Prognostic Impact of Indocyanine Green Plasma Disappearance Rate in Hepatocellular Carcinoma Patients after Radiofrequency Ablation: A Prognostic Nomogram Study

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Abstract

Objective Radiofrequency ablation has been used widely for the local ablation of hepatocellular carcinoma, particularly in its early stages. The study aim was to identify significant prognostic factors and develop a predictive nomogram for patients with hepatocellular carcinoma who have undergone radiofrequency ablation. We also developed the formula to predict the probability of 3- and 5-year overall survival based on clinical variables.

Methods We retrospectively studied 96 consecutive patients with hepatocellular carcinoma who had undergone radiofrequency ablation as a first-line treatment. Independent and significant factors affecting the overall survival were selected using a Cox proportional hazards model, and a prognostic nomogram was developed based on these factors. The predictive accuracy of the nomogram was determined by Harrell’s concordance index and compared with the Cancer of the Liver Italian Program score and Japan Integrated Staging score.

Results A multivariate analysis revealed that age, indocyanine green plasma disappearance rate, and log (des-gamma-carboxy prothrombin) level were independent and significant factors influencing the overall survival. The nomogram was based on these three factors. The mean concordance index of the nomogram was 0.74±0.08, which was significantly better than that of conventional staging systems using the Cancer of the Liver Italian Program score (0.54±0.03) and Japan Integrated Staging score (0.59±0.07).

Conclusion This study suggested that the indocyanine green plasma disappearance rate and age at radiofrequency ablation (RFA) and des-gamma-carboxy-prothrombin (DCP) are good predictors of the prognosis in hepatocellular carcinoma patients after radiofrequency ablation. We successfully developed a nomogram using obtainable variables before treatment.

Key words: hepatocellular carcinoma, indocyanine green plasma disappearance rate, nomogram, radiofrequency ablation, des-gamma-carboxy prothrombin

Introduction

Surgical resection should be the first-line option for patients with solitary hepatocellular carcinoma (HCC) and a well-preserved liver function (1-3); however, only 20% of patients with HCC are candidates for resection due to their tumor stage, liver function, performance status, or comorbidities (4). Radiofrequency ablation (RFA) has recently become the most frequently used treatment option for early-stage HCC and an alternative for patients with HCC who are not eligible for surgical resection (1-3, 5, 6). Shiina et
al. reported estimated 5- and 10-year survival rates for patients undergoing RFA of 60.2% and 27.3%, respectively (7). Several studies have compared the survival prognosis between surgical resection and RFA; Livraghi et al. and Chen et al. reported that, compared with resection, RFA was less invasive and associated with fewer complications (8, 9). Furthermore, Sato et al. reported that the percentages of in-hospital deaths among patients who underwent hepatectomy and RFA were 2.60% and 0.25%, respectively (10). Therefore, RFA is considered the treatment of choice for patients with single HCC.

Many staging systems have been developed to evaluate HCC severity. The Child-Pugh classification has been widely used to evaluate the liver function. Prognostic staging systems for HCC, such as the Cancer of the Liver Italian Program (CLIP) score and the Japan Integrated Staging (JIS) score, reflect the tumor, node, metastasis stage and the Child-Pugh score (11-13). Other staging systems using nomograms have recently been developed to predict the prognosis of patients with HCC (14-17). These nomograms are more sophisticated than those using conventional variables such as the CLIP or JIS score. However, prognostic nomograms for patients who have undergone local ablation therapy for HCC have not been sufficiently established.

This study’s aim was to clarify the significant prognostic factors and construct a predictive nomogram for patients with HCC who have undergone RFA. Predictive outcomes using the herein-described nomogram can be obtained with widely used clinical variables, and its concordance index (c-index) can be determined (18, 19). We also developed an original formula that enables easier and more rapid prediction of the 3- and 5-year overall survival (OS). This nomogram and corresponding formula may be useful for determining a treatment strategy and predicting the prognosis in clinical practice.

Materials and Methods

Patients

At Niigata University Medical and Dental Hospital, 109 patients underwent RFA as first-line treatment from January 2000 to December 2013. We excluded patients who had (i) undergone previous first-line treatments for HCC in other hospitals (n=5), (ii) undergone combined RFA and resection for multiple HCC (n=5), and (iii) been diagnosed with a simultaneous malignant tumor or recurrent tumor (n=3). Thus, the medical records for 96 consecutive patients with HCC were reviewed. All were analyzed in this study. However, the indocyanine green plasma disappearance rate (ICG-PDR) was not obtained for five patients, and the des-gamma-carboxy prothrombin (DCP), also known as protein induced by vitamin K absence of antagonist (PIVKA-II), level was not obtained for two. Therefore, the data of 89 patients were used to develop the nomogram. This retrospective study was approved by the institutional review board of Niigata University Medical and Dental Hospital (number 2041), and informed consent was waived because of the low risk associated with this study. The study protocol conformed to the ethical guidelines of the World Medical Association Declaration of Helsinki (as revised in 2008).

Diagnosis

HCC was diagnosed according to the guidelines of the Japan Society of Hepatology and the European Association for the Study of the Liver. Nodules were diagnosed as HCC requiring treatment based on typical imaging features showing areas of early arterial enhancement and delayed washout in the venous or delayed phases of dynamic computed tomography (CT) or dynamic contrast-enhanced magnetic resonance imaging (MRI) (1, 2, 20). Patients who were not diagnosed with typical HCC by dynamic CT or dynamic MRI underwent contrast-enhanced ultrasonography or CT arteriportography (21). Fifteen patients who could not be diagnosed by these imaging techniques underwent a tumor biopsy, and all were pathologically diagnosed with HCC (2, 22).

Treatment

All nodules diagnosed as HCC were treated by RFA according to the guidelines of the Japan Society of Hepatology. The patients investigated in this study were divided into four groups according to tumor node metastasis (TNM) stages. Stage IV had only one patient, who was a 74-year-old woman with 3 stage IV HCC lesions of a maximum 26 mm diameter and a suspected 8-mm para-aortic lymph node metastasis. Her hepatic reserve was good, and RFA was performed with the objective of controlling the intrahepatic lesions. (Table 1) Thirty-one of the 96 patients in this study underwent transcatheter arterial embolization (TAE) or transcatheter arterial chemoembolization (TACE) before RFA. A 2- or 3-cm Cool-tip needle and the Cool-tip system (Covidien, Mansfield, MA, USA) were used for ablation, ensuring an ablative margin of ≥5 mm. Dynamic CT was conducted within two days of RFA to confirm the absence of an obvious remnant tumor. All blood biochemical, CT, MRI, endoscopy, and ultrasound findings were obtained within three months before RFA.

Data collection

Table 1 shows the patients’ demographic data and preoperative clinical factors. Information on age at the time of RFA, sex, hepatitis B surface antigen status, and hepatitis C virus antibody status were gathered in this study. The presence of esophageal and gastric varices was confirmed by endoscopy. The presence of splenomegaly and the maximum tumor diameter (mm) was confirmed by abdominal ultrasound. The number of tumors and presence or absence of bilateral tumors were also determined by dynamic CT or dynamic MRI. The levels of the tumor markers α-fetoprotein (ng/mL) and DCP (mAU/mL) were measured. The laboratory findings also included the levels of aspartate...
Table 1. Demographics and Clinical Characteristics of Patients with Hepatocellular Carcinoma.

| Variable          | Category | Distribution | %    |
|-------------------|----------|--------------|------|
| Age               | Years    |              | 69.9 (8.8) |
| Sex               |          | Male         | 57   |
|                   |          | Female       | 39   |
| Child-Pugh class  | A        | 86           | 89.6 |
|                   | B        | 10           | 10.4 |
| TNM stage         | I        | 45           | 46.9 |
|                   | II       | 35           | 36.5 |
|                   | III      | 15           | 15.6 |
|                   | IV       | 1            | 1.0  |
| CLIP score        | 0        | 91           | 94.8 |
|                   | 1        | 5            | 5.2  |
| JIS score         | 0        | 38           | 39.6 |
|                   | 1        | 38           | 39.6 |
| HCV antibody      | +        | 80           | 83.3 |
|                   | -        |              |      |
| TAE/TACE          | +        | 65           | 67.7 |
|                   | -        | 31           | 32.3 |
| Gastric varices   | +        | 7            | 7.3  |
|                   | -        | 89           | 92.7 |
| Splenomegaly      | +        | 73           | 76.0 |
|                   | -        | 23           | 24.0 |
| Maximum diameter  | mm       |              | 20.0 (0.78) |
| Number of tumors  | 1        | 69           | 71.9 |
|                   | 2        | 18           | 18.8 |
|                   | 3        | 7            | 7.3  |
|                   | 4        | 2            | 2.1  |
| Main tumor (134)  | S1       | 1            | 0.7  |
|                   | S2       | 6            | 4.5  |
|                   | S3       | 15           | 11.2 |
|                   | S4       | 8            | 6.0  |
|                   | S5       | 29           | 21.6 |
|                   | S6       | 21           | 15.7 |
|                   | S7       | 17           | 12.7 |
|                   | S8       | 37           | 27.6 |
| Bilateral tumors  | +        | 12           | 12.5 |
|                   | -        | 84           | 87.5 |

| Variable          | Category | Distribution | %    |
|-------------------|----------|--------------|------|
| AFP (ng/mL)       |          |              | 14 (0-999) |
| DCP (mAU/mL)      |          | 22 (9-2026)  |
| AST (U/L)         |          | 52 (20-228)  |
| ALT (U/L)         |          | 40 (12-270)  |
| γ-GTP (U/L)       |          | 47 (12-444)  |
| ALP (U/L)         |          | 314 (98-827) |
| LDH (IU/L)        |          | 232 (126-832)|
| ChE (IU/L)        |          | 182 (70.5)   |
| Hb (g/dL)         |          | 12.5 (1.8)   |
| Pt (×10^10/μL)    |          | 100 (35-250) |
| Alb (g/dL)        |          | 3.7 (0.46)   |
| Cre (mg/dL)       |          | 0.7 (0.4-9.9)|
| T-Bil (μL)        |          | 0.9 (0.1-3.7)|
| NH₃ (μg/dL)       |          | 64 (3-164)   |
| PT% (%)           |          | 79 (14)      |
| ICG-PDR (%/min)   |          | 10.1 (2.5-22.0) |

Data are expressed as the median (range) or the mean (standard deviation) unless otherwise indicated.

TNM: tumor node metastasis, CLIP: Cancer of the Liver Italian Program, JIS: Japan Integrated Staging, HBs: hepatitis B surface, HCV: hepatitis C virus, TAE: transcatheter arterial embolization, TACE: transcatheter arterial chemoembolization, AFP: α-fetoprotein, DCP: des-gamma-carboxy prothrombin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GTP: γ-glutamyltransferase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, ChE: cholinesterase, Hb: hemoglobin, Pt: platelet, Alb: albumin, Cre: creatinine, T-Bil: total bilirubin, NH₃: ammonia, PT%: prothrombin activity percentage, ICG-PDR: indocyanine green plasma disappearance rate.

aminotransferase (U/L), alanine aminotransferase (U/L), γ-glutamyltransferase (U/L), alkaline phosphatase (U/L), lactate dehydrogenase (U/L), cholinesterase (U/L), hemoglobin (g/dL), albumin (g/dL), creatinine (mg/dL), total bilirubin (IU/L), and ammonia (μg/dL); platelet count (×10^3/μL); prothrombin activity percentage; and ICG-PDR (%/min). The Child-Pugh class, CLIP score, and JIS score were calculated based on the imaging and laboratory findings.

Statistical analyses

For descriptive statistics, continuous variables are presented as mean ± standard deviation or median (range), and discrete variables are presented as frequency and proportion. Normality of the distributions of continuous variables was tested by the Shapiro-Wilk test. The OS among the groups was stratified by a single factor and estimated by the Kaplan-Meier method. Significant differences were assessed by the log-rank test. In reference to previous studies, continuous variables were converted to binary variables. A Cox proportional hazards regression analysis (Cox analysis) was used to select the significant and independent prognostic factors that significantly affected OS with a forward stepwise regression method. Our nomogram was based on the variables selected by the Cox analysis using the rms package of R version 2.14.1 (19, 23). Nomogram accuracy was measured by Harrell's c-index (18). Bootstraps with 1,000 resamples were used for these activities. Student’s t-test was performed to compare distribution of the c-index of our nomogram with that based on the CLIP and JIS scores (11, 12). All analyses were carried out using SPSS version 20.0 (IBM Corp, Armonk, NY, USA) In all analyses, a p value of <0.05 was considered significant.

Results

Baseline characteristics

Table 1 shows patients’ baseline characteristics. The male and female distribution was 57 (59%) and 39 (41%), respectively, and the mean age at RFA was 69.9±8.8 years. The proportions of tumor, node, metastasis stage I, II, III, and IV tumors were 47%, 37%, 16%, and 1%, respectively, and the positivity rates for hepatitis B surface antigen and hepatitis C virus were 16.7% and 67.7%, respectively. RFA treatment was conducted for 134 tumors in 96 patients. The median maximum diameter was 18.6 (8.0-45.0) mm. With respect to tumor markers, the median α-fetoprotein and DCP levels were 14 (0-909) ng/mL and 22 (9-2026) mAU/mL respectively. The median follow-up period for all 96 patients was 46.8 months (range 1.6-137.9 months).

Overall survival

Fifty deaths were observed during the follow-up period. The estimated 3- and 5-year OS rates were 71.1% and 56.1%, respectively (Fig. 1). Table 2 shows the estimated 1-, 3-, and 5-year OS rates and results of log-rank tests for geo-
Nomograms are widely used to predict the cancer prognosis because of their ability to estimate the probability of an event, such as death, tailored to the profile of an individual patient. They are also often used to obtain patients’ informed consent (24).

Several studies have found that age is an independent risk factor for OS after RFA (7, 25-27). Kao et al. concluded that younger patients with HCC had a better OS and lower recurrence rate after RFA than older patients (27). Our results showed that the OS rate of 54 patients aged ≥70 years was significantly lower than that of 42 patients aged <70 years, and that age was an independent risk factor for OS after RFA (Table 2, 3). However, previous studies have described the efficacy and safety of RFA for elderly patients with HCC (28, 29). Therefore, elderly patients with HCC should be treated according to the same strategy as that used for non-elderly patients.

In this study, log(DCP) was selected as a continuous variable for predicting the prognosis. Takahashi et al. concluded that DCP was the best prognostic predictor post-RFA (30). Hagiwara et al. suggested that HCC frequently infiltrated the portal vein in patients with a DCP level of ≥100 mAU/mL (31). Asaoka et al. reported that DCP level is the most useful predisposing parameter for development of vascular invasion (32). They found that patients with microvascular invasion had a poor prognosis and other treatment strategies should therefore be explored for such patients. In the present study, the OS rate of 11 patients with a DCP level of ≥200 mAU/mL was significantly lower than that of 83 patients at <200 mAU/mL (log-rank test, p=0.001).

**Multivariate analysis**

We performed a Cox analysis with forward stepwise regression in which all variables in the log-rank test in Table 2 were used as prognostic variable candidates. The Cox analysis indicated that age, ICG-PDR, and log(DCP) were independent and significant prognostic factors affecting the OS (Wald test: age, p=0.003; ICG-PDR, p=0.001; log(DCP), p=0.002) (Table 3).

**Nomogram development and validation**

A prognostic nomogram was constructed based on the estimated regression coefficients identified in the Cox analysis and the rms package of R version 2.14.1 (Fig. 2) (17, 18). The c-index of the nomogram was estimated as 0.74±0.08 using 1,000 data sets created by the bootstrap method. The estimated c-index was found to be significantly better than that of conventional staging using the CLIP score (0.54±0.03, p<0.001) and JIS score (0.59±0.07, p<0.001). Fig. 3 illustrates the calibration of this nomogram (Fig. 3). The vertical bars indicate 95% confidence intervals (CIs) on the 1,000 bootstrap analysis, and the dashed line represents the performance of an ideal nomogram. Calibration appears to be accurate for the prediction. The estimated 3- and 5-year OS rates were calculated using the following formula:

\[
\text{3 years OS rate} = (0.803)^{(0.057\times \text{Age} + 0.162\times \text{ICG-PDR} + 0.329\times \text{log(DCP)} - 3.485)}
\]

\[
\text{5 years OS rate} = (0.626)^{(0.057\times \text{Age} + 0.162\times \text{ICG-PDR} + 0.329\times \text{log(DCP)} - 3.485)}
\]

**Discussion**

Nomograms are widely used to predict the cancer prognosis because of their ability to estimate the probability of an
### Table 2. Estimated Survival Rate by Kaplan-Meier and Log-rank Tests.

| Factor (years) | Category | Distribution | Estimated survival rate | 5-y (%) | Log-rank p value |
|---------------|----------|--------------|-------------------------|---------|-----------------|
| Age (years)   | ≥70      | 54           | 93.9                    | 61.4    | 42.7            | 0.004 |
|               | <70      | 42           | 100.0                   | 82.4    | 71.0            |       |
| Sex           | Male     | 57           | 98.1                    | 75.6    | 62.7            | 0.270 |
|               | Female   | 39           | 94.9                    | 65.4    | 47.2            |       |
| Child-Pugh class | A    | 86           | 97.6                    | 73.3    | 58.0            | 0.045 |
|               | B        | 10           | 87.5                    | 50.0    | 37.5            |       |
| TNM Stage     | I, II   | 80           | 96.0                    | 70.2    | 59.8            | 0.255 |
|               | III, IV | 16           | 100.0                   | 75.0    | 43.8            |       |
| CLIP score    | 0       | 91           | 100.0                   | 74.3    | 59.6            | <0.001|
|               | 1       | 5            | 80.0                    | 0.0     | 0.0             |       |
| JIS score     | 0-1     | 76           | 95.8                    | 70.4    | 61.1            | 0.129 |
|               | 2-3     | 20           | 100.0                   | 73.7    | 42.1            |       |
| HBs antigen   | +       | 16           | 93.8                    | 75.0    | 66.7            | 0.044 |
|               | -       | 80           | 97.3                    | 70.1    | 53.6            |       |
| HCV antibody  | +       | 65           | 98.3                    | 72.8    | 55.5            | 0.341 |
|               | -       | 31           | 93.5                    | 67.7    | 56.5            |       |
| TAE/TACE      | +       | 31           | 96.6                    | 85.4    | 59.8            | 0.577 |
|               | -       | 65           | 96.8                    | 64.6    | 54.5            |       |
| Esophageal varices | +     | 20           | 94.7                    | 55.7    | 31.0            | 0.030 |
|               | -       | 76           | 97.2                    | 75.2    | 62.8            |       |
| Gastric varices | +     | 7            | 100.0                   | 57.1    | 42.9            | 0.056 |
|               | -       | 89           | 96.4                    | 72.4    | 57.3            |       |
| Splenomegaly  | +       | 73           | 100.0                   | 60.9    | 56.2            | 0.115 |
|               | -       | 23           | 95.6                    | 74.8    | 55.7            |       |
| Maximal diameter | ≥20 mm | 35           | 97.1                    | 63.3    | 39.7            | 0.016 |
|               | <20 mm  | 61           | 96.5                    | 75.8    | 66.7            |       |
| Number of tumors | 1     | 69           | 95.4                    | 72.2    | 63.8            | 0.125 |
|               | ≥2      | 27           | 100.0                   | 68.4    | 40.2            |       |
| Bilateral tumors | 1     | 12           | 100.0                   | 81.8    | 54.5            | 0.888 |
|               | ≥2      | 84           | 96.3                    | 69.6    | 56.6            |       |
| AFP (ng/mL)   | ≥20     | 40           | 94.9                    | 60.1    | 42.1            | 0.035 |
|               | <20     | 56           | 98.1                    | 79.5    | 67.2            |       |
| DCP (mAU/mL)  | ≥200    | 11           | 90.9                    | 40.4    | 15.2            | 0.002 |
|               | <200    | 83           | 97.5                    | 74.8    | 60.6            |       |
| AST (U/L)     | ≥50     | 51           | 97.9                    | 66.7    | 45.1            | 0.119 |
|               | <50     | 45           | 95.5                    | 75.9    | 67.6            |       |
| ALT (U/L)     | ≥50     | 36           | 97.0                    | 71.0    | 52.0            | 0.937 |
|               | <50     | 60           | 96.6                    | 71.2    | 58.2            |       |
| γ-GTP (U/L)   | ≥50     | 46           | 97.7                    | 72.5    | 60.1            | 0.475 |
|               | <50     | 50           | 95.8                    | 70.0    | 52.6            |       |
| ALP (U/L)     | ≥300    | 52           | 96.0                    | 65.1    | 43.7            | 0.081 |
|               | <300    | 44           | 97.6                    | 79.2    | 72.5            |       |
| LDH (IU/L)    | ≥200    | 62           | 94.8                    | 66.0    | 47.1            | 0.003 |
|               | <200    | 34           | 100.0                   | 80.4    | 72.7            |       |
| ChE (IU/L)    | ≥200    | 33           | 96.9                    | 83.7    | 71.4            | 0.079 |
|               | <200    | 63           | 96.6                    | 64.4    | 47.8            |       |
| Hb (g/dL)     | ≥12.0   | 60           | 96.5                    | 75.8    | 60.6            | 0.021 |
|               | <12.0   | 36           | 97.1                    | 63.2    | 48.3            |       |
| Plt (×10^3/μL) | ≥100   | 61           | 97.1                    | 72.2    | 58.7            | 0.770 |
|               | <100    | 35           | 95.5                    | 68.2    | 49.1            |       |
| Alb (g/dL)    | ≥3.8    | 45           | 95.5                    | 81.1    | 65.1            | 0.297 |
|               | <3.8    | 51           | 97.9                    | 61.3    | 46.8            |       |
| Cre (mg/dL)   | ≥0.7    | 59           | 96.4                    | 66.9    | 52.5            | 0.344 |
|               | <0.7    | 37           | 97.2                    | 77.3    | 61.3            |       |
| T-Bil (IU/L)  | ≥1.0    | 39           | 100.0                   | 62.2    | 50.0            | 0.065 |
|               | <1.0    | 57           | 94.4                    | 78.4    | 61.0            |       |
| NH3 (μg/dL)   | ≥60     | 51           | 97.8                    | 76.0    | 61.2            | 0.383 |
|               | <60     | 45           | 95.5                    | 64.9    | 49.5            |       |
| PT% (%)       | ≥70     | 72           | 97.1                    | 72.2    | 58.7            | 0.077 |
|               | <70     | 24           | 95.5                    | 68.2    | 49.1            |       |
| ICG-PDR (%/min)| ≥10.0 | 46           | 95.5                    | 80.6    | 68.6            | 0.003 |
|               | <10.0   | 45           | 100.0                   | 66.3    | 47.5            |       |

Data are expressed as the median (range) or the mean (standard deviation) unless otherwise indicated.

TNM: tumor node metastasis, CLIP: Cancer of the Liver Italian Program, JIS: Japan Integrated Staging, HBs: hepatitis B surface, HCV: hepatitis C virus, TAE: transcatheter arterial embolization, TACE: transcatheter arterial chemoembolization, AFP: α-fetoprotein, DCP: des-gamma-carboxy prothrombin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GTP: γ-glutamyltranspeptidase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, ChE: cholinesterase, Hb: hemoglobin, Plt: platelet, Alb: albumin, Cre: creatinine, T-Bil: total bilirubin, NH3: ammonia, PT%: prothrombin activity percentage, ICG-PDR: indocyanine green plasma disappearance rate.
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In our nomogram, the ICG-PDR had the longest line, with
PDR as a continuous variable by a Cox analysis (p=0.001).
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Table 3. Multivariate Analysis of Prognostic Factors for Overall Survival.

| Variable          | Estimated regression coefficient | SE  | HR (95%CI)       | p value† |
|-------------------|---------------------------------|-----|-----------------|----------|
| ICG-PDR (%/min)   | -0.162                          | 0.047| 0.850 (0.776-0.932) | 0.001    |
| Age (years)       | 0.057                           | 0.019| 1.059 (1.019-1.100) | 0.003    |
| log (DCP) (mAU/mL)| 0.329                           | 0.108| 1.389 (1.124-1.717) | 0.002    |

SE: standard error of regression coefficient, HR: hazard ratio, CI: confidence interval, ICG-PDR: indocya-
nine green plasma disappearance rate, DCP: des-gamma-carboxy prothrombin
†Wald test

Figure 2. Nomogram predicting the probability of 3-and
5-year overall survival after radiofrequency ablation. Each
point can be determined by drawing a line straight upward
from each predictor to the point axis. Total points can be cal-
culated by summing each point. The probability of 3- and 5-year
overall survival can be found by drawing a line straight down
from the total points axis. ICG-PDR: indocyanine green plasma
disappearance rate, DCP: des-gamma-carboxy prothrombin

Figure 3. The calibration curve of the nomogram predicting
survival rate. The x-axis is the prediction of the nomogram,
and the y-axis is the actual survival probability by the Kaplan-
Meier method.

nosis of patients with HCC. Our study selected the ICG-
PDR as a continuous variable by a Cox analysis (p=0.001).
In our nomogram, the ICG-PDR had the longest line, with
100 points, showing it is the most useful variable for pre-
dicting the prognosis of patients with HCC post-RFA.
Therefore, the ICG-PDR appears to be an extremely impor-
tant factor for determining the treatment strategy, including
recommendations for hepatectomy, and we strongly recom-
mand checking the ICG-PDR before treatment. Kaneko et
al. concluded that an ICG-PDR of ≥ 6.0 in patients under-
going portal resection is valid because of the acceptable mor-
bidity and mortality associated with this criterion (35). We
propose the same criterion (ICG-PDR ≥ 6.0) for RFA.
To our knowledge, this is the first prognostic nomogram
to use ICG-PDR for patients with HCC. Compared with a
regression formula for the precise estimation of survival,
nomograms are more useful in clinical settings because they
provide an easily accessible visual representation of the ap-
proximate estimated rate and the effect of different factors
on survival.

Certain limitations associated with the present study war-
rant mention. This was a single-center retrospective study,
and the method of selecting treatment strategies may have
introduced bias. We evaluated 89 patients, which is fewer
than in previous studies of nomograms for HCC. Because a
limited number of cases were used to develop this nomo-
gram and calculate the c-index, external validation is
needed.

The authors state that they have no Conflict of Interest (COI).

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