Cerrahpaşa Med J 2026; 50: 1-11 ORIGINAL ARTICLE

Survival and Dosimetry in Advanced Hepatocellular Carcinoma with Tumor Sizes Up to 20 cm: A High Tumor Volume Institutional Cohort

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What is already known on this topic?

- *Survival outcomes after transarterial radioembolization with yttrium-90 (Y-90 TARE) vary widely, and prognostic factors in patients with large, bilobar, or high tumor burden disease are not clearly defined.*

What does this study add on this topic?

- *In patients with advanced hepatocellular carcinoma and large tumor burden, bilobar tumor distribution was the strongest independent predictor of poor survival after Y-90 TARE.*
- *Tumor absorbed dose and infused activity were not independently associated with overall survival in this high-volume cohort.*

Abstract

Objective: Transarterial radioembolization with yttrium-90 (Y-90 TARE) is a well-established locoregional therapy for hepatocellular carcinoma (HCC) in patients who are not candidates for transarterial chemoembolization (TACE); however, its clinical benefit and prognostic determinants in advanced-stage, high-volume, or bilobar disease remain unclear.

Methods: A total of 51 patients with Barcelona Clinic Liver Cancer (BCLC)-B and BCLC-C stage HCC who underwent Y-90 TARE between 2009 and 2018 and were unsuitable for TACE due to diffuse, bilobar, or infiltrative tumor morphology were retrospectively analyzed. Dosimetric data were evaluated in a subgroup treated with glass microspheres. Kaplan–Meier and Cox regression analyses were used to assess overall survival (OS) and its associations with clinical, anatomical, and dosimetric parameters.

Results: The median OS for the cohort was 11.05 months (95% CI: 8.8-18.0), with 12-, 24-, and 36-month survival rates of 46.9%, 23.0%, and 17.9%, respectively. Unilobar disease, albumin–bilirubin grade 1, and absence of portal vein thrombosis were associated with numerically longer survival. Multivariate analysis identified bilobar tumor distribution as the only independent predictor of mortality (hazard ratio: 3.07, $P = .039$). Tumor absorbed dose >100 Gy, higher tumor volume, and infused activity >40 mCi were not significantly associated with OS.

Conclusion: Transarterial radioembolization with yttrium-90 provides modest survival benefit in advanced HCC patients with large and bilobar tumors, particularly in those with preserved liver function and unilobar involvement. While tumor dose and activity did not independently predict survival, these findings underscore the importance of anatomical disease distribution and the need for refined dosimetric strategies, especially in bilobar disease.

Keywords: Advanced hepatocellular carcinoma, dosimetry, radioembolization, survival analysis, tumor burden, yttrium-90

Introduction

Each year, approximately 865 000 people worldwide are diagnosed with hepatocellular carcinoma (HCC), and 757 000 individuals lose their lives due to HCC-related causes.[1] Despite advances in cancer treatment, the 5-year survival rate remains low, ranging between 5% and 18%.[2] Although it is the sixth most commonly diagnosed cancer, it is the third most common cause of cancer-related deaths.

In advanced-stage HCC, particularly in patients with large tumor burdens, treatment options are limited and survival outcomes are poor. Larger, infiltrative, bilobar or extrahepatic spreading tumors pose additional therapeutic challenges due to their aggressive nature and vascular complexity. Systemic therapy remains the primary recommendation according to the 2022 Barcelona Clinic Liver Cancer (BCLC) guidelines; however, transarterial radioembolization with yttrium-90 (Y-90 TARE) has emerged as a promising locoregional therapy for selected patients.[3]

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Recently, several studies have evaluated the outcomes of Y-90 TARE in earlier-stage disease, often incorporating patient groups eligible for surgical resection or transplantation and using different dosimetric strategies including conventional and personalized dosimetry.[4,5] However, the cohort is fundamentally different, composed exclusively of BCLC-B and BCLC-C patients who were deemed unsuitable for transarterial chemoembolization (TACE) due to their diffuse, bilobar, multinodular, or infiltrative disease patterns. At minimum, lobar therapy was applied, and some patients underwent sequential or simultaneous bilobar treatments. This patient population is clinically comparable to those typically considered for systemic therapy alone.

Large randomized trials such as SorAfenib Versus RADIOEMBOLIZATION in Advanced Hepatocellular Carcinoma (SARAH) and SorAfenib Versus RADIOEMBOLIZATION in Advanced Hepatocellular Carcinoma (SARAH) and Selective Internal Radiation Therapy (SIRT) Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma (HCC) (SIRveNIB) did not demonstrate a significant survival advantage of Y-90 TARE over sorafenib, possibly due to suboptimal dosimetry and heterogeneous patient selection.[6-8] More recently, retrospective cohort studies have begun to explore the efficacy of combination therapies. Notably, a recent retrospective analysis evaluating bilobar Y-90 TARE in conjunction with systemic atezolizumab/bevacizumab treatment demonstrated improved survival outcomes compared to historical controls receiving TARE alone.[9]

The purpose of this study is to evaluate survival outcomes following Y-90 TARE in patients with advanced HCC, with particular emphasis on patient characteristics and dosimetric parameters. Additionally, survival results are compared with those reported in studies of systemic treatment agents to contextualize the efficacy of Y-90 TARE within the current therapeutic landscape.

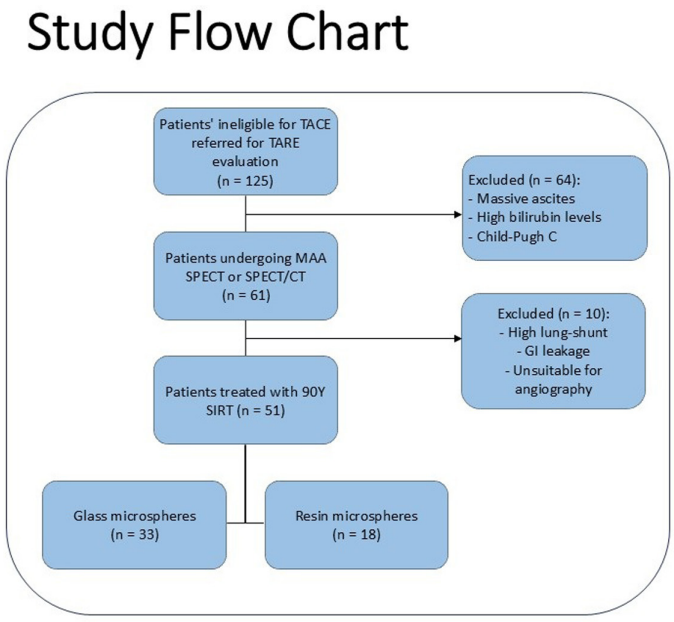


Figure 1. Flow diagram outlining the patient selection process. Of the 125 patients referred for transarterial radioembolization (TARE) evaluation due to transarterial chemoembolization ineligibility, 64 were excluded primarily due to massive ascites, elevated bilirubin, or Child-Pugh C liver function. A total of 61 patients underwent macroaggregated albumin SPECT or SPECT/computed tomography, with an additional 10 excluded due to high lung shunt, gastrointestinal leakage, or angiographic unsuitability. The final study population included 51 patients treated with yttrium-90 TARE.

Methods

Patient Population

This observational study was conducted between January 2009 and December 2018. During this period, 125 patients diagnosed with HCC presented to the clinic for Y-90 TARE treatment. The inclusion criteria involved patients with no indication for potentially curative treatments (surgery, ablation, or transplantation) following multidisciplinary assessment, who were ineligible for TACE, had anEastern Cooperative Oncology Group Performance Status (ECOG)performance score < 2, and were within Child-Pugh classes A-B8. The exclusion criteria include contraindication for angiography, lung shunt > 20%, uncorrectable flow to the gastrointestinal tract observed during Tc-99m macroaggregated albumin intrahepatic perfusion scintigraphy (Tc-99m MAA), tumor burden exceeding 70% of the whole liver volume, and presence of massive ascites. 64 patients were deemed ineligible for TARE treatment at the initial evaluation, and in that MAA planning scintigraphy was not applied. An additional 10 patients were found unsuitable for treatment after MAA planning (Figure 1). The remaining 51 patients were suitable for Y-90 TARE treatment. The mean post-therapeutical follow-up duration is 16.40 months (range: 1-77 months).

Pre-Treatment Evaluation

All patients included in the study were required to have an ECOG performance score of less than 2, be aged over 18 years, and have no contraindications for angiography. Whether the patients received previous local or systemic liver treatment was determined. Serum liver function tests were checked at the time of patient admission. The Child-Pugh scores were calculated, and the patients with a score of B8 or less were included in the study. Patients were staged according to the BCLC system. The albumin–bilirubin (ALBI) scoring system, calculated using the logarithmic values of albumin and total bilirubin levels, was also retrospectively applied to the study group.

All patients were managed by a multidisciplinary committee and were considered unsuitable for other local therapies. Pre-treatment contrast-enhanced upper abdominal magnetic resonance imaging (MRI) and F-Flurodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) images were obtained.

Transarterial Radioembolization Procedure

As the first step, planning celiac angiography combined with Tc-99m MAA was performed to define tumor vascularity and potential extrahepatic shunting as well as to calculate therapeutic dose planning of Y-90 TARE. All patients were given 300 mg of perchlorate per oral 30 minutes before angiography to prevent any possible non-specific gastric uptake due to the availability of free Tc-99m pertechnetate component within the Tc-99m MAA kit. Access to the hepatic artery via the celiac artery was achieved using angiography, and then 5-10 mCi (185-370 MBq) of Tc-99m MAA was administered into one of the hepatic artery branches. Following the angiography procedure, planar scintigraphy covering the thoracoabdominal area and also an additional SPECT/CT imaging from the upper abdomen were acquired within the first hour after injection by using a dual-head SPECT gamma camera integrated with a 16-detector CT gantry (Symbia T16, Siemens

Healthcare). The acquisition parameters for SPECT were a 128 · 128 matrix with 64 frames (20 s/frame). A low-dose CT scan was performed for attenuation correction and morphological mapping of the liver. In the study cohort, the targeted tumor dose was set at least 120 Gy with glass-based treatment by using a multicompartmental dosimetry approach; the activity of resin microspheres was calculated according to the body surface area (BSA) method.[10] The lung shunt fraction was calculated using planar region of interest (ROIs) and was planned not to exceed 30 Gy for single treatment and 50 Gy for dual treatment.[11] Patients with gastrointestinal leaks did not undergo treatment.

Within 14 days of the planning procedure, the intended dose of Y-90 TARE was administered by reaching the same location of the hepatic artery via a second celiac angiography. The choice between resin and glass microspheres was based on availability; if both were available, the decision was made non-randomly according to the clinician's preference. Of the 51 patients included in the study, 33 (65%) were treated with glass microspheres and 18 (35%) with resin microspheres. In patients needing bilobar treatment, the other lobe is treated with lobar therapy at the third month of treatment.

Statistical Analyses

Descriptive and inferential statistical analyses were performed using both SPSS version 29 (IBM SSPS Corp., Armonk, NY, USA) and R (version 4.4.3). Numerical data are presented as median and SD, or as mean and range, where appropriate. Categorical data are presented as frequencies (n) and percentages (%). The chi-square test was used to compare categorical variables, and differences in continuous variables were assessed using the Mann–Whitney *U*-test for 2-group comparisons or the Kruskal–Wallis test for 3 or more groups. Kaplan–Meier curves for overall survival (OS) were plotted for both clinical and dosimetric subgroups, and log-rank tests were performed to compare survival distributions. Overall survival was defined as the time in months from treatment initiation to the date of death or last follow-up. Confidence intervals for survival medians were estimated using a bootstrap resampling method with 1000 iterations. Univariate Cox proportional hazards regression analysis was conducted using a broad range of clinical and dosimetric parameters. Variables with $P < .100$ in univariate analysis and no multicollinearity were included in multivariate Cox regression analysis. Hazard ratios (HR) and 95% CIs were reported for all models. All tests were 2-sided, and a *P*-value < .05 was considered statistically significant. Analyses were conducted programmatically using R packages including survival, survminer, officer, and flextable to ensure reproducibility, and SPSS was used to complement model building and subgroup analyses. Statistical scripts in R were used to ensure reproducibility, including the generation of Word and PowerPoint outputs for tabular and graphical survival summaries. Kaplan–Meier survival curves were generated using the survminer package in R, allowing for visual comparison across clinical and dosimetric subgroups.

Ethical Approval

This retrospective observational study was approved by the Clinical Research Ethics Committee of İstanbul University–Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval No: 70920, Decision Date: May 7, 2019; Document Date: May 9, 2019). The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant national regulations. Written informed consent was obtained from all patients prior to treatment, and patient data were analyzed anonymously.

Results

Patients

Table 1 summarizes the baseline characteristics of the study population (n = 51). The median age at diagnosis was 66.6 years (SD = 8.8), and the majority of patients were male (84%). Hepatitis B (49%) and hepatitis C (41%) infections constituted the main etiologies of liver disease. Cirrhosis was present in 43% of patients, and 29.4% had received prior liver-directed therapy.

Unilobar tumor distribution was observed in 55% of patients, while 45% had bilobar disease. The median largest tumor diameter was 7.0 cm (interquartile range: 4.3-12.0), with 31% of patients having tumors ≥10 cm, including 5 patients (9.8%) with tumor diameters ≥15 cm. Portal vein thrombosis (PVT) was present in 33% of patients, and extrahepatic disease was detected in 49%. According to BCLC staging, 41% were classified as BCLC-B and 59% as BCLC-C. Most patients were ALBI grade 1 (80%) and Child-Pugh class A (86%).

When comparing the baseline characteristics between patients treated with glass and resin microspheres, cirrhosis was more frequently observed in the resin group (67% vs. 30%, $P = .01$). In addition, the diagnosis was confirmed by biopsy in all patients in the resin group, whereas MRI-based diagnosis was used in 8 patients (24%) in the glass group ($P = .02$). No statistically significant differences were observed in other baseline characteristics between the 2 groups. The median largest tumor size was slightly higher in the resin group (8.37 ± 5.14 cm vs. 7.72 ± 4.62 cm, $P = .65$).

Table 2 summarizes the dosimetric and volumetric characteristics of the cohort, including tumor dose, liver exposure, lung shunt, and infused activity. The median tumor absorbed dose was 121.5 Gy (SD: 44.9), while the irradiated liver dose and lung dose were 50.8 Gy (SD: 25.1) and 9.2 Gy (SD: 10.6), respectively. The median tumor volume was 346.0 cm^3, and the target liver volume was 853.5 cm^3, corresponding to approximately 49.5% of the total liver volume.

The median infused Y-90 activity was 51.6 mCi (SD = 28.5), with a slightly higher dose administered in the glass group (60.6 mCi) compared to the resin group (52.6 mCi). The median lung shunt fraction was 10.0% (SD = 6.6), and the median dose per volume delivered to the tumor was 0.42 Gy/cm^3 (SD = 0.29).

Prognostic Factors

The median OS for the entire cohort was 11.05 months (95% CI: 8.8-18.0), as determined by Kaplan–Meier analysis. The OS rates at 12, 24, and 36 months were 46.9%, 23.0%, and 17.9%, respectively (Figure 2). Out of the 8 surviving patients, 1 (5.6%) received treatment with resin microspheres while 7 others (21.2%) were treated with glass microspheres.

Kaplan–Meier Subgroup Analyses

In subgroup analysis, age <65 years was associated with a numerically longer median OS of 15.6 months compared to 9.7 months in older patients ($P = .16$). Similarly, etiologic subtypes did not significantly impact survival ($P = .63$), although median OS was longer in patients with hepatitis C virus–related HCC (13.4 vs. 10.2 months for hepatitis B virus). Albumin–bilirubin grade was a strong predictor of survival: patients with ALBI grade 1 had a significantly longer OS than those with grade 2 (15.6 vs. 4.1 months, $P < .001$) (Figure 3A). Tumor distribution was another significant prognostic factor ($P = .018$); patients with unilobar disease had more than double the median OS compared to those with bilobar disease (18.0 vs. 8.8 months) (Figure 3B). Alpha-fetoprotein levels ≥400 ng/mL were associated with numerically shorter survival

Table 1. Characteristics of Patients

	n = 51	*P*
Age at diagnosis (years), ± SD	66.6 ± 8.8	.122
<65 years, n (%)	20 (39)	
≥65 years, n (%)	31 (61)	
Male sex, n (%)	43 (84)	
Etiology of liver disease, n (%)		.072
HBV	25 (49)	
HCV	21 (41)	
Alcohol	4 (8)	
Other	1 (2)	
Prior liver treatment, n (%)		
Present	15 (29.4)	
Absent	36 (70.6)	
Cirrhosis, n (%)	22 (43)	
Ascites, n (%)		.368
None	39 (76)	
Grade 1	6 (12)	
Grade 2	6 (12)	
Distribution, n (%)		
Unilobar	28 (55)	
Bilobar	22 (45)	
Largest tumor size	7.0 (IQR: 4.3-12.0)	.001
≤5 cm	20 (39.2)	
5-10 cm	15 (29.4)	
10-15 cm	13 (21.6)	
≥15 cm	5 (9.8)	
Portal vein thrombosis		
Branch	17 (33)	
Absent	34 (67)	
Method of diagnosis		
Biopsy	43 (84)	
MRI	8 (16)	
Extrahepatic disease, n (%)	25 (49)	
AFP (ng/mL)		
<400	35 (69)	
≥400	16 (31)	
Liver function		
Albumin (g/dL) ± SD	3.80 ± 0.55	
Total Bilirubin (mg/dL) ± SD	0.80 ± 0.47	
INR ± SD	1.17 ± 0.23	
Child-Pugh, n (%)		
A	44 (86)	
B-B8	7 (14)	
ALBI, n (%)		
ALBI 1	41 (80)	
ALBI 2	10 (20)	
BCLC		
BCLC-B	21 (41)	
BCLC-C	30 (59)	
Y-90 Particles		
Glass	33 (65)	
Resin	18 (35)	

AFP, alpha-fetoprotein; ALBI, albumin–bilirubin grade; BCLC, Barcelona Clinic Liver Cancer; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range.

compared to lower levels (8.0 vs. 11.2 months, $P = .46$) (Figure 3C). Similarly, PVT was associated with numerically shorter OS (5.4 vs. 15.6 months, $P = .20$) (Figure 3D).

No significant differences in OS were observed between patients with or without prior liver-directed therapy ($P = .79$), cirrhosis ($P = .99$), or ascites ($P = .95$), with nearly overlapping survival curves in all comparisons. No survival difference was detected across Child-Pugh classes (A vs. B, $P = .83$), or between BCLC-B and BCLC-C stages (15.6 vs. 9.3 months, $P = .43$).

Among dosimetric parameters, patients receiving tumor absorbed doses >100 Gy had a numerically lower OS (8.8 vs. 11.2 months, $P = .59$) (Figure 4A). Tumor volume also showed no significant correlation with survival ($P = .56$), although larger tumors (>320 cm^3) had slightly shorter OS (Figure 4B). Likewise, infused activity >40 mCi (Figure 4C) and higher dose per volume values (Figure 4D) were not associated with improved survival.

Other volumetric and composite parameters also showed no significant association with OS, including liver dose >50 Gy ($P = .39$) and target liver volume >850 cm^3 ($P = .41$). Notably, infused activity was the only available dose metric for the entire cohort, owing to the use of BSA-based calculations in all patients treated with resin Y-90 microspheres.

Detailed Kaplan–Meier survival curves for each variable are included in Supplementary Data 1.

Univariate and Multivariate Analysis Summary

In the univariate Cox regression analysis, several variables were found to be associated with OS. These included total bilirubin (HR: 2.50, 95% CI: 1.195-5.234, $P = .015$), bilobar tumor distribution (HR: 2.10, 95% CI: 1.124-3.902, $P = .020$), ALBI grade 2 (HR: 3.15, 95% CI: 1.497-6.630, $P = .003$), and whole liver volume (HR: 1.001, 95% CI: 1.000-1.001, $P = .012$). Albumin level was borderline significant (HR: 0.559, 95% CI: 0.308-1.015, $P = .056$).

Table 2. Descriptive Statistics of Dosimetric and Volumetric Features

	Median	SD	*P*
Dose			
Tumor dose (Gy)	121.50	44.86	
Irradiated non-tumoral liver dose (Gy)	50.81	25.07	
Irradiated lung dose (Gy)	9.18	10.56	
Infused Y-90 dose (mCi)	51.60	28.49	.221
Infused Y-90 glass dose	60.59	30.70	
Infused Y-90 resin dose	52.58	23.85	
Lung shunt fraction	10.00	6.62	
Volume			
Target volume (cm^3)	853.50	727.87	
Tumor volume (cm^3)	346.00	382.65	
Whole liver volume	1805.50	1047.41	
Irradiated liver volume - whole liver ratio	49.46	23.71	
Dose per volume (Gy/cm^3)	0.42	0.29	

cm^3, cubic centimeter; Gy, gray (absorbed radiation dose); mCi, millicurie; SD, standard deviation; Y-90, yttrium-90. Lung shunt fraction represents the percentage of administered activity shunted to the lungs. The irradiated liver-to-whole liver volume ratio represents the percentage of the whole liver volume exposed to radiation. Values are presented as median and SD.

In the multivariate analysis, bilobar tumor distribution remained independently associated with worse survival (HR: 3.07, 95% CI: 1.06-8.89, *P* = .039), while whole liver volume showed a borderline association (HR: 1.000, 95% CI: 1.000-1.001, *P* = .085). Table 3 presents the full results of univariate and multivariate Cox regression.

Discussion

In this cohort of advanced HCC patients treated with Y-90 TARE, ALBI score demonstrated a strong prognostic association with OS. Patients with ALBI grade 1 had significantly longer survival than those with grade 2 (15.6 vs. 4.1 months, *P* = .0014), a finding supported by univariate analysis (HR: 3.15, *P* = .003). Although ALBI grade did not retain significance in the multivariate model, this may reflect multicollinearity with other liver function indicators such as bilirubin and albumin.

These results reinforce the well-established role of ALBI in TARE outcomes, as seen across multiple studies regardless of microsphere type.[12,13] Both resin- and glass-based series—including those using BSA, partition, and medical internal radiation dosimetry (MIRD) dosimetry—have highlighted ALBI as a key predictor of not only survival but also treatment-related hepatic toxicity. Notably, Jeschke et al also found ALBI to be predictive of radioembolization-induced liver disease (REILD) development, particularly in bilobar Y-90 TARE. While the study did not report toxicity outcomes, the prognostic importance of ALBI for survival in advanced HCC remains consistent. Given its simplicity and reproducibility, ALBI should be incorporated into routine pre-treatment assessment in advanced HCC patients considered for TARE, especially when individualized dosimetry is not available.

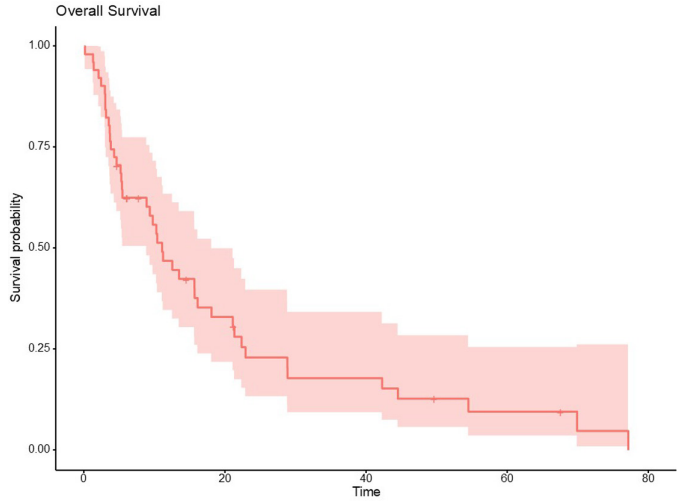


Figure 2. Kaplan–Meier curve showing the overall survival (OS) of the entire cohort. The median OS was 11.05 months (95% CI: 8.8-18.0). The 12-, 24-, and 36-month survival rates were 46.9%, 23.0%, and 17.9%, respectively.

In the cohort of advanced HCC patients undergoing Y-90 TARE, tumor distribution was one of the most significant prognostic factors for OS. Patients with unilobar disease had a median OS of 18.0 months compared to only 8.8 months for those with bilobar involvement (*P* = .018). This difference persisted in multivariate Cox analysis (HR: 3.07, 95% CI: 1.06-8.89, *P* = .039), confirming bilobar tumor distribution as an independent predictor of worse outcome.

The findings are directly supported by the results of Jeschke et al, who analyzed outcomes in a large, multi-center cohort and found that bilobar Y-90 TARE was associated with significantly shorter survival and higher risk of REILD, particularly in patients with compromised liver function.[9] Although REILD incidence was not evaluated in the study, the adverse prognostic impact of bilobar disease likely reflects several overlapping factors—greater tumor burden, technical complexity, and limited capacity for selective therapy.

Moreover, the frequent need for sequential or simultaneous bilobar treatments in this group may increase cumulative liver exposure, particularly when dosimetry is not personalized. While some recent reports advocate for selective bilobar TARE using cone-beam CT and advanced partition models, such approaches remain challenging in real-world advanced-stage populations with infiltrative or diffuse tumors.

Collectively, the data and the external literature confirm that bilobar tumor distribution remains a major determinant of post-TARE prognosis and should be carefully considered when selecting advanced HCC patients for treatment.

In the cohort of advanced HCC patients, high tumor burden was common: 31% of patients had tumors ≥10 cm, and nearly 10% had lesions ≥15 cm. Despite this, median OS was 11.05 months, a result that compares favorably with outcomes reported in the SARAH and SIRveNIB trials, where median tumor diameters were typically smaller.[6-8]

Tumor volume itself was not a statistically significant predictor of survival in the Kaplan–Meier subgroup analysis (*P* = .56), nor in the multivariate model. However, the consistently shorter survival observed in patients with larger tumors aligns with biological expectations. Notably, tumor distribution (unilobar vs. bilobar)

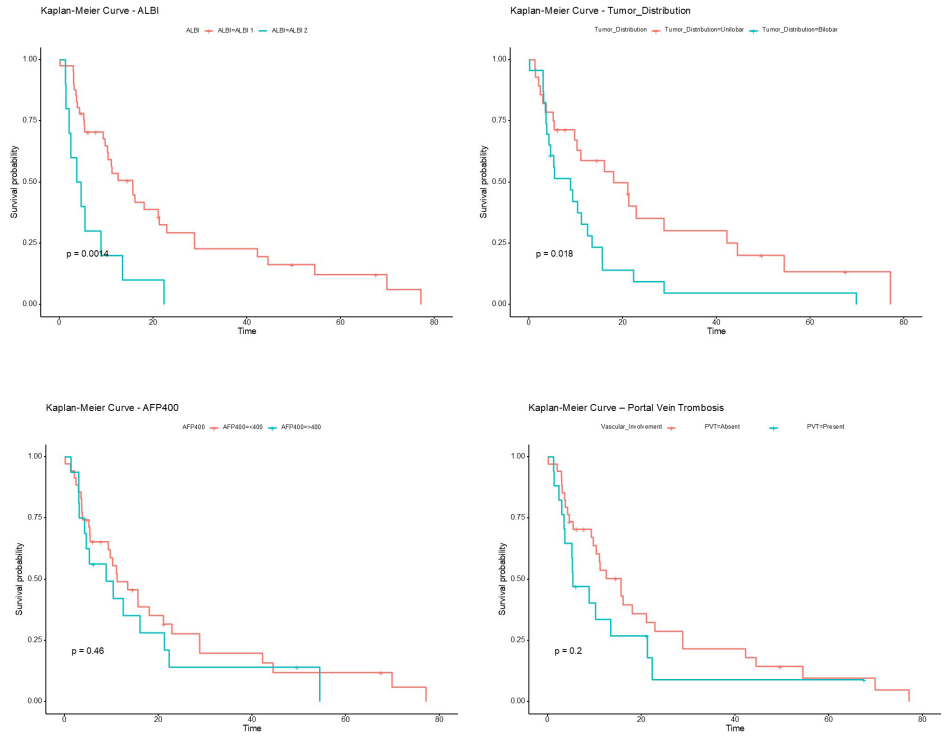


Figure 3. Kaplan–Meier survival analysis for selected prognostic factors: (A) Barcelona Clinic Liver Cancer stage, (B) Albumin–bilirubin grade, (C) Tumor distribution (unilobar vs. bilobar), (D) Portal vein thrombosis.

appeared to be a stronger determinant of prognosis than absolute tumor size, suggesting that anatomical extent and feasibility of selective treatment may override sheer volume in influencing outcomes.

Unlike the SARAH and SIRveNIB trials, which primarily used BSA-based activity and did not incorporate dosimetric data, the study included detailed tumor and liver dosimetry in patients treated with glass Y-90 TARE. This allowed for a more refined

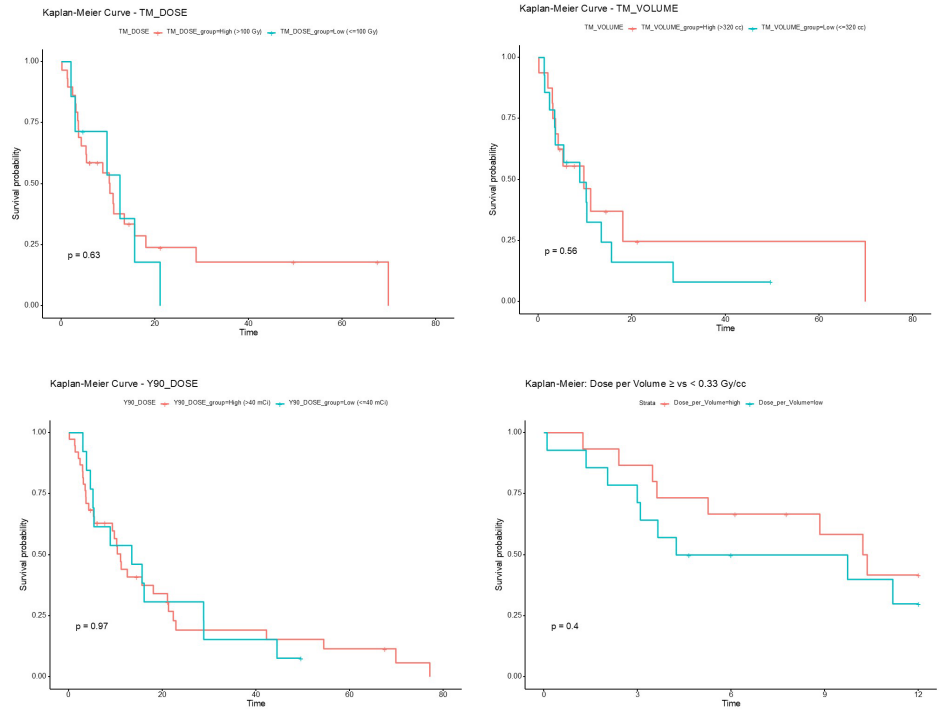


Figure 4. Kaplan–Meier survival curves demonstrate overall survival (OS) according to key dosimetric and volumetric parameters: (A) tumor absorbed dose >100 Gy vs. ≤100 Gy, (B) tumor volume >320 cm^3 vs. ≤320 cm^3, (C) infused yttrium-90 activity >40 mCi vs. ≤40 mCi, and (D) dose per tumor volume (Gy/cm^3) ≥0.33 vs. <0.33. None of these parameters showed a statistically significant association with OS in this cohort.

Table 3. Univariate Analysis of Variables Associated with Survival in Y-90 TARE.

	Univariate			Multivariate		
	HR	**95% CI**	***P***	**HR**	**95% CI**	***P***
Treatment age	1.003	0.973-1.034	.857			
Largest tumor size	1.030	0.962-1.103	.392			
AFP	1.000	1.000-1.000	.219			
INR	2.701	0.780-9.359	.117			
Bilirubin	2.501	1.195-5.234	**.015**	2.391	0.682-8.376	.173
Albumin	0.559	0.308-1.015	.056	0.821	0.294-2.292	.707
Prior liver treatment	1.095	0.566-2.119	.787			
Cirrhosis	0.995	0.541-1.830	.987			
Ascites	1.025	0.497-2.110	.947			
Tumor distribution	2.096	1.124-3.902	**.020**	3.070	1.060-8.887	**.039**
Portal vein thrombosis	1.534	0.798-2.948	.199			
EHD	1.540	0.836-2.828	.165			
BCLC	1.281	0.689-2.377	.432			
ALBI	3.148	1.497-6.630	**.003**			
Y-90 device (glass vs. resin)	0.681	0.360-1.286	.236			
Tumor dose	0.990	0.978-1.003	.128			
Liver target dose	0.996	0.982-1.011	.640			
Lung dose	1.004	0.969-1.041	.809			
Y-90 dose	1.006	0.994-1.018	.311			
Lung shunt ratio	1.033	0.983-1.087	.201			
Target volume	1.000	1.000-1.001	.103			
Tumor volume	1.000	0.999-1.001	.756			
Whole liver volume	1.001	1.000-1.001	**.012**	1.000	1.000-1.001	**.085**
Target/liver percentage	1.001	0.984-1.018	.945			
Dose per volume	1.001	0.419-2.388	.998			

P-value < .05 considered as significant.
AFP, alpha-fetoprotein; ALBI, albumin–bilirubin grade; BCLC, Barcelona Clinic Liver Cancer; EHD, extrahepatic disease; HR, hazard ratio; TARE, transarterial radioembolization; Y-90, yttrium-90 microspheres.

analysis of how volumetric tumor characteristics interact with absorbed dose. The data suggest that large tumor size alone should not be considered a contraindication for Y-90 TARE, particularly in experienced centers capable of adapting treatment strategies to anatomical complexity.

In the study, no dosimetric or volumetric parameter showed a statistically significant association with OS, either in univariate Kaplan–Meier analysis or multivariate modeling. This includes tumor absorbed dose (Gy), mean liver dose, lung dose, infused activity, and dose per volume metrics. Interestingly, in several comparisons, patients receiving higher activity or higher dose appeared to have numerically shorter survival. This seemingly paradoxical trend likely reflects treatment selection bias, where patients with more extensive or aggressive disease were assigned higher doses or larger target volumes based on clinical judgment.

Importantly, dosimetric analysis was only available for patients treated with glass Y-90 TARE, while infused activity in mCi was analyzed across the entire cohort, all of whom were treated using BSA-based planning with resin microspheres. The lack of survival correlation with absolute activity reinforces the limitations of BSA dosimetry, which does not account for tumor burden, distribution, or liver function.

Similarly, infused activity >40 mCi was not associated with improved outcomes (11.1 vs. 13.4 months, $P = .97$). In fact, patients who received higher activities had numerically shorter survival, likely reflecting treatment selection bias in favor of higher dose delivery in patients with more extensive disease. This observation

emphasizes the limitations of BSA-based dosing, where activity is prescribed based on BSA without accounting for tumor burden, anatomical distribution, or liver function. The lack of correlation between infused activity and survival in the study does not contradict the value of dosimetry; rather, it highlights the need for personalized or image-based treatment planning to avoid both under- and overtreatment.

One additional explanation may relate to the large tumor burden observed in a considerable proportion of the cohort. In patients with very large tumors, the maximum deliverable activity is often constrained by lung shunt fraction and safety limits, which may restrict the achievable tumor absorbed dose despite large treatment volumes. In such situations, survival may be more strongly influenced by the amount of remaining functional liver parenchyma rather than the absolute tumor dose delivered. Conversely, higher absorbed doses are generally easier to achieve in patients with smaller tumors and preserved liver reserve, where treatment activity can be escalated more safely and dose distribution is more homogeneous.

Comparison with Systemic Therapy Trials

The OS observed in the cohort of patients with advanced HCC (median OS: 11.05 months) should be interpreted in the context of previously reported outcomes from randomized trials evaluating both locoregional and systemic therapies. Direct cross-trial comparisons are inherently limited because of differences in patient selection, tumor burden, liver function, and treatment allocation strategies across studies. In addition, survival outcomes in the control arms of pivotal trials vary substantially, and therefore treatment effects reported as hazard ratios within randomized studies may provide a more balanced estimate of therapeutic benefit than absolute median survival values alone.

Two phase 3 randomized trials, SARAH and SIRveNIB, compared Y-90 TARE with sorafenib in patients with locally advanced HCC. Both trials failed to demonstrate superiority of Y-90 TARE over sorafenib. In the SARAH trial, median OS was 8.0 months with Y-90 TARE and 9.9 months with sorafenib (hazard ratio (HR) 1.15), while the SIRveNIB trial reported median OS of 8.8 months with Y-90 TARE compared with 10.0 months with sorafenib (HR 1.10). These results initially limited the adoption of Y-90 TARE as a first-line therapy in advanced HCC. However, it should be noted that both trials applied BSA-based dosimetry rather than personalized partition dosimetry, which may influence tumor absorbed radiation dose and treatment efficacy.

In the cohort, the median OS of 11.05 months exceeds the survival reported for Y-90 TARE in both SARAH and SIRveNIB, despite the presence of several adverse baseline characteristics. A considerable proportion of the patients presented with bilobar disease (45%), large tumors (≥10 cm in 31%), and PVT (33%), indicating a cohort with advanced intrahepatic tumor burden.

A key observation in the study is the marked survival difference according to intrahepatic tumor distribution. Patients with unilobar disease demonstrated substantially longer survival (median OS: 18.0 months), whereas those with bilobar involvement had shorter survival (median OS: 8.8 months). This finding suggests that anatomical tumor distribution represents a critical determinant of treatment outcomes following Y-90 TARE. Similar observations have been reported in a retrospective analysis by Jeschke et al, in which Y-90 TARE outcomes appeared more favorable in patients with limited intrahepatic disease, whereas bilobar involvement was associated with poorer survival and an increased risk of radiation-induced liver disease. Collectively, these findings support the concept that disease distribution within the liver may outweigh other clinical factors in determining the effectiveness of locoregional therapies.

During the past decade, systemic treatment options for advanced HCC have evolved considerably with the introduction of immune checkpoint inhibitors and anti-angiogenic agents. In the IMbrave150 trial, the combination of atezolizumab plus bevacizumab significantly improved survival compared with sorafenib, with a reported median OS of 19.2 months versus 13.4 months, respectively (HR = 0.66).[14] Similarly, the single tremelimumab regular interval durvalumab (STRIDE) regimen evaluated in the HIMALAYA trial (Durvalumab and tremelimumab as first-line treatment in patients with advanced hepatocellular carcinoma) demonstrated improved survival compared with sorafenib, with a median OS of 16.4 months versus 13.8 months (HR = 0.78).[15,16] These results highlight the substantial therapeutic progress achieved with immunotherapy-based combinations in advanced HCC. To further evaluate the safety and effectiveness of this regimen in broader clinical practice beyond the selected trial population of HIMALAYA, the phase 3b SIERRA study (Durvalumab and tremelimumab as first line treatment in participants with advanced hepatocellular carcinoma) was subsequently initiated. However, mature OS data have not yet been reported.[17]

Nevertheless, it is important to recognize that randomized systemic therapy trials typically enroll selected patient populations, most commonly including patients with preserved liver function (Child-Pugh A) and good performance status. Moreover, these studies generally do not stratify patients according to intrahepatic tumor distribution, such as unilobar versus bilobar disease. Consequently, the influence of anatomical tumor burden on treatment outcomes remains insufficiently characterized in systemic therapy trials.

Real-world analyses may provide complementary insights into treatment effectiveness in broader patient populations. In a retrospective study by Jeschke et al, median OS of 13.0 months was reported for patients treated with atezolizumab plus bevacizumab, while patients with bilobar disease achieved a median OS of approximately 12.1 months.[9] In contrast, bilobar disease in the cohort was associated with shorter survival following Y-90 TARE. These observations suggest that systemic therapy may provide more effective disease control in patients with extensive intrahepatic tumor burden, particularly in cases where selective Y-90 TARE becomes technically challenging or when the risk of radiation-induced liver disease increases.

Taken together, the findings support a more nuanced treatment selection strategy in advanced HCC. Transarterial radioembolization with yttrium-90 may remain an effective locoregional option for carefully selected patients with preserved liver function and limited intrahepatic disease distribution, particularly in unilobar or segmental involvement. In contrast, patients with extensive bilobar disease may derive greater benefit from systemic immunotherapy-based regimens. Future studies integrating tumor distribution, personalized dosimetry, and evolving systemic therapy strategies may further refine patient selection and optimize treatment outcomes.

The survival outcomes across these studies are summarized in Table 4, which compares the findings with previously published randomized and real-world data according to treatment modality and tumor distribution.

Technical Considerations

Bilobar HCC presents unique technical and clinical challenges for Y-90 TARE. In the cohort, all patients with bilobar disease were treated using either sequential or same-day bilobar TARE, depending on functional reserve and tumor distribution. Given

Table 4. Comparison of Overall Survival Across Studies

Study	Treatment	Overall OS (months)	Unilobar OS (months)	Bilobar OS (months)	HR
Current Study	Y-90 TARE (resin + glass)	11.05	18.0	8.8	
SARAH (2017)	Sorafenib	9.9	N/A	N/A	
SARAH (2017)	Y-90 TARE (resin, BSA)	8.0	N/A	N/A	1.15
SIRveNIB (2018)	Sorafenib	10.2	N/A	N/A	
SIRveNIB (2018)	Y-90 TARE (resin, BSA)	8.8	N/A	N/A	1.10
IMbrave150 (2022)	Atezolizumab + bevacizumab	19.2	N/A	N/A	0.66
IMbrave150 (2022)	Sorafenib	13.4	N/A	N/A	
Jeschke et al (2023)	Atezolizumab + bevacizumab	13.0	13.1	12.1	
Jeschke et al (2023)	Y-90 TARE (bilobar, mostly glass)	8.1	13.0	7.1	
HIMALAYA (2025)	Durvalumab plus tremelimumab	16.4	N/A	N/A	0.78
HIMALAYA (2025)	Sorafenib	13.8	N/A	N/A	

In Jeschke et al, Y-90 TARE was predominantly administered using glass microspheres with partition dosimetry.
BSA, body surface area method; HR, hazard ratio; N/A, not available; OS, overall survival; Y-90 TARE, yttrium-90 transarterial radioembolization.

the extensive treatment volume, especially when approaching or exceeding 50% of the total liver, careful staging and recovery monitoring are essential.

In the cohort, 5 patients (9.8%) received Y-90 TARE with 100% target liver volume, indicating whole liver treatment. This group is of particular concern regarding post-treatment hepatic recovery. A recent prospective study by Allimant et al demonstrated that following glass Y-90 TARE with personalized dosimetry, whole liver function declined by up to 32% at 2 weeks and remained below baseline levels for at least 3 months post-treatment, even in the absence of REILD.[18]

These findings have major implications for treatment sequencing in bilobar disease. In the absence of clear guidelines, there is no established interval for sequential lobar treatments. While 3 months is often considered a reasonable waiting period for contralateral liver regeneration and functional compensation, the dataset indicates that this may not be sufficient for all patients. Notably, 11 patients (21.6%) in the study had OS shorter than 3 months. For such patients, a sequential lobar approach may not provide sufficient therapeutic benefit before death and may increase the risk of liver decompensation.

Personalised vs. Standard Dosimetry

The DOSISPHERE-01 trial was a landmark randomized phase 2 study that demonstrated the superiority of personalized dosimetry over standard BSA-based planning in patients with locally advanced HCC. However, direct comparison with the cohort highlights important differences in patient selection and treatment context. While the study included patients with more extensive disease burden—including 49% with extrahepatic spread — DOSISPHERE-01 excluded all cases with extrahepatic metastasis and focused exclusively on intrahepatic disease with preserved liver function. The outcomes appear numerically lower compared to the personalized arm of DOSISPHERE-01 (median OS: 11.0 vs. 26.6 months),

While the personalized dosimetry approach in DOSISPHERE-01 was supported by advanced angiographic techniques—including segmental catheterization, flow redistribution, and cone-beam CT-guided planning—such methods were not routinely employed in the center during the study period. The planning angiography relied on conventional digital subtraction angiography with lobar catheterization, and treatment activity was primarily determined using the BSA method in the resin group and simplified MIRD in the glass group.

The absence of advanced targeting tools such as cone-beam CT or flow diversion techniques likely limited the ability to achieve highly selective delivery and maximize tumor-to-liver dose differentials. These technical factors, combined with the greater tumor burden and impaired liver function in the cohort, may explain the more modest outcomes observed compared to the personalized dosimetry arm in DOSISPHERE-01.

Nonetheless, the results highlight the real-world applicability and safety of Y-90 TARE in advanced HCC, even without full adoption of modern dosimetric and interventional techniques. The findings underscore the growing need for personalized dosimetry protocols and angiographic precision in order to expand the therapeutic potential of TARE in complex cases.

Tumor Volume and Dose Efficiency

Tumor volume is a critical parameter in Y-90 TARE planning, on par with tumor absorbed dose (Gy), and should be considered a core element in interventional decision-making. In the study, the median tumor volume was 346.0 cm^3, while the target liver volume was 853.5 cm^3—indicating a substantial tumor burden relative to the treated area. Despite delivering a median infused activity of 60.6 mCi in the glass group, the resulting median tumor absorbed dose was 121.5 Gy, suggesting a limited dose efficiency per unit volume.

In contrast, Tahir et al achieved higher tumor doses (>180 Gy) using lower infused activity (median 1.59 GBq) and a smaller target volume (444 cm^3) by applying single-compartment MIRD dosimetry with resin microspheres. This resulted in significantly longer survival (18.1 months) and a dose-response effect, where patients receiving >180 Gy had markedly better outcomes than those with lower doses ($P = .01$).[5]

The apparent increase in tumor absorbed dose observed by Tahir et al, despite lower infused activity and smaller target volumes, may in part be explained by their cohort's markedly smaller

median tumor volumes. This inverse relationship highlights the critical influence of tumor size on dose distribution and emphasizes the need for scalable treatment planning in advanced HCC.

In clinical practice, such findings may unintentionally encourage operators to apply uniform high-dose thresholds, regardless of tumor volume. However, a dose prescription suitable for a 100 cm^3 tumor may be inadequate—or even unsafe—when scaled to a 300 cm^3 lesion, and certainly inappropriate for the largest tumors in the study, which reached up to 1230 cm^3. These scenarios underscore the importance of volume-adapted dosimetry, wherein treatment planning must account not only for desired absorbed dose but also for tumor geometry, perfusion heterogeneity, and liver reserve.

Risk Factors

The multivariate Cox regression analysis identified bilobar tumor distribution as the only independent predictor of OS, with a hazard ratio of 3.07 (P = .039). This finding aligns with previous evidence suggesting that bilobar involvement reflects not only greater tumor burden but also anatomical complexity that limits selective delivery and increases non-target exposure. This variable was also strongly associated with poor outcomes in univariate analysis (P = .020), reinforcing its clinical significance.

Total bilirubin and ALBI grade 2 were significant in univariate analysis but lost significance in the multivariate model, likely due to collinearity with liver volume and other hepatic reserve indicators. Notably, whole liver volume showed a borderline association with survival (HR 1.000, P = .085), suggesting that larger hepatic volumes may be a surrogate for more extensive disease, bilobar treatment, or impaired parenchymal function.

Although no statistically significant difference in survival was observed between BCLC-B and BCLC-C stages in the cohort (15.6 vs. 9.3 months, P = .43), this finding should be interpreted in the context of the study population. The lack of separation between these 2 groups may be due to the overlapping nature of clinical characteristics in this cohort, where many BCLC-B patients were deemed ineligible for TACE due to tumor morphology or distribution, and a substantial proportion of BCLC-C patients had preserved liver function with normal liver function tests (LFTs). This convergence likely minimized the prognostic discrimination typically associated with the BCLC staging system.

These findings emphasize that in advanced HCC, anatomical distribution and global hepatic involvement may outweigh isolated laboratory metrics in predicting prognosis following Y-90 TARE. Additionally, the data support the notion that volumetric disease burden—especially when coupled with suboptimal liver function—requires tailored treatment planning and may define a subgroup of patients less likely to benefit from standard TARE protocols.

Limitations

This study has several limitations that should be acknowledged. First, its retrospective, single-center design introduces the possibility of selection bias, especially in treatment allocation between resin and glass Y-90 microspheres. The choice of dosimetric methodology (BSA vs. MIRD) was not randomized but rather based on institutional protocols and clinical feasibility, which may limit the comparability of treatment groups.

Second, personalized dosimetry was not performed in all patients. Detailed dose calculations were only available in the glass subgroup, whereas all resin-treated patients were dosed using the BSA method. As such, key dosimetric variables like tumor absorbed dose were missing for a substantial portion of the cohort, precluding a unified dose-response analysis across the entire population.

Third, advanced imaging techniques such as cone-beam CT, segmental catheterization, and flow diversion were not routinely utilized during treatment planning. These technologies have become increasingly relevant in enhancing the selectivity and safety of TARE, particularly in bilobar or infiltrative disease. Their absence may have influenced both dosimetric outcomes and toxicity profiles.

Fourth, treatment-related toxicity (e.g., REILD) or post-treatment liver function dynamics were not systematically assessed. As a result, the safety profile of TARE in this advanced population could not be formally quantified, and subclinical toxicities may have gone undetected.

Finally, the sample size (n = 51), though reflective of a high-volume cohort, remains relatively limited, particularly for multivariate modeling and subgroup survival analyses. Some trends, while clinically relevant, may not have reached statistical significance due to power limitations.

Future Directions

There is also a growing need for volume-adapted dosimetry algorithms. As the findings and others suggest, tumor volume critically affects absorbed dose distribution, and current fixed-threshold models may not adequately capture this complexity. Future protocols should explore tumor-to-liver dose ratios, dose-per-cm^3 thresholds, and composite scoring systems that integrate anatomy, function, and disease extent.

Additionally, the potential for combining Y-90 TARE with systemic immunotherapy (e.g., atezolizumab/bevacizumab) remains a promising area of investigation, particularly for patients with bilobar or extrahepatic disease where monotherapy may be insufficient. Hybrid treatment strategies, such as sequential TARE followed by immunotherapy, may offer synergistic benefits and should be evaluated in randomized trials.

In this retrospective analysis of advanced HCC patients treated with Y-90 TARE, it was found that tumor distribution and hepatic reserve were the most significant predictors of survival, whereas absolute dose parameters—such as infused activity or tumor absorbed dose—did not independently predict outcome. Patients with unilobar disease and preserved liver function (ALBI grade 1) experienced significantly longer survival, emphasizing the importance of anatomical and functional patient selection in TARE planning. While tumor volume alone was not statistically associated with survival, its interaction with dosimetric efficiency suggests that volume-adapted, personalized dosimetry may enhance therapeutic outcomes.

Compared to prior randomized trials and systemic therapy benchmarks, the results highlight the feasibility and real-world utility of Y-90 TARE in a high-burden, bilobar-predominant population. However, the absence of personalized planning in the majority of patients and lack of advanced interventional techniques underscore a critical gap in optimizing treatment delivery. Moving forward, integration of image-based dosimetry, volumetric modeling, and hybrid treatment strategies may offer a more precise and effective therapeutic approach for advanced HCC.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Artificial Intelligence Usage Statement: The authors declared that no Artificial Intelligence tool was used in the preparation of the manuscript.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University–Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval No: 70920, Decision Date: May 7, 2019; Document Date: May 9, 2019).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – K.S.; Design – S.S.; Supervision – K.S., S.S.; Resources – K.S., S.S.; Materials – K.S., S.S.; Data Collection and/or Processing – S.B.; Analysis and/or Interpretation – S.B.; Literature Search – S.B.; Writing Manuscript – S.B.; Critical Review – U.S., S.S., K.S.

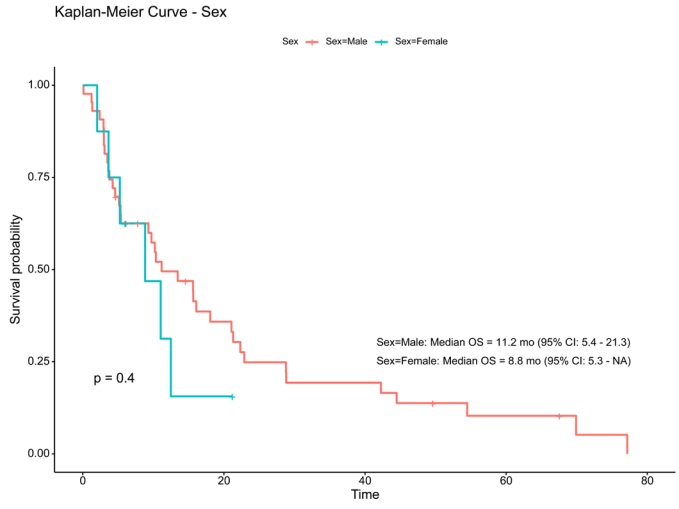
Declaration of Interests: The authors have no conflict of interest to declare.

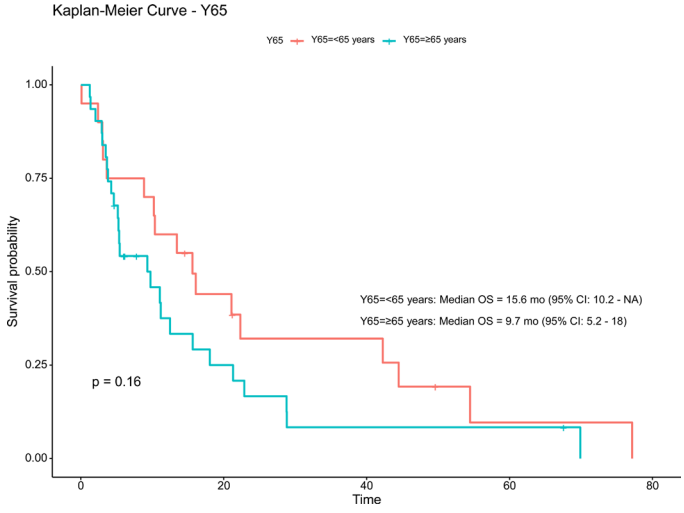
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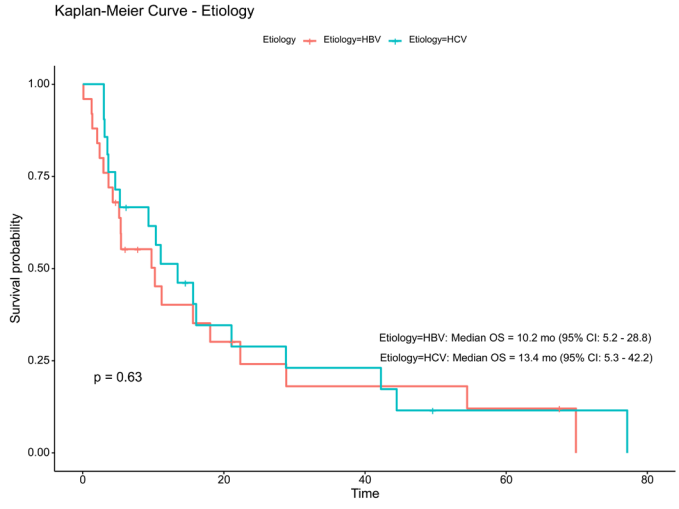
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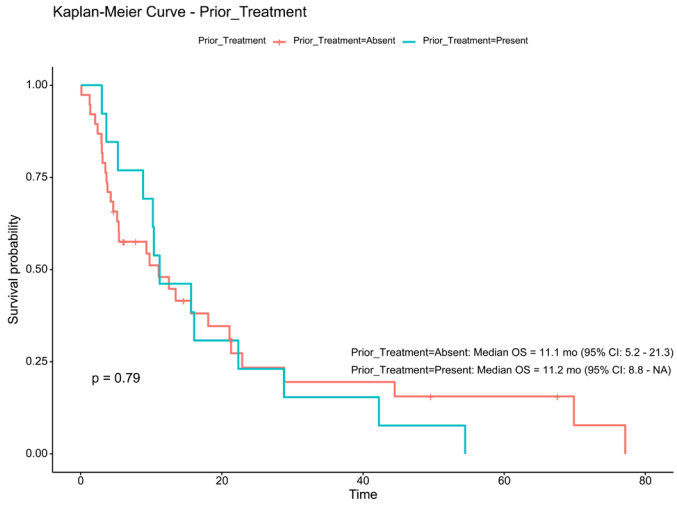
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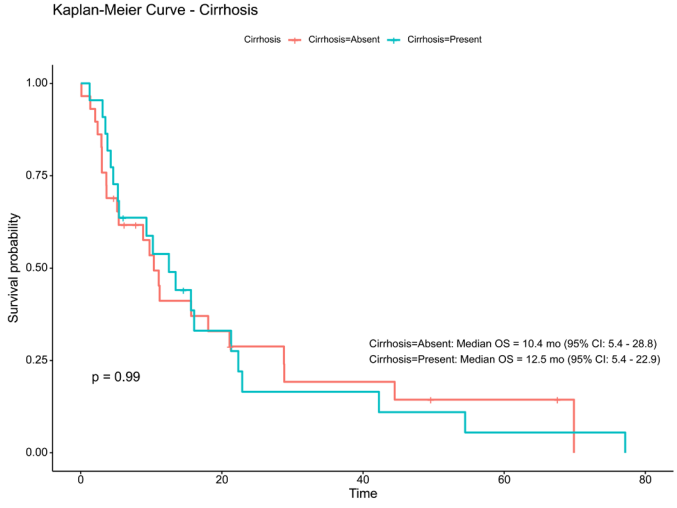
Supplementary Data 1.

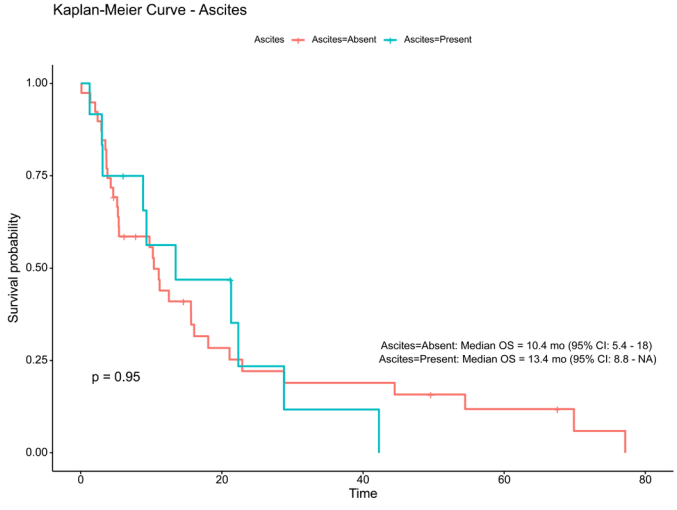


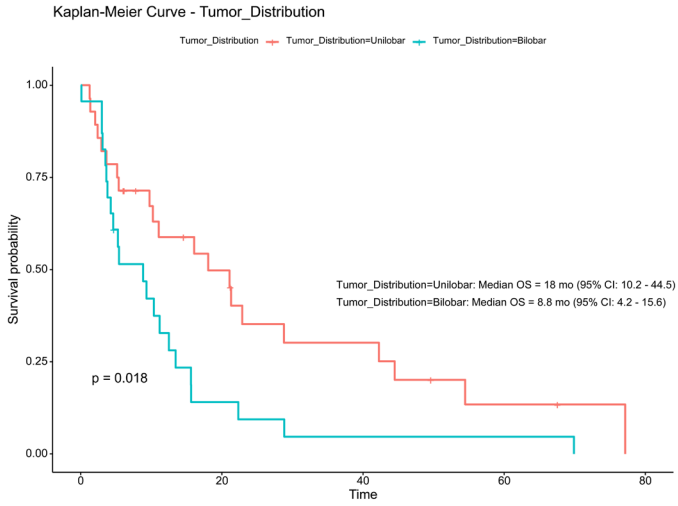


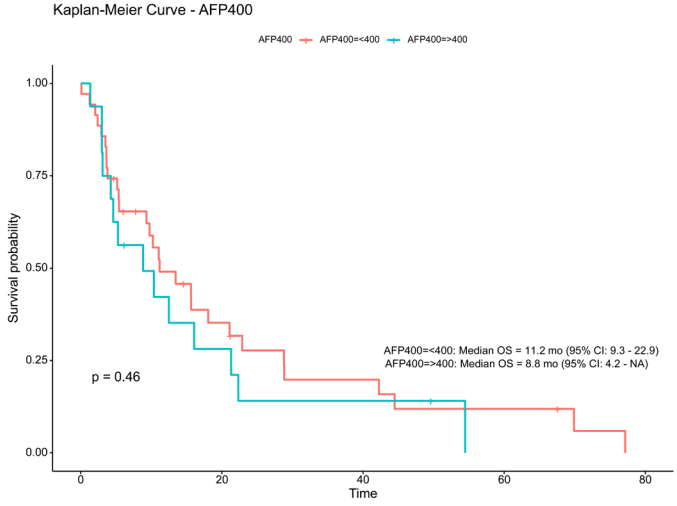


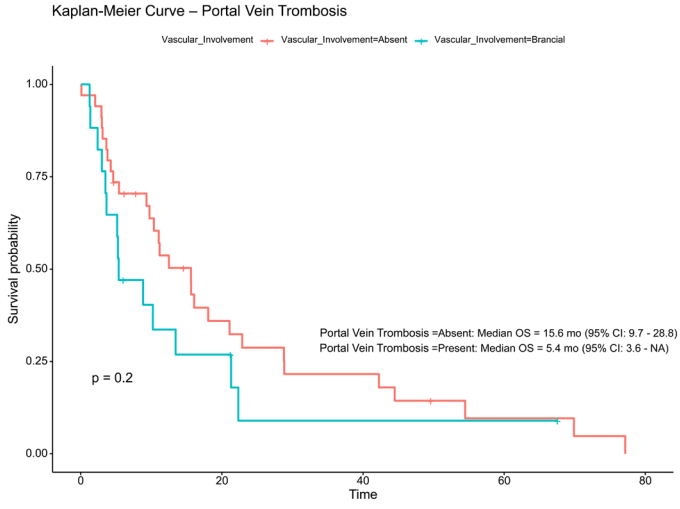

Kaplan-Meier Curve - Prior_Treatment
Prior_Treatment
Prior_Treatment=Absent
Prior_Treatment=Present
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.79
Prior_Treatment=Absent: Median OS = 11.1 mo (95% CI: 5.2 - 21.3)
Prior_Treatment=Present: Median OS = 11.2 mo (95% CI: 8.8 - NA)
0
20
40
60
80
Time

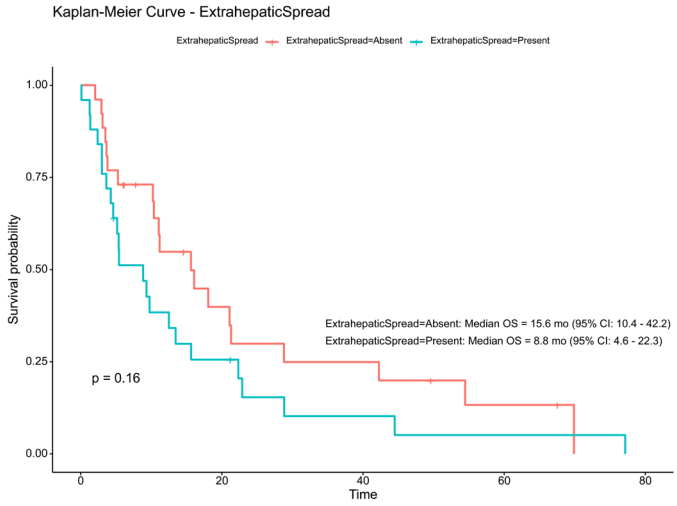

Kaplan-Meier Curve - Cirrhosis
Cirrhosis
Cirrhosis=Absent
Cirrhosis=Present
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.99
Cirrhosis=Absent: Median OS = 10.4 mo (95% CI: 5.4 - 28.8)
Cirrhosis=Present: Median OS = 12.5 mo (95% CI: 5.4 - 22.9)
0
20
40
60
80
Time

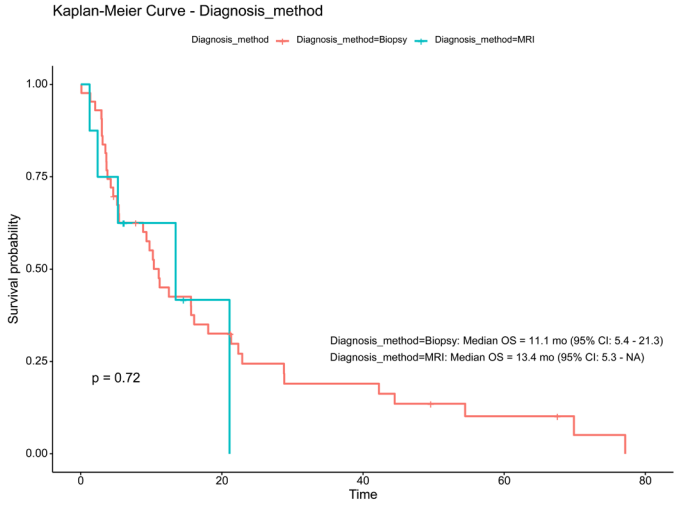

Kaplan-Meier Curve - Ascites
Ascites
Ascites=Absent
Ascites=Present
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.95
Ascites=Absent: Median OS = 10.4 mo (95% CI: 5.4 - 18)
Ascites=Present: Median OS = 13.4 mo (95% CI: 8.8 - NA)
0
20
40
60
80
Time

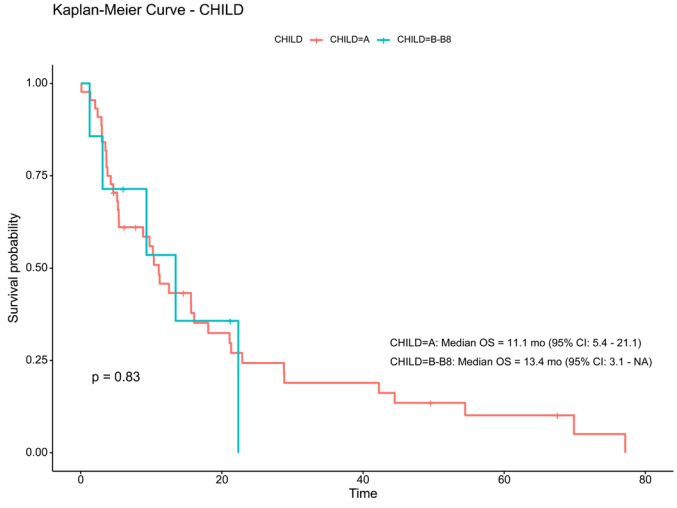

Kaplan-Meier Curve - Tumor_Distribution
Tumor_Distribution
Tumor_Distribution=Unilobar
Tumor_Distribution=Bilobar
Survival probability
1.00
0.75
0.50
0.25
0.00
Tumor_Distribution=Unilobar: Median OS = 18 mo (95% CI: 10.2 - 44.5)
Tumor_Distribution=Bilobar: Median OS = 8.8 mo (95% CI: 4.2 - 15.6)
p = 0.018
0
20
40
60
80
Time

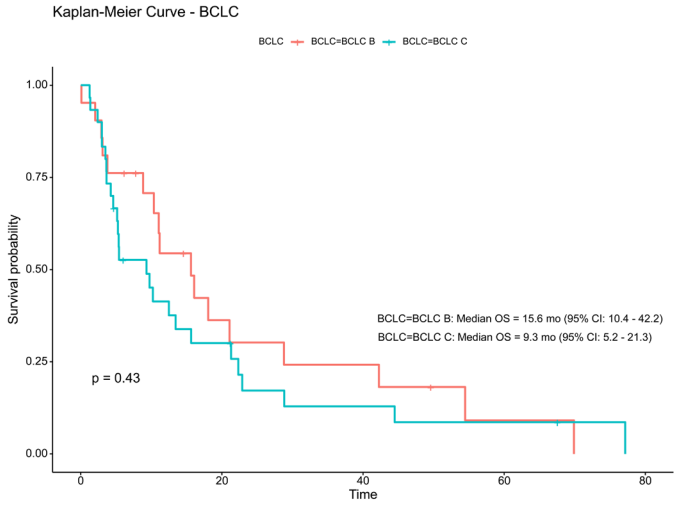

Kaplan-Meier Curve - AFP400
AFP400
AFP400=<400
AFP400=>400
Survival probability
1.00
0.75
0.50
0.25
0.00
AFP400=<400: Median OS = 11.2 mo (95% CI: 9.3 - 22.9)
AFP400=>400: Median OS = 8.8 mo (95% CI: 4.2 - NA)
p = 0.46
0
20
40
60
80
Time

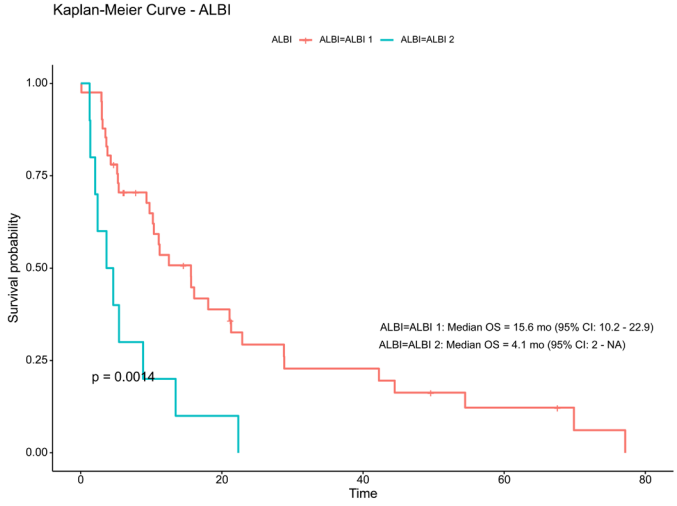

Kaplan-Meier Curve – Portal Vein Trombosis
Vascular_Involvement
Vascular_Involvement=Absent
Vascular_Involvement=Brancial
Survival probability
1.00
0.75
0.50
0.25
0.00
Portal Vein Trombosis =Absent: Median OS = 15.6 mo (95% CI: 9.7 - 28.8)
Portal Vein Trombosis =Present: Median OS = 5.4 mo (95% CI: 3.6 - NA)
p = 0.2
0
20
40
60
80
Time

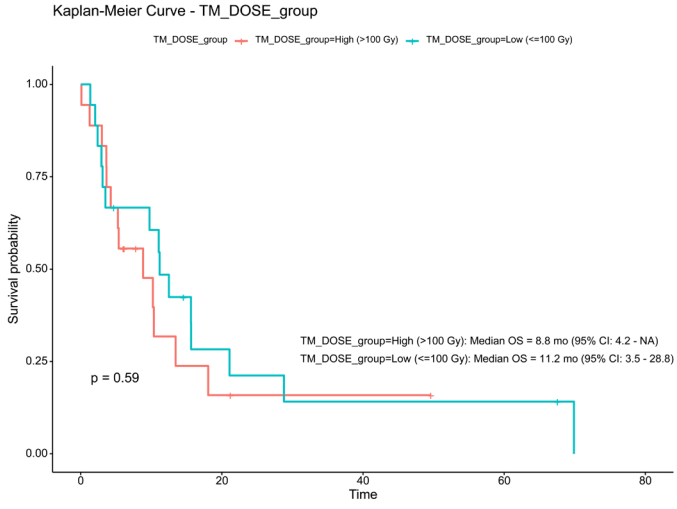

Kaplan-Meier Curve - ExtrahepaticSpread
ExtrahepaticSpread
ExtrahepaticSpread=Absent
ExtrahepaticSpread=Present
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
ExtrahepaticSpread=Absent: Median OS = 15.6 mo (95% CI: 10.4 - 42.2)
ExtrahepaticSpread=Present: Median OS = 8.8 mo (95% CI: 4.6 - 22.3)
p = 0.16

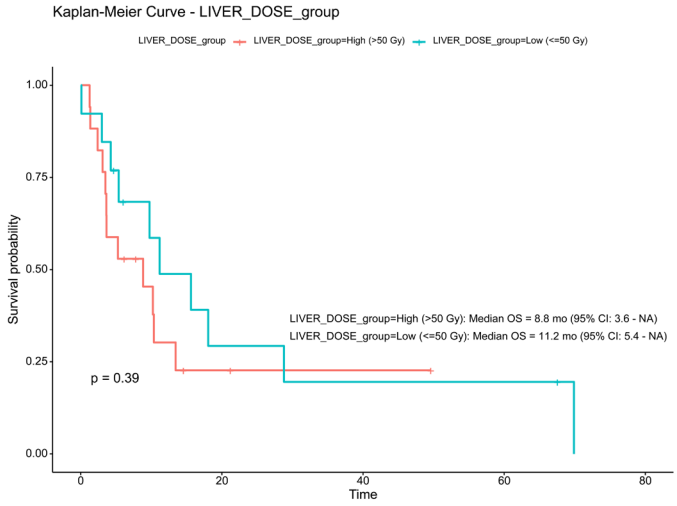

Kaplan-Meier Curve - Diagnosis_method
Diagnosis_method
Diagnosis_method=Biopsy
Diagnosis_method=MRI
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
Diagnosis_method=Biopsy: Median OS = 11.1 mo (95% CI: 5.4 - 21.3)
Diagnosis_method=MRI: Median OS = 13.4 mo (95% CI: 5.3 - NA)
p = 0.72

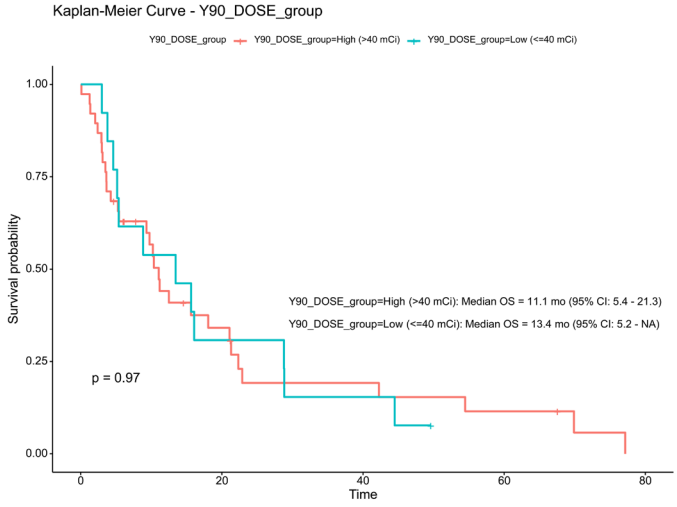

Kaplan-Meier Curve - CHILD
CHILD
CHILD=A
CHILD=B-B8
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
CHILD=A: Median OS = 11.1 mo (95% CI: 5.4 - 21.1)
CHILD=B-B8: Median OS = 13.4 mo (95% CI: 3.1 - NA)
p = 0.83

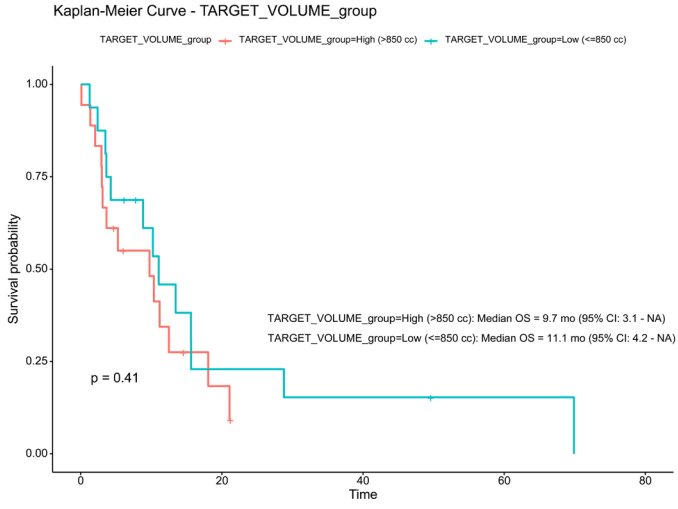

Kaplan-Meier Curve - BCLC
BCLC
BCLC=BCLC B
BCLC=BCLC C
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
BCLC=BCLC B: Median OS = 15.6 mo (95% CI: 10.4 - 42.2)
BCLC=BCLC C: Median OS = 9.3 mo (95% CI: 5.2 - 21.3)
p = 0.43

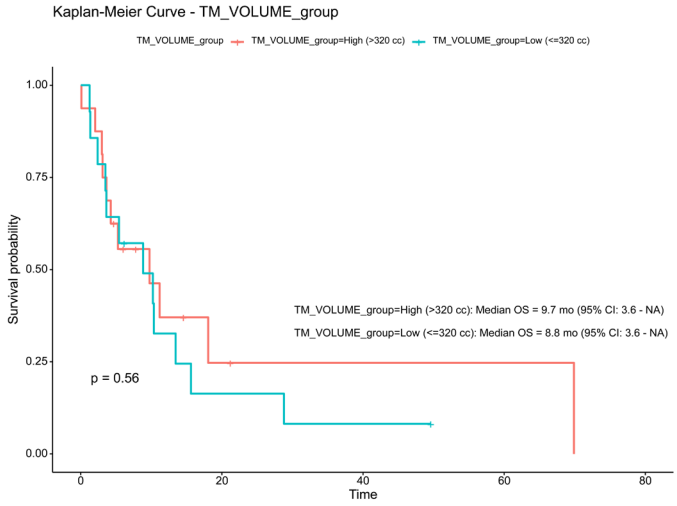

Kaplan-Meier Curve - ALBI
ALBI
ALBI=ALBI 1
ALBI=ALBI 2
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
ALBI=ALBI 1: Median OS = 15.6 mo (95% CI: 10.2 - 22.9)
ALBI=ALBI 2: Median OS = 4.1 mo (95% CI: 2 - NA)
p = 0.0014

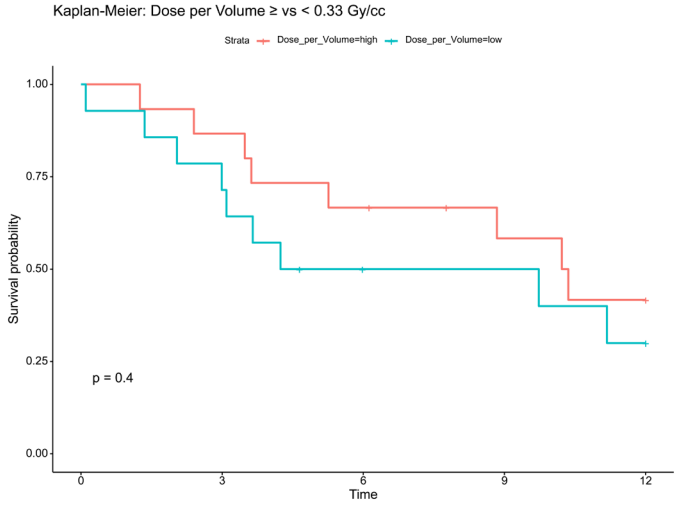

Kaplan-Meier Curve - TM_DOSE_group
TM_DOSE_group
TM_DOSE_group=High (>100 Gy)
TM_DOSE_group=Low (<=100 Gy)
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
TM_DOSE_group=High (>100 Gy): Median OS = 8.8 mo (95% CI: 4.2 - NA)
TM_DOSE_group=Low (<=100 Gy): Median OS = 11.2 mo (95% CI: 3.5 - 28.8)
p = 0.59


Kaplan-Meier Curve - LIVER_DOSE_group
LIVER_DOSE_group
LIVER_DOSE_group=High (>50 Gy)
LIVER_DOSE_group=Low (<=50 Gy)
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
LIVER_DOSE_group=High (>50 Gy): Median OS = 8.8 mo (95% CI: 3.6 - NA)
LIVER_DOSE_group=Low (<=50 Gy): Median OS = 11.2 mo (95% CI: 5.4 - NA)
p = 0.39


Kaplan-Meier Curve - Y90_DOSE_group
Y90_DOSE_group
Y90_DOSE_group=High (>40 mCi)
Y90_DOSE_group=Low (<=40 mCi)
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
Y90_DOSE_group=High (>40 mCi): Median OS = 11.1 mo (95% CI: 5.4 - 21.3)
Y90_DOSE_group=Low (<=40 mCi): Median OS = 13.4 mo (95% CI: 5.2 - NA)
p = 0.97


Kaplan-Meier Curve - TARGET_VOLUME_group
TARGET_VOLUME_group
TARGET_VOLUME_group=High (>850 cc)
TARGET_VOLUME_group=Low (<=850 cc)
Survival probability
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time
TARGET_VOLUME_group=High (>850 cc): Median OS = 9.7 mo (95% CI: 3.1 - NA)
TARGET_VOLUME_group=Low (<=850 cc): Median OS = 11.1 mo (95% CI: 4.2 - NA)
p = 0.41


Kaplan-Meier Curve - TM_VOLUME_group
TM_VOLUME_group
TM_VOLUME_group=High (>320 cc)
TM_VOLUME_group=Low (<=320 cc)
Survival probability
1.00
0.75
0.50
0.25
0.00
TM_VOLUME_group=High (>320 cc): Median OS = 9.7 mo (95% CI: 3.6 - NA)
TM_VOLUME_group=Low (<=320 cc): Median OS = 8.8 mo (95% CI: 3.6 - NA)
p = 0.56
0
20
40
60
80
Time


Kaplan-Meier: Dose per Volume ≥ vs < 0.33 Gy/cc
Strata
Dose_per_Volume=high
Dose_per_Volume=low
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.4
0
3
6
9
12
Time