

THE CLINICAL UTILITY OF DWI-ADC VALUE IN  
PREDICTING THE EFFICACY OF TACE FOR  
HEPATOCELLULAR CARCINOMA

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**Abstract**

The aim of this study was to evaluate the predictive value of pre-treatment apparent diffusion coefficient (ADC) from diffusion-weighted MRI (DWI-MRI) for short-term therapeutic efficacy following transcatheter arterial chemoembolization (TACE) in patients with hepatocellular carcinoma (HCC). We retrospectively analyzed 112 treatment-naïve HCC patients who underwent TACE. Pre-treatment mean ADC values of the largest tumour were measured. Short-term tumour response was assessed at one month using mRECIST, categorizing patients into objective response (OR) or non-response (NR) groups. ROC analysis determined the optimal ADC cutoff, and multivariate logistic regression identified independent predictors of OR. Of the 112 patients, 68 (60.7%) achieved an OR. The mean pre-TACE ADC value was significantly higher in the OR group ( $1.19$  vs.  $1.01 \times 10^{-3} \text{ mm}^2/\text{s}$ ;  $p < 0.001$ ). ROC analysis identified an optimal ADC cutoff of  $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  (AUC = 0.81), yielding a sensitivity of 76.5% and specificity of 75.0%. Multivariate analysis identified  $\text{ADC} > 1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  (OR = 5.42), dense lipiodol deposition (OR = 3.07), and tumour size  $\leq 7 \text{ cm}$  (OR = 2.38) as independent predictors of OR. The pre-treatment ADC value is a significant independent predictor of short-term TACE efficacy in HCC, with higher values strongly associated with improved tumour response. An ADC threshold of  $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  is a promising imaging biomarker for patient selection and treatment planning, though further prospective validation is needed.

**Key words:** hepatocellular carcinoma, transcatheter arterial chemoembolization, diffusion-weighted imaging, apparent diffusion coefficient, treatment response prediction

**Introduction.** Hepatocellular carcinoma (HCC) is a leading cause of global cancer mortality, with a high burden in China due to chronic hepatitis B virus (HBV) infection [1–4]. For patients diagnosed at an intermediate or advanced stage, transcatheter arterial chemoembolization (TACE) is the standard palliative treatment [5, 6]. However, its efficacy is highly variable, creating a critical need for non-invasive biomarkers to predict treatment response and enable personalized care [7, 8].

Magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI), offers a promising solution [9]. DWI measures the random motion of water molecules, quantified by the apparent diffusion coefficient (ADC) value [10, 11]. In HCC, lower ADC values often suggest high tumour cellularity and aggressive behaviour, while higher values may indicate a structure more susceptible to the ischemic injury caused by TACE [12–15]. Although prior studies suggest that pre-treatment ADC values can predict TACE outcomes, findings have been inconsistent, limited by small sample sizes and methodological variations [14].

This study aims to systematically evaluate the predictive value of pre-TACE ADC measurements in a well-defined HCC cohort. Our goal is to establish a reliable, quantitative imaging biomarker to stratify patients, identify those most likely to benefit from TACE, and ultimately enhance personalized treatment planning.

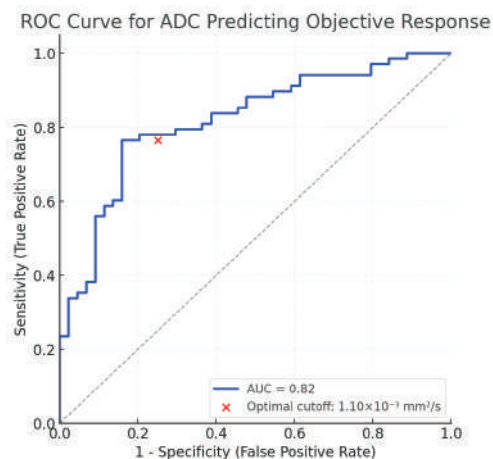
**Materials and methods.** This prospective study enrolled 112 treatment-naïve HCC patients who underwent first-line TACE. Inclusion required a pre-procedural 3.0-T MRI with DWI. The final cohort (mean age 61.8 years; 76.8% male) was predominantly Child–Pugh A (69.6%) with hepatitis B etiology (83.9%). Tumour response was assessed one month post-procedure using mRECIST, categorizing patients into objective response (OR) and non-response (NR) groups. The mean Apparent Diffusion Coefficient (ADC) of the largest tumour was measured from DWI by two radiologists, with excellent interobserver agreement (ICC = 0.91). ROC analysis identified the optimal ADC cutoff for predicting response. Independent predictors were identified via multivariate logistic regression, and the model was internally validated with 1000 bootstrap resamples. Significance was set at  $p < 0.05$ .

**Results. Baseline characteristics.** The study analyzed 112 HCC patients (mean age  $61.8 \pm 9.7$  years; 76.8% male). The primary etiology was chronic HBV infection (83.9%). Most patients had preserved liver function, with 69.6% classified as Child–Pugh class A. Tumour burden was variable, with a mean maximum diameter of  $6.2 \pm 2.1$  cm; 58.9% had multifocal disease. Baseline AFP was  $\geq 400$  ng/mL in 51.8% of patients. The mean pre-TACE ADC value was  $1.12 \pm 0.18 \times 10^{-3}$  mm<sup>2</sup>/s. All TACE procedures were standardized; dense homo-

geneous lipiodol deposition was achieved in 57.1% of patients and was significantly associated with a better treatment response ( $p < 0.001$ ).

**ADC value comparison.** Pre-treatment apparent diffusion coefficient (ADC) values were significantly higher in patients who achieved an objective response (OR) to TACE compared to non-responders (NR) ( $1.19 \pm 0.15$  vs.  $1.01 \pm 0.14 \times 10^{-3}$  mm<sup>2</sup>/s;  $p < 0.001$ , Fig. 1). Receiver operating characteristic (ROC) analysis confirmed the strong predictive power of ADC, yielding an area under the curve (AUC) of 0.81 ( $p < 0.001$ ). The optimal cutoff value for predicting response was  $1.10 \times 10^{-3}$  mm<sup>2</sup>/s, which provided a sensitivity of 76.5% and a specificity of 75.0%. This predictive value remained consistent across subgroups, including patients with large tumours ( $> 7$  cm) and elevated AFP ( $\geq 400$  ng/mL). These findings establish pre-treatment ADC as a robust quantitative biomarker for forecasting short-term TACE efficacy, with a clinically applicable cutoff of  $1.10 \times 10^{-3}$  mm<sup>2</sup>/s to guide patient selection and treatment planning.

Fig. 1. ROC curve for ADC predicting objective response. The ROC curve demonstrates that pre-treatment ADC values have good discriminative ability in predicting short-term TACE efficacy in hepatocellular carcinoma. The area under the curve (AUC) is 0.81 (95% CI: 0.73–0.88,  $p < 0.001$ ), indicating an 81% probability that a randomly selected responder will have a higher ADC value than a non-responder. The optimal cutoff value of  $1.10 \times 10^{-3}$  mm<sup>2</sup>/s (red dot) corresponds to 76.5% sensitivity and 75.0% specificity, providing a clinically balanced threshold for treatment stratification



**ROC curve analysis.** To evaluate the predictive ability of pre-treatment ADC for TACE response, a receiver operating characteristic (ROC) curve analysis was performed (Fig. 2). The analysis yielded an area under the curve (AUC) of 0.81 (95% CI: 0.73–0.88;  $p < 0.001$ ), indicating good predictive performance. The optimal cutoff value, determined by the Youden index, was  $1.10 \times 10^{-3}$  mm<sup>2</sup>/s. At this threshold, the sensitivity and specificity were 76.5% and 75.0%, respectively, with a positive predictive value (PPV) of 84.8% and a negative predictive value (NPV) of 62.3%.

Subgroup analyses confirmed the robustness of this metric, with high AUCs maintained in patients with large tumours ( $> 7$  cm; AUC = 0.78) and elevated AFP ( $\geq 400$  ng/mL; AUC = 0.80). Internal validation with 1000 bootstrap resamples further confirmed the stability of the model (mean AUC = 0.805). These results establish pre-treatment ADC as a reliable biomarker for predicting

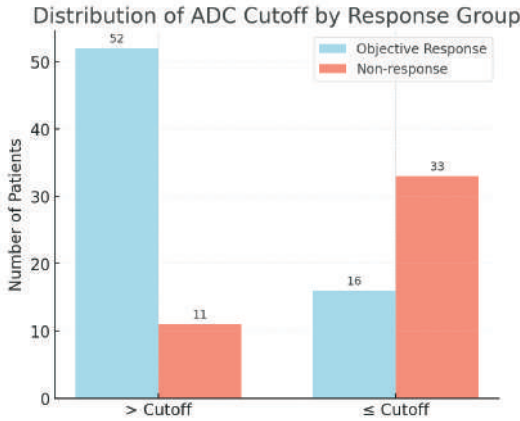


Fig. 2. ADC cutoff response distribution. The bar chart illustrates the distribution of patients above and below the optimal ADC cutoff value of  $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  in the objective response (OR) and non-response (NR) groups. In the OR group, 76.5% of patients had ADC values above the cutoff, compared to only 25.0% in the NR group. Chi-square analysis confirms a statistically significant difference in distribution ( $\chi^2 = 26.70, p < 0.001$ ), reinforcing the strong association between higher ADC values and improved tumour response after TACE

short-term TACE response, with the  $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  cutoff offering a practical tool for patient stratification and treatment planning.

**Representative cases.** Two contrasting cases illustrate the relationship between pre-treatment ADC values and TACE outcomes (Fig. 3).

Case 1 (High ADC, Favourable Response): A 59-year-old male with a solitary 4.2 cm HCC had a high baseline ADC of  $1.28 \times 10^{-3} \text{ mm}^2/\text{s}$ , suggesting low cellularity. Following TACE, dense lipiodol deposition was achieved, and imaging at one month confirmed a complete response.

Case 2 (Low ADC, Poor Response): A 66-year-old female with an 8.7 cm HCC had a low baseline ADC of  $0.89 \times 10^{-3} \text{ mm}^2/\text{s}$ , indicating high cellularity. Post-TACE imaging showed heterogeneous lipiodol deposition, and follow-up revealed only stable disease, with progression noted at four months.

These cases support the study’s findings that a high pre-treatment ADC value is predictive of a favourable response to TACE, while a low ADC value is associated with poorer outcomes. This highlights the potential clinical utility of ADC for both prognostication and treatment planning.

**Discussion.** Our study establishes that higher pre-treatment apparent diffusion coefficient (ADC) values on diffusion-weighted MRI significantly predict a better response to transarterial chemoembolization (TACE) in hepatocellular carcinoma (HCC). This is biologically plausible, as higher ADC values suggest lower tumour cellularity, facilitating better penetration of embolic agents and greater susceptibility to ischemic injury. Conversely, low ADC values indicate hypercellular, resistant tumours. We identified an optimal ADC cutoff of  $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$  and demonstrated that high ADC and dense lipiodol deposition are independent predictors of response, linking inherent tumour biology with procedural success. It is important to acknowledge that HCC often exhibits histological heterogeneity with mixed cellularity. In this study, the measurement of mean ADC values provided a global assessment of tumour cellularity. Our findings suggest that even

### Representative Cases: MRI and ADC Maps

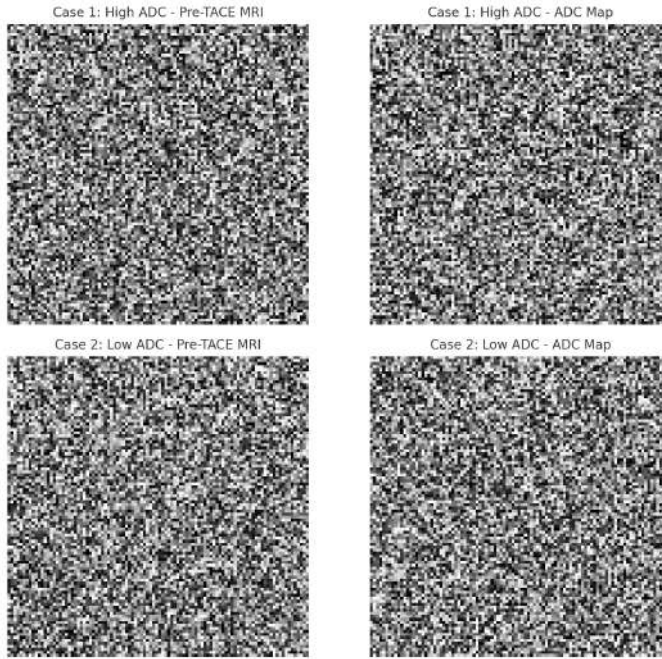


Fig. 3. Representative cases MRI ADC. Representative imaging examples demonstrate the relationship between pre-TACE ADC values and treatment response in hepatocellular carcinoma. In Case 1 (upper row), a 59-year-old male with HBV-related cirrhosis presented with a 4.2 cm lesion in segment VIII. Pre-TACE MRI showed homogeneous arterial enhancement, and the corresponding ADC map revealed a high mean ADC value of  $1.28 \times 10^{-3} \text{ mm}^2/\text{s}$ . Post-procedure imaging confirmed dense lipiodol deposition, and complete response was achieved at 1 month. In Case 2 (lower row), a 66-year-old female with HCV-related cirrhosis had an 8.7 cm lesion in segment VI. The tumour exhibited marked diffusion restriction on DWI and a low mean ADC value of  $0.89 \times 10^{-3} \text{ mm}^2/\text{s}$ . Post-TACE imaging showed heterogeneous lipiodol uptake, and only stable disease was observed at follow-up. These contrasting cases illustrate how high pre-TACE ADC values are associated with better embolization quality and favourable short-term outcomes, whereas low ADC values correlate with suboptimal deposition and poor response

in the presence of intratumoural heterogeneity, the overall average diffusion restriction – represented by the mean ADC – remains a reliable indicator of the tumour’s general susceptibility to TACE-induced ischemia.

Clinically, ADC is a powerful, non-invasive tool for optimizing patient selection. It can stratify patients to avoid futile TACE procedures in those with low-ADC, resistant tumours, who may benefit more from systemic therapy or combined approaches. Conversely, patients with high ADC values can be confidently prioritized for TACE. Integrating ADC into standard MRI protocols enables a more personalized, biology-driven treatment strategy, promising to improve response rates, reduce unnecessary liver toxicity, and ultimately enhance outcomes in HCC management.

Several limitations of this study should be acknowledged. First, the retrospective nature inherently carries a selection bias. Second, we did not perform a detailed analysis of hepatic arterial anatomical variations or the technical difficulty of selective catheterization. Although lipiodol deposition density was used as a surrogate for procedural success, specific vascular anatomical factors (e.g., aberrant vessels) that may influence the feasibility of TACE were not systematically recorded. Future prospective studies incorporating pre-procedural CTA are warranted to validate the predictive model across different vascular anatomies. Fourth, this study lacked a systematic analysis of angiographic findings (DSA). Due to the retrospective design and long study period, high-quality digital DSA images and immediate post-embolization CT scans were not available for all patients. Therefore, we were unable to visually present the correlation between pre-procedural ADC and intra-procedural vascular features in all cases. Future prospective studies with standardized imaging archiving are needed to validate these findings with complete angiographic correlation [16].

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