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Multivariate Analysis of Prognostic Factors for Survival following Doxorubicin-eluting Bead Transarterial Chemoembolization for Hepatocellular Carcinoma

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Abstract

Purpose: To identify prognostic factors for survival in patients with hepatocellular carcinoma (HCC) treated with transarterial chemoembolization with doxorubicin-eluting beads (DEBs).

Materials and Methods: In a retrospective, single-center analysis, tumor- and patient-related factors were recorded for univariate and multivariate analyses via Kaplan–Meier and Cox regression. Infiltrative HCC phenotype and portal vein invasion (PVI) were correlated, and patients with either or both were classified as having radiographically advanced (RAdv) HCC. The primary endpoint was overall survival, which was calculated from the time of first DEB chemoembolization procedure.

Results: A total of 168 patients underwent 248 procedures, of which 215 (86.7%) were outpatient procedures. Mean length of stay was 0.33 days, and 25 patients (10.1%) were readmitted within 30 days. A total of 33 patients underwent liver transplantation and were excluded from survival analyses. A total of 130 had cirrhosis; 62, 50, and 18 had Child class A, B, and C disease, respectively. Forty-one patients had infiltrative HCC phenotype, 28 of whom also had PVI. Multivariate analysis of survival in all patients showed α -fetoprotein (AFP), performance status (PS), RAdv HCC, Child classification, albumin level, and ascites to predict survival. In patients without RAdv HCC, AFP, PS, Child classification, albumin level, and International Normalized Ratio were independent predictors. Increased bilirubin level was not an independent risk factor for death.

Conclusions: Independent prognostic factors in patients with HCC undergoing DEB chemoembolization have been identified. Increased bilirubin level was not an independent risk factor. These data can be used in HCC patient selection and counseling for DEB chemoembolization.

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None of the other authors have identified a conflict of interest.

Conventional transarterial chemoembolization with lipiodol and doxorubicin (1) or cisplatin (2) is known to prolong survival in certain patients with unresectable hepatocellular carcinoma (HCC), including some with unilateral portal vein invasion (PVI) (2). According to established guidelines, however, patients with Child class B and C cirrhosis and patients with PVI are poor candidates for transarterial chemoembolization (3,4). Transarterial chemoembolization with doxorubicin-eluting beads (DEBs) is a relatively new modality associated with favorable systemic doxorubicin exposure/toxicity and liver-specific toxicity compared to conventional chemoembolization. Studies have documented its safety and efficacy (5,6). DEB chemoembolization also significantly increased objective response compared with conventional chemoembolization in patients with more advanced HCC in a randomized trial (6).

As DEB chemoembolization is becoming more widely practiced, it is important to know which variables independently predict survival and whether conventional chemoembolization limitations are applicable. This information would provide a basis on which evidence-based treatment decisions can be made in multidisciplinary settings. As most patients with HCC in the United States have competing (ie, cirrhosis vs cancer) risks for death, tumor- and patient-related variables are relevant. The aim of the present effort was to identify prognostic factors for survival in a large, single-center cohort of patients with HCC treated with DEB chemoembolization.

MATERIALS AND METHODS

Patients and Variables

Data were collected and reported in accordance with published guidelines (7). This is a retrospective review of patients with HCC referred from the hepatobiliary and liver transplantation services of Piedmont Hospital (Atlanta, Georgia) who underwent chemoembolization procedures with DEBs (LC Bead; Biocompatibles, Farnham, United Kingdom) between March 2006 and February 2011; the end of the study was October 2011. The authors' liver transplantation program began in 2005, and we had limited experience with conventional transarterial chemoembolization before our DEB chemoembolization experience, preventing meaningful comparison of the two procedures at our center. Survival was calculated from the time of first DEB chemoembolization procedure. Investigational review board approval was obtained.

HCC was confirmed based on American Association for the Study of Liver Diseases criteria (4) and/or biopsy. Patient-related data collected included age, race, sex, Eastern Cooperative Oncology Group (ECOG) performance status (PS) (8), clinically apparent ascites, hepatic encephalopathy, complete blood count, International Normalized Ratio (INR), and serum levels of creatinine, total bilirubin, and albumin. Child classification and Child–Turcotte–Pugh (CTP) and Model for End-stage Liver Disease (MELD) scores were calculated. Tumor-related data collected included pretreatment α -fetoprotein (AFP) levels, discrete/measurable lesion(s) versus infiltrative HCC phenotype (ie, no discrete border between lesions[s] and hepatic parenchyma), PVI on cross-sectional contrast-enhanced imaging, and maximum tumor diameter. PVI was defined as tumor-related invasion of the left or right main portal vein or a primary branch; thrombosis of the main portal vein or any branch not

contiguous with the tumor was not classified as PVI. In patients with multifocal HCC, the largest tumor diameter was used in analyses. Infiltrative HCC phenotype and/or PVI in a patient undergoing DEB chemoembolization were classified as representing “radiographically advanced” (RAdv) HCC, which was included as a single variable in the analyses because of increased statistical significance of this composite variable (as detailed later); moreover, as most patients with PVI had infiltrative HCC and vice versa, doing so reduced the risk of diluting one’s effect by the other (ie, multi- collinearity). In addition, patients without RAdv HCC were analyzed separately.

Before undergoing DEB chemoembolization, all patients were presented at a multidisciplinary hepatobiliary tumor board and deemed to have unresectable disease by experienced hepatobiliary surgeons. Unilateral PVI alone in an otherwise appropriate surgical candidate (ie, Child class A disease, no biochemical or radiographic evidence of portal hypertension, ECOG PS of 0, noninfiltrative HCC) was not a contraindication to resection.

For patients with multiple lesions, treatment planning was based on intrahepatic tumor burden, proximity of lesions, and perceived hepatic reserve (based on CTP score); eg, a patient with Child B cirrhosis with bilateral disease would be counseled that lesions in each hemiliver would be treated sequentially and not in one setting. Per our standard practice, follow-up consisted of triple-phase cross-sectional imaging and appropriate laboratory assessment 30 days after DEB chemoembolization in all surviving patients; patients in whom imaging was believed to show residual viable tumor and who had tolerated the previous procedure(s) were treated again. Laboratory and radiographic assessment were repeated at 90-day intervals. Imaging studies before and after treatment were reviewed at a multidisciplinary hepatobiliary tumor board. New lesions and lesions deemed to have persistent viable tumor (based on nodular arterial hyperenhancement with venous washout) underwent subsequent DEB chemoembolization. Follow-up of patients treated multiple times was the same as outlined earlier.

Patients were not excluded from DEB chemoembolization based solely on segmental PVI, Child B or C disease classification or ECOG PS greater than 1, all contraindications to chemoembolization according to American Association for the Study of Liver Diseases (4), or the Barcelona Clinic Liver Cancer (BCLC) staging/treatment algorithm (3).

Readmission within 30 days of the procedure and the reason for admission were recorded. Postembolization syndrome was defined as nausea/vomiting, fever, leukocytosis, and/or otherwise unexplained abdominal pain (7).

Treatment

All patients were treated with doxorubicin-containing LC Bead particles (Biocompatibles) that were 100–300 μ m and/or 300–500 μ m in diameter. The sizes varied in the same patient in separate procedures, preventing meaningful analysis of the effect of bead size on outcome.

Patients received sedation with intravenous midazolam, fentanyl, and hydromorphone. All procedures were performed by using common femoral artery access; pretreatment celiac and superior mesenteric arteriography was obtained through 4–5-F diagnostic catheters. Infusions were performed through a 0.027-inch microcatheter advanced coaxially into the tumor feeding vessel(s) under fluoroscopic guidance. Doxorubicin (150 mg) was prepared, and each vial's contents were resuspended in contrast agent–containing diluent to create a final administration volume of 20 mL. Subsequent infusion was performed at approximately 1–3-mL solutions per minute under fluoroscopic observation until the treatment endpoint (stasis or near-stasis in first- or second-order tumor-feeding vessels or complete administration of the beads) was reached, followed by completion angiography. Two patients participating in a clinical trial received “lobar” infusions as directed by the trial protocol; otherwise, all infusions were into segmental or higher-order arteries.

In the recovery area, patients were given as-needed analgesic and antiemetic medications and intravenous hydration for 2–6 hours and then assessed to determine if discharge or admission were appropriate based on need for pain and/or nausea control. A 6–12-day course of oral prednisone (5 mg) and as-needed oral acetaminophen/hydrocodone (325 mg/5 mg) and promethazine (25 mg) suppositories were prescribed.

Statistical Analyses

Statistical analyses were performed with Stata (version 11.2; Stata, College Station, Texas). All laboratory values and other patient characteristics used in the analyses were those that existed at first treatment. Univariate survival analyses were done by using the Kaplan–Meier method for categorical variables and Cox regression for continuous variables; multivariate analyses were done by using Cox regression. Variables with a *P* value $\leq .10$ on univariate analysis were included in multivariate analyses. Statistical significance was defined by a *P* value $\leq .05$. Total bilirubin level, hereafter referred to as bilirubin level, was analyzed as a continuous variable and also categorized as less than 1.0, 1.5, 2.0, 3.0, 3.5, and 4.0 mg dL⁻¹ to identify any significant threshold(s). AFP was analyzed as a categorical value with cutoff levels of greater than 9.0 (upper limit of normal in our laboratory), 50, 100, 200, 300, 400, 500, and 1,000 ng mL⁻¹. All other numerical laboratory values (eg, albumin, INR) were analyzed as continuous variables. Child classification was analyzed as a composite variable in Cox regression modeling, and the individual laboratory and clinical components of Child classification were analyzed in separate models to minimize the impact of multicollinearity. Where appropriate, means are given $\pm$ standard deviation; each hazard ratio (HR) is accompanied by the corresponding 95% confidence interval (CI).

RESULTS

A total of 168 patients underwent DEB chemoembolization treatment for HCC. Thirty-three underwent liver transplantation and were excluded from survival analyses, as their procedures were as a “bridge” to transplantation and not as definitive HCC therapy. Liver transplantation in these patients was performed a mean of 159.4 days $\pm$ 193.7 after DEB chemoembolization; one patient who was being treated as a bridge to transplantation died of spontaneous bacterial peritonitis on postprocedure day 17 and was included in survival

analyses. This patient and the other 134 patients underwent 248 DEB chemoembolization procedures (mean, 1.91 procedures per patient). Patient characteristics are listed in Table 1 (overall population) and Table 2 (those with cirrhosis). Of the four patients with bilirubin levels of more than 4.0 mg dL⁻¹ (Table 1), the values were 5.8, 6.1, 10.8, and 18.1 mg dL⁻¹; the respective intervals to death were 1,091, 415, 15, and 40 days.

Mean length of stay was 0.33 days $\pm$ 1.31 (range, 0–14 d). Patients were discharged home on the day of the procedure for 215 of 248 procedures (86.7%); discharge was on postprocedure day 1 for 120 procedures (8.1%), day 2 for three procedures, day 3 for five procedures, days 5 and 8 for two procedures each, and day 14 for one procedure. There were 25 (10.1%) hospital admissions within 30 days related to the procedure for postembolization syndrome (n 11), encephalopathy (n 5), gastrointestinal bleeding (n 4), spontaneous bacterial peritonitis (n 3), gastric ulceration in a patient with a replaced left hepatic artery (n 1), and pancreatitis (n 1). Death occurred within 30 days of 10 of 248 procedures (4.0%) and resulted from complications of cirrhosis/portal hypertension (n 7), pneumonia (n 1), and unknown causes (n 2). Unadjusted survival is shown in Figure 1; 86 patients (63.7%) were dead at the end of the study.

Most patients with PVI had infiltrative HCC, and vice versa. Forty-one patients had infiltrative HCC, including 28 with PVI; 11 patients had PVI without infiltrative HCC. Therefore, 39 patients had PVI, and a total of 52 patients were classified as having RAdv HCC. One of the earliest patients seen during the study period (fifth overall) had Child class B cirrhosis (CTP score of 7), PVI, and infiltrative HCC; tolerated three DEB chemoembolization procedures without complication; and survived 1,190 days. Another patient, who was also receiving sorafenib, with Child class A cirrhosis, PVI, and infiltrative HCC, tolerated seven procedures without complication and survived 579 days.

Survival Analyses

Overall.—On univariate analysis, the following characteristics were significantly associated with survival: all AFP categories, including abnormal AFP (ie, 4–9 ng · mL⁻¹, the upper limit of normal; $P = .0009$; Fig 2) and AFP level greater than 1,000 ng mL⁻¹ ($P = .0001$); infiltrative HCC ($P = .0001$); PVI ($P = .0003$); RAdv HCC ($P = .0001$; Fig 3); albumin level ($P = .0001$); ascites ($P = .0002$); encephalopathy ($P = .001$); INR ($P = .0001$); ECOG PS ($P = .0001$); multifocal HCC ($P = .0005$); MELD score greater than 10 ($P = .008$); and Child class ($P = .0001$; Fig 4a). Bilirubin as a continuous variable and categorized as greater than 1.5 mg dL⁻¹ ($P = .017$) and greater than 2.0 mg dL⁻¹ ($P = .037$; Fig 5a) was also significant on univariate analysis; no other bilirubin category was significant, which did not change after eliminating those with bilirubin levels greater than 4.0 mg dL⁻¹. Additionally, for those with measurable lesion(s) (ie, not infiltrative), a largest tumor size of more than 5.0 cm was not significantly associated with survival ($P = .32$), nor was it significant as a continuous variable ($P = .06$).

Of all individual variables analyzed, infiltrative HCC phenotype had the highest predictive value (w2 test statistic, 24.15) on univariate analysis, almost twice the test statistic for the next highest, PVI (w2 test statistic, 12.92); combining infiltrative HCC and PVI into RAdv

HCC yielded an w_2 test statistic of 30.29. The median survival durations for those with and without RAdv HCC were 176 and 640 days, respectively (Fig 3).

Multivariate analysis of all patients showed AFP levels greater than 9 ng mL⁻¹ (HR, 2.3 [95% CI, 1.2–4.3]), ECOG PS greater than 0 (HR, 2.1 [95% CI, 1.3–3.4]), RAdv HCC, (HR, 1.7 [95% CI, 1.0–2.7]), and Child class to be independent predictors of death; the HRs for Child class B and C disease were 2.3 (95% CI, 1.4–3.9) and 5.7 (95% CI, 3.0–11.1), respectively (Table 3). MELD score greater than 10 was not independently significant. We replaced Child class with its five individual components in an otherwise identical Cox regression model, and albumin level (HR, 0.5 [95% CI, 0.3–0.7]) and ascites (HR, 1.9 [95% CI, 1.2–3.0]) were the only significant variables on multivariate analysis (Table 3). Bilirubin as a continuous variable (HR, 1.0 [95% CI, 0.9–1.1]), and all categoric levels, was not; as earlier, eliminating patients with bilirubin levels greater than 4.0 mg dL⁻¹ had no meaningful impact on this. Encephalopathy (HR, 1.0 [95% CI, 0.6–2.0]) and INR (HR, 1.0 [95% CI, 0.4–2.8]) were also not statistically significant.

Patients without RAdv HCC.—It was believed to be relevant to separately investigate prognostic factors in those without PVI and/or infiltrative HCC (n 83), as DEB chemoembolization perhaps should be restricted to this group. In these patients, ECOG PS ($P=1/4$.0002), ascites ($P=1/4$.004), all AFP categoric levels, albumin level ($P=0$.0001), INR ($P=0$.0001), multifocal HCC ($P=0$.046), MELD score greater than 10 ($P=0$.045), and Child class ($P=0$.0001) were significantly associated with survival on univariate analyses. Bilirubin was not; Figure 5b shows the survival curves in those with bilirubin levels greater than 2.0 mg dL⁻¹ versus 2.0 mg dL or lower.

On multivariate analysis in those without RAdv HCC, ECOG PS greater than 0 (HR, 2.6 [95% CI, 1.3–5.3]), AFP (for AFP 4–9 ng mL⁻¹, HR, 2.3 [95% CI, 1.3–6.7]), and

Analyzing the individual components of Child class in the Cox model with AFP level greater than 200 ng mL⁻¹ showed albumin (HR, 0.4 [95% CI, 0.3–0.7]) and INR (HR, 21.5 [95% CI, 3.2–146.2]) as the only significant Child class variables. Ascites (HR, 0.8 [95% CI, 0.3–2.0]) and encephalopathy (HR, 0.8 [95% CI, 0.3–2.2]) were not independently significant. Interestingly, the HR in this multivariate analysis for bilirubin was 0.64 (95% CI, 0.4–0.9), indicating a lower chance of death with increasing bilirubin. However, in univariate analysis, as a continuous variable, bilirubin was not significant (HR, 0.98 [95% CI, 0.7–1.4]); moreover, none of the categoric levels of bilirubin were significant by Kaplan–Meier analysis.

DISCUSSION

The increasing incidence of cirrhosis and HCC mandate ongoing efforts to refine and expand the array of treatment options for HCC. Liver transplantation and surgical resection are potentially curative but limited to a minority of patients. DEB chemoembolization is becoming more widely practiced, as the HCC incidence is increasing (9–11) and initial clinical trial results were promising (5,6). Because most patients with HCC in the United States have cirrhosis and are at significant risk of non-tumor-related death, non-tumor-

related variables are important to include in survival analyses. Such variables associated with outcomes after conventional transarterial chemoembolization have been reported (12–17). As the role of DEB chemoembolization is expanding, it is important that we understand the pretreatment factors associated with survival following DEB chemoembolization, and whether the same prognostic factors associated with conventional chemoembolization apply—especially given one study’s finding of a potentially superior side-effect profile of DEB chemoembolization and better objective response rate in patients with more advanced disease states, defined as Child class B cirrhosis, ECOG PS of 1, disease in both hemilivers, or recurrent disease (6). Overall differences in response rate in that study, however, were not statistically significant ($P=.11$); a difference in survival between conventional and DEB chemoembolization was not assessed (6). Others have also not found significant differences in tumor response rates and survival upon prospectively comparing conventional versus DEB chemoembolization (18).

Generally, risk factors for death in the patients in the present study were similar to those reported for conventional chemoembolization: worse survival is associated with more advanced tumor characteristics and liver dysfunction. Specifically, our data show the independent significance of several variables, including AFP, ECOG PS, and Child class; infiltrative HCC phenotype and PVI were the two most predictive of death. Combining these two variables into a single category, RAdv HCC, resulted in stronger and independent statistical association with outcome. Bilirubin level, a frequently used value in determining advisability of DEB chemoembolization, had no practical prognostic value on multivariate analyses, had little univariate association with survival in the overall cohort, and had no univariate association with survival in the group without RAdv HCC. This is in contrast to a retrospective univariate analysis (19). A more recent multivariate analysis of prognostic factors for survival after conventional chemoembolization in 362 patients (15) did not specifically evaluate bilirubin but showed similar independent risk factors to ours: Child class, PVI, and AFP; tumor size and multiple tumors were independent predictors of death in their cohort (15). Multifocal disease was significant in our population on univariate analysis, and tumor size as a continuous variable trended toward significance, but both lost significance after controlling for other factors.

As other variables did have independent significance, our data suggest it is reasonable to not use bilirubin level as a sole factor in determining DEB chemoembolization candidacy. Rather, albumin level and ascites had better and more practical predictive value overall, where as albumin level and INR were more predictive in those without RAdv HCC. Our patients with bilirubin levels greater than 4.0 mg dL⁻¹ and short survival times had other significant prognostic factors, possibly explaining the lack of independent significance of bilirubin when controlling for those factors. Child class, which incorporates multiple variables and better signifies overall functional hepatic reserve, was independently significant in both cohorts, and therefore appears more useful than its individual variables. Additionally, Child class was more predictive in our population than MELD score, and it has also been shown in one study (20) to be superior to MELD score in predicting survival after conventional chemoembolization; similar to our data, these authors showed albumin to be the Child classification variable most predictive of survival after conventional chemoembolization (20). An experience with 172 patients (16) included World Health

Organization radio- graphic criteria in a Cox model and found observation of a response per these criteria, PVI, extrahepatic metastases, and AFP to independently predict survival; Child class did not have independent prognostic significance (16).

In the patients in the present review who did not have RAdv HCC, we found that AFP, ECOG PS, and Child class remained independent predictors of survival. It is interesting that all AFP cutoff levels were independently significant, including AFP level greater than 9 ng mL⁻¹, the upper limit of normal. This is at least somewhat attributable to the high impact of those with AFP levels of more than 400 ng mL⁻¹, as eliminating this subgroup rendered AFP levels greater than 9 ng mL⁻¹ statistically insignificant on univariate and multivariate analyses. AFP levels greater than 200 ng mL⁻¹, however, remained an important threshold, as this level did independently predict outcome in those patients who had AFP levels lower than 400 ng mL⁻¹.

It is important to note that our RAdv HCC cohort is not identical to the “advanced-stage” subgroup in the BCLC classification (ie, BCLC stage C) (3), as our composite variable is tumor-related only and therefore does not incorporate ECOG PS or Child class. Additionally, the BCLC staging system does not directly account for infiltrative HCC phenotype. As such, our data with respect to RAdv HCC do not pertain to advanced disease in staging systems that incorporate patient-related variables, including BCLC, and we are not proposing an additional variable to consider in the field of HCC research. However, given the statistical magnitude of its association with outcome in our population (Table 3, Fig 3), we believed it worthy of being included in our report, and it seems reasonable to use this variable in treatment decision-making. These patients did significantly worse (Fig 3), and our data suggest that they might be better served with other therapeutic options, or perhaps even observation on a case-by-case basis.

Patients with Child class B/C cirrhosis undergoing DEB chemoembolization should be counseled as to their increased risk of death. Our data suggest that Child class B/C cirrhosis may not be an absolute contraindication to chemoembolization but should be balanced against these patients’ perceived tumor-related risk of death, and we incorporate it in treatment planning; eg, multiple and/or bilateral tumors are treated sequentially, and as super- selectively as feasible, rather than simultaneously. It is also sensible to incorporate liver transplantation candidacy in treatment planning. Our data indicate that a person with Child class C cirrhosis who is not a transplantation candidate would derive little benefit by undergoing DEB chemoembolization (Fig 4); again, other treatment options may be considered. Alternatively, if a patient with Child class B or C cirrhosis who is a transplantation candidate needs effective tumor control while waiting, the risk/benefit analysis may favor DEB chemoembolization.

The present study is retrospective and has limitations. Selection bias undoubtedly exists, as we do not present data on patients referred for DEB chemoembolization who were denied the treatment. It is also possible that our patient selection changed over time, given the lack of rigid inclusion criteria from the beginning. Our early successes in patients with poor prognostic factors (eg, Child class B disease, PVI, infiltrative HCC) perhaps created a willingness to continue to treat patients with these traits. We did not question this until we

undertook the objective analysis of our data for the present report, and therefore do not think our selection criteria became significantly more restrictive during the study period; as a result of our data, however, we are now more restrictive, especially with patients with Child class B/C disease and those with PVI and/or infiltrative HCC. Additionally, the data presented are from a single center and are observational only, and therefore we are not able to firmly state which factors are most important in terms of patient selection for other centers.

In summary, our data show that prognostic factors for survival following DEB chemoembolization are similar to those reported for conventional chemoembolization. Our experience confirms that, even though DEB chemoembolization can be performed safely in the outpatient setting in patients with HCC, patient survival is often limited by non-tumor-related (eg, Child classification, ECOG PS) and tumor-related (eg, AFP level, PVI, infiltrative phenotype) factors; and DEB chemoembolization may not provide the benefit we anticipated in our early experience. With the increasing incidence of HCC, however, continued growth in the number of patients appropriately undergoing DEB chemoembolization is expected. Child classification is seemingly superior to its individual variables in predicting survival in these patients.

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ABBREVIATIONS

AFP	a-fetoprotein
BCLC	Barcelona Clinic Liver Cancer
CI	confidence interval
CTP	Child–Turcotte–Pugh
DEB	doxorubicin-eluting bead
ECOG	Eastern Cooperative Oncology Group
HCC	hepatocellular carcinoma
HR	hazard ratio
INR	International Normalized Ratio
MELD	Model for End-stage Liver Disease
PS	performance status
PVI	portal vein invasion
RAdv	radiographically advanced

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Figure 1.
Overall survival.

Figure 2.
Survival in all patients by a-fetoprotein (AFP) $4.9 \text{ ng} \times \text{mL}^{-1}$, the upper limit of normal.

Figure 3. Survival in all patients by radiographically advanced (RAdv) hepatocellular carcinoma (HCC).

Figure 4. Survival by Child class in all patients (a) and in only those without radiographically advanced (RADv) hepatocellular carcinoma (HCC) (b).

Figure 5. Survival by total bilirubin in all patients (a) and in only those without radiographically advanced (RADv) hepatocellular carcinoma (HCC) (b).

Table 1 .

Patient Characteristics: Overall (N 1/4 135)

Characteristic	Value
Male sex	105 (77.8)
Cirrhosis	130 (96.3)
DEB chemoembolization procedures	
1	67 (49.6)
2	38 (28.1)
3	20 (14.8)
4	7 (5.2)
5	2 (1.5)
7	1 (0.7)
Total bilirubin	
o 1.0 mg · dL ⁻¹	45 (33.3)
1.0–1.9 mg · dL ⁻¹	60 (44.4)
2.0–3.0 mg · dL ⁻¹	21 (15.6)
3.1–4.0 mg · dL ⁻¹	5 (3.7)
4 4.0 mg · dL ⁻¹	4 (3.0)
Albumin	
4 3.5 mg · dL ⁻¹	24 (17.8)
2.8–3.5 mg · dL ⁻¹	67 (49.6)
o 2.8 mg · dL ⁻¹	44 (32.6)
INR	
o 1.7	127 (94.1)
1.7–2.3	8 (5.9)
4 2.3	0
AFP	
o 9 ng · mL ⁻¹ (ULN)	37 (27.4)
9.1–200 ng · mL ⁻¹	43 (31.9)
201–400 ng · mL ⁻¹	8 (5.9)
401–1,000 ng · mL ⁻¹	9 (6.7)
4 1,000 ng · mL ⁻¹	38 (28.2)
ECOG PS	
0	86 (63.7)
1	38 (28.1)
2	11 (8.1)
Infiltrative HCC	41 (30.3)
Segmental PVI	39 (28.9)
“Advanced HCC”	52 (38.5)
Largest tumor 4 5.0 cm ⁿ	29 (30.9)

Values in parentheses are percentages. DEB 1/4 doxorubicin- eluting bead, ECOG 1/4 Eastern Cooperative Oncology Group, HCC 1/4 hepatocellular carcinoma, INR 1/4 International Normal- ized Ratio, PS 1/4 performance status, PVI 1/4 portal vein invasion, ULN 1/4 upper limit of normal.

ⁿExcluding those with infiltrative HCC (n 1/4 94).

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Table 2 .

Patient Characteristics: Patients with Cirrhosis (n 1/4 130)

Characteristic	Value
Etiology of liver disease	
Hepatitis C	76 (58.5) ⁿ
Hepatitis B	17 (13.10)
Alcohol	16 (12.3)
Nonalcoholic fatty liver disease	10 (7.7)
Other	4 (3.0)
Child classification	
A	62 (47.7)
B	50 (38.5)
C	18 (13.9)
Total bilirubin	
o 1.0 mg · dL ⁻¹	41 (31.5)
1.0–1.9 mg · dL ⁻¹	60 (46.2)
2.0–3.0 mg · dL ⁻¹	20 (15.4)
3.1–4.0 mg · dL ⁻¹	5 (3.9)
4 4.0 mg · dL ⁻¹	4 (3.1)
Albumin	
4 3.5 mg · dL ⁻¹	21 (16.1)
2.8–3.5 mg · dL ⁻¹	65 (50.0)
2.8 mg · dL ⁻¹	44 (33.9)
INR	
o 1.7	122 (93.9)
1.7–2.3	8 (6.2)
4 2.3	0
AFP	
o 9 ng · mL ⁻¹ (ULN)	34 (26.2)
9.1–200 ng · mL ⁻¹	43 (33.1)
201–400 ng · mL ⁻¹	8 (6.2)
401–1,000 ng · mL ⁻¹	9 (6.9)
4 1,000 ng · mL ⁻¹	36 (27.7)
ECOG PS	
0	84 (64.6)
1	35 (26.9)
2	11 (8.5)

AFP 1/4 a-fetoprotein, ECOG 1/4 Eastern Cooperative Oncology Group, INR 1/4 International Normalized Ratio, PS 1/4 performance status, ULN upper limit of normal.

ⁿNine patients also had abused alcohol.

Table 3 .

HRs of Independently Significant Variables in All Patients

Variable	HR (95% CI)	P Value
Advanced HCC	1.7 (1.0–2.7)	.045
ECOG PS 4 0	2.1 (1.3–3.4)	.001
AFP 4 9 ng · mL ⁻¹	2.3 (1.2–4.3)	.008
Child class		
A	Reference	–
B	2.3 (1.4–3.9)	.001
C	5.7 (3.0–11.1)	o.0001
Albumin ⁿ	0.5 (0.3–0.7)	.0001
Ascites ⁿ	1.9 (1.2–3.0)	.01

AFP 1/4 a-fetoprotein, CI 1/4 confidence interval, ECOG 1/4 East- ern Cooperative Oncology Group, HCC 1/4 hepatocellular carcinoma, HR 1/4 hazard ratio, PS 1/4 performance status.

ⁿ Analyzed separately from Child classification.

Table 4 .

HRs of Independently Significant in Patients without Advanced HCC

Variable	HR (95% CI)	P Value
ECOG PS 4 0	2.8 (1.4–5.6)	.003
AFP 4 9 ng · mL ⁻¹	2.3 (1.3–6.7)	.0096
Child class		
A	Reference	–
B	2.3 (1.1–4.8)	.031
C	6.9 (1.3–20.3)	.0005
Albumin ⁿ	0.4 (0.3–0.7)	.02
INR ⁿ	21.5 (3.2–146.2)	.002

AFP 1/4 a-fetoprotein, CI 1/4 confidence interval, ECOG 1/4 East- ern Cooperative Oncology Group, HCC 1/4 hepatocellular carcinoma, HR 1/4 hazard ratio, INR 1/4 International Normalized Ratio, PS performance status.

ⁿ Analyzed separately from Child classification.