studies have reported HCC-CL to be 3.2-7.6% resected [6, 7, 12, 13] that is consistent with our result, 6.7%.

Takayasu et al. reported in 1986 that patients with HCC-CL might have a poorer prognoses and more intrahepatic metastases than those with HCC-NCL [5]. Tanaka et al. reported that the five-year OS rates of 15 patients with HCC-CL were poorer than those of patients with HCC-NCL, 25.9% vs. 54.1%, respectively [6]. However, Ikegami et al. demonstrated that five-year OS and RFS were not different between HCC-CL vs. HCC-NCL, 66.7% vs. 68.6%, and 34.6% vs. 32.8%, respectively [7]. Sakamoto et al. reported that five-year OS and RFS of patients with solitary caudate lobe and

other segment HCCs were not significantly different, 76% vs. 64%, and 44% vs. 40%, respectively [13]. The prognoses for those with HCC-CL remain controversial. In our study, there were not significant differences for the five-year OS rates between the CL and the NCL groups, 59% vs 72%, respectively ($p = 0.43$). RFS was significantly more unfavorable in the CL group than that in the NCL group, 16 months vs. 38 months, respectively ($p = 0.03$). Regarding the discrepancy between OS and RFS, treatments after recurrence were relatively comparable because liver functions were not so different among two groups. Therefore, OS might be not so different among two groups. Furthermore, the RFS of HCC with vp was more unfavorable in the CL group ($p = 0.04$). There were not significant differences for RFS of HCC without vp between the two groups ($p = 0.39$). While clinicopathological characteristics of CL patients were almost same with those of NCL patients, interestingly, the frequency of vp3/vp4 was significantly higher in the CL group. However, vp rates were not significantly different. HCC-CL might have a poorer RFS rate due to the anatomical structure. Since the caudate branches of the PV directly arise from the left and right branches of the PV, tumor cells may disseminate into the main portal branches.

Liu et al. reported that HCC located in the Spiegel lobe showed a better prognosis than that in the caudate process or paracaval portion and that surgical margin, and cirrhosis were prognostic factors for HCC located in the caudate lobe [14]. However, in this study, the median RFS time of the cases with R1 was 20 months and that of the cases with R0 was 16 months in the CL group ($p = 0.55$). These were not significant. Our study showed that tumor size ≥ 5 cm and presence of vp were independent unfavorable prognostic factors for both OS and RFS in this study. PIVKA-II ≥ 120

mAU/ml was an independent unfavorable prognostic factor for RFS. The reason why the presence of vp is an unfavorable factor may be due to the anatomical structure as explained previously. Furthermore, larger tumors and high PIVKA-II were risk factors for vp [15-17]. These cases should be performed anatomical hepatectomy such as total caudate lobectomy. The patients should be followed with contrast enhanced computed tomography [CT] scan of the chest and abdomen or contrast enhanced magnetic resonance imaging [MRI] of the abdomen and non-contrast CT of the chest every 3 months.

Hepatic resection is the main therapeutic method even for HCC-CL. Surgical procedures for HCC-CL are classified into three forms: 1) partial resection (mostly, Spiegel lobe), 2) resection combined with another lobe, and 3) isolated caudate lobectomy with a high dorsal resection technique [18] or anterior transection [19]. Partial resection should be performed if the tumor is located in the Spiegel lobe or caudate process [20]. On the other hand, partial resection without resection of another lobe is not suitable for tumors in the whole caudate lobe or the paracaval portion. While resection combined with another lobe is a relatively simple and easy procedure in these cases, this option is not appropriate for patients with poor liver function. An isolated caudate lobectomy using a high dorsal resection technique is a rational and suitable procedure for these patients [18]. However, the high dorsal resection technique is challenging. This procedure requires mastery of advanced techniques and anatomical comprehension. Liu et al. reported that the complication rate (10% vs. 43%), time of vascular occlusion (33 minutes vs. 52 minutes), blood loss (460 ml vs. 780 ml), blood transfusion (55% vs. 87%), operative time (170 min vs. 240 min), and

hospital stay (13 days vs. 18 days) were significantly lower and shorter in the combined caudate lobectomy than those in the isolated caudate lobectomy, respectively [21]. Zhou et al. reported that time of vascular occlusion (23 min vs. 31 min), blood loss (615 ml vs. 1011 ml), and operative time (202 min vs. 316 min) were significantly lower in the combined caudate lobectomy than those in the isolated caudate lobectomy, respectively [22]. However, their study reported similar morbidity and mortality rates [18]. In our study, blood loss and complication rates tended to be higher with the high dorsal resection technique, although significant differences were not identified.

In our current study, laparoscopic hepatectomy for the caudate lobe were not performed, however, this technique was reported. Since Dulucq et al. reported 2 cases in 2006 [23], some reports for small cases about laparoscopic caudate lobectomy have been shown [24, 25]. The indication for laparoscopic caudate lobectomy should be carefully considered.

In conclusion, HCC originating from the caudate lobe showed poorer RFS than that of HCC originating from other segments. Patients with tumor size ≥ 5 cm, PIVKA-II ≥ 120 mAU/ml, portal venous invasion, and LF or LC should be followed-up closely, as they represent a high-risk group prone to recurrence.

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1 **Figure captions**

2 **Fig. 1**

3 (a) Overall survival curves for patients with HCC located in the caudate lobe vs. the non-caudate
4 lobe.

5 (b) Relapse-free survival curves for patients with HCC located in the caudate lobe vs. the non-
6 caudate lobe.

Table 1. Clinicopathological characteristics of HCC at caudate lobe

Characteristics		CL (n = 39)	NCL (n = 545)	<i>p</i>
Epidemiology				
Age	< 60	13 (33 %)	213 (39 %)	0.47
	≥ 60	26 (67 %)	332 (61 %)	
Sex	Male	32 (82 %)	436 (82 %)	0.75
	Female	7 (18 %)	109 (18 %)	
HBs-Ag	Positive	13 (33 %)	198 (36 %)	0.70
	Negative	26 (67 %)	347 (64 %)	
HCV-Ab	Positive	20 (51 %)	213 (39 %)	0.13
	Negative	19 (49 %)	332 (61 %)	
NBNC	Yes	7 (18 %)	143 (26 %)	0.25
	No	32 (82 %)	402 (74 %)	
Biochemical Factors				
Platelets	< 100,000 /mm ³	10 (26 %)	110 (20 %)	0.41
	≥ 100,000 /mm ³	29 (74 %)	435 (80 %)	
Albumin	< 4.0 g/dl	10 (26 %)	230 (42 %)	0.04
	≥ 4.0 g/dl	29 (74 %)	315 (58 %)	
Total bilirubin	≥ 1.5 mg/dl	3 (8 %)	31 (6 %)	0.60
	< 1.5 mg/dl	36 (92 %)	514 (94 %)	
PT	< 80%	6 (15 %)	81 (15 %)	0.92
	≥ 80%	33 (85 %)	464 (85 %)	
ICGR15	≥ 15%	18 (46 %)	240 (44 %)	0.79
	< 15%	21 (54 %)	305 (56 %)	
AFP	≥ 20 ng/ml	22 (56 %)	228 (42 %)	0.07
	< 20 ng/ml	17 (44 %)	317 (58 %)	
PIVKA-II	≥ 120 mAU/ml	16 (41 %)	188 (34 %)	0.40
	< 120 mAU/ml	23 (59 %)	357 (66 %)	
Tumor Factors				
Tumor size	≥ 5cm	10 (26 %)	158 (29 %)	0.65
	< 5cm	29 (74 %)	387 (71 %)	
Surgical procedure				
Lobectomy	Yes	12 (31%)	121 (22%)	0.46
	No	27 (69%)	424 (78%)	

Histological Factors

vp	Yes	8 (21 %)	103 (19 %)	0.80
	No	31 (79 %)	442 (81 %)	
vp3/vp4	Yes	3 (8 %)	13 (2 %)	0.04
	No	36 (92%)	532 (98 %)	
vv	Yes	3 (8 %)	26 (5 %)	0.41
	No	36 (92%)	519 (95 %)	
vv3	Yes	0 (0%)	2 (0.4%)	0.70
	No	39 (100%)	543 (99.6 %)	
Differentiation	poor	12 (31 %)	120 (22 %)	0.20
	well/moderate/others	27 (69 %)	425 (78 %)	
Surgical margin	positive	2 (5%)	10 (2%)	0.37
	negative	37 (95%)	535 (98%)	
Cirrhosis	LF or LC	20 (51 %)	290 (53 %)	0.81
	CH or NL	19 (49 %)	255 (47 %)	

HBs-Ag, HBs-antigen; HCV-Ab, HCV-antibody; NBNC, without HBV and HCV; PT, prothrombin time; ICGR15, indocyanine green retention rate at 15 min; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence-II; vp, portal venous invasion; vp3, tumor thrombus in the first branch of the portal vein; vp4, tumor thrombus extension to the trunk or the opposite side branch of the portal vein; vv, hepatic venous invasion; vv3, tumor thrombus in the inferior vena cava; LF, liver fibrosis; LC, liver cirrhosis; CH, chronic hepatitis; NL, normal liver.

Table 2. Surgical outcome

(a) Surgical outcome of caudate lobe and non-caudate lobe

	CL (n = 39)	NCL (n = 545)	<i>p</i>
Median blood loss (range) ml	430 (20-6050)	470 (0-10907)	0.61
Median operative time (range) min	318 (120-546)	321 (78-1019)	0.95
Morbidity			
Pleural effusion	0 (0 %)	2 (0.4 %)	0.70
Ascites	2 (5.1 %)	21 (3.8 %)	0.69
Postoperative bleeding	1 (2.6 %)	9 (1.7 %)	0.67
Bile leakage	3 (7.7 %)	28 (5.1 %)	0.49
Wound infection	1 (2.6 %)	12 (2.2 %)	0.88
Mortality			
30-day	0 (0 %)	1 (0.2 %)	0.78
90-day	0 (0 %)	4 (0.7 %)	0.59

CL, caudate lobe group; NCL, non-caudate lobe group.

Table 2. Surgical outcome

(b) Surgical outcome of each procedure for caudate lobe

	Partial caudate lobectomy (n = 21)	Isolated total caudate lobectomy (n = 6)	Combined with hemi- hepatectomy. (n = 12)	<i>p</i>
Median blood loss (range) ml	390 (20- 6050)	500 (250-2200)	486 (120- 4605)	<i>0.48</i>
Median operative time (range) min	291 (120- 530)	339 (177-504)	377 (253- 546)	<i>0.10</i>
Morbidity				
Pleural effusion	0 (0 %)	0 (0 %)	1 (8.3 %)	<i>0.17</i>
Ascites	2 (9.5 %)	0 (0 %)	0 (0 %)	<i>0.19</i>
Postoperative bleeding	0 (0 %)	1 (16.7 %)	0 (0 %)	<i>0.65</i>
Bile leakage	1 (4.8 %)	1 (16.7 %)	1 (8.3 %)	<i>0.59</i>
Wound infection	1 (4.8 %)	0 (0 %)	0 (0 %)	<i>0.36</i>
Mortality				
30-day	0 (0 %)	0 (0 %)	0 (0 %)	-
90-day	0 (0 %)	0 (0 %)	0 (0 %)	-

Table 3. Initial recurrence patterns

	CL (n = 39)	NCL (n = 545)	<i>p</i>
Recurrence cases	29 (74.4 %)	340 (62.4 %)	<i>0.13</i>
Median recurrence duration (range) months	13 (0.9-115)	20 (0.4-255)	<i>0.13</i>
Recurrence site			
Liver	28 (97 %)	317 (93.2 %)	<i>0.48</i>
Lung	2 (5.1 %)	13 (3.8 %)	<i>0.42</i>
Others	0 (0 %)	8 (2.4 %)	<i>0.40</i>

CL, caudate lobe group; NCL, non-caudate lobe group.

Table 4. Prognostic factors for relapse-free survival of solitary HCC which tumor size <10 cm

Relapse-free survival		
Characteristics	Univariate (<i>p</i>)	Multivariate (<i>p</i>) (hazard ratio) (95% CI)
Epidemiology		
Age ≥ 60	0.83	
Sex Male	0.24	
HBs-Ag positive	0.63	
HCV-Ab positive	0.03	0.25 (1.152) (0.904-1.467)
NBNC	0.03	0.27 (0.852) (0.639-1.136)
Biochemical Factors		
Platelets < 100,000 /mm ³	0.04	0.05 (1.309) (0.998-1.718)
Albumin < 4.0 g/dl	<0.01	<0.01 (1.398) (1.113-1.756)
T-bil ≥ 1.5 mg/dl	0.20	
PT < 80 %	0.13	
ICGR15 ≥ 15 %	<0.01	0.22 (1.081) (0.952-1.229)
AFP ≥ 20 ng/ml	<0.01	0.02 (1.269) (1.027-1.568)

PIVKA-II ≥ 120 mAU/ml	<0.01	0.01 (1.315) (1.048-1.649)
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Surgical Factors

Blood loss ≥ 300 ml	0.05
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Operative time ≥ 300 min	0.64
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Tumor Factors

Tumor size ≥ 5 cm	<0.01	0.03 (1.296) (1.017-1.650)
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Tumor location caudate/non-caudate	0.03	0.01 (1.620) (1.106-2.371)
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Histological Factors

vp	<0.01	0.03 (1.363) (1.024-1.814)
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vv	0.05
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Differentiation poor	<0.01	0.04 (1.302) (1.004-1.688)
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Surgical margin positive	0.13
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Cirrhosis (LF or LC)	<0.01	0.09 (1.206) (0.966-1.504)
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HBs-Ag, HBs-antigen; HCV-Ab, HCV-antibody; T-bil, Total bilirubin; PT, prothrombin time; ICGR15, indocyanine green retention rate at 15 min; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence-II; vp, portal venous invasion; vv, hepatic venous invasion; LF, liver fibrosis; LC, liver cirrhosis.

Table 4. Prognostic factors for survival and recurrence of solitary HCC which tumor size <10 cm in the caudate lobe

Characteristics	Overall Survival		Relapse-free survival	
	Univariate (<i>p</i>)	Multivariate (<i>p</i>) (hazard ratio) (95% CI)	Univariate (<i>p</i>)	Multivariate (<i>p</i>) (hazard ratio) (95% CI)
Epidemiology				
Age ≥ 60	0.60		0.16	
Sex Male	0.09		0.02	0.86 (1.130) (0.269-4.745)
HBs-Ag positive	0.47		0.24	
HCV-Ab positive	0.21		0.62	
NBNC	0.47		0.07	
Biochemical Factors				
Platelets < 100,000 /mm ³	0.47		0.21	
Albumin < 4.0 g/dl	0.42		0.30	
T-bil ≥ 1.5 mg/dl	<0.01	<0.01 (545.103) (11.463-25919.513)	0.01	0.40 (0.471) (0.080-2.759)
PT < 80 %	0.16		0.79	
ICGR15 ≥ 15 %	<0.01	0.32 (0.486) (0.117-2.016)	0.01	0.23 (0.501) (0.160-1.571)
AFP ≥ 20 ng/ml	0.36		0.26	
PIVKA-II ≥120 mAU/ml	0.02	0.52 (0.500) (0.058-4.291)	0.02	0.02 (4.523) (1.197-17.092)

Surgical Factors				
Blood loss $\geq$ 300 ml	0.04	0.38 (0.47) (0.086-2.572)	0.01	0.99 (1.000) (0.190-5.253)
Operative time $\geq$ 300 min	0.90		0.04	0.73 (0.762) (0.162-3.580)
Tumor Factors				
Tumor size $\geq$ 5 cm	0.03	0.02 (5.694) (1.192-27.179)	0.04	0.03 (3.702) (1.127-12.154)
Tumor location Paracaval/Process	0.58		0.82	
Histological Factors				
vp	<0.01	<0.01 (85.527) (5.489-1332.587)	<0.01	<0.01 (7.752) (1.835-32.749)
vv	0.30		0.73	
Differentiation poor	0.51		0.32	
Surgical margin positive	0.29		0.55	
Cirrhosis (LF or LC)	0.04	<0.01 (11.126) (1.971-62.800)	0.04	0.01 (3.906) (1.345-11.342)

HBs-Ag, HBs-antigen; HCV-Ab, HCV-antibody; T-bil, Total bilirubin; PT, prothrombin time; ICGR15, indocyanine green retention rate at 15 min; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence-II; vp, portal venous invasion; vv, hepatic venous invasion; LF, liver fibrosis; LC, liver cirrhosis.

Fig.1.

