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Original Article

Delayed percentage attenuation ratio (DPAR) on multiphase CT as a quantitative predictor of early response in hepatocellular carcinoma

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Abstract

Hepatocellular carcinoma (HCC) remains a major cause of cancer-related mortality, and transarterial chemoembolization (TACE) is the standard therapy for intermediate-stage disease. However, response to TACE is variable, and reliable quantitative imaging biomarkers are needed to support early treatment decision-making. This study aimed to evaluate the predictive value of the delayed percentage attenuation ratio (DPAR) measured from pre-TACE multiphasic computed tomography (CT) in forecasting early therapeutic response. A retrospective cross-sectional study was conducted involving patients with a definitive diagnosis of HCC who underwent their first TACE session and had complete multiphasic CT imaging before and after treatment. Quantitative washout parameters, delayed percentage attenuation ratio (DPAR), absolute washout (WOAbs), and relative washout (WORel) were measured using standardized region of interest (ROI) placement by three radiologists. Treatment response was assessed four to six weeks post-TACE based on modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria and classified into responders and non-responders. Diagnostic performance was evaluated using receiver operating characteristic (ROC) analysis, and interobserver reliability was assessed using intraclass correlation coefficient (ICC) and Cohen's κ. A total of 49 HCC patients were included and analyzed. Responders demonstrated significantly higher DPAR values compared with non-responders (median 134.5 vs 113.0; $p<0.001$). DPAR showed the strongest discriminative performance with an area under the curve (AUC) of 0.898, outperforming WOAbs (AUC 0.689) and WORel (AUC 0.704). The optimal DPAR threshold of ≥120.5 provided 84.4% sensitivity and 88.2% specificity to predict early post-TACE treatment response. Interobserver reliability was excellent for all washout parameters (ICC 0.98–0.99), and agreement for mRECIST classification was also excellent (κ=0.867). In conclusion, pre-TACE DPAR is a robust and reproducible quantitative imaging biomarker that accurately predicts early response to TACE in HCC. A threshold value of ≥120.5 may assist in treatment planning and patient selection in routine clinical practice.

Keywords: Hepatocellular carcinoma, transarterial chemoembolization, computed tomography, DPAR, imaging biomarker

Introduction

Hepatocellular carcinoma (HCC) accounts for approximately 75% of primary liver cancers and represents a major global health burden [1,2]. According to the Global Cancer Observatory 2020,

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liver cancer ranks among the seven most common malignancies worldwide and the third leading cause of cancer-related death, with an incidence of 9.5 and mortality of 8.5 per 100,000 population annually [2–4]. Prognosis remains poor, with a 5-year survival rate of only 19% in the United States, and the highest prevalence is observed in East and Southeast Asia as well as North Africa [2,3]. In Indonesia, HCC is the fourth most common cancer among men, with an age-standardized incidence rate of 13.4 per 100,000 [5]. Major etiologic factors include chronic hepatitis B or C infection, cirrhosis, excessive alcohol consumption, and non-alcoholic steatohepatitis [5].

For patients with intermediate-stage HCC, transarterial chemoembolization (TACE) remains the standard of care; however, treatment response is highly variable, emphasizing the need for reliable prognostic imaging biomarkers. Multiphase computed tomography (CT) and magnetic resonance imaging (MRI) provide a noninvasive diagnosis of HCC by assessing enhancement patterns across arterial, portal venous, and delayed phases. The characteristic imaging features include arterial phase hyperenhancement, delayed washout, and capsular enhancement [6,7]. Quantitative assessment of washout, defined as hypoattenuation of the lesion relative to the surrounding liver during the portal venous phase or delayed (equilibrium) phase, has emerged as a promising approach not only for diagnosis but also for predicting outcomes following locoregional therapy such as TACE. This phenomenon is commonly referred to as delayed-phase washout in hepatocellular carcinoma imaging [8–10].

Although delayed-phase washout has long been recognized in HCC, previous studies have largely relied on qualitative or subjective evaluation [8,11,12]. Recent evidence indicates that a quantitative index called the delayed-phase attenuation ratio (DPAR), defined as the ratio of liver-to-lesion attenuation measured on the delayed phase, may outperform conventional washout metrics in predicting post-TACE response, offering standardized and reproducible measurements [9,10]. However, current findings remain heterogeneous across centers and imaging protocols, and variations in delayed-phase acquisition timing (typically 2–5 minutes) may affect measurement reliability and threshold applicability [8,9]. Therefore, there is a need for single-center validation of quantitative washout parameters to determine which metric best predicts early post-TACE response and to establish a clinically actionable cut-off applicable to routine multiphasic CT. This study aimed to evaluate whether pre-TACE quantitative washout parameters differ between responders and non-responders, and to determine the most discriminative metric and its optimal cut-off for predicting early treatment response, with a particular focus on the DPAR measured on multiphasic CT.

Methods

Study design and setting

A retrospective, cross-sectional, non-experimental comparative study was conducted at a tertiary referral hospital in Yogyakarta, Indonesia, from February 2020 to February 2024. The study received ethical clearance from the Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, with administrative permission from Dr. Sardjito General Hospital, Yogyakarta, Indonesia, and the requirement for written informed consent was waived in accordance with the Declaration of Helsinki. Consecutive non-random sampling was utilized, involving patients with a definitive diagnosis of HCC who underwent their first session of TACE and had available multiphasic contrast-enhanced abdominal CT examinations before and after treatment.

Patients' criteria

Diagnosis of HCC was established using noninvasive imaging criteria according to European Association for the Study of the Liver clinical practice guideline (EASL 2018), the American Association for the Study of Liver Diseases practice guidance (AASLD 2018), or Liver Imaging Reporting and Data System (LI-RADS) category 5 (2018), characterized by arterial phase hyperenhancement with portal or delayed-phase washout and/or an enhancing capsule. Inclusion criteria consisted of: (1) definitive HCC without hepatic steatosis; (2) availability of multiphasic CT (pre-contrast, arterial, portal venous, and delayed phases) performed at the same

institution; (3) aortic attenuation of 100–150 Hounsfield units (HU) at the level of the celiac axis; (4) no prior definitive HCC therapy; and (5) age above 18 years. Patients were excluded if their CT examination was incomplete or if they had chronic kidney disease with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m².

Eligibility for TACE was determined through multidisciplinary tumor board discussion based on the Barcelona Clinic Liver Cancer staging system and major international guideline recommendations (EASL 2018 and AASLD 2018) [6,7,13]. For multifocal disease, the largest viable lesion was selected as the index lesion according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria, while in bilobar involvement, the dominant measurable lesion was chosen. Infiltrative or diffuse-type HCC was excluded due to the inability to obtain a reliable region of interest (ROI)-based quantitative assessment. Only one target lesion per patient was included in the analysis. A priori sample size estimation required approximately 26 patients per group (total 52), and the final analytic sample of 49 patients approached this requirement.

Multiphasic computed tomography (CT) procedure

Multiphasic CT examinations were performed using four phases, consisting of pre-contrast, arterial (approximately 35–45 seconds), portal venous (approximately 60–75 seconds), and delayed-phases acquired 2–5 minutes after contrast administration. The delayed-phase timing followed institutional protocol consistent with common clinical practice and prior evidence showing stable DPAR measurement within this interval. Only examinations meeting the predefined aortic attenuation threshold of 100–150 HU at the level of the celiac axis were included to ensure standardized arterial enhancement. All scans were obtained using a 128-slice multidetector CT scanner (Brilliance 64, Philips Medical Systems, Best, Netherlands) with acquisition parameters of 120 kVp, 200–300 mAs, a section thickness of 1 mm with a 0.5 mm increment (range 1–3 mm acceptable), and a section scan time of 4–6 seconds. A non-ionic iodinated contrast agent (300 mg I/mL) was administered intravenously at 1 mL/kg with an injection rate of 3–5 mL/s, followed by a saline flush.

Computed tomography (CT) acquisition

All CT images were retrieved from the institutional Picture Archiving and Communication System (PACS) and reviewed using a Digital Imaging and Communication in Medicine (DICOM) viewer. Measurements were independently performed by three radiologists with different levels of clinical experience, two with more than five years and one with less than five years, following a brief calibration. Circular ROIs approximately 1 cm in diameter were placed within viable tumor portions and adjacent normal liver parenchyma across all phases, avoiding necrotic areas, intratumoral hemorrhage, visible vessels, bile ducts, calcifications, and peripheral margins. ROI placement was maintained on corresponding axial slices to minimize variability.

The primary quantitative variable was the DPAR, calculated as:

$$\text{DPAR} = \left(\frac{HU_{liver,delayed}}{HU_{lesion,delayed}} \right) \times 100$$

This formula was adopted based on a prior study demonstrating superior predictive performance compared with other washout metrics [14]. To enable comparison with additional washout parameters, absolute washout (WOAbs) and relative washout (WORel) were also calculated using established formulas [8]:

$$\text{WOAbs} = \left(\frac{HU_{arterial} - HU_{delayed}}{HU_{arterial}} \right) \times 100$$

$$\text{WORel} = \left(\frac{HU_{arterial} - HU_{delayed}}{HU_{arterial} - HU_{pre-contrast}} \right) \times 100$$

All quantitative measurements were independently performed by three radiologists. For treatment response assessment, two radiologists were blinded to post-TACE outcomes, and

disagreements were resolved by consensus with adjudication by a third senior radiologist when required.

Treatment and response evaluation

All patients underwent conventional transarterial chemoembolization (cTACE) performed by an interventional radiologist according to the institutional protocol. After selective or superselective catheterization of the tumor-feeding hepatic arteries, a mixture of chemotherapeutic agent (doxorubicin) and iodized oil (lipiodol) was administered, followed by embolization using gelatin sponge particles until near-stasis ("sub-stasis") of arterial flow was achieved. The same cTACE technique was consistently applied to all patients included in this study.

Treatment response was evaluated on follow-up multiphasic CT performed four to six weeks after the procedure using the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Response categories included complete response, partial response, stable disease, and progressive disease. For statistical analysis, outcomes were dichotomized into responders (complete response or partial response) and non-responders (stable disease or progressive disease).

Statistical analysis

Data normality was assessed using the Shapiro–Wilk test. Because one response group violated normality assumptions, the Mann–Whitney U test was applied to compare DPAR values between responders and non-responders. Receiver operating characteristic (ROC) analysis was performed to evaluate diagnostic performance, reporting the area under the curve (AUC) with 95% confidence intervals. The optimal DPAR cut-off point was determined using the Youden index along with corresponding sensitivity and specificity.

Interobserver reliability for continuous variables was assessed using the intraclass correlation coefficient (ICC) based on a two-way random-effects model with absolute agreement for average measurements (ICC(2,3)) with 95% confidence intervals. Agreement for treatment response classification (responders vs non-responders) was evaluated using Cohen's κ statistic. Statistical analyses were conducted using commercial software SPSS version 21 (IBM, New York, USA), with statistical significance defined as two-sided $p<0.05$.

Results

Patients' characteristics

A total of 49 patients with HCC who underwent initial TACE were included, consisting of 32 responders and 17 non-responders based on mRECIST assessment (**Figure 1**). A total of 168 patients underwent multiphasic abdominal CT for suspected HCC, of whom 121 met the inclusion criteria. Seventy-two patients were excluded due to incomplete multiphasic CT (absence of arterial, venous, or delayed-phase) or chronic kidney disease with an eGFR <30 mL/min/1.73 m², leaving 49 patients for final analysis.

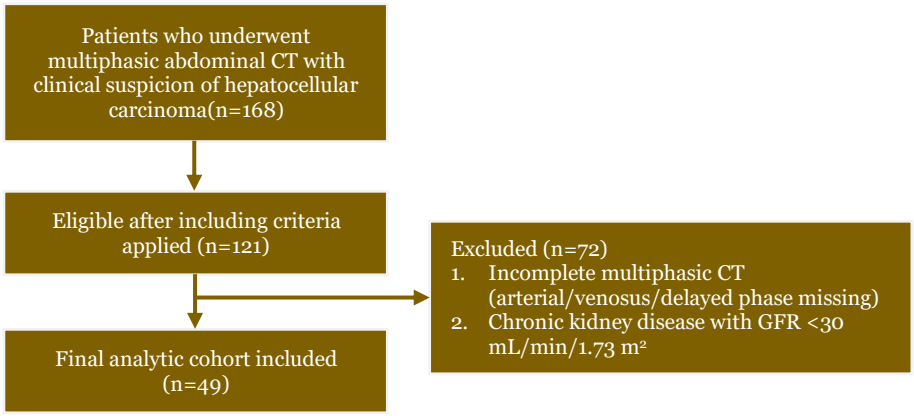

Figure 1. Patient inclusion and selection flow diagram of the study.

The baseline characteristics of patients are presented in **Table 1**. Most patients were aged ≥50 years (90.6%) and male (72.5%). Chronic viral hepatitis B or C was present in 57.1% of patients, and 71.4% had serum alpha-fetoprotein (AFP) levels <200 ng/mL. Large tumors (≥5 cm) were observed in 91.8% of cases. Solitary lesions were identified in 65.3% of patients, and unilateral disease distribution in 67.3%. Irregular lesion margins were present in 57.1%. Additional findings included necrosis in 67.3%, cirrhosis in 16.3%, ascites in 12.2%, tumor thrombus in 4.1%, and arterioportal fistula in 2.0% (**Table 1**). Comparative analysis showed that most baseline characteristics did not differ significantly between responders and non-responders (all $p>0.05$), except for lesion margin ($p=0.046$) and lesion location ($p=0.004$), which demonstrated significant associations with treatment response (**Table 1**).

Table 1. Comparison of the baseline characteristics between responders and non-responders (n=49)

Characteristic	Total n (%)	TACE treatment response		*p*-value
		Responders (n=32) n (%)	Non-responders (n=17) n (%)	
Age				
≥50 years	44 (89.8)	29 (90.6)	15 (88.2)	1.000 [a,*]
<50 years	5 (10.2)	3 (9.4)	2 (11.8)	
Sex				
Male	36 (73.5)	23 (71.9)	13 (76.5)	0.729 [a]
Female	13 (16.5)	9 (28.1)	4 (23.5)	
Chronic liver disease				
HBV/HCV	28 (57.1)	16 (50.0)	12 (70.6)	0.166 [a]
Non-viral	21 (42.9)	16 (50.0)	5 (29/4)	
Alpha-fetoprotein				
≥200 ng/mL	14 (28.6)	7 (53.1)	7 (41.2)	0.155 [b]
<200 ng/mL	35 (71.4)	25 (78.1)	10 (58.8)	
Lesion margin				
Regular	21 (42.9)	17 (53.1)	4 (23.5)	0.046 [b]
Irregular	28 (57.1)	15 (46.9)	13 (76.5)	
Tumor size				
≥5 cm	45 (91.8)	29 (90.6)	16 (94.1)	1.000 [a,*]
<5 cm	4 (8.2)	3 (9.4)	1 (5.9)	
Number of lesions				
Solitary	32 (65.3)	23 (71.9)	9 (52.9)	0.185 [b]
Multiple	17 (34.7)	9 (28.1)	8 (47.1)	
Lesion location				
Bilateral	16 (32.7)	6 (18.8)	10 (58.8)	0.004 [b]
Unilateral	33 (67.3)	26 (81.2)	7 (41.2)	
Tumor thrombus				
Present	2 (4.1)	1 (3.1)	1 (5.9)	1.000 [a,*]
Absent	47 (95.9)	31 (96.9)	16 (94.1)	
Arterioportal fistula				
Present	1 (2.0)	0 (0.0)	1 (5.9)	1.000 [a]
Absent	48 (98.0)	32 (100.0)	16 (94.1)	
Necrosis				
Present	33 (67.3)	19 (59.4)	14 (82.4)	1.000 [a]
Absent	16 (32.7)	13 (40.6)	3 (17.6)	
Cirrhosis				
Present	8 (16.3)	7 (21.9)	1 (5.9)	0.149 [a]
Absent	41 (83.7)	25 (78.1)	16 (94.1)	
Ascites				
Present	6 (12.2)	5 (15.6)	1 (5.9)	0.650 [a,*]
Absent	43 (87.8)	27 (84.4)	16 (94.1)	

HBV: hepatitis B virus; HCV: hepatitis C virus; TACE: transarterial chemoembolization
[a] Analyzed using Fisher's exact test
[b] Analyzed using Chi-square test
*Statistically significant at $p<0.05$

Quantitative washout analysis

Quantitative washout values measured before TACE were compared between two groups based on the mRECIST criteria, with partial response and complete response classified as responders, and progressive disease and stable disease classified as non-responders (**Table 2**). Responders demonstrated significantly higher washout values across all three quantitative parameters. For

WOAbs, the mean value in responders was 41.19±33.83 compared with 25.65±18.49 in non-responders (p=0.030). For WORel, responders had a mean value of 14.97±8.21 versus 10.06±7.72 in non-responders (p=0.020). Similarly, DPAR values were markedly higher in responders (139.41±19.86) compared with non-responders (114.41±13.44) (p<0.001). This finding indicated that patients achieving partial or complete response exhibited visibly higher pre-TACE washout values compared with those with progressive or stable disease.

Table 2. Comparison of quantitative washout parameters between responder and non-responder groups of in patients with hepatocellular carcinoma (HCC) before transarterial chemoembolization (TACE)

Washout parameter	Group	Mean±SD	Median (min-max)	p-value
WOAbs	Responders (n=32)	41.19±33.83	29.50 (14–175)	0.030*
	Non-responders (n=17)	25.65±18.49	22.00 (3–69)	
WORel	Responders (n=32)	14.97±8.21	12.50 (4–34)	0.020*
	Non-responders (n=17)	10.06±7.72	7.00 (1–25)	
DPAR	Responders (n=32)	139.41±19.86	134.50 (110–184)	<0.001*
	Non-responders (n=17)	114.41±13.44	113.00 (100–160)	

DPAR: delayed percentage attenuation ratio; WOAbs: absolute washout; WORel: relative washout
*Statistically significant at p<0.05

Receiver operating characteristic (ROC) analysis

ROC analysis demonstrated clear differences in diagnostic performance among the three quantitative washout parameters (**Figure 2**). The DPAR showed the strongest predictive ability for distinguishing responders from non-responders after the first TACE session. DPAR achieved an AUC of 0.898, followed by the WORel with an AUC of 0.704, and the WOAbs with an AUC of 0.689 (**Table 3**). All three ROC curves were positioned above the reference line, indicating acceptable discriminative power; however, DPAR demonstrated superior performance, falling within the "good" AUC classification range and showing the greatest separation from the diagonal reference line. These findings support DPAR as the most reliable quantitative washout metric for predicting early post-TACE therapeutic response.

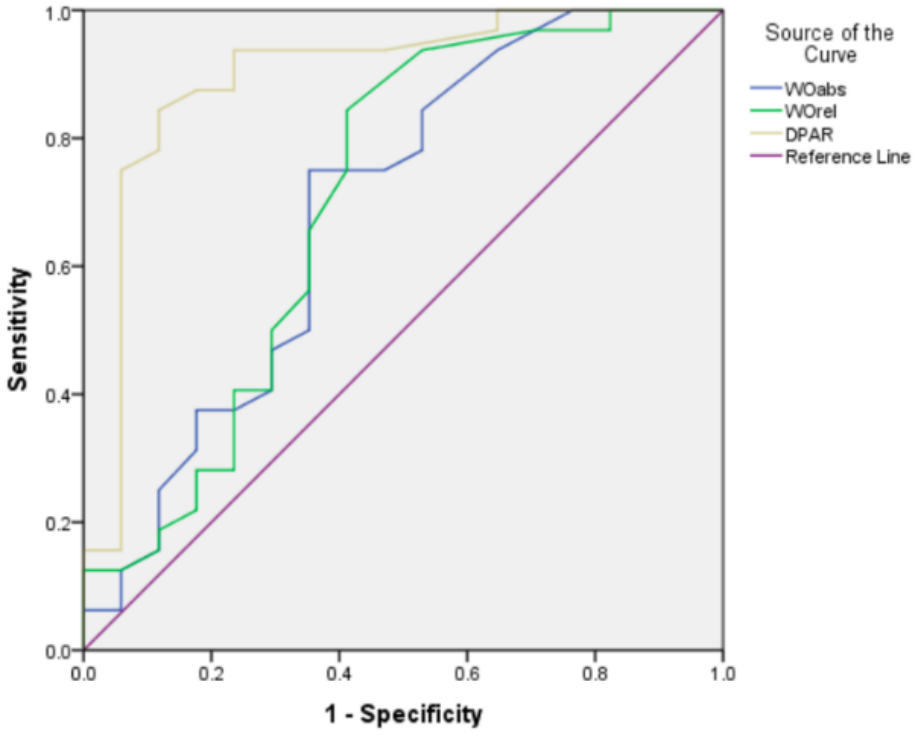

Figure 2. Receiver operating characteristic (ROC) curve of the three washout parameters in predicting post-TACE therapeutic response in patients with hepatocellular carcinoma (HCC).

Table 3. Diagnostic performance of quantitative washout parameters in predicting post-TACE response in patients with hepatocellular carcinoma (HCC)

Parameter	Cut-off	AUC (95%CI)	Sensitivity	Specificity
WOAbs	26.5	0.689 (0.521–0.857)	0.656	0.647
WORel	9.5	0.704 (0.533–0.875)	0.656	0.647
DPAR	120.5	0.898 (0.792–1.000)	0.844	0.882

AUC: area under the receiver operating characteristic curve; DPAR: delayed percentage attenuation ratio; WOAbs: absolute washout; WORel: relative washout

Cut-off point analysis

Cut-off analysis showed that the DPAR value provided the most accurate threshold for predicting early treatment response after the first TACE session. Using the Youden index, the optimal cut-off for DPAR was ≥120.5, yielding a sensitivity of 0.84 and a specificity of 0.88. These values indicate a strong discriminative ability, where lesions with DPAR values below 120.5 were more likely to exhibit stable disease or progressive disease, while those above the threshold were predominantly classified as partial response or complete response. For comparison, the cut-off values obtained from the WOAbs and WORel formulas were 26.5 and 9.5, respectively. Both metrics demonstrated lower diagnostic performance, each showing 66% sensitivity and 65% specificity, reflecting moderate predictive accuracy. These findings are consistent with the ROC curve evaluation, which also identified DPAR as the most reliable washout parameter (**Figure 3**).

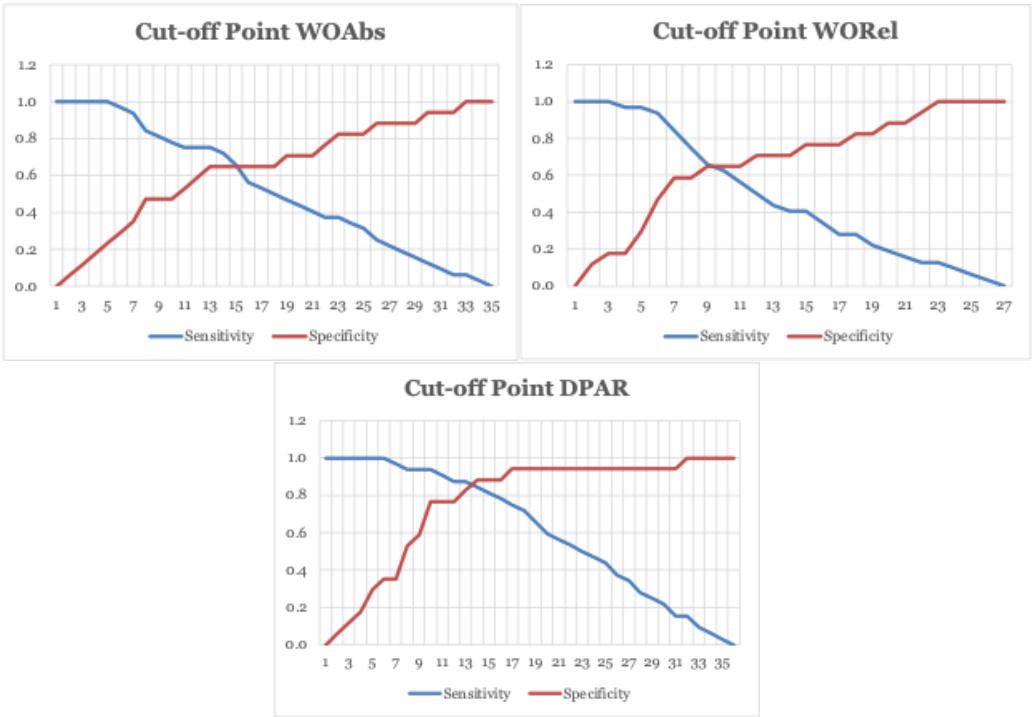

Figure 3. Cut-off analysis of WOAbs, WORel, and DPAR for predicting the response post-transarterial chemoembolization (TACE) in patients with hepatocellular carcinoma (HCC).

Reliability

Interobserver reliability for washout quantification was excellent. Three radiologists with different levels of experience (>5 years, 3–4 years, and 2 years) independently placed ROIs within viable tumor regions and adjacent normal liver parenchyma while avoiding necrotic, hemorrhagic, vascular, and calcified areas. The ICCs ranged from 0.98 to 0.99, indicating excellent reproducibility (ICC > 0.90). For treatment response classification based on mRECIST, interobserver agreement assessed using Cohen's κ was 0.86, also demonstrating excellent reliability (**Table 4**). This observation is consistent with the representative case (**Figure 4**), where a lesion with a high DPAR value (163) demonstrated a 65% reduction in viable tumor area according to mRECIST following the first TACE session.

Table 4. Interobserver reliability for washout quantification and mRECIST response classification

Parameter	Reliability Metric	Value	95%CI (lower-upper)	Interpretation
WOAbs (delayed)	ICC (single measure)	0.966	0.904–0.991	Excellent
	ICC (average measures)	0.988	0.966–0.997	Excellent
WORel (delayed)	ICC (single measure)	0.987	0.962–0.996	Excellent
	ICC (average measures)	0.996	0.987–0.999	Excellent
DPAR (delayed)	ICC (single measure)	0.993	0.980–0.998	Excellent
	ICC (average measures)	0.998	0.993–0.999	Excellent
mRECIST response classification	Cohen's κ	0.867	—	Excellent

ICC values >0.90 and κ values >0.80 indicate excellent interobserver agreement

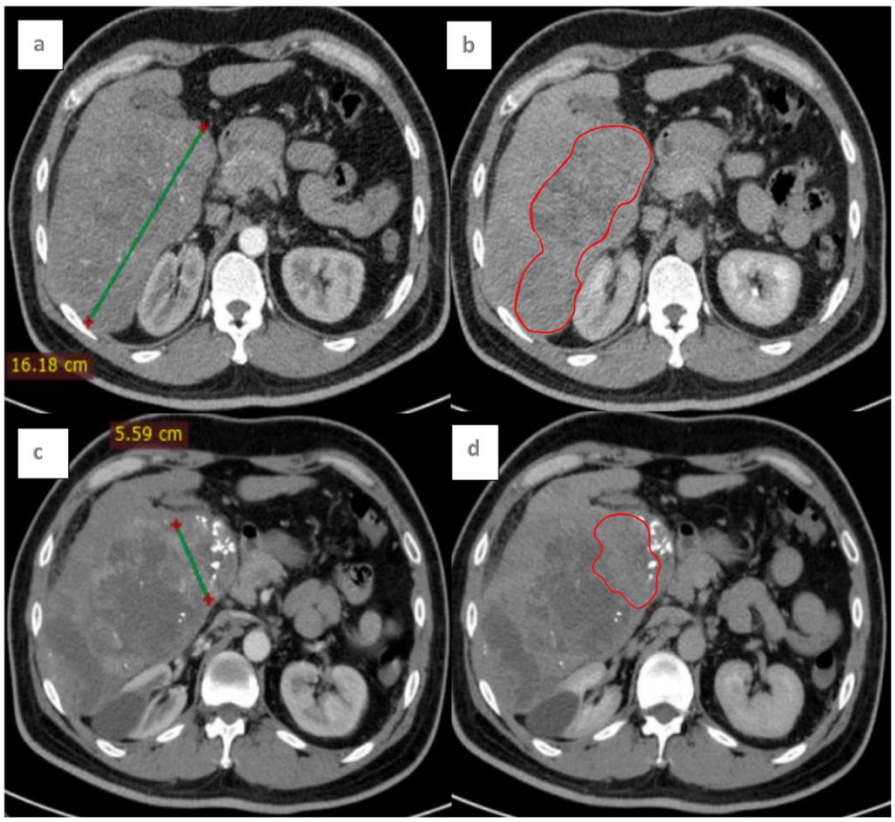

Figure 4. Example of mRECIST-based treatment response evaluation. Pre-TACE arterial (A) and delayed phase (B) CT images demonstrate a large hepatocellular carcinoma with a maximal diameter of 16.18 cm; the viable enhancing component is outlined. Follow-up CT after TACE (C and D) shows a reduction of the viable portion to 5.59 cm, representing a 65% decrease in viable tumor area and fulfilling the criteria for objective response according to mRECIST. The pre-treatment DPAR value for this case was 163.

Discussion

This retrospective single-center study showed that the DPAR derived from pre-TACE multiphasic CT was the most discriminative quantitative imaging parameter for predicting early therapeutic response in HCC patients. Responders demonstrated significantly higher DPAR values than non-responders (p<0.001). ROC analysis further confirmed excellent diagnostic performance, with an AUC of 0.89 (95%CI, 0.79–1.00) and an optimal cut-off of 120.5, providing 84.4% sensitivity and 88.2% specificity. These findings suggest that DPAR may serve as a practical and reliable imaging biomarker to support early treatment stratification in patients undergoing TACE [9,10].

In addition to quantitative parameters, previous studies found that several morphologic characteristics also showed significant associations with treatment response [9,10]. Lesions with regular margins and unilateral tumor distribution were more likely to achieve favorable outcomes (p=0.046 and p=0.004, respectively), suggesting that more localized and well-defined disease may facilitate more effective embolization [15]. Measurement reliability across observers was

excellent, with ICC values of 0.98–0.99 for washout parameters and a Cohen's κ of 0.867 for mRECIST classification, indicating consistently reproducible assessments. These morphologic patterns likely reflect more compact tumor architecture and more localized arterial feeders, enabling more complete embolization, whereas irregular or bilobar tumors may exhibit diffuse vascularization that reduces embolization efficacy despite technically adequate procedures.

Patient selection for TACE in this cohort followed a structured, guideline-based clinical pathway. Eligibility for locoregional therapy was determined through multidisciplinary tumor board discussions using the Barcelona Clinic Liver Cancer staging system and major international recommendations [16,17]. This approach ensured that only patients with appropriate tumor burden, preserved liver function, and adequate performance status underwent TACE, reducing heterogeneity in treatment suitability and strengthening internal validity by minimizing selection bias.

A major strength of this study lies in its pragmatic design, which reflects real-world clinical practice in a tertiary referral setting. Methodological rigor was ensured through strict inclusion criteria, standardized multiphasic CT acquisition, enforcement of arterial-phase quality using predefined aortic attenuation thresholds (100–150 HU), and blinded ROI placement by three independent radiologists. These measures enhanced internal consistency and supported the reproducibility of washout quantification. The predominance of large tumors (≥5 cm in 92% of patients) further extends the applicability of DPAR to more advanced disease stages, in which reliable imaging biomarkers are critically needed. Importantly, variations in arterial-phase enhancement within the acceptable 100–150 HU range did not materially affect DPAR values because this parameter is calculated from delayed-phase attenuation.

This study also provides several contributions that enhance its clinical relevance. It includes an Asian patient cohort—an underrepresented population in quantitative washout research despite known regional differences in liver disease patterns and treatment response. Arterial-phase quality was systematically standardized, improving the reliability of attenuation-based metrics. Interobserver reproducibility was excellent across radiologists with different experience levels, supporting the robustness of the measurement protocol. Finally, patient selection was based on multidisciplinary tumor board discussions, reflecting real-world clinical workflow and supporting the external validity of DPAR in routine TACE decision-making.

The findings of this study are consistent with previous reports showing that delayed-phase washout metrics outperform early-phase–based formulas in predicting post-TACE response [8–10]. Previous studies demonstrated that DPAR cut-off values near 120 produced AUCs of approximately 0.85–0.90 [9,10]. Our results showed comparable performance, with DPAR achieving an AUC of 0.898 and providing the strongest discrimination among the three evaluated washout parameters, whereas WOAbs and WORel exhibited lower predictive accuracy. Importantly, while many earlier studies evaluated smaller tumors (mean diameter ~2 cm), our findings confirm that a DPAR threshold ≥120.5 remains predictive even in larger tumors, as 92% of our cohort had lesions ≥5 cm [9,10,18]. This supports the robustness and relative size-independence of DPAR as an imaging biomarker. Morphologic predictors, such as regular margins and unilateral involvement, also align with previous findings, possibly reflecting more localized arterial supply and technically more complete embolization [9,10]. The influence of portal venous anatomy, particularly lesion proximity to major bifurcations, may also affect embolization efficacy, although this factor was not specifically assessed in our cohort [15].

The physiologic basis of DPAR's superior performance likely contributes to these results. HCC demonstrates predominantly arterialized vascular supply, whereas normal liver parenchyma derives most of its perfusion from the portal vein [12,19,20]. This creates relative hypoattenuation of HCC during venous and delayed phases [18]. Because DPAR is calculated within a single phase, it reduces variability arising from contrast dose, injection rate, timing errors, and arterial enhancement differences [21]. In contrast, WOAbs and WORel rely partly on arterial or pre-contrast measurements, making them more susceptible to technical variation [21,22]. Lipiodol deposition did not influence washout quantification in this study because all attenuation values were obtained from pre-TACE imaging [23,24].

Although DPAR showed strong discriminative performance, multivariate analyses were not performed due to the relatively limited sample size and the imbalance between responder and

non-responder groups, which could compromise the stability of multivariable modeling. As these covariates are known to influence post-TACE outcomes, the independent predictive value of DPAR cannot be fully established. Future studies should incorporate multivariate logistic or survival-based modeling to determine whether DPAR retains prognostic significance after adjustment.

Infiltrative or diffuse-type HCC was excluded due to its lack of discrete margins, which preclude reproducible ROI-based attenuation measurements. This approach aligns with previous washout studies but limits the applicability of the present findings primarily to nodular and mass-forming HCC [9,10,25]. Additional research is needed to evaluate whether DPAR-based metrics can be extended to infiltrative tumor subtypes.

For clinical implementation, standardized ROI placement using approximately 1 cm circular regions within viable tumor tissue while avoiding necrotic or vascular areas, and consistent delayed-phase acquisition around 3 minutes, is recommended to optimize measurement reproducibility. Incorporating DPAR into structured radiology reports, together with morphologic features such as lesion margin and laterality, may support more informed TACE treatment planning. Future work should include prospective, multicenter validation, integration with established prognostic indicators, and external reproducibility testing to determine whether threshold recalibration is required before broad clinical adoption.

This study has some limitations, including its retrospective single-center design and modest sample size, which may limit statistical precision and generalizability. Variability in delayed-phase acquisition timing (2–5 minutes) could influence attenuation consistency, and dichotomizing responses into two groups may oversimplify biological heterogeneity. Restricting analysis to a single index lesion may underrepresent multifocal disease. Furthermore, survival outcomes and multivariable prognostic analyses were not performed, limiting assessment of long-term predictive value.

Conclusion

This study demonstrated that the DPAR measured on pre-TACE multiphasic CT was a reliable and reproducible quantitative imaging biomarker for predicting early treatment response in HCC patients. A threshold value of ≥120.5 was significantly associated with objective response, supporting the use of DPAR as a practical tool to guide therapeutic planning and patient selection for transarterial chemoembolization.

Ethics approval

Ethical clearance was granted by the Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada (approval number: KE/FK/0359/EC/2024), with administrative permission obtained from Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

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Competing interests

All the authors declare that there are no conflicts of interest.

Funding

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study utilized artificial intelligence (AI) tools solely to support manuscript preparation. An AI-based language model (ChatGPT) was employed for language enhancement, sentence refinement, and technical writing assistance to improve clarity and readability. AI tools were not used for data collection, analysis, interpretation, modeling, or drawing scientific conclusions. All AI-assisted outputs were critically reviewed, verified, and revised by the authors to ensure accuracy and consistency. The final decisions, interpretations, and content of this manuscript reflect the authors' independent academic judgment and intellectual contributions.

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