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ORIGINAL RESEARCH

Extent of Embolization as an Independent Prognostic Factor in Superselective Conventional Transarterial Chemoembolization for Hepatocellular Carcinoma

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Purpose: Superselective conventional transarterial chemoembolization (ss-cTACE) guided by angiography–multidetector CT (AMDCT) improves feeder detection but can broaden the treated territory and compromise hepatic reserve. We asked whether restricting the embolized area to <1 Couinaud sector-equivalent is associated with better prognosis in treatment-naïve hepatocellular carcinoma (HCC). Our primary estimand was the covariate-adjusted hazard ratio (HR) comparing extended (≥1 sector-equivalent) vs limited (<1 sector-equivalent) embolization.

Patients and Methods: We conducted a single-center retrospective cohort including 195 consecutive patients with newly diagnosed HCC who underwent initial ss-cTACE/AMDCT (2010-10-01 to 2023-08-31; median age 75 years). Post-procedural imaging classified patients as Group L (<1 sector-equivalent; n=136) or Group E (≥1; n=59). Endpoints were progression-free survival (PFS) and overall survival (OS); liver-related death was modeled with cause-specific hazards. Multivariable Cox models were prespecified as primary, with propensity-score overlap weighting as a complementary sensitivity analysis; short-term hepatic safety was assessed by post-TACE ALBI within 1 month.

Results: Compared with Group L, Group E showed shorter PFS (median 7 vs 12 months; aHR 1.7, 95% CI 1.1–2.5; p =.01) and OS (median 21 vs 33 months; aHR 2.1, 95% CI 1.2–3.5; p =.003). Short-term hepatic safety did not differ: the post-TACE ALBI score assessed within 1 month was similar between groups (−2.1 ± 0.4 vs −2.0 ± 0.4; p =.16). In Group L, liver-related survival exceeded OS (113 vs 57 months; p =.01). Adjusted analyses confirmed embolization extent as an independent prognostic factor beyond stage, tumor burden, location, and liver function (PFS aHR 1.7; OS aHR 2.1). Among Group L decedents, HBV/HCV was independently associated with liver-related death (OR 6.9, 95% CI 1.8–34; p =0.009).

Conclusion: During initial ss-cTACE/AMDCT, restricting embolization to <1 sector-equivalent was associated with longer PFS/OS and fewer liver-related deaths, supporting treatment planning that minimizes ischemic parenchymal injury, particularly in older or vulnerable patients.

Plain Language Summary: Transarterial chemoembolization (TACE) treats liver cancer (HCC) by blocking blood flow to the tumor. Using a combined angiography–CT system (AMDCT), doctors can find very small feeding arteries and target them precisely. However, when many tiny branches are involved, the treated area can unintentionally become wide and may harm healthy liver tissue. We reviewed 195 patients who received their first TACE at our hospital. After treatment, we grouped patients by how much of the liver was embolized: less than one anatomical sector (limited) or one sector or more (extended). Patients in the limited group lived longer without needing further treatment and lived longer overall than those in the extended group. They also had fewer deaths caused by liver problems, suggesting that preserving liver reserve is crucial for long-term outcomes. These findings were confirmed using additional statistical checks designed to make fairer comparisons between the two groups. Importantly, short-term liver function measured about a month after TACE was not worse in the limited group.

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What does this mean? For many patients—especially older adults or those with fragile liver function—planning TACE to keep the treated area as small as reasonably possible may lower the chance of liver-related complications and help patients live longer. These results support careful, territory-sparing strategies when technically feasible.

Keywords: hepatocellular carcinoma, transarterial chemoembolization, angiography–MDCT, embolization extent, survival, propensity score, cause-specific hazard

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Introduction

Transarterial chemoembolization (TACE) is generally recommended for Barcelona Clinic Liver Cancer (BCLC) stage B (intermediate-stage) hepatocellular carcinoma (HCC), though it can be considered in selected advanced-stages or for patients ineligible for surgery or radiofrequency ablation (RFA).[1,2] Conventional TACE (cTACE) has become the standard treatment technique for HCC in many treatment algorithms.[3–7] In cTACE, lipiodol (iodized oil) plays an important role as a potent embolic material for microvasculature, including not only tumor-feeding arteries and tumor blood sinusoids but also hepatic arteries, portal venules, and hepatic sinusoids in the surrounding liver, when followed by particulate emboli such as gelfoam particles.[3–6]

From a clinical standpoint, unintended embolization of a broad parenchymal territory may accelerate chronic deterioration of hepatic reserve and limit eligibility for subsequent systemic or locoregional therapies. Prior studies have largely contrasted lobar versus superselective TACE techniques or focused on imaging guidance platforms, but few have explicitly quantified the embolized territory itself as a prognostic factor under AMDCT-guided superselective cTACE. A territory-sparing strategy that confines embolization to the smallest feasible vascular unit could therefore be particularly important in older patients and those with marginal hepatic reserve.

Although the utility of AMDCT in identifying tumor feeders is well established,[8] its impact on clinical outcomes when managing multiple subsegmental branches remains unclear. Therefore, this study retrospectively evaluated whether restricting the extent of embolization during ss-cTACE/AMDCT is associated with better prognosis in patients undergoing initial treatment for HCC. In this study, the primary estimand is a covariate-adjusted hazard ratio for the association between the achieved embolization extent—quantified post-procedurally as sector-equivalent (Group L <1 vs Group E ≥ 1)—and prognosis under AMDCT-guided ss-cTACE. Accordingly, we adopt multivariable Cox models as the main analysis, viewing propensity-based methods and balancing weights as complementary sensitivity tools rather than mandatory replacements.[9–11]

Materials and Methods

Participants and Study Design

This retrospective cohort design was selected as the most feasible and clinically appropriate approach to assess the prognostic association of the achieved embolization extent under AMDCT guidance in real-world practice. The Institutional Review Board of Kanazawa University approved this retrospective cohort study (approval number: 114488–1; date of approval: March 13, 2024) and waived the requirement for written informed consent because of the retrospective design, the exclusive use of data generated during routine clinical care, and the minimal risk to participants. All data were anonymized before analysis, and no identifiable personal information was included in the dataset. The study was conducted outside the United States; therefore, HIPAA compliance was not applicable. All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments. This patient cohort has not been previously reported. Between October 1, 2010, and August 31, 2023, we reviewed medical records of patients initially treated with TACE for newly diagnosed HCC at our institution. Patients were eligible if they underwent ss-cTACE/AMDCT as the first-line treatment. Patients were excluded if they received TACE techniques other than ss-cTACE/AMDCT (eg, drug-eluting bead TACE or TACE using alternative anticancer agents),[12] underwent preoperative ss-cTACE, had BCLC stage C or D disease, or lacked adequate hepatic imaging or clinical data. The detailed patient selection process and the number of exclusions are described in the Results section.

Treatment Strategy and Indication for TACE

At our institution, treatment selection for HCC is made by a multidisciplinary board in accordance with the BCLC guidelines. When surgical resection or stand-alone radiofrequency ablation (RFA) is technically unfeasible, the board preferentially opts for super-selective conventional TACE (ss-cTACE), often followed by RFA; however, the final plan may be modified to respect patient preferences. Further details are provided in the Supplemental Material and Methods.

Ss-cTACE Procedure Under AMDCT Guidance

Digital subtraction arteriography and CT during hepatic arteriography (CTHA) were performed for the precise detection and final diagnosis of HCC, as previously reported.[13] In principle, the microcatheter was advanced to the subsegmental (or more distal) level for each tumor feeder to achieve a superselective approach while minimizing healthy parenchymal damage. When anatomically necessary, protective embolization was used only to prevent extrahepatic reflux and was not intended to modulate the intrahepatic territory treated. Whenever complete occlusion of all tumor feeders was indicated, catheters were positioned at or beyond the subsegmental level, ensuring coverage of every branch without unnecessary embolization of normal tissue. The ss-cTACE procedure and technique are detailed in Supplemental Methods.

Definition of Embolization Extent

Because this was a retrospective study, the final embolized area was determined post-procedurally based on angiographic and CT imaging. Although the microcatheter was generally advanced into subsegmental or distal arteries for ss-cTACE, multiple feeders often combined to produce coverage tantamount to at least one hepatic sector. In principle, a single Couinaud sector contains two subsegmental arteries; however, some sectors can harbor more than two, and arteries from different segments may collectively supply the equivalent of a single sector. To avoid under- or overestimating the embolization area when branches were physically separate (eg, A2 and A8) or anomalously clustered within one segment, the final extent was expressed in "sector-equivalent" terms. Any combined coverage matching or exceeding one sector's equivalence was defined as beyond-sector-equivalent (Group E). Conversely, treatments confined to less than one sector-equivalent were classified as one sector-equivalent-limited (Group L). This classification is illustrated in Figure 1. In both panels, the red outlines represent the embolized area, the dashed lines indicate Couinaud segment boundaries, and the blue circles correspond to hepatocellular carcinoma nodules. This classification was used to stratify patients based on the final embolization extent in superselective conventional TACE.

Outcome Measures and Prognostic Factors

Factors related to patient background, tumor burden and progression, tumor location (central vs peripheral), imaging surrogates of tumor aggressiveness—specifically the presence or absence of low signal intensity on hepatobiliary-phase (HBP) gadoxetic-acid–enhanced MRI—and background liver function were examined.[14–20] Details are provided in Supplemental Methods. Ss-cTACE followed by RFA within a few weeks as an Initial treatment (sequential RFA) and split ss-cTACE were specified to identify markers that might contribute to prognosis beyond the effects of ss-cTACE alone. Furthermore, molecular targeted therapy, whole-liver therapy, and additional RFA were evaluated as variables to enhance the overall treatment strategy when ss-cTACE alone was insufficient for controlling recurrent tumors (definitions detailed in Supplemental Methods).

The analysis recorded patient outcomes including progression-free survival (PFS), overall survival (OS), and liver-related survival. In this study, PFS was operationally defined as the interval from the date of the initial ss-cTACE /AMDCT to the initiation of any additional locoregional or systemic therapy for intrahepatic tumor recurrence, including marginal recurrence at the treated site or the appearance of new intrahepatic lesions. Progression prompting additional treatment was determined radiologically on follow-up contrast-enhanced CT or gadoxetic acid–enhanced MRI, consistent with mRECIST progressive disease thresholds (ie, ≥20% increase in viable/enhancing tumor burden and/or the appearance of new intrahepatic lesions), and was confirmed at a multidisciplinary tumor board in routine practice. Because this study was retrospective and the event time was defined by treatment initiation, we did not perform centralized post-hoc re-measurement to assign full mRECIST response categories. Patients who were alive without additional treatment at last

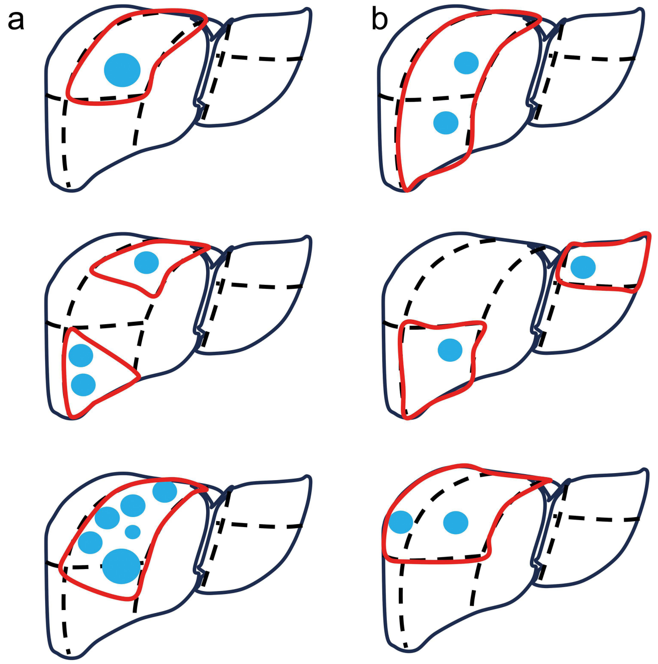

Figure 1 Schematic classification of embolization extent. (**a**) Group L: Sector-limited embolization defined as <1 Couinaud sector-equivalent. Embolization is confined to a limited area such as a single subsegment or adjacent distal branches. (**b**) Group E: Beyond-sector embolization defined as ≥1 sector-equivalent. Multiple subsegments, often across different sectors, are embolized due to complex arterial supply or extensive tumor burden. In both panels, the red-shaded hepatic areas correspond to Couinaud segment units and illustrate the parenchymal territory considered embolized; when two or more contiguous segments are included, this represents ≥1 sector-equivalent. Dashed lines indicate Couinaud segment boundaries, and blue circles represent hepatocellular carcinoma nodules.

imaging follow-up and those who died without receiving additional treatment were censored at the date of their last evaluable imaging or at death, respectively. OS was defined as the time from the initial ss-cTACE/AMDCT to death from any cause or last follow-up. Significant prognostic factors were identified, and further analysis was conducted on factors related to liver-related death. Deaths due to HCC, liver failure, and hemorrhage from variceal rupture were defined as liver-related deaths.[21,22] Liver-related death was defined a priori as death attributable to HCC progression, hepatic failure, or variceal bleeding; all other deaths were considered non–liver-related. For liver-related survival, we fitted cause-specific Cox models, treating non–liver-related deaths as censored events at the time of death.

Short-term Hepatic Safety

Short-term liver reserve was assessed at two timepoints: baseline (≤14 days pre-TACE) and within 1 month post-TACE. The safety outcome was the ALBI score measured within 1 month after TACE.

Statistical Analysis

The statistical approach involved descriptive analysis, with continuous variables presented as means with standard deviations or medians with interquartile ranges (IQRs), and categorical variables as counts and percentages. PFS and OS were analyzed using Cox proportional hazards models,[23] and OS curves were compared using Kaplan–Meier and Log rank tests. For two-group comparisons between group L and E, continuous variables were compared using a *t*-test, and categorical variables were compared using the χ^2-test or Fisher's exact test. Clinically relevant factors (eg, tumor burden, Child–Pugh classification, BCLC stage) were included in the multivariable Cox model even if they were not significant in univariate analysis, in order to account for potential confounding. Multivariable Cox proportional hazards models were fit with BCLC 0 and Group L (<1 sector-equivalent) as reference categories. Covariates (BCLC stage, tumor burden: Up-to-Seven and 5-5-500, tumor location, Child–Pugh class, sex) were forcibly included a priori; liver-related survival was analyzed with a cause-specific hazard approach treating non–liver deaths as competing risks. Because our etiologic question concerned the instantaneous (cause-specific) hazard of liver-related death, the cause-specific Cox model was prespecified as the primary approach; alternative subdistribution models were not pursued in the main analysis to avoid diluting the estimand. Hazard ratios (HRs) indicate the relative instantaneous risk of the event. The multivariate model was constructed using variables with both clinical relevance and statistical significance, while multicollinearity was avoided. OS curves were compared based on clinical and statistical significance. For risk assessment, logistic regression was applied following univariate analysis, with significant variables entered into a multivariate model to control for confounders. All statistical analyses were two-sided, with the significance level set at $p < 0.05$. Data analysis using GraphPad Prism version 10.1.1 (GraphPad Software, La Jolla, CA, USA) was conducted by K.O. and supervised by K.K. A priori power calculation was not conducted owing to the observational nature of the study. We aimed to increase the generalizability of the findings and identify potential correlations. Multivariate models were used for statistical analysis to ensure accuracy. Liver-related mortality was analyzed using a cause-specific hazard model, treating non–liver-related death as censoring. A cause-specific hazard approach was used to evaluate liver-related mortality while treating non–liver-related death as a competing risk. The resulting hazard ratios (HRs) thus reflect the cause-specific hazard for liver-related death in relation to relevant covariates. Full specifications and diagnostics for the overlap-weighting sensitivity analyses (covariates, balance metrics, and effective sample size) are provided in the Supplemental Methods and Results.

Results

Patient Characteristics and Group Classification

After applying the inclusion and exclusion criteria described in the Methods section, 195 patients with newly diagnosed HCC were included in the survival analysis, as illustrated in Figure 2. Baseline characteristics are summarized in Table 1. The median age was 75 years (IQR: 68–82), and 134 patients (69%) were men. Based on the final embolization extent, 136 patients (70%) were classified as Group L (<1 sector-equivalent) and 59 (30%) as Group E (≥1 sector-equivalent). The median follow-up duration was 11 months (IQR: 5–23) for progression-free survival (PFS) and 27 months (IQR: 14–48) for overall survival (OS). During the observation period, 90 patients (46%) died, including 57 (29%) from liver-related causes. Significant between-group differences were observed in sex distribution ($p = 0.01$), BCLC stage ($p = 0.01$), Up-to-Seven criteria ($p < 0.001$), 5-5-500 criteria ($p < 0.001$), and tumor location ($p < 0.001$). In contrast, liver function parameters were comparable between the two groups.

The differences in various baseline variables between group L and group E patients were analyzed (Table 2). Among these baseline characteristics, sex distribution differed significantly (group L: 86 males, 50 females vs group E: 48 males, 11 females; $p = 0.01$). BCLC stages also varied between group L (0: 16%, A: 41%, B: 43%) and group E (0: 3%, A: 36%, B: 61%; $p = 0.01$). Differences were observed for the Up-to-seven (group L: 85% within, 15% beyond vs group E: 61% within, 39% beyond; $p < 0.001$) and 5-5-500 criteria (group L: 79% within, 21% beyond vs group E: 53% within, 47% beyond; $p < 0.001$). Within 1 month after TACE, the post-TACE ALBI score did not differ significantly between groups (group L: -2.1 ± 0.4 vs group E: -2.0 ± 0.4; $p = 0.16$). Nodule location (group L: 61% peripheral, 39% central vs group E: 32% peripheral, 68% central; $p < 0.001$) also differed significantly. In contrast, the median follow-up times for PFS (group L: 12 months vs group E: 7 months) and OS (group L: 33 months vs group E: 21 months), as well as the total deaths (group L: 54 [40%] vs group E: 36 [61%]) and liver-related deaths (group L: 31 [23%] vs group E: 26 [44%]) are time-dependent outcomes rather than baseline characteristics. Therefore, these values are reported descriptively without p-values in Table 2, and their statistical comparisons were instead assessed using appropriate survival analyses (ie, Kaplan–Meier and Cox proportional hazards models).

Clinical and Survival Outcomes

Figure 3 and the Figure S1 illustrate a representative case of ss-cTACE/AMDCT in which embolization was strictly confined to less than one sector-equivalent (sector-limited). The Cox proportional hazards analysis, illustrated via a forest plot (Figure 4), showed that group E and BCLC-B significantly reduced the interval before additional treatment. Group E was associated with a 70% higher hazard of requiring subsequent treatment (HR, 1.7; 95% CI: 1.1, 2.5; $p = 0.01$), and BCLC-B with a 280% increased risk (HR, 3.8; 95% CI: 1.7, 10; $p = 0.003$). No significant differences in the hazard of requiring subsequent treatment were observed for the other assessed variables (Figure 4, Tables S1 and S2). In

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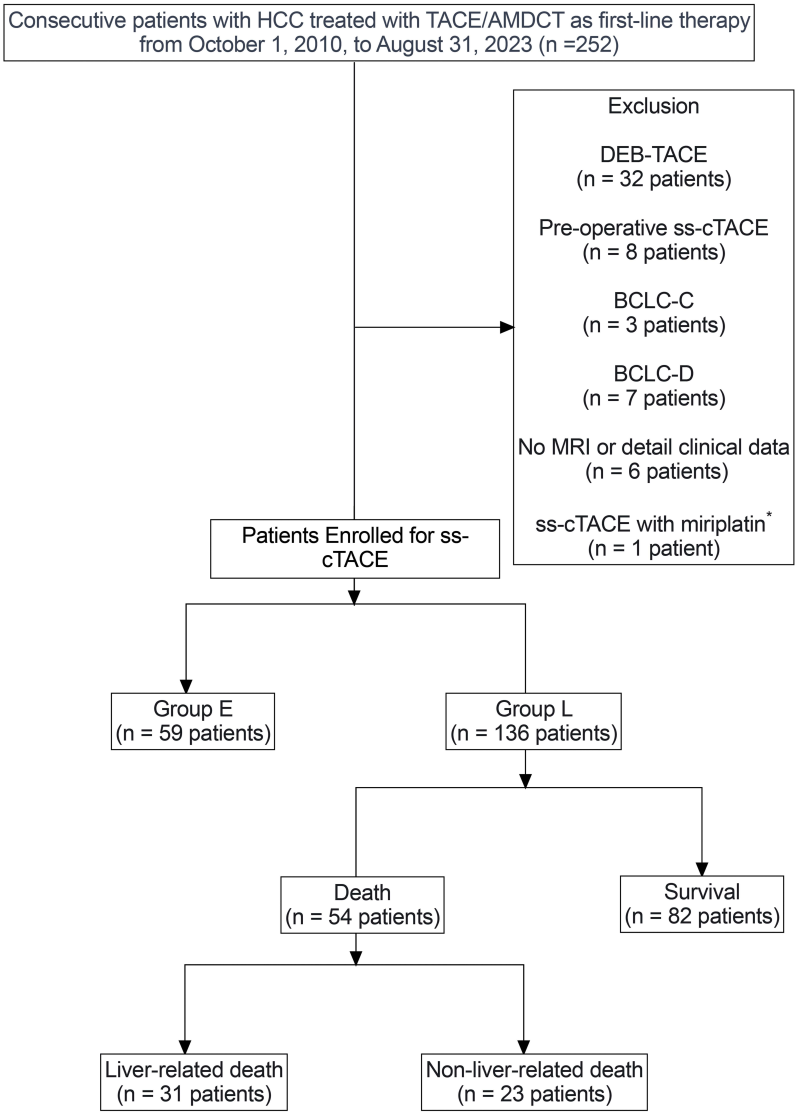

Figure 2 Flowchart illustrating the selection process. Initial screening of 252 patients with hepatocellular carcinoma for transarterial chemoembolization (TACE) under combined angiography and multidetector CT system guidance, detailing inclusion/exclusion criteria and final analysis of 195 patients. Except where indicated, categorical variables are presented as the number of patients (percentage), and continuous variables are presented as means ± standard deviations (SD). Age, alpha-fetoprotein, protein induced by vitamin K absence-II, and follow-up time for progression-free and overall survival are presented as medians with interquartile ranges (IQRs) in parentheses. The sum of the percentage values may not be 100% because of rounding. Child–Pugh classification, Serum PIVKA level, and HBP signal intensity ratio of the liver were not available for 11, 12, and 19 patients, respectively. * Reasons for exclusion included the use of miriplatin, as it may worsen the outcomes of ss-cTACE (12).

Abbreviations: TACE/AMDCT, transarterial chemoembolization under combined angiography and multidetector CT system guidance; HCC, hepatocellular carcinoma; ss-cTACE, superselective conventional transarterial chemoembolization; DEB-TACE, drug-eluting beads transarterial chemoembolization; BCLC, Barcelona Clinic Liver Cancer.

pre-specified propensity-score sensitivity analyses using overlap weighting, balance was excellent across all baseline covariates (all weighted SMDs < 0.10; Figure S2; Table S1); full diagnostics and marginal estimates are provided in the Supplementary Materials (Figure S3; Table S3; Supplemental Results).

Multivariate analyses highlighted that elevated serum protein induced by vitamin K absence-II levels (HR, 1.0; 95% CI: 1.0–1.0; p =0.004), Child–Pugh classification (HR, 1.9; 95% CI: 1.1, 3.0; p =0.02), treatment with embolized area group E (HR, 2.1; 95% CI: 1.2, 3.5; p =0.003), and being beyond the Up-to-seven criteria (HR, 2.8; 95% CI: 1.1, 6.7; p =0.03) were associated with a poorer prognosis in patients undergoing ss-cTACE/AMDCT for initial HCC. Conversely, high signal intensity on hepatobiliary phase MRI indicated a more favorable prognosis (HR, 0.2; 95% CI:0.03, 0.6; p =0.046). However, being beyond the 5-5-500 rule (HR, 1.1; 95% CI: 0.5, 2.1; p =0.78), split ss-cTACE/AMDCT (HR, 0.5; 95% CI: 0.2, 1.2; p =0.13), combination of ss-cTACE/AMDCT and RFA (HR, 1.3; 95% CI: 0.8, 2.3; p =0.32), and

Table 1 Patient Characteristics

Characteristics	**All Patients (n = 195)**
Sex: Male / Female	134 (69) / 61 (31)
Age	75 (IQR: 68–82)
Background liver; Nonviral / Hepatitis B or C	107 (55) / 88 (45)
Child–Pugh Classification; A / B	135 (69) / 49 (25)
BCLC; 0 / A / B	24 (12) / 77 (39) / 94 (48)
Up-to-Seven; Within / Beyond	151 (77) / 44 (23)
5-5-500; Within / Beyond	138 (71) / 57 (29)
Serum albumin level, g/dL	3.6 ± 0.5
Serum bilirubin level, mg/dL	0.9 ± 0.4
ALBI score	−2.3 ± 0.5
Serum AFP level, ng/mL	11 (IQR: 5–49)
Serum PIVKA-II level, mAU/mL	68 (IQR: 26–327)
HBP signal intensity ratio of the liver	2.0 ± 0.5
HBP signal intensity of all nodules; Not only / only high intensity	182 (93) / 13 (7)
Location in All nodules; All HCCs in peripheral / any HCCs in central zone	102 (52) / 93 (48)
Group L / Group E	136 (70) / 59 (30)
Type of initial HCC treatment	
Single -session ss-cTACE	115 (59)
Split ss-cTACE	30 (15)
Sequential RFA	51 (26)
Treatment of second or subsequent for recurrent/new HCC	
Combination ss-cTACE and RFA*	78 (38)
Systemic chemotherapy	33 (17)
Whole-liver therapy	41 (21)
Median follow-up time for PFS, Month	11 (IQR: 5–23)
Median follow-up time for OS, Month	27 (IQR: 14–48)
All death	90 (46)
Liver-related death	57 (29)
Survival	105 (54)

Notes: * Includes the application of RFA to recurrent lesions, as well as RFA after TACE for initial HCC. Group L, total embolized area <1 sector-equivalent; Group E, total embolized area ≥1 sector-equivalent.

Abbreviations: AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; cTACE, conventional lipiodol-transarterial chemoembolization; HBP, hepatobiliary phase; HCC, hepatocellular carcinoma; PIVKA-II, protein induced by vitamin K absence-II; RFA, radiofrequency ablation; PFS, progression-free survival; OS, overall survival.

whole-liver therapy (HR, 1.6; 95% CI: 0.9, 2.2; p =0.05) did not significantly affect prognosis (Figure 5, Table S2). Although group E demonstrated a higher hazard for worse outcomes, these patients also had more advanced disease features (eg, beyond Up-to-seven or 5-5-500 criteria), suggesting that extensive embolization may reflect or overlap with greater tumor burden.

Liver-Related vs All-Cause Mortality

Across all patients, the median cause-specific survival for liver-related death was 73 months, whereas the median overall survival (all-cause) was 48 months (log-rank p =0.006). In Group L, the median cause-specific survival for liver-related death was 113 months, compared with a median overall survival of 57 months (p =0.01). These findings suggest that limiting the embolization extent may help preserve liver function and reduce liver-related mortality, thereby contributing to longer-term survival in selected patients (Figure 6a, Table 3). For patients in Group L, the median overall survival was 57 months. Notably, liver-related causes were associated with a substantially prolonged median survival of 113 months (p

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Table 2 Characteristics of Subgroups Treated with Superselective Conventional Transarterial Chemoembolization (cTACE) That Covered ≥1 Sector-Equivalent (Group E) versus <1 Sector-Equivalent (Group L)

Characteristics	**Group L (n = 136)**	**Group E (n = 59)**	**p-value**
Sex: Male / Female	86 (63) / 50 (37)	48 (81) / 11 (19)	0.01
Age	75 (IQR: 68–82)	75 (IQR: 68–82)	0.83
Background liver; Nonviral / Hepatitis B or C	77 (57) / 59 (43)	30 (51) / 29 (49)	0.46
Child–Pugh Classification; A / B	95 (70) / 32 (24)	40 (68) / 17 (29)	0.63
BCLC; 0 / A / B	22 (16) / 56 (41) / 58 (43)	2 (3) / 21 (36) / 36 (61)	0.01
Up-to-Seven; Within / Beyond	115 (85) / 21 (15)	36 (61) / 23 (39)	<0.001
5-5-500; Within / Beyond	107 (79) / 29 (21)	31 (53) / 28 (47)	<0.001
Serum albumin level, g/dL	3.7 ± 0.5	3.5 ± 0.5	0.14
Serum bilirubin level, mg/dL	1.0 ± 0.5	0.9 ± 0.5	0.72
ALBI score	−2.3± 0.5	−2.2 ± 0.4	0.18
Post-TACE ALBI score (within one month)	−2.1± 0.4	−2.0± 0.4	0.16
Serum AFP level, ng/mL	10 (IQR: 5–41)	14 (IQR: 5–74)	0.63
Serum PIVKA-II level, mAU/mL	64 (IQR: 23–211)	102 (IQR: 29–670)	0.89
HBP signal intensity ratio of the liver	2.0 ± 0.5	2.0 ± 0.5	0.42
HBP signal intensity of all nodules; Not only / only high intensity	125 (92) / 11 (8)	57 (97) / 2 (3)	0.35
Location in All nodules; All HCCs in peripheral / any HCCs in central zone	83 (61) / 53 (39)	19 (32) / 40 (68)	<0.001
Type of initial HCC treatment			
Single -session ss-cTACE	85 (63)	30 (51)	N/A
Split ss-cTACE	15 (11)	15 (25)	N/A
Sequential RFA	36 (26)	15 (25)	N/A
Treatment of second or subsequent for recurrent/new HCC			
Combination ss-cTACE and RFA*	57 (42)	21 (36)	N/A
Systemic chemotherapy	21 (15)	12 (20)	N/A
Whole-liver therapy	25 (18)	16 (27)	N/A
Median follow-up time for PFS, Month	12 (IQR: 6–27)	7 (IQR: 4–14)	N/A
Median follow-up time for OS, Month	33 (IQR: 14–56)	21 (IQR: 14–34)	N/A
All death	54 (40)	36 (61)	N/A
Liver-related death	31 (23)	26 (44)	N/A.

Note: Except where indicated, categorical variables are presented as the number of patients (percentage), and continuous variables are presented as means ± standard deviations (SD). Age, alpha-fetoprotein, protein induced by vitamin K absence-II, and follow-up time for progression-free and overall survival are presented as medians with interquartile ranges (IQRs) in parentheses. The sum of the percentage values may not be 100% because of rounding. Child–Pugh classification, Serum PIVKA level, and HBP signal intensity ratio of the liver were unavailable for 11, 12, and 19 patients, respectively. Statistical analyses for categorical variables were performed using either the chi-square test or Fisher's exact test, depending on the expected cell frequencies. For continuous variables, the *t*-test was employed to compare means between two independent groups. * Includes the application of RFA to recurrent lesions, as well as RFA after ss-cTACE for initial HCC. Group E, total embolized area ≥1 sector-equivalent; Group L, total embolized area <1 sector-equivalent.

Abbreviations: AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; ss-cTACE, superselective conventional transarterial chemoembolization; HBP, hepatobiliary phase; HCC, hepatocellular carcinoma; PIVKA-II, protein induced by vitamin K absence-II; RFA, radiofrequency ablation; PFS, progression-free survival; OS, overall survival; N/A, not applicable.

=0.01), suggesting that limiting the embolized area may help suppress liver-related mortality and contribute to favorable long-term outcomes (Figure 6b, Table 3).

Predictors of Liver-Related Mortality

To investigate factors associated with liver-related mortality among patients who underwent sector-limited embolization (Group L), clinical characteristics were compared between those who died from liver-related causes and those who died from non–liver-related causes (Table 4, Figure 7). Hepatitis B or C infection was identified as a significant independent risk factor for liver-related death (OR: 6.9; 95% CI: 1.8–34; p =0.009). Although elevated serum bilirubin (OR: 6.8; 95% CI: 1.3–67; p =0.05) and combination treatment with RFA (OR: 3.6; 95% CI: 0.9–15; p =0.07) showed trends toward association, statistical significance was not reached. Notably, none of the 31 patients with liver-related death exhibited

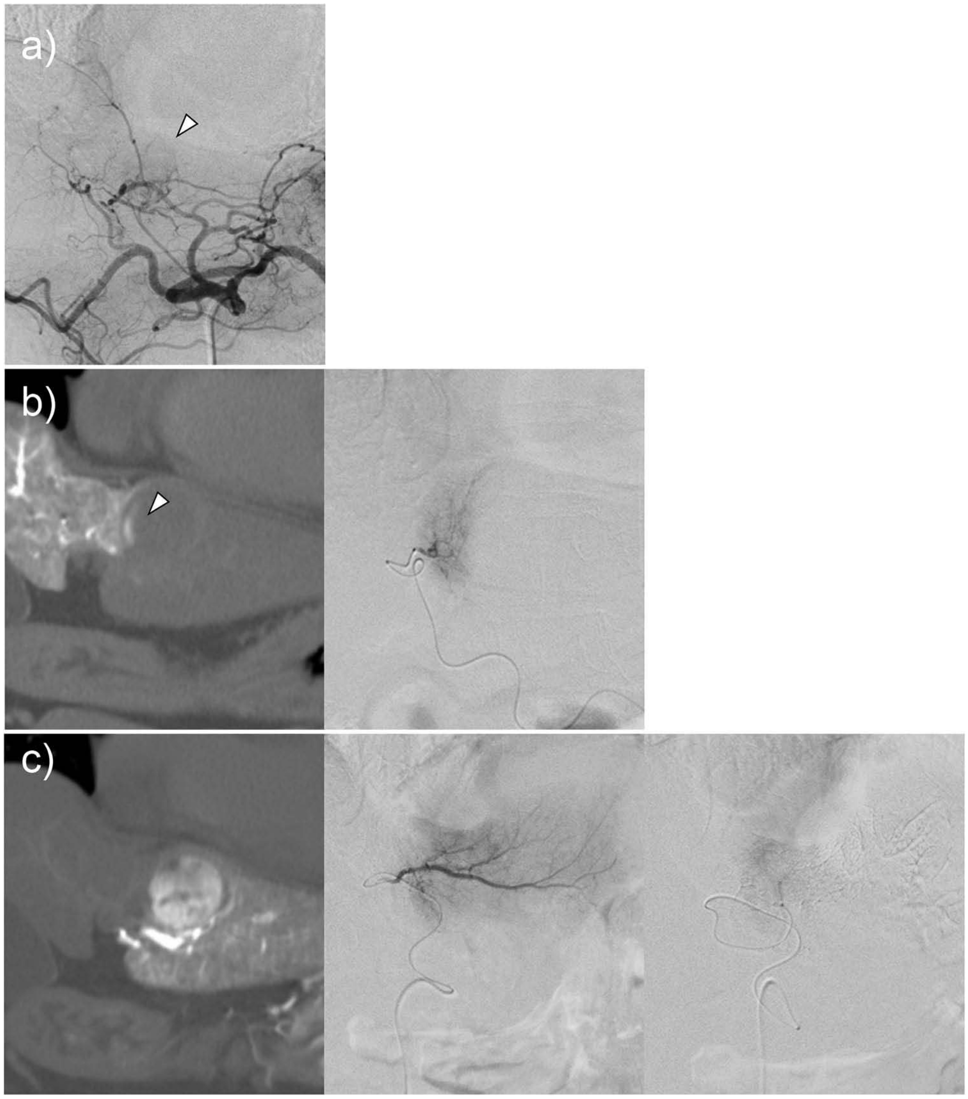

Figure 3 Representative case of Angio-MDCT-guided conventional transarterial chemoembolization showing tumor-feeding arteries and embolization outcomes. A 76-year-old female with chronic liver disease who tested positive for hepatitis C virus. After conventional transarterial chemoembolization restricted to <1 sector-equivalent, combined with radiofrequency ablation, the patient has been recurrence-free for 10 years. (**a**) Celiac angiography. The arrow points to the HCC in the central Zone. (**b**) Arterial phase of CTHA (CT hepatic arteriography), Coronal view (left). The arrow indicates blood supply originating from the periphery of A4. DSA image with a selected peripheral branch of A4 (right). Superselective conventional transarterial chemoembolization (ss-cTACE) was performed as distally as possible within the subsegmental branches. (**c**) Arterial phase of CTHA, Coronal view. Blood supply from the periphery of A2 and A3 was confirmed (left). DSA with selected A2 branch (center). Ss-cTACE was conducted due to suspected blood supply from multiple fine branches at the subsegmental branch level, resulting in an embolization range equal to a Couinaud segment. DSA image of fine branches heading cephalad from A3 (right). Ss-cTACE was performed, resulting in an embolization range less than subsegmental. Although multiple feeders were treated, the total embolization remained under one sector-equivalent, as shown by localized lipiodol accumulation in Supplemental Figure 1.

hyperintense signal on hepatobiliary phase imaging, whereas such signal was observed in 2 of 23 patients with non–liver-related death, precluding odds ratio calculation (Figure 7). This analysis is restricted to Group L (<1 sector-equivalent). Odds ratios (ORs) with 95% CIs are shown; variables entered in the multivariable model were those significant on univariable analysis. When multivariate analysis was performed, the observation of high signal intensity on HBP in all nodules became unavailable due to data separation. Multivariate analysis was conducted using logistic regression on variables that demonstrated significant differences in the univariate analysis. ORs with 95% CIs are presented for each variable. Points to the left of the vertical line indicate a protective effect, whereas points to the right indicate an increased risk. Gray circles and multivariate analysis indicated by black squares represent univariate analyses.

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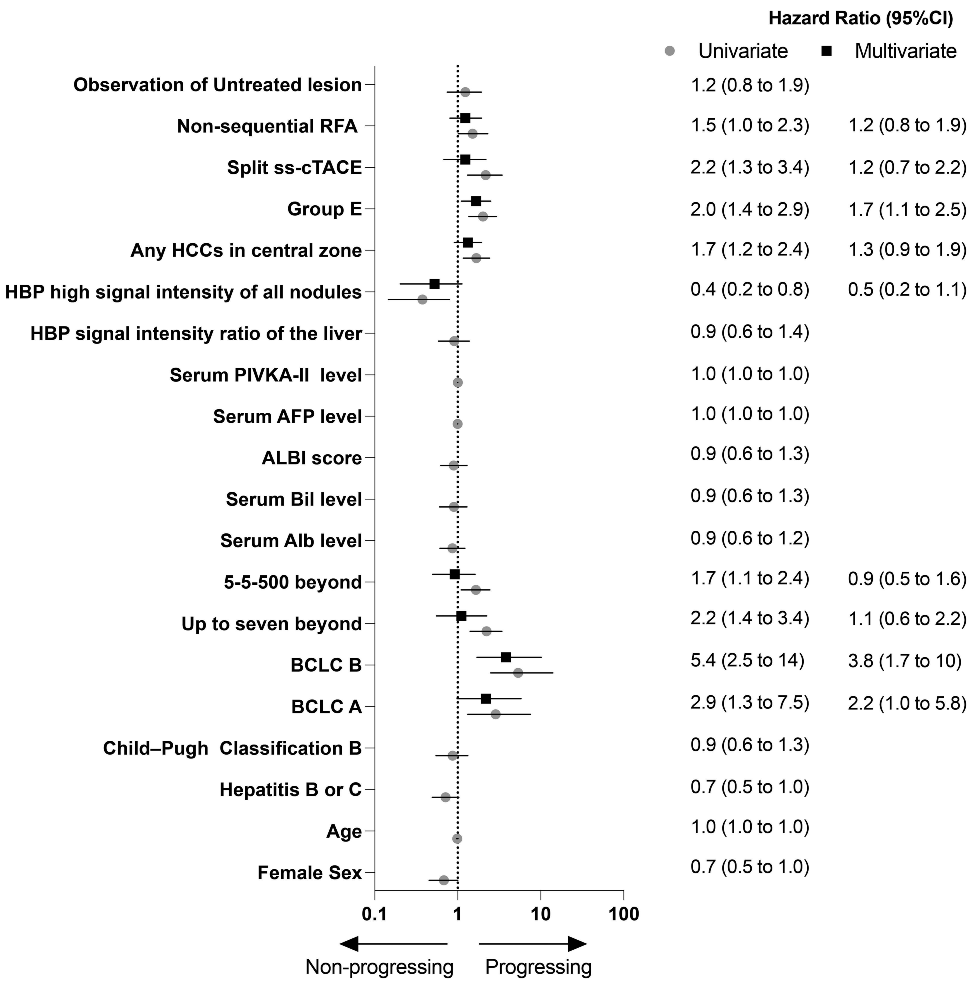

Figure 4 Forest plot of factors influencing progression-free survival (PFS) in patients with initial hepatocellular carcinoma (HCC) after superselective conventional transarterial chemoembolization (ss-cTACE). This forest plot presents the results of univariate and multivariate Cox proportional hazards analyses focusing on factors influencing PFS in patients undergoing initial treatment for HCC with ss-cTACE. Multivariate analysis was conducted using Cox proportional hazards regression on variables that demonstrated significant differences in the univariate analysis. HRs with 95% CIs are shown for each variable, providing insight into the impact of various factors on the duration until subsequent treatment or progression. Points to the left of the vertical line suggest a favorable effect on PFS, while points to the right indicate a detrimental effect. Gray circles denote results from univariate analysis, and black squares indicate results from multivariate analysis. This analysis was conducted to identify the critical determinants that extend the time to progression or subsequent treatment in patients with initial HCC following ss-cTACE. Reference categories: BCLC 0; Group L (<1 sector-equivalent).

Abbreviations: RFA, radiofrequency ablation; ss-cTACE, superselective conventional transarterial; HCC, hepatocellular carcinoma; Group E, total embolized area ≥1 sector-equivalent; HBP, hepatobiliary phase; PIVKA-II, protein induced by vitamin K absence-II; AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval.

Discussion

This study investigated whether restricting the extent of embolization in superselective conventional TACE under angiography–MDCT guidance to less than one sector-equivalent improves prognosis in patients with HCC. Although broader embolization (≥1 sector-equivalent) appeared to reflect more advanced disease, multivariate analysis revealed it as an independent predictor of shorter progression-free and overall survival. In contrast, limiting embolization to <1 sector-equivalent significantly prolonged survival, particularly for liver-related deaths, highlighting the prognostic importance of treatment extent itself.

A simple two-group comparison might suggest that the more favorable outcomes in Group L could be attributed to less advanced disease at baseline. However, even after adjusting for multiple prognostic factors in a Cox proportional hazards model, patients in Group E remained significantly associated with shorter PFS and OS. This finding implies that broader embolization itself, rather than disease stage alone, may contribute to poorer prognosis. Moreover, the addition of tumor location (peripheral vs central) and other variables to the model did not alter this result, highlighting the

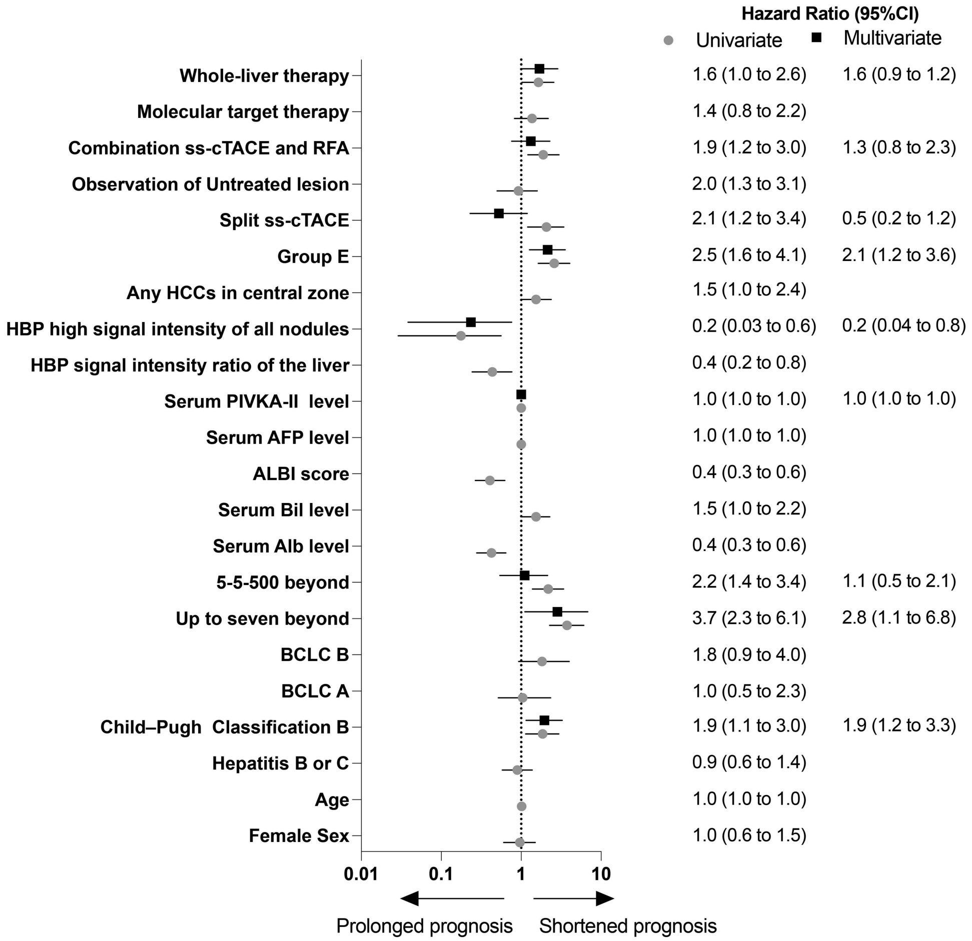

Figure 5 Forest plot of prognostic factors in patients with initial hepatocellular carcinoma (HCC) treated with superselective conventional transarterial chemoembolization (ss-cTACE): results from univariate and multivariate Cox proportional hazards analyses for overall survival (OS). This forest plot illustrates the results of univariate and multivariate Cox proportional hazards analyses identifying prognostic factors in patients undergoing ss-cTACE for initial HCC treatment. Multivariate analysis was conducted using Cox proportional hazards regression on variables that demonstrated significant differences in the univariate analysis. HRs with 95% CIs are presented for each variable. Points to the left of the vertical line indicate decreased risk, whereas points to the right indicate increased risk. Gray circles represent univariate analysis results; black squares represent multivariate analysis results. This analysis was conducted to identify the key factors contributing to the prognosis of patients with ss-cTACE treatment for initial HCC. In the univariate analysis, significant differences were observed in serum albumin level, bilirubin level, ALBI score, Child–Pugh classification, and HBP signal intensity ratio of the liver (pre- and post-administration of gadoxetic acid). Reference categories: BCLC 0; Group L (<1 sector-equivalent). For multivariate analysis, the Child–Pugh classification was selected as the representative variable for liver reserve function because its variance inflation factor was <10, indicating a lower risk of multicollinearity among the significant variables identified (Table S1).

Abbreviations: RFA, radiofrequency ablation; ss-cTACE, superselective conventional transarterial; HCC, hepatocellular carcinoma; Group E, total embolized area ≥1 sector-equivalent; HBP, hepatobiliary phase; PIVKA-II, protein induced by vitamin K absence-II; AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval.

importance of limiting the embolized area to preserve liver function and improve survival. This result may reflect differences in hepatic ischemia caused by ss-cTACE or in the preservation of liver reserve. As supporting evidence, the Child–Pugh score was also confirmed as an independent factor influencing OS. Additionally, although previous studies have reported better ss-cTACE outcomes in peripheral HCC,[18] tumor location was not an independent predictor in our cohort—likely because AMDCT guidance enabled us to selectively catheterize smaller branches, even for centrally located lesions. Nonetheless, in some central HCCs, the feeding artery may arise too proximally to allow true superselective access. In such cases, the embolized area could extend beyond one sector-equivalent, potentially worsening outcomes.

Our findings revealed that patients in group L had better survival outcomes for liver-related deaths than for all-cause mortality, implying that minimizing embolization to <1 sector-equivalent may offer benefits for selected HCC patients. In our study, patients treated with <1 sector-equivalent ss-cTACE (Group L) showed better survival specifically for liver-related deaths, indicating a genuine survival benefit. However, in those with nonviral etiologies, more frequent non–liver-

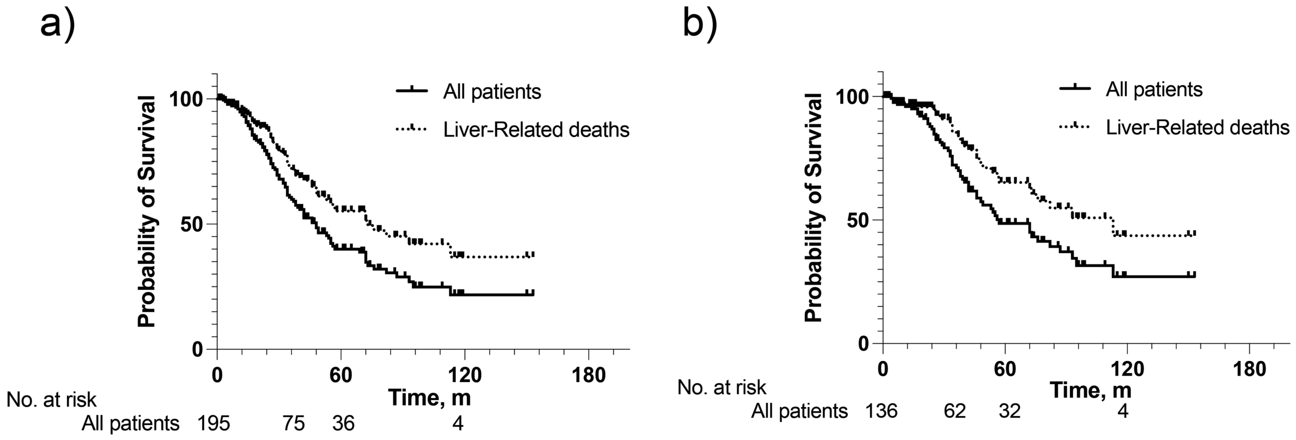

Figure 6 Survival outcomes in patients with initial hepatocellular carcinoma (HCC) treated with superselective conventional transarterial chemoembolization (ss-cTACE): a cause-specific hazard for liver-related death. (**a**) Comparison of overall survival between all patients and those with liver-related deaths, illustrating a statistically significant difference (p =0.006). (**b**) Group L indicated a significant difference (p =0.01). In the Kaplan–Meier survival analyses, the "No. at risk" is presented at the critical time points of 0, 36, 60, and 120 months.

related deaths may overshadow this advantage, resulting in an underestimation of the procedure's overall survival benefit. Although viral hepatitis was a risk factor for liver-related mortality (as previously reported),[24] it is likely that such patients typically have fewer non–liver-related comorbidities. Consequently, effective HCC control in the viral hepatitis group can lead to a more pronounced extension of overall survival.

Most prior HCC survival studies involved younger (40–60 years) patients with viral etiologies, in whom liver-related deaths predominated; younger age has also been shown to predict longer survival.[25] The median age in our cohort was 75, which may underestimate 5- and 10-year survival rates. However, when focusing on liver-related mortality, the findings are broadly consistent with earlier reports. Additionally, cone-beam CTHA—one of the essential imaging methods for detailed assessment of HCCs and supplemental arteries[26–28]—guided ss-cTACE has shown 5-year survival rates of up to 60%,[29–32] comparable to or exceeding those of resection, RFA, and systemic therapies.[33–37] Although combining TACE with sequential RFA can enhance survival,[38,39] the TACE method in those studies was often not strictly defined. Here, sequential RFA was not a significant prognostic factor, suggesting that once a truly limited ss-cTACE is attained, additional ablation may yield only marginal benefit. Furthermore, prior studies have indicated that the survival outcomes of superselective TACE in patients with limited tumor burden may be comparable to those of surgical resection, and that the additional benefit of RFA may be limited under such conditions.[40] These findings are consistent

Table 3 Survival Analysis of Patients with Initial HCC Undergoing Superselective Conventional Transarterial Chemoembolization: Median Survival and Rates at Various Time Points

Variables	Patients (Numbers)	Median Survival (Months)	Survival Rate (%) in Months						p-value
			12	24	36	48	60	120	
All patients	195								
All deaths	90	48	94	78	60	49	40	22	0.006
Liver-related death	57	73	95	88	72	62	55	37	
Group L	136								
All deaths	54	57	96	87	71	57	49	27	0.01
Liver-related death	31	113	97	96	84	73	65	44	

Note: This table summarizes the median survival in months and survival rates at 12, 24, 36, 48, 60, and 120 months for all patients who underwent their first superselective conventional transarterial chemoembolization (ss-cTACE) for HCC. Survival rates were presented as percentages, reflecting the proportion of patients alive at each specified time point. The Kaplan–Meier method was used to estimate survival curves, and differences in survival between groups were assessed using the Log rank test, with p <0.05 considered statistically significant. These analyses provide insights into the long-term efficacy of ss-cTACE in treating HCC and emphasize the influence of procedural specificity on patient outcomes.

Abbreviations: Group L, total embolized area <1 sector-equivalent; HCC, hepatocellular carcinoma.

Table 4 Patient Characteristics in Liver-Related and Non-Liver-Related Deaths Among Patients Treated with Superselective Conventional Transarterial Chemoembolization Restricted to <1 Sector-Equivalent

Variables	**All Deceased Patients (n = 54)**	**Cause of Death**		**Univariate Analysis**	**Multivariate Analysis**
		Liver-Related Death (n = 31)	**Non-liver-Related Death (n = 23)**		
Sex: Male / Female	32 (59) / 22 (41)	17 (54) / 14 (46)	15 (65) / 8 (35)	0.72	
Age	72 (IQR: 66–79)	71 (IQR: 60–77)	76 (IQR: 69–82)	0.41	
Background liver; Nonviral / Hepatitis B or C	27 (50) / 27 (50)	11 (35) / 20 (65)	16 (70) / 7 (30)	0.02	0.009
Child–Pugh Classification; A / B	33 (61) / 17 (31)	19 (61) / 11 (35)	14 (60) / 6 (26)	0.10	
BCLC; 0 / A / B	9 (17) / 20 (37) / 25 (46)	6 (19) / 12 (39) / 13 (42)	3 (13) / 8 (35) / 12 (52)	0.33 / 0.37 / 0.84	
Up-to-Seven; Within / Beyond	41 (76) / 13 (24)	23 (74) / 8 (26)	18 (78) / 5 (22)	0.44	
5−5−500; Within / Beyond	40 (74) / 14 (26)	24 (77) / 7 (23)	16 (70) / 7 (30)	0.21	
Serum albumin level, g/dL	3.5 ± 0.5	3.4 ± 0.6	3.5 ± 0.4	0.34	
Serum bilirubin level, mg/dL	1.0 ± 0.6	1.2 ± 0.6	0.8 ± 0.3	0.045	0.05
ALBI score	−1.9 ± 0.4	−1.9 ± 0.4	−1.9 ± 0.4	0.29	
Serum AFP level, ng/mL	13 (IQR: 7–98)	13 (IQR: 7–150)	12 (IQR: 7–98)	0.46	
Serum PIVKA-II level, mAU/mL	90 (IQR: 24–877)	79 (IQR: 30–218)	95 (IQR: 20–3998)	0.50	
HBP signal intensity ratio of the liver	1.9 ± 0.5	1.9 ± 0.5	1.9 ± 0.4	0.29	
HBP signal intensity of all nodules; Not only /only high intensity	52 (96) / 2 (4)	31 (100) / 0 (0)	21 (90) / 2 (9)	N/A †	
Location in All nodules; All HCCs in peripheral / any HCCs in central zone	29 (54) / 25 (46)	19 (61) / 12 (39)	10 (43) / 13 (57)	0.10	
Treatment of second or subsequent for recurrent/new HCC					
Combination ss-cTACE and RFA*	26 (48)	19 (61)	7 (30)	0.03	0.07
Split ss-cTACE for initial HCC	8 (15)	3 (10)	5 (22)	0.48	
Observation of Untreated Lesion	12 (22)	9 (29)	3 (13)	0.10	
Molecular target therapy	15 (28)	11 (35)	4 (20)	0.87	
Whole-liver therapy	18 (33)	12 (39)	6 (26)	0.74	

Note: Deaths due to hepatocellular carcinoma (HCC), liver failure, and hemorrhage from variceal rupture were defined as liver-related deaths. Patients were categorized into liver-related death and non-liver-related death groups, and variables that showed significant differences in the univariate analysis were subsequently analyzed using multivariate logistic regression. Except where indicated, categorical variables are presented as the number of patients (percentage), and continuous variables are presented as means ± standard deviations (SD). Age, alpha-fetoprotein, and protein induced by vitamin K absence-II are presented as medians with interquartile ranges (IQRs) in parentheses. The sum of the percentage values may not be 100% because of rounding. Child–Pugh classification was not available for four patients. * Includes the application of RFA to recurrent lesions and RFA after ss-cTACE for initial HCC. †Logistic regression could not be adequately fitted owing to perfect separation; therefore, p-values are unavailable.

Abbreviations: AFP, alpha-fetoprotein; ALBI, albumin–bilirubin; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; ss-cTACE, superselective conventional transarterial chemoembolization; HBP, hepatobiliary phase; HCC, hepatocellular carcinoma; N/A, not applicable; PIVKA-II, protein induced by vitamin K absence-II; RFA, radiofrequency ablation.

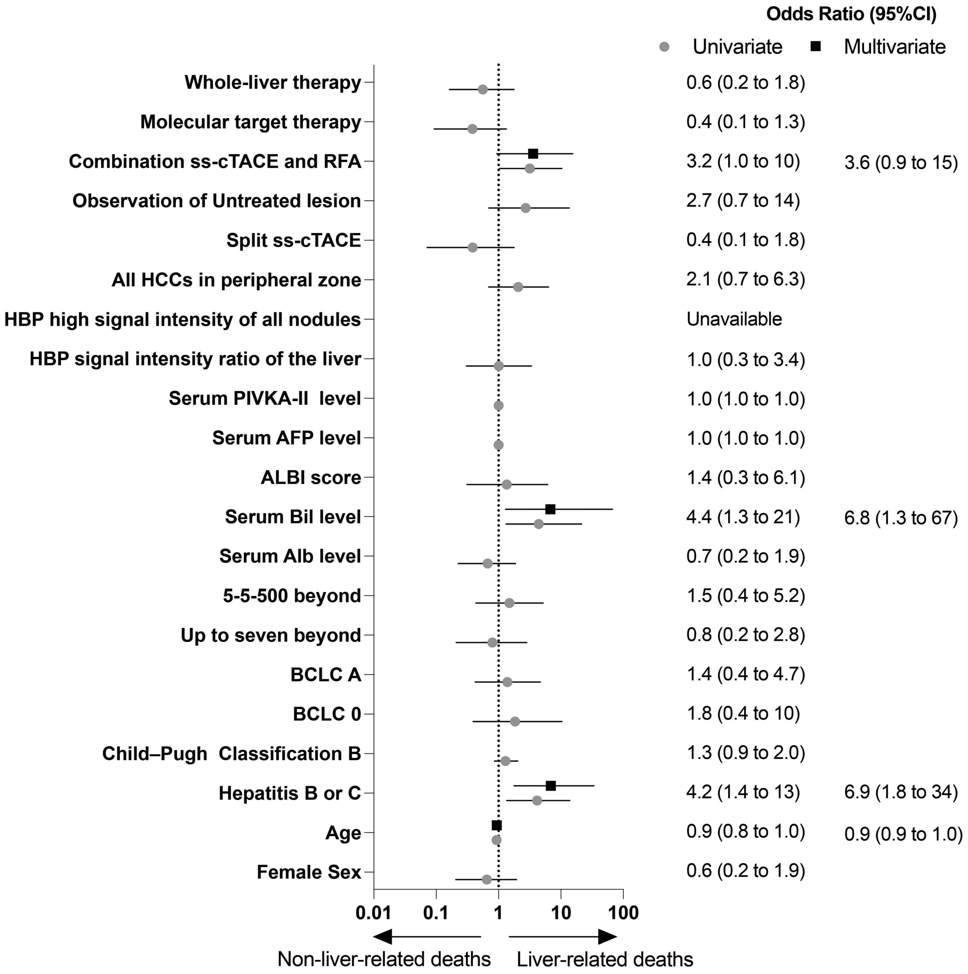

Figure 7 Forest plot of univariate and multivariate logistic regression restricted to Group L (<1 sector-equivalent), comparing liver-related vs non-liver-related deaths (see Table 4). This analysis is restricted to Group L (<1 sector-equivalent). Odds ratios (ORs) with 95% CIs are shown; variables entered in the multivariable model were those significant on univariable analysis. When multivariate analysis was performed, the observation of high signal intensity on HBP in all nodules became unavailable due to data separation. Multivariate analysis was conducted using logistic regression on variables that demonstrated significant differences in the univariate analysis. ORs with 95% CIs are presented for each variable. Points to the left of the vertical line indicate a protective effect, whereas points to the right indicate an increased risk. Gray circles and multivariate analysis indicated by black squares represent univariate analyses.

Abbreviations: RFA, radiofrequency ablation; ss-cTACE, superselective conventional transarterial; HCC, hepatocellular carcinoma; Group E, total embolized area ≥1 sector-equivalent; HBP, hepatobiliary phase; PIVKA-II, protein induced by vitamin K absence-II; AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval.

with the present study, in which sequential RFA was not identified as a significant prognostic factor once truly limited embolization was achieved. And, these findings may indicate that, in addition to tumor size and number, the extent of embolization could be relevant to therapeutic decision-making in ss-cTACE. Such considerations might complement existing frameworks like the BCLC staging system. When disease anatomy suggests that ≥1 sector-equivalent would be unavoidably treated in a single session, clinicians should be aware of the potential for greater parenchymal ischemia and deterioration of liver reserve in susceptible patients. In such situations, staged treatments or temporary/flow-modulating embolics (eg, DSM-TACE) may be considered to preserve liver function, acknowledging the trade-off of multiple sessions. Our cohort was not designed to compare embolic platforms; therefore, these considerations are hypothesis--generating and warrant prospective evaluation. Also, we did not systematically capture antiviral treatment status or baseline viral load (HBV DNA or HCV RNA levels), and therefore we could not examine how the degree of viral suppression might have modified the association between embolization extent and liver-related mortality. This represents an important limitation that should be addressed in future prospective cohorts.

This study had some limitations. First, the retrospective design may introduce selection bias; however, this risk was minimized by the use of a consecutive case selection method. Second, the generalizability of our findings may be limited due to patient demographics. However, careful consideration of the variability in prognoses associated with different HCC etiologies enhances the robustness of our findings. Third, because subgroup counts for specific liver-related causes were small and attribution can be intrinsically ambiguous in HCC (overlap between tumor progression and hepatic decompensation), we did not present formal between-group cross-tabulations of specific causes for Group L vs Group E. Instead, we relied on cause-specific hazards as the primary estimand to minimize misclassification bias. Fourth, treatment protocols evolved during the study period; nevertheless, incorporating these changes as independent variables in the analysis helped maintain the integrity of the outcomes. The limited follow-up duration for specific participants may have excluded instances of late recurrence or long-term adverse effects. Nonetheless, the inclusion of cases with follow-up exceeding 10 years provides substantial evidence of the long-term efficacy of the treatments. Finally, hepatic reserve was formally assessed only up to 1 month after ss-cTACE using the ALBI score, and we did not systematically collect longitudinal liver function trajectories or hepatic decompensation events. As such, our hypothesis that broader embolization may accelerate chronic deterioration of liver function should be interpreted as mechanistic speculation and warrants confirmation in prospective studies with long-term hepatic toxicity data.

Clinical Implications

Our findings support a territory-sparing planning principle for ss-cTACE under AMDCT guidance: when multiple small feeders are identified, operators should aim for distal microcatheter positions and avoid cumulative embolization that exceeds one sector-equivalent in a single sitting. If the anticipated treated territory would reach ≥1 sector, adopting a staged approach or using temporary/flow-modulating embolics may mitigate parenchymal ischemia with acceptable trade-offs. These considerations are particularly relevant in elderly patients or those with limited hepatic reserve. Prospective studies should test whether protocolized territory-sparing strategies can causally improve liver-related survival.

Conclusion

Restricting the embolized area during superselective conventional TACE under angiography–MDCT guidance to less than one sector-equivalent was independently associated with improved survival in patients with HCC. Although broader embolization reflected more advanced disease in some cases, its extent itself emerged as a significant prognostic factor. Notably, patients with viral hepatitis benefited more from this approach in terms of liver-related survival, while nonviral etiologies were more often associated with non–liver-related deaths. These findings highlight the need to consider both tumor burden and embolization extent when planning ss-cTACE, particularly in elderly patients or those with comorbidities.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Chen S, Peng Z, Zhang Y, et al. Lack of response to transarterial chemoembolization for intermediate-stage hepatocellular carcinoma: abandon or repeat? *Radiology*. 2021;298:680–692. doi:10.1148/radiol.2021202289
2. Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol*. 2022;76:681–693. doi:10.1016/j.jhep.2021.11.018
3. Mendiratta-Lala M, Aslam A, Bai HX, et al. Ethiodized oil as an imaging biomarker after conventional transarterial chemoembolization. *Eur Radiol*. 2024;34:3284–3297. doi:10.1007/s00330-023-10326-7
4. Ikeda M, Arai Y, Inaba Y, et al. Conventional or drug-eluting beads? Randomized controlled study of chemoembolization for hepatocellular carcinoma: JIVROSG-1302. *Liver Cancer*. 2022;11:440–450. doi:10.1159/000525500
5. Miyayama S, Matsui O. Superselective conventional transarterial chemoembolization for hepatocellular carcinoma: rationale, technique, and outcome. *J Vasc Interv Radiol*. 2016;27:1269–1278. doi:10.1016/j.jvir.2016.04.014
6. Miyayama S. Treatment strategy of transarterial chemoembolization for hepatocellular carcinoma. *Appl Sci*. 2020;10:7337. doi:10.3390/app10207337
7. Xiang J, Li Y, Mei S, et al. Novel diagnostic and therapeutic strategies based on PANoptosis for hepatocellular carcinoma. *Cancer Biol Med*. 2025;22:928–939. doi:10.20892/j.issn.2095-3941.2025.0150
8. Taiji R, Lin EY, Lin YM, et al. Combined angio-CT systems: a roadmap tool for precision therapy in interventional oncology. *Radiol Imaging Cancer*. 2021;3:e210039. doi:10.1148/rycan.2021210039

9. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46:399–424. doi:10.1080/00273171.2011.568786
10. Li F, Li F. Propensity score weighting for causal inference with multiple treatments. *Ann Appl Stat*. 2019;13:2389–2415. doi:10.1214/19-AOAS1282
11. Okumura K. Comment on: "Controlling nutritional status (CONUT) score is associated with overall survival in patients with HCC treated with cTACE"-is propensity score matching necessary? *Cardiovasc Intervent Radiol*. 2025 doi:10.1007/s00270-025-04197-2.
12. Miyayama S, Yamashiro M, Shibata Y, et al. Comparison of local control effects of superselective transcatheter arterial chemoembolization using epirubicin plus mitomycin C and miriplatin for hepatocellular carcinoma. *Jpn J Radiol*. 2012;30:263–270. doi:10.1007/s11604-011-0043-6
13. Hayashi M, Matsui O, Ueda K, Kawamori Y, Gabata T, Kadoya M. Progression to hypervascular hepatocellular carcinoma: correlation with intranodular blood supply evaluated with CT during intraarterial injection of contrast material. *Radiology*. 2002;225:143–149. doi:10.1148/radiol.2251011298
14. Ma B, Xu H, Wu X, et al. Evaluation of liver function using Gd-EOB-DTPA-enhanced MRI with T1 mapping. *BMC Med Imaging*. 2023;23:73. doi:10.1186/s12880-023-01028-z
15. Liu MT, Zhang XQ, Lu J, et al. Evaluation of liver function using the hepatocyte enhancement fraction based on gadoxetic acid-enhanced MRI in patients with chronic hepatitis B. *Abdom Radiol*. 2020;45:3129–3135. doi:10.1007/s00261-020-02478-7
16. Shinkawa H, Tanaka S, Takemura S, et al. Prognostic value of expanded liver transplantation criteria-the 5-5-500 rule-in patients with hepatic resection for intermediate-stage hepatocellular carcinoma. *J Hepatobiliary Pancreat Sci*. 2020;27:682–689. doi:10.1002/jhbp.792
17. Inmutto N, Nimitrungtawee N, Srisuwan T, Kattipathanapong T, Jantarangkoon A, Puttisri O. Investigating up-to-seven criteria and APRI (AST platelet ratio) as prognostic factors in intermediate-stage hepatocellular carcinoma patients who received transarterial chemoembolization. *Asian Pac J Cancer Prev*. 2022;23:3939–3946. doi:10.31557/APJCP.2022.23.11.3939
18. Asano K, Kageyama K, Yamamoto A, et al. Transcatheter arterial chemoembolization for treatment-naive hepatocellular carcinoma has different treatment effects depending on central or peripheral tumor location. *Liver Cancer*. 2023;12:576–589. doi:10.1159/000530441
19. Bae JS, Kim JH, Lee DH, Kim JH, Han JK. Hepatobiliary phase of gadoxetic acid-enhanced MRI in patients with HCC: prognostic features before resection, ablation, or TACE. *Eur Radiol*. 2021;31:3627–3637. doi:10.1007/s00330-020-07499-w
20. Kitao A, Matsui O, Zhang Y, et al. Dynamic CT and gadoxetic acid-enhanced MRI characteristics of P53-mutated hepatocellular carcinoma. *Radiology*. 2023;306:e220531. doi:10.1148/radiol.220531
21. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. *J Hepatol*. 2023;79:516–537. doi:10.1016/j.jhep.2023.03.017
22. Mosconi C, Gramenzi A, Biselli M, et al. Survival and tolerability of transarterial chemoembolization in greater versus less than 70 years of age patients with unresectable hepatocellular carcinoma: a propensity score analysis. *Cardiovasc Intervent Radiol*. 2020;43:1015–1024. doi:10.1007/s00270-020-02451-3
23. Chung GE, Lee JH, Kim HY, et al. Transarterial chemoembolization can be safely performed in patients with hepatocellular carcinoma invading the main portal vein and may improve the overall survival. *Radiology*. 2011;258:627–634. doi:10.1148/radiol.10101058
24. Vitale A, Svegliati-Baroni G, Ortolani A, et al. Epidemiological trends and trajectories of MAFLD-associated hepatocellular carcinoma 2002-2033: the ITA.LI.CA database. *Gut*. 2023;72:141–152. doi:10.1136/gutjnl-2021-324915
25. Niu XK, He XF. Development of a computed tomography-based radiomics nomogram for prediction of transarterial chemoembolization refractoriness in hepatocellular carcinoma. *World J Gastroenterol*. 2021;27:189–207. doi:10.3748/wjg.v27.i2.189
26. Tacher V, Radaelli A, Lin M, Geschwind JF. How I do it: cone-beam CT during transarterial chemoembolization for liver cancer. *Radiology*. 2015;274:320–334. doi:10.1148/radiol.14131925
27. Lin EY, Jones AK, Chintalapani G, Jeng ZS, Ensor J, Odisio BC. Comparative analysis of intra-arterial cone-beam versus conventional computed tomography during hepatic arteriography for transarterial chemoembolization planning. *Cardiovasc Intervent Radiol*. 2019;42:591–600. doi:10.1007/s00270-018-2116-8
28. De baere T, Ronot M, Chung JW, et al. Initiative on superselective conventional transarterial chemoembolization results (INSPIRE). *Cardiovasc Intervent Radiol*. 2022;45:1430–1440. doi:10.1007/s00270-022-03233-9
29. Matsui O, Kadoya M, Yoshikawa J, et al. Small hepatocellular carcinoma: treatment with subsegmental transcatheter arterial embolization. *Radiology*. 1993;188:79–83. doi:10.1148/radiology.188.1.8390073
30. Matsui O, Miyayama S, Sanada J, et al. Interventional oncology: new options for interstitial treatments and intravascular approaches: superselective TACE using iodized oil for HCC: rationale, technique and outcome. *J Hepatobiliary Pancreat Sci*. 2010;17:407–409. doi:10.1007/s00534-009-0234-z
31. Miyayama S. Ultraselective conventional transarterial chemoembolization: when and how? *Clin Mol Hepatol*. 2019;25:344–353. doi:10.3350/cmh.2019.0016
32. Miyayama S, Yamashiro M, Sugimori N, Ikeda R, Okimura K, Sakuragawa N. Outcomes of patients with hepatocellular carcinoma treated with conventional transarterial chemoembolization using guidance software. *J Vasc Interv Radiol*. 2019;30:10–18. doi:10.1016/j.jvir.2018.08.009
33. Zhong JH, Ke Y, Gong WF, et al. Hepatic resection associated with good survival for selected patients with intermediate and advanced-stage hepatocellular carcinoma. *Ann Surg*. 2014;260:329–340. doi:10.1097/SLA.0000000000000236
34. Yau T, Tang VY, Yao TJ, Fan ST, Lo CM, Poon RT. Development of Hong Kong liver cancer staging system with treatment stratification for patients with hepatocellular carcinoma. *Gastroenterology*. 2014;146:1691–700.e3. doi:10.1053/j.gastro.2014.02.032
35. Ohama H, Hiraoka A, Tada F, et al. Clinical usefulness of surgical resection including the complementary use of radiofrequency ablation for intermediate-stage hepatocellular carcinoma. *Cancers*. 2022;15:236. doi:10.3390/cancers15010236
36. Bai XM, Cui M, Yang W, et al. The 10-year survival analysis of radiofrequency ablation for solitary hepatocellular carcinoma 5 cm or smaller: primary versus recurrent HCC. *Radiology*. 2021;300:458–469. doi:10.1148/radiol.2021200153
37. Yang W, Yan K, Goldberg SN, et al. Ten-year survival of hepatocellular carcinoma patients undergoing radiofrequency ablation as a first-line treatment. *World J Gastroenterol*. 2016;22:2993–3005. doi:10.3748/wjg.v22.i10.2993
38. Chu HH, Kim JH, Yoon HK, et al. Chemoembolization combined with radiofrequency ablation for medium-sized hepatocellular carcinoma: a propensity-score analysis. *J Vasc Interv Radiol*. 2019;30:1533–1543. doi:10.1016/j.jvir.2019.06.006

39. Hirooka M, Hiraoka A, Ochi H, et al. Transcatheter arterial chemoembolization with or without radiofrequency ablation: outcomes in patients with barcelona clinic liver cancer stage B hepatocellular carcinoma. *AJR Am J Roentgenol*. 2018;210:891–898. doi:10.2214/AJR.17.18177
40. Miyayama S, Yamashiro M, Ikeda R, et al. Efficacy of superselective conventional transarterial chemoembolization using guidance software for hepatocellular carcinoma within three lesions smaller than 3 cm. *Cancers*. 2021;13:6370. doi:10.3390/cancers13246370