ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.americanjir.com

American Journal of Interventional Radiology

Interventional Oncology *Original Research*

Survival impact of C-Arm cone-beam computed tomography on hepatocellular carcinoma patients undergoing chemoembolization

Mohamed E. Abdelsalam[1], Tomas M. Appleton Figueira[2], Joe Ensor[3], Alda L. Tam[1], Rony Avritscher[1], Ahmed O. Kaseb[4], Sanjay Gupta[1]

[1]Department of Interventional Radiology, The University of Texas MD Anderson, Houston, Texas, [2]Department of Radiology, Upstate University Hospital, Syracuse, New York, [3]Department of Biostatistics, Houston Methodist Research Institute, Houston, Texas, [4]Department of Medical Oncology, The University of Texas MD Anderson, Houston, Texas, United States.

***Corresponding author:**
Mohamed E. Abdelsalam, Department of Interventional Radiology, The University of Texas MD Anderson, Houston, Texas, United States.

meabdelsalam@mdanderson.org

Received : 24 March 2021
Accepted : 06 May 2021
Published : 04 June 2021

DOI
10.25259/AJIR_7_2021

Quick Response Code:

ABSTRACT

Objectives: The objectives of the study were to evaluate the use of C-arm cone-beam computed tomography (CBCT) for tumor targeting for transarterial chemoembolization (TACE) and its impact on overall survival (OS) in hepatocellular carcinoma patients.

Material and Methods: Two groups were retrospectively evaluated according to the date of the first TACE session before and after C-arm CBCT installation in late 2005 (group A [n = 34], 2004–2005; group B [n = 104], 2008+). The years 2006 and 2007 were excluded to allow for the incorporation of this new imaging technology into clinical practice. The vessel selection order was recorded for all TACE sessions. Univariate and multivariate analyses were performed to assess the impact on and predictors of survival.

Results: The average TACE selection order for each patient was significantly higher in group B than in group A ($P < 0.0001$). The median OS was significantly longer in group B (29.34 months) than in group A (19.65 months; $P = 0.0088$), and the difference in duration was most pronounced in patients with tumor burdens < 25% (n = 93; $P = 0.0075$), in whom the 3-year survival rate was 56.1% in group B and 15.3% in group A. In these 93 patients, the OS was significant longer ($P = 0.018$) for high (41.07 months) versus low (19.65 months) vessel selection order across both groups. In multivariate analyses, both the period in which TACE was performed ($P = 0.022$) and the use of C-arm CBCT ($P = 0.0075$) were significant predictors of improved OS.

Conclusion: Use of advanced C-arm CBCT during TACE enhances the operating physician's ability to deliver targeted, effective therapy for hepatocellular carcinoma, an aggressive approach that favorably impacts survival.

Keywords: Cone-beam computed tomography, HCC, Transarterial chemoembolization

INTRODUCTION

Transarterial chemoembolization (TACE) is a frontline therapeutic option for hepatocellular carcinoma in patients who are not candidates for transplantation or resection. Two randomized controlled trials established the survival benefit of TACE in this patient population in 2002.[1,2] In general, the median overall survival (OS) and 2-year survival durations and rates in patients with preserved liver function and limited disease with well-defined tumor margins (Okuda stage I and Barcelona Clinic Liver Cancer [BCLC] stage A/B disease) ranged from 16 to 28 months and

from 40% to 63%, respectively, in many Western series for both TACE and radioembolization.[1,3-7] As with any surgery or invasive procedure, controllable variables can impact the efficacy, safety, and outcome of TACE. These include (1) the experience and skill of the operating physician and his or her diligence in identifying and selectively catheterizing all vessels (both hepatic and extrahepatic) supplying the tumor or tumors, (2) the imaging technique used during the intervention, (3) the chemoembolic regimen used, and (4) the patient selection criteria. Many of these variables are interrelated, but one particular variable that has not received adequate attention with regard to its impact on the efficacy and outcome of TACE is the imaging technique used to plan and guide it. Only recently has this become a controllable variable with the development of a new imaging technology, C-arm cone-beam computed tomography (CBCT), that was released commercially as an option for angiography systems in late 2005.

The quality of the imaging technology used during TACE and its ability to provide the necessary imaging information to identify all tumors and their complete arterial supply is important to optimizing the efficacy of the therapy. Conventional angiography systems in most interventional Radiology procedure suites have used only fluoroscopy and digital subtraction angiography (DSA) to perform this complex therapy [Figure 1a and b]. DSA provides two-dimensional images of the arterial anatomy and flow and identifies the target lesion, as iodinated contrast material is taken up by the tumor more rapidly and in greater amounts than by the surrounding liver (commonly referred to as a hypervascular lesion).

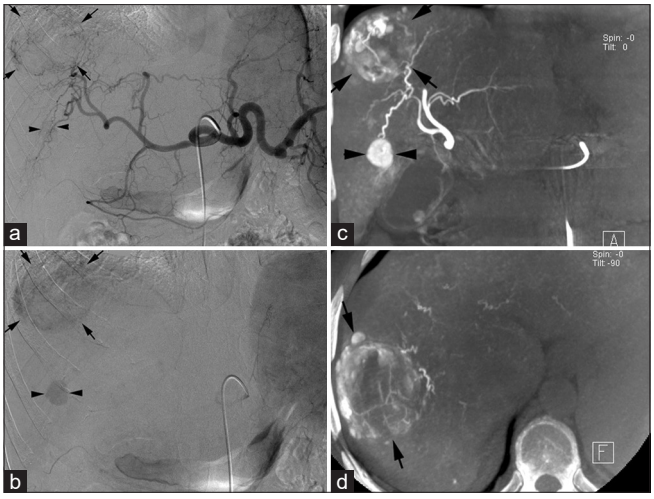

Figure 1: A 65-year-old male with known liver cirrhosis developed multifocal HCC. (a) Early arterial phase digital subtraction angiogram (DSA) of the celiac artery showing a dominant hepatic lesion (arrows) and another poorly identified lesion (arrowhead). (b) Late arterial phase of the DSA showing better delineation of both lesions. (c) Coronal and (d) axial C-arm cone-beam computed tomography (CBCT) showing the enhanced detail of the dominant tumor mass (arrows) and a satellite nodule (arrowheads) within the right lobe of the liver and the sharp depiction of its arterial supply depicted in the C-arm CBCT images reconstructed compared to frontal projection DSA images.

Physicians performing TACE quickly recognized the advantages of C-arm CBCT over conventional DSA.[8-11] C-arm CBCT acquires a three-dimensional data set as the C-arm of the angiography unit rotates around the patient, acquiring multiple two-dimensional projections along an arc of more than 200°. The images obtained are reconstructed to produce "computed tomography-like" images [Figure 1c and d], providing hepatic parenchymal (soft tissue) information not previously obtainable with DSA. With this imaging information, a physician performing TACE can place catheters into more subselective arterial branches to deliver the chemoembolic regimen as close to the tumor as possible. Many practitioners widely believe that subselective (segmental or subsegmental) catheterization of tumor-feeding arteries is more effective and leads to better outcomes and higher degrees of tumor necrosis than does less selective or lobar catheterization in patients with hepatocellular carcinoma undergoing TACE.[12-14] Although researchers have confirmed that subselective catheterization produces higher degrees of tumor necrosis than does lobar catheterization in explant reviews, they have yet to adequately validate the impact of subselective catheterization and therapy on survival. Therefore, in the present retrospective study, we sought to analyze the clinical outcomes in patients undergoing TACE for hepatocellular carcinoma in two different time periods (before and after incorporation of C-arm CBCT into routine clinical practice) to determine whether the operating physicians' ability to be more subselective with delivery of the chemoembolic regimen using C-arm CBCT impacted survival.

MATERIAL AND METHODS

All patients with hepatocellular carcinoma who underwent TACE from January 2004 to December 2005 or from January 2008 to January 2011 at The University of Texas MD Anderson Cancer Center (n = 138) were considered in this retrospective single-institution study. This Health Insurance Portability and Accountability Act-compliant study was approved by the MD Anderson Institutional Review Board, and a waiver of informed consent was granted. C-arm CBCT was initially installed at MD Anderson in late 2005. To determine the impact of this new imaging technology on TACE and mitigate the impact of the transition period for C-arm CBCT adoption and incorporation into clinical practice, TACE sessions performed in 2006 and 2007 were excluded from the study. Thus, treatments performed in two time periods were compared: 2004–2005 (Group A;

34 patients) and 2008 and later (Group B; 104 patients). Diagnosis of hepatocellular carcinoma was based on imaging and/or histology in all patients before TACE. Imaging consisted of triple-phase computed tomography or magnetic resonance imaging within 1 month before the initial treatment.

All TACE sessions were performed using a commercially available single-plane, ceiling-mounted angiography system (AXIOM Artis dTA; Siemens AG, Healthcare Sector, Forchheim, Germany). Conventional DSA was performed with all TACE procedures. A C-arm CBCT system upgrade that enabled three-dimensional image rendering (DynaCT; Siemens AG, Healthcare Sector) was performed in late 2005. Two patients in Group A underwent TACE with C-arm CBCT after its installation, whereas 90 patients in group B underwent TACE with C-arm CBCT. C-arm CBCT was used at the discretion of the operating physician and was recorded as used for a patient if it was performed at least once for treatment planning during any of the patient's sessions.

All patient data, images, and reports were reviewed, and the number and selection order of arterial branches embolized was recorded. Each chemoembolized hepatic vessel was assigned a branch catheterization order to reflect the selective nature of catheterization. Specifically, the chemoembolized branches were categorized as 0, 1, 2, 3, etc., according to this branching vessel ordering system. The hepatic artery proper replaced and/or accessory right hepatic artery arising from the superior mesenteric artery and gastrohepatic trunk was considered zero-order branches. The right and left hepatic arteries and replaced left hepatic artery from a gastrohepatic artery were considered first-order branches. Assignment of second, third, and higher orders was based on branch selection beyond the first order artery. The average TACE vessel selection order for each patient was calculated by dividing the sum of the orders for each vessel embolized by the number of vessels embolized in each session and then dividing that quotient by the total number of sessions.

In addition, the total number, sizes, and border characteristics of all lesions were recorded, and patients were further grouped according to morphology-based on these variables. The longest transaxial tumor dimension measured through imaging was used to determine lesion size and the lesion margins were categorized as well-defined or ill-defined/infiltrative.

In group B, the potential impact of the TACE regimen and adjuvant use of sorafenib (Bayer HealthCare Pharmaceuticals, Wayne, NJ) on survival was evaluated. A conventional TACE (cTACE) regimen consisting of an emulsion of cisplatin (100 mg), doxorubicin (Adriamycin; 50 mg), and mitomycin (10 mg) with ethiodized oil (Ethiodol; Savage Laboratories, Melville, NY) followed by particulate embolization was used for all procedures in 2008 and earlier, whereas a drug-eluting bead (DEB)-TACE regimen (LC Beads; Biocompatibles UK Limited, Surrey, UK) consisting of doxorubicin (50–100 mg depending on lesion size and vascularity) bound to 100–300-μM particles was used for most of the TACE procedures in 2009 and after. Patients were considered to have received adjuvant sorafenib if administration of it was initiated or continued after any of the TACE sessions for more than 60 days.

Assessment of response of hepatocellular carcinoma to "TACE" was based on post-TACE computed tomographic or magnetic resonance imaging assessment of the index lesion or lesions treated in the first TACE session after completion of all sessions and on the modified Response Evaluation Criteria in Solid Tumors (modified RECIST) including the decline or loss of arterial enhancement.[15,16] Survival durations were recorded for all patients starting with the first TACE session; if another hepatic directed therapy was performed after TACE (ablation, radioembolization, transplantation, or resection), the patient was censored according to the date of the first post-TACE intervention.

Survival analysis was conducted using the Kaplan–Meier method and differences in survival duration were determined using either the log-rank or stratified log-rank test. The method described by Brookmeyer and Crowley was used to construct 95% confidence intervals (CIs) for the median survival duration. Two-sample *t*-tests were used to determine the mean differences in demographics and TACE procedures. Frequency distribution differences for demographic and tumor morphology variables were tested using the Pearson Chi-squared test or Fisher's exact test when appropriate. All statistical analyses and graphs were produced using the SAS software program (version 9.2; SAS Institute Inc., Cary, NC). $P < 0.05$ were considered statistically significant.

RESULTS

The study patients' demographic and tumor morphology characteristics are outlined in Table 1. The patients consisted of 93 men (67%) and 45 women (32%). The median follow-up duration in all patients was 15.9 months (95% CI, 12.9–18.9 months). The median OS duration was significantly longer ($P = 0.0088$) in group B (29.34 months [95% CI, 21.52]) than in group A (19.65 months [95% CI, 12.94–24.02]) [Table 2 and Figure 2a]. The rate of C-arm CBCT use was 87% in group B but only 6% in group A. When we compared OS in the two groups based on the use of C-arm CBCT, the survival benefit was significantly better ($P = 0.002$) in the group that underwent C-arm CBCT with DSA (median survival duration, 41.07 months [95% CI, 21.98, 46.06]) than in the group that underwent TACE with DSA alone (median survival duration, 19.65 months [95% CI, 12.94–24.02) [Table 2 and Figure 2b]. Our initial multivariate analyses [Table 3A] demonstrated that the later time period (group B, 87% C-arm CBCT use), in

which the first TACE session was performed, was a significant predictor of prolonged survival duration ($P = 0.022$). Since 90 (87%) of the patients in group B underwent TACE with C-arm CBCT, the multivariate analysis in Table 3A was performed again but for the use of C-arm CBCT rather than for time period [Table 3B]. This multivariate analysis demonstrated that the use of C-arm CBCT with TACE was a significant predictor of prolonged survival duration ($P = 0.0075$), confirming that the use of C-arm CBCT was the reason for the better survival durations in group B than in group A.

When we stratified the patients in each group according to Okuda stage, the survival advantage with C-arm CBCT remained, with 2-year survival rates of 57% (95% CI, 21–69%) and 39% (95% CI, 21–57%) in groups B and A, respectively, for Okuda stage 1 disease [Table 2].

The survival difference was most pronounced in patients with tumor burdens <25% ($P = 0.0075$; $n = 93$), with 2- and 3-year survival rates of 61% (95% CI, 45–74%) and 56% (95% CI, 38–71%), respectively, in group B and 31% (95% CI, 13–51%) and 15% (95% CI, 4–34%), respectively, in group A [Table 2 and Figure 2c]. In this subgroup of patients with tumor burden <25%, the survival difference remained significantly better ($P = 0.0005$) with 2- and 3-year survival rates of 63% (95% CI, 48–76%) and 58% (95% CI, 42–72%), respectively, when TACE was performed with C-arm CBCT compared to 2- and 3-year survival rates of 24% (95% CI, 8–44%) and 6% (95% CI, 0–24%), respectively, when TACE was performed with DSA alone [Table 2 and Figure 2d].

The average number of arteries chemoembolized in the two groups did not differ significantly (3.125 and 2.500 in groups B and A, respectively; $P = 0.12$), but we did observe a higher frequency of subselective catheterization during TACE in group B, as the average TACE catheterization score was significantly higher ($P < 0.0001$) in group B (2.36) than in group A (1.62). In the subgroup with tumor burdens <25%, the median OS duration was significantly longer ($P = 0.018$) for high (41.07 months) than for low (19.65 months) TACE selection scores in both groups. The low and high vessel selection scores were defined as <2 and ≥2, respectively, as an average of all sessions for each TACE patient [Figure 3].

Table 1: Demographic and tumor morphology characteristics.

Variable		*n* (%)		*P* Value
		Group A (*n*=34)	Group B (*n*=104)	
Median age (± standard deviation), years		69.5 (±10.7)	66.0 (±12.4)	0.1376
Sex	Female	11 (32)	34 (33)	0.9708
	Male	23 (68)	70 (67)	
Imaging	DSA	32 (94)	14 (13)	
	DSA+C-arm CBCT	2 (6)	90 (87)	
Lesion morphology				
A	≤3 lesions with each lesion ≤3 cm or a single lesion ≤5 cm; well-defined borders	9 (26)	34 (33)	0.5517
B	Single lesion ≥5 cm; well-defined borders	9 (26)	16 (15)	
C	≤4 lesions, any diameter >3 cm; well-defined borders	8 (24)	21 (20)	
D	>4 lesions; well-defined borders	3 (9)	16 (15)	
E	Any lesion with infiltrative/ill-defined borders or satellite nodules	5 (15)	17 (16)	
Okuda stage	1	27 (79)	90 (87)	0.3152
	2	7 (21)	14 (13)	
Child-Pugh score	A	32 (94)	101 (97)	0.4168
	B	2 (6)	3 (3)	
Etiology of liver disease	Hepatitis B	3 (9)	14 (13)	0.0502
	Hepatitis C	7 (21)	36 (35)	
	Hepatitis B and C	4 (12)	1 (1)	
	Non-viral	6 (18)	17 (16)	
	None	14 (41)	36 (35)	
Tumor burden	<25%	21 (62)	72 (69)	0.0374
	25–50%	8 (24)	29 (28)	
	>50%	5 (15)	3 (3)	
Sorafenib use	No (or ≤60 days)	34 (100)	62 (60)	
	Yes	0 (0)	42 (40)	

DSA: Digital subtraction angiography, CBCT: Cone-beam computed tomography

Table 2: Survival rates stratified by patient group (time period) and by use of C-arm CBCT.

Survival rates stratified by patient group (time period)	Group A					Group B					*P*-value
	1 year (%)	2 year (%)	3 year (%)	5 year (%)	Median (months)	1 year (%)	2 year (%)	3 year (%)	5 year (%)	Median (months)	
Overall	73.5	37.0	15.4	12.3	19.65	75.7	59.6	48.2	--	29.34	0.0088
Okuda											
Stage 1	74.10	39.40	19.70	15.70	19.65	76.30	57.40	50.30	--	--	0.0338
Stage 2	71.40	28.60	--	--	21.26	70.70	70.70	37.70	--	28.12	0.0707
Tumor burden											
<25%	76.2	30.6	15.3	10.2	19.65	81.1	61.2	56.1	--	--	0.0075
25–50%	62.5	50.0	25.0	25.0	21.17	61.0	52.9	37.8	--	24.44	0.8278
>50%	60.0	40.0	0.0	--	21.26	100	100	0.0	--	28.12	0.0826
Survival rates stratified by use of C-arm CBCT	**DSA alone**					**Cone-beam+DSA**					***P*-value**
	1 year (%)	2 year (%)	3 year (%)	5 year (%)	Median (months)	1 year (%)	2 year (%)	3 year (%)	5 year (%)	Median (months)	
Overall	70.20	34.80	12.70	12.70	19.65	77.60	61.20	50.00	41.70%	41.07	0.002
Okuda											
Stage 1	72.10	38.10	16.90	16.90	19.65	77.50	58.40	51.70	41.30%	41.07	0.0191
Stage 2	63.50	25.40	0.00	--	21.26	77.80	77.80	41.50	--	28.12	0.0203
Tumor burden											
<25%	77.10	23.70%	5.90	5.90	18.92	82.60	63.30	58.80	49.00%	41.07	0.0005
25–50%	61.50	52.80	31.70	31.70	30.06	61.90	52.40	34.90	--	24.44	0.9479
>50%	100	100	0.0	--	28.12	60.0	40.0	0.0	--	21.26	0.0826

CBCT: Cone-beam computed tomography, DSA: Digital subtraction angiography

Table 3: Multivariate analysis for overall survival according to time period in which the first TACE session was performed and by the use of C-arm CBCT.

A	**Time period in which the first TACE session was performed**				
Effect	**Parameter estimate**	***P*-value**	**Hazard ratio**	**95% Hazard ratio confidence limits**	
Time Period	−0.62856	0.0222	0.533	0.311	0.914
Age	−0.00599	0.6121	0.994	0.971	1.017
Sex	−0.00963	0.9714	0.99	0.585	1.677
Tumor burden	0.30691	0.2696	1.359	0.788	2.344
Average vessel selection score	0.00303	0.9885	1.003	0.665	1.513
B	**Use of C-arm CBCT**				
Effect	**Parameter estimate**	***P*-value**	**Hazard ratio**	**95% Hazard ratio confidence limits**	
C-arm CBCT	−0.80163	0.0075	0.449	0.249	0.807
Age	−0.00551	0.6393	0.995	0.972	1.018
Sex	−0.04628	0.8631	0.955	0.564	1.616
Tumor burden	0.23633	0.394	1.267	0.736	2.181
Average vessel selection score	0.12683	0.5735	1.135	0.73	1.766

A: Multivariate Cox proportional hazards model for overall survival included as predictors in: (1) Time Period with "2005 and Before" as the reference level, (2) Age as a continuous variable, (3) Sex with "Male" as the reference level, (4) Disease Burden with "<25%" as the reference level, and (5) Average vessel Selection Score as a continuous variable, B: Multivariate Cox proportional hazards model for overall survival included as predictors: (1) C-arm CBCT, with "DSA Alone" as the reference level, (2) Age as a continuous variable, (3) Sex with "Male" as the reference level, (4) Tumor Burden with "<25%" as the reference level, and (5) Average vessel Selection Score as a continuous variable. CBCT: Cone-beam computed tomography, TACE: Transarterial chemoembolization

In group B, the survival rate did not differ significantly according to the TACE regimen ($P = 0.64$) [Table 4]. cTACE regimen was used in $n = 32$ (31%) in 2008 compared to (DEB-TACE) regimen used in $n = 67$ (64%) in 2009 and after. Five patients underwent TACE using both regimens and were excluded from the study. The patients who received

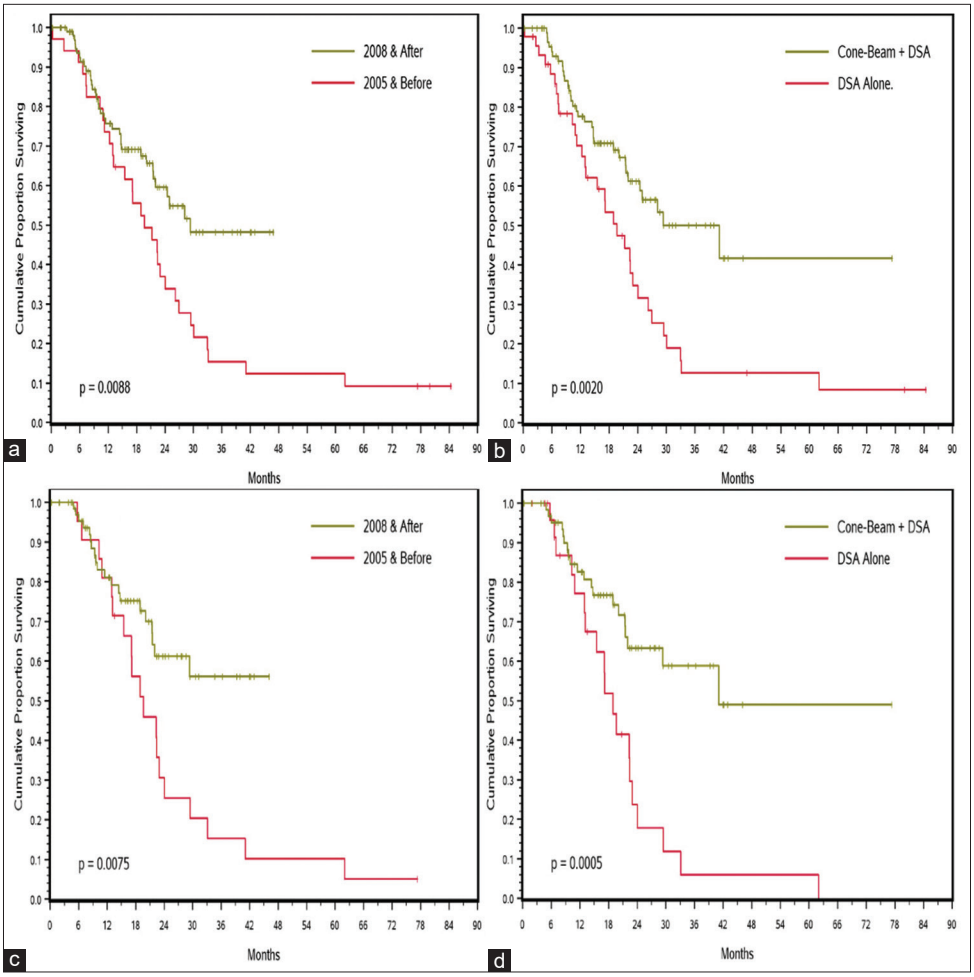

Figure 2: (a) Kaplan–Meier estimates of overall survival (OS) by time period (group A vs. group B) in all patients who underwent transarterial chemoembolization (TACE). (b) Kaplan–Meier estimates of OS according to the use of C-arm cone-beam computed tomography (CBCT) with digital subtraction angiogram (DSA) or the use of DSA alone during TACE. (c) Kaplan-Meier estimates of OS by time period (group A vs. group B) in patients with tumor burdens <25%. (d) Kaplan–Meier estimates of OS according to the use of C-arm CBCT with DSA or the use of DSA alone during TACE in patients with tumor burdens <25%.

Table 4: Survival rates stratified according to TACE regimen in Group B.

Regimen	*n*	1 year	2 year	3 year	Median duration (Months)	*P*-value
cTACE	32	81.20%	62.10%	45.30%	29.34	0.6403
DEB TACE	67	72.50%	58.80%	50.40%	--	

Five patients underwent TACE using both regimens and were excluded from analysis. TACE: Transarterial chemoembolization, cTACE: Conventional transarterial chemoembolization, DEB TACE: Drug-eluting bead transarterial chemoembolization

Table 5: Survival stratified by Sorafenib use in Group B.

Sorafenib use	*n*	1 year	2 year	3 year	Median duration (Months)	*P*-value
No	62	84.10%	69.90%	54.50%	--	0.007
Yes*	42	62.50%	43.70%	37.50%	14.75	

*Patients who received sorafenib for fewer than 60 days were included in this group.

sorafenib had significantly lower survival rates ($P = 0.0067$) than did the patients who did not receive sorafenib or received it for fewer than 60 days [Table 5]. The majority of the 42 patients in group B who received sorafenib after TACE had multifocal disease beyond Milan criteria (morphology A; $n = 31$). Twenty of these patients had disease burdens >25% and six had imaging findings of portal vein invasion or infiltrative. Based on the modified Response Evaluation Criteria in Solid Tumors, the response rates for TACE (complete and partial) were 76% and 82% in groups A and B, respectively, for patients who underwent adequate follow-

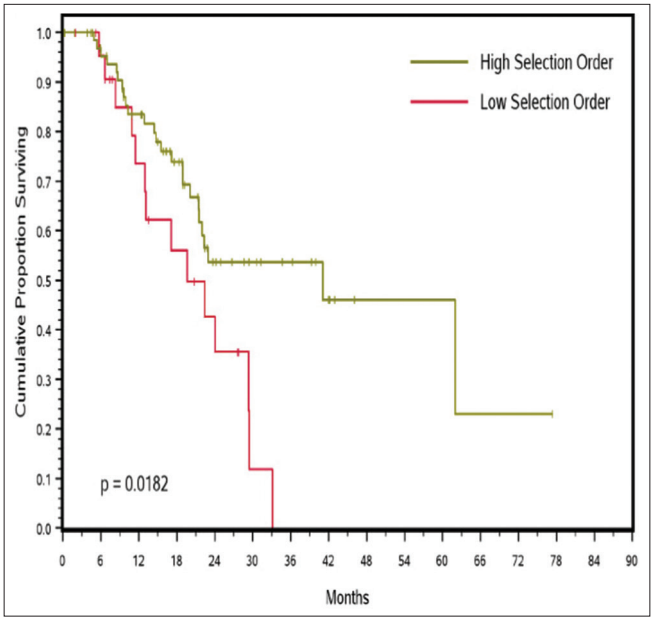

Figure 3: Kaplan–Meier estimates of overall survival by low (<2) and high (2 or more) transarterial chemoembolization vessel selection order in both time periods (group A vs. group B) in patients with tumor burdens <25%.

up imaging. The progression-free survival (PFS) durations did not differ significantly between groups A and B overall ($P = 0.86$) or in patients with tumor burdens <25% ($P = 0.84$). These durations also did not differ significantly ($P = 0.45$) in patients with complete responses (group B [$n = 34$]: 2-year PFS rate, 35.6%; group A [$n = 14$]: 2-year PFS rate, 33.3%).

DISCUSSION

This study demonstrated that the use of the new imaging technology C-arm CBCT as an adjunct to conventional DSA during TACE provided the necessary information to significantly increase selectivity (increased TACE selection order) in delivering the chemoembolic regimen. This increase in vessel selection order and its resulting effect of delivering the chemoembolic regimen closer to the target tumor may have had a positive impact on survival. Specifically, the median survival duration was significantly longer after C-arm CBCT installation (group B) than before it (group A). Patients with low-volume disease (tumor burden < 25%) benefited the most from the use of C-arm CBCT.

The desire to increase selectivity with this therapy is related to the premise that an increase in the selectivity of catheterization would result in delivery of an increased dose to the target lesion or lesions and reduce the amount of collateral uninvolved liver exposed to the therapeutic regimen and thus improve the efficacy, safety, and tolerability of the intervention and ultimately improve OS. Several authors have advocated reporting higher rates of complete necrosis with subselective and/or subsegmental TACE compared to lobar TACE. For example, Uchida *et al.*,[12] Matsui *et al.*,[13] and Matsuo *et al.*[14] reported complete necrosis rates ranging from 63% to 83% in small series of patients who underwent subselective TACE before resection for hepatocellular carcinoma. A subsequent study confirmed the benefits of selective/superselective TACE over lobar TACE in a group of liver transplant recipients.[17] In that series of 67 patients who underwent TACE as a bridging ($n = 53$) or downstaging ($n = 14$) maneuver before transplantation, the patients who underwent selective/superselective TACE had a significantly higher mean necrosis rate (73.0%) than did the patients who underwent lobar TACE (52.8%; $P = 0.002$). The complete necrosis rates in the selective/superselective and lobar groups were 53.8% and 29.8%, respectively.

TACE performed at our institution in 2004 and 2005 relied on conventional DSA for subselective catheterization, which has been the standard for this purpose since the early to middle 1990s. The median survival duration of 19.65 months in group A is in keeping with results in series in the West having median OS and 2-year survival durations and rates for Okuda stage I or BCLC stage A/B hepatocellular carcinoma ranging from 16 to 28 months and from 40% to 63%, respectively, for both TACE and radioembolization.[1,3-7] TACE procedures performed at our institution since 2008 reflect the adoption and integration of C-arm CBCT into routine clinical practice for treatment planning. Thus, the major differences between the two periods compared in our study are the use of C-arm CBCT and resulting increase in the average TACE selection order resulting from the use of this new imaging technology. We excluded TACE sessions performed in 2006 and 2007 to reduce the effects associated with the adoption of this new technology and to account for the time required to learn how to best use it. In comparing the two periods represented by groups A and B, instead of simply comparing TACE with and without C-arm CBCT, we reduced the chance of bias toward the tendency to use this advanced imaging technique for chemoembolization in complex cases that may require high branch vessel selection orders.

Univariate [Table 2] and multivariate [Table 3A] analyses both demonstrated prolonged survival durations in group B across all variables. To support our belief that the predominant reason for this survival prolongation was the use of C-arm CBCT, we performed the same univariate [Table 2] and multivariate [Table 3B] analyses, replacing the time period of the first TACE session with the use of C-arm CBCT across both time periods, observing that 90 (87%) patients in group B and 2 (6%) patients in group A underwent this new imaging modality. These analyses also demonstrated prolonged OS as well as prolonged survival across all variables and stratifications in the patients who underwent TACE with C-arm CBCT, which supported our hypothesis.

We performed the two sets of analyses to strengthen the validity of our findings and reduce the potential impact of bias on the data.

Quantifying the impact of new imaging technology on a procedure like TACE is difficult. Several authors reported that using C-arm CBCT during TACE provided additional imaging information over that provided with DSA imaging that impacted the outcome of the procedure in 19–39% of cases.[8,11,18] This impact on procedure outcome may have included a change in catheter position, a search for additional branches supplying the tumor, avoidance of branches not supplying the target lesion, and avoidance of non-targeted structures to reduce the potential for adverse events. Other series demonstrated the superiority of lesion detection using C-arm CBCT with DSA over that using DSA alone,[8,9] especially when lesions were angiographically occult.[19] Unlike these early series, in the present study, we attempted to quantify the impact of C-arm CBCT on the outcome of TACE patients in a less subjective and potentially less biased way by simply assessing two groups of patients with similar disease burdens separated by time according to the first TACE session, in which the critical variables that changed were the use of C-arm CBCT and resulting increase in average TACE selection order.

Aside from the inherent issues associated with the retrospective nature of this study, two variables that appeared during the time period represented by group B may have impacted survival: the TACE regimen used and the incorporation of sorafenib in the treatment algorithm. We addressed these issues by performing a subanalysis of group B, in which we did not observe a significant difference in the patients who underwent cTACE and DEB-TACE. However, we did observe a significant negative impact of sorafenib use on survival, favoring patients in group B who did not receive sorafenib. This finding most likely reflects that the majority of the patients who received sorafenib had advanced disease or unfavorable imaging characteristics (e.g., multinodular disease, infiltrative lesions, and satellite/daughter nodules) and thus would be expected to have shorter survival durations. Physicians did not routinely use sorafenib in the treatment regimens, with only 40% of the patients in group B receiving the drug after TACE.

CONCLUSION

The present study showed that the use of C-arm CBCT during TACE for hepatocellular carcinoma increases the OS. This may be related to the increased vessel selectivity.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Llovet JM, Real MI, Montana X, Planas R, Coll S, Aponte J, *et al*. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: A randomised controlled trial. Lancet 2002;359:1734-9.
2. Lo CM, Ngan H, Tso WK, Liu CL, Lam CM, Poon RT, *et al*. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology 2002;35:1164-71.
3. Geschwind JF, Salem R, Carr BI, Soulen MC, Thurston KG, Goin KA, *et al*. Yttrium-90 microspheres for the treatment of hepatocellular carcinoma. Gastroenterology 2004;127 5 Suppl 1:S194-205.
4. Salem R, Lewandowski RJ, Atassi B, Gordon SC, Gates VL, Barakat O, *et al*. Treatment of unresectable hepatocellular carcinoma with use of 90Y microspheres (TheraSphere): Safety, tumor response, and survival. J Vasc Interv Radiol 2005;16:1627-39.
5. Salem R, Lewandowski RJ, Kulik L, Wang E, Riaz A, Ryu RK, *et al*. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterology 2011;140:497-507.e2.
6. Sangro B, Carpanese L, Cianni R, Golfieri R, Gasparini D, Ezziddin S, *et al*. Survival after yttrium-90 resin microsphere radioembolization of hepatocellular carcinoma across Barcelona clinic liver cancer stages: A European evaluation. Hepatology 2011;54:868-78.
7. Brown DB, Pilgram TK, Darcy MD, Fundakowski CE, Lisker-Melman M, Chapman WC, *et al*. Hepatic arterial chemoembolization for hepatocellular carcinoma: Comparison of survival rates with different embolic agents. J Vasc Interv Radiol 2005;16:1661-6.
8. Tognolini A, Louie JD, Hwang GL, Hofmann LV, Sze DY, Kothary N. Utility of C-arm CT in patients with hepatocellular carcinoma undergoing transhepatic arterial chemoembolization. J Vasc Interv Radiol 2010;21:339-47.
9. Kakeda S, Korogi Y, Ohnari N, Moriya J, Oda N, Nishino K, *et al*. Usefulness of cone-beam volume CT with flat panel detectors in conjunction with catheter angiography for transcatheter arterial embolization. J Vasc Interv Radiol 2007;18:1508-16.
10. Iwazawa J, Ohue S, Mitani T, Abe H, Hashimoto N, Hamuro M, *et al*. Identifying feeding arteries during TACE of hepatic tumors: Comparison of C-arm CT and digital subtraction angiography. Am J Roentgenol 2009;192:1057-63.
11. Wallace MJ, Murthy R, Kamat PP, Moore T, Rao SH, Ensor J, *et al*. Impact of C-arm CT on hepatic arterial interventions for

hepatic malignancies. J Vasc Interv Radiol 2007;18:1500-7.
12. Uchida H, Ohishi H, Matsuo N, Nishimine K, Ohue S, Nishimura Y, *et al*. Transcatheter hepatic segmental arterial embolization using lipiodol mixed with an anticancer drug and Gelfoam particles for hepatocellular carcinoma. Cardiovasc Intervent Radiol 1990;13:140-5.
13. Matsui O, Kadoya M, Yoshikawa J, Gabata T, Arai K, Demachi H, *et al*. Small hepatocellular carcinoma: Treatment with subsegmental transcatheter arterial embolization. Radiology 1993;188:79-83.
14. Matsuo N, Uchida H, Nishimine K, Soda S, Oshima M, Nakano H, *et al*. Segmental transcatheter hepatic artery chemoembolization with iodized oil for hepatocellular carcinoma: Antitumor effect and influence on normal tissue. J Vasc Interv Radiol 1993;4:543-9.
15. Bruix J, Sherman M, Llovet JM, Beaugrand M, Lencioni R, Burroughs AK, *et al*. Clinical management of hepatocellular carcinoma. Conclusions of the Barcelona-2000 EASL conference. European association for the study of the liver. J Hepatol 2001;35:421-30.
16. Shim JH, Lee HC, Kim SO, Shin YM, Kim KM, Lim YS, *et al*. Which response criteria best help predict survival of patients with hepatocellular carcinoma following chemoembolization? A validation study of old and new models. Radiology 2012;262:708-18.
17. Golfieri R, Cappelli A, Cucchetti A, Piscaglia F, Carpenzano M, Peri E, *et al*. Efficacy of selective transarterial chemoembolization in inducing tumor necrosis in small (<5 cm) hepatocellular carcinomas. Hepatology 2011;53:1580-9.
18. Virmani S, Ryu RK, Sato KT, Lewandowski RJ, Kulik L, Mulcahy MF, *et al*. Effect of C-arm angiographic CT on transcatheter arterial chemoembolization of liver tumors. J Vasc Interv Radiol 2007;18:1305-9.
19. Miyayama S, Yamashiro M, Okuda M, Yoshie Y, Sugimori N, Igarashi S, *et al*. Usefulness of cone-beam computed tomography during ultraselective transcatheter arterial chemoembolization for small hepatocellular carcinomas that cannot be demonstrated on angiography. Cardiovasc Intervent Radiol 2009;32:255-64.

How to cite this article: Abdelsalam ME, Appleton-Figueira TM, Ensor J, Tam AL, Kaseb AO, Gupta S. Survival impact of C-Arm cone-beam computed tomography on hepatocellular carcinoma patients undergoing chemoembolization. Am J Interv Radiol 2021;5:9.