# The value of computed tomography perfusion for assessing the response of hepatocellular carcinoma to transarterial chemoembolization

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## ABSTRACT

We determined the value of computed tomography perfusion (CTP) for assessing the response of hepatocellular carcinoma (HCC) to transarterial chemoembolization (TACE). 20 post-TACE HCC patients were re-evaluated with contrast-enhanced computed tomography and CTP. Patients with persistent arterial vascularization [non-response (NR)] or those with no arterial vascularization in the mass, but with signs of new nodules, underwent digital subtraction angiography (DSA), which was used to analyze image characteristics and CTP parameters of TACE-treated HCC. 27 post-TACE HCC masses (mean size 4.21 cm, range 2-6.5 cm) were observed in the 20 patients. The values yielded by CTP were 78.30±40.41 mL/min/100g and 33.67±38.74 mL/min/100g for hepatic arterial blood flow (HABF) and 51.40±17.80% and 25.60±26.53% for hepatic arterial fraction (HAF) in the NR group and complete response group, respectively. The NR group's cutoff value of HABF was ≥55.95 mL/min/100g, with a sensitivity of 91.7% and specificity of 71.42%, and that of HAF was ≥32.55%, with a sensitivity of 92.3% and specificity of 83.33%. The CTP and DSA techniques showed high agreement in assessing the post-TACE responses of liver tumors (κ=0.872). The perfusion parameters HABF and HAF have high value for assessing post-TACE responses of HCC.

## Introduction

Hepatocellular carcinoma (HCC) is one of the most common liver cancers.[1] Although evaluation of liver tumor response and recurrence after transarterial chemoembolization (TACE) is essential for treatment planning, there are limitations to assessing the enhancement of TACE-treated tumors because lipiodol fills the mass.[2] Computed tomography perfusion (CTP), which accurately estimates the perfusing blood flow through liver parenchyma and the vascular changes of malignant liver diseases,[3,4] is a promising technique for evaluating the response of HCC after TACE. The basic principle of CTP involves combining pre- and post-contrast images to create a dynamic image over time at a specific liver tissue site. This process is used to generate a density-time curve.[5]

Perfusion parameters in perfusion maps represent vascular changes in tumors - the abnormal neovascularization of liver parenchyma, ranging from neoplastic to dysplastic nod-

ules and HCC. Vascular proliferation increases gradually in this order.[5,6] Post-treatment HCC with persistent arterial vascularization or residual tumor tissue exhibits higher hepatic arterial blood flow (HABF) and hepatic arterial fraction (HAF) compared to normal liver parenchyma.[7,8] High HABF and HAF represent vascular proliferation that originates from the hepatic artery and decreased perfusion originating from the portal vein.[9] Therefore, in this study, we evaluated imaging characteristics and the merits of CTP for assessing the post-TACE response of HCC.

## Materials and Methods

### Patients

This study was approved by the Hanoi Medical University Institutional Ethical Review Board (Ref: 1888/QĐ-DHYHN) and conducted according to the ethical standards of the 1964 Declaration of Helsinki and its later amendments. We obtained the medical records and contrast-enhanced computed tomography (CECT) and CTP images of 20 HCC patients receiving TACE at our hospital from August 2021 to September 2022. Overall, the 20 cases involved 27 tumors, including 14 non-responses (NRs) and 13 complete responses (CRs) on CTP. Of the 19 liver tumors undergoing digital subtraction angiography (DSA) after CTP, 13 were NRs and 6 were CRs. The remaining eight tumors were not subjected to DSA and were followed up with CECT after two months. We recorded other data, including age, history of hepatitis B and hepatitis C infection, and serum alpha-fetoprotein (AFP) values, for each patient in this study.

### Contrast-enhanced computed tomography

Imaging was performed with the Revolution 256 series CT machine (GE Healthcare Systems, United States) by scanning the hepatic area from the diaphragm to the pelvis, including in the pre-injection phase, arterial phase (30 s after contrast injection), and venous phase (60 s after contrast injection). Parameters used for the three phases were 120 kV, 200 mAs, 1 mm thin slice, 0.0625 mm reconstruction, 80 ml contrast medium at 5 ml/s, and 30 ml saline solution.

### Computed tomography perfusion imaging

Imaging was performed with a 256-slide Revolution CT machine (GE Healthcare Systems), with a detector coverage of 16 cm, focusing on the liver tumor area with parameters 120 kV, 80 mAs, matrix 512×512, 50 ml contrast medium at 5 ml/s, 5 mm slice thickness, 1.25 mm reconstructed slice thickness, and 30 ml saline solution.[10]

### Transarterial chemoembolization

The TACE technique was performed by doctors having more than 10 years of experience. The maximum dose of lipiodol was 20-30 ml, with the amount selected based on tumor size and mass perfusion flow.[10,11]

### Imaging analysis

The CECT and CTP imaging data were stored on PACS (Carestream PACS; Carestream Health, Eemnes, The Netherlands) and analyzed independently by two radiologists (a 2nd-year resident and a doctor with 10 years of experience in gastrointestinal imaging) blinded to the results of the DSA and CECT examination after two months. Disagreements between the two doctors were resolved through discussion.

Computed tomography perfusion images were reproduced with integrated registration and CT perfusion 3D software (GE Medical Systems) pre-installed on the workstation. The analysis of CT images was performed using CT Perfusion 3D software. This software generated functional color maps (quantitative), and perfusion parameters (quantitative) were calculated automatically, with compensation for respiratory error recordings. On the axial plane of the original image, two regions of interest (ROIs) were identified, the first in the abdominal aorta and the second in the portal vein, so that the ROI was located in the center of the blood vessel, extravascular deviation. The contrast density in the lumen was plotted over time (Figure 1), reflecting

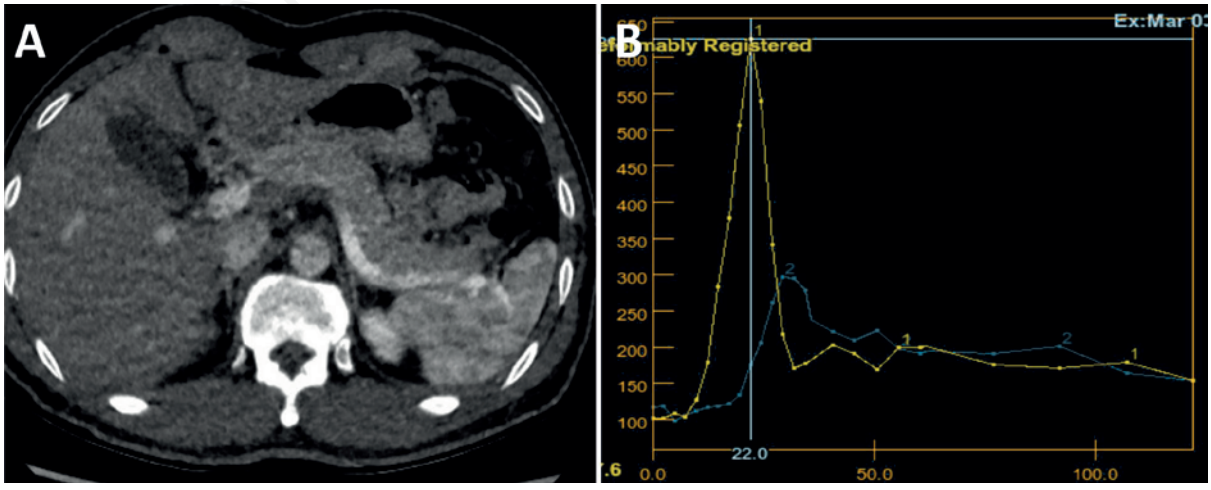


**Figure 1.** Computed tomography perfusion image (A) of two regions of interest in the aorta (yellow) and portal vein (blue), yielding a density-time curve of intravascular contrast concentration (B).

the perfusion capacity of liver tissue as shown in functional perfusion maps.

The functional perfusion maps included those for hepatic arterial blood flow (HABF; ml/min/100g), hepatic arterial fraction (HAF; %), blood volume (BV; ml/100g), blood flow (BF; ml/min/100g), mean transit time (MTT; s), time to peak (TTP; s), and permeability surface area product (PS; ml/min/100g). Pre-formatted color-coded perfusion maps show liver tissue perfusion, with colors ranging from blue to red to indicate varying levels of perfusion.

Next, two ROIs in the post-treatment liver tumor area and basal liver parenchyma were demarcated. The post-treatment tumor area was defined as the area of the liver tumor with a perfusion signal (indicated by color) on perfusion maps, with lipiodol not deposited; this area could be enhanced or not enhanced on CECT. Basal liver parenchyma was defined as the area of liver parenchyma that did not change density compared to the remaining liver parenchyma, except for the liver tumor area. The first ROI was placed within the post-treatment liver tumor site, encompassing the maximum tumor area. The ROI placement was guided by CTP images and cross-checked with CECT to ensure the avoidance of lipiodol deposition.[12,13] The placement of this ROI was repeated three times, and the resulting measurements were averaged. The second ROI located in the basal liver parenchyma avoided arteries and veins. The perfusion parameters were calculated for the treated tumor area and collected from the non-neoplastic liver parenchyma.

Residual or angiogenic liver tumor after TACE (NR) was defined as the part of the tumor with higher values of HABF and HAF perfusion parameters than the surrounding liver parenchyma.[14] HABF and HAF were evaluated qualitatively and quantitatively, based on the color signal in the dark-to-light color range on the perfusion map. NR was lighter in color than the surrounding liver parenchyma on the HABF map (Figure 2A) and HAF map (Figure 2B) and the strong enhancement on the arterial-phase CECT film (Figure 2C) was confirmed by DSA. NR HCC after treatment showed angiogenesis on DSA (Figure 2D).

Complete-response liver tumor after TACE was defined as a tumor completely devoid of color signals on HABF and HAF perfusion maps (Figure 3C, D). On CECT, the liver tumor was filled with lipiodol without enhancement residue (Figure 3A, B). Upon reevaluation with CECT after two

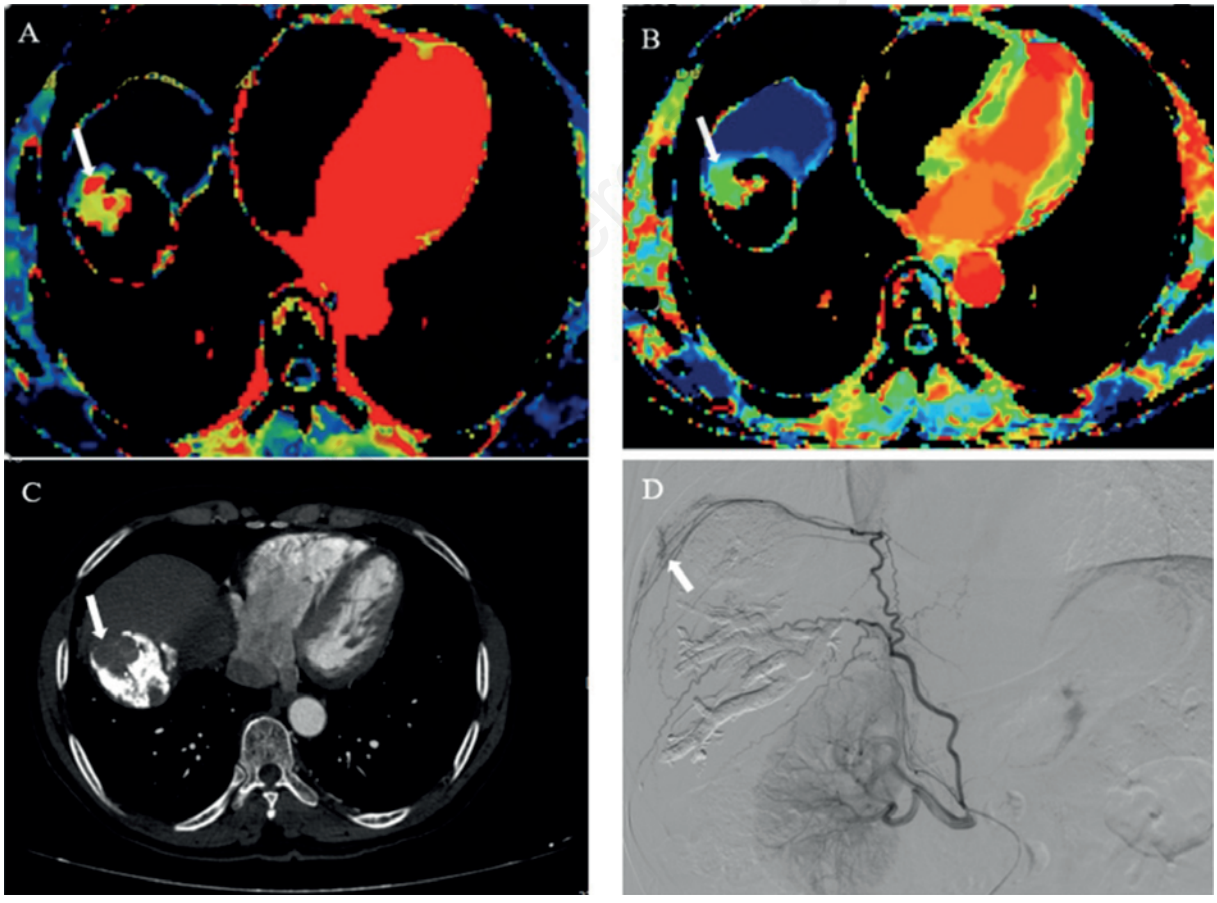


**Figure 2.** A 69-year-old male patient with non-response hepatocellular carcinoma after transarterial chemoembolization confirmed with contrast-enhanced computed tomography, computed tomography perfusion, and digital subtraction angiography. Perfusion maps of (A) hepatic arterial blood flow and (B) hepatic arterial fraction of post-treatment liver tumor show increased angiogenesis (indicated by arrow). (C) The contrast-enhanced computed tomography image shows post-injection enhancement of the hepatic artery tumor after angiogenesis (indicated by arrow). (D) digital subtraction angiography image shows the angiogenic portion of the liver tumor with blood supply from the right subdiaphragmatic artery (indicated by arrow).

months, there was no increase in the size of the liver tumor, and no enhancement tissue was detected (Figure 3E). This further was confirmed by the absence of angiogenesis on DSA (Figure 3F).

## Statistical analysis

Data were analyzed with SPSS 26.0. Qualitative data are described as frequencies ± %. Quantitative data are described as mean ± standard deviation (SD). The chi-square test was used to compare ratios between two qualitative variables. When more than 20% of the expected number of observations was less than 5, the chi-square correction was performed with Fisher's exact test. Paired post-treatment HCC groups were compared using t-tests if the data were normally distributed and the Mann-Whitney U test if the distribution was non-normal.

Receiver operating characteristic (ROC) curves were analyzed based on indicators that were significantly different in two-group comparisons of response. The combination of these indicators was used to find the cutoff point. The area under the curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive value were calculated. A P-value of <0.05 was considered statistically significant.

# Results

This study involved 20 patients (15 men and 5 women). Their mean age was 63.65±7.77 years and they collectively had a total of 27 HCC after TACE. Fourteen patients were infected with hepatitis B virus and one patient was infected with hepatitis C virus. The average tumor size was 4.21±14.07cm. The AFP level of the NR and CR groups was 13.05 ng/ml and 29.07 ng/ml, respectively. Radiation dose of CTP mean is 30.9±7.0mSv (min 23.4mSv; max 42.8mSv), and radiation dose of CECT mean is 25.6±6.8mSv (min 18.6mSv; max 36.5mSv).

The characteristics of HABF, HAF, BV, BF, MTT, TTP, and PS perfusion parameters of HCC after TACE are presented in Table 1. HABF of the NR and CR groups was 78.30±40.41 ml/min/100g and 33.67±38.74 ml/min/100g, respectively; the difference was statistically significant (P=0.028). HAF of the NR and CR groups was 51.40±17.80% and 25.60±26.53%, respectively; this difference was also statistically significant (P=0.035) (Table 1). The differences in mean BV, BF, MTT, TTP, and PS between the two groups were not statistically significant (P>0.05).

Characteristics of the relative ratios, rHABF, rHAF, rBV, rBF, rMTT, rTTP, and rPS, of HCC after TACE are presented in Table 2. rTTP of the NR and CR groups was 0.91 and 1.74, respectively, a statistically significant difference (P=0.031). However, the differences in relative ratios (rHABF, rHAF, rBV, rBF, rMTT, and rPS) of perfusion parameters for HCC after TACE between the NR and CR groups were not statistically significant (P>0.05).

Data on the predictive value of perfusion parameters for diagnosing liver tumor angiogenesis after TACE are presented in Table 3. HABF, with AUC=0.821, had a high value for assessing the response of liver tumors after TACE. The HABF cutoff of ≥55.95 ml/min/100g showed a sensitivity of 91.7%, specificity of 71.42%, positive predictive value of 84.6%, and

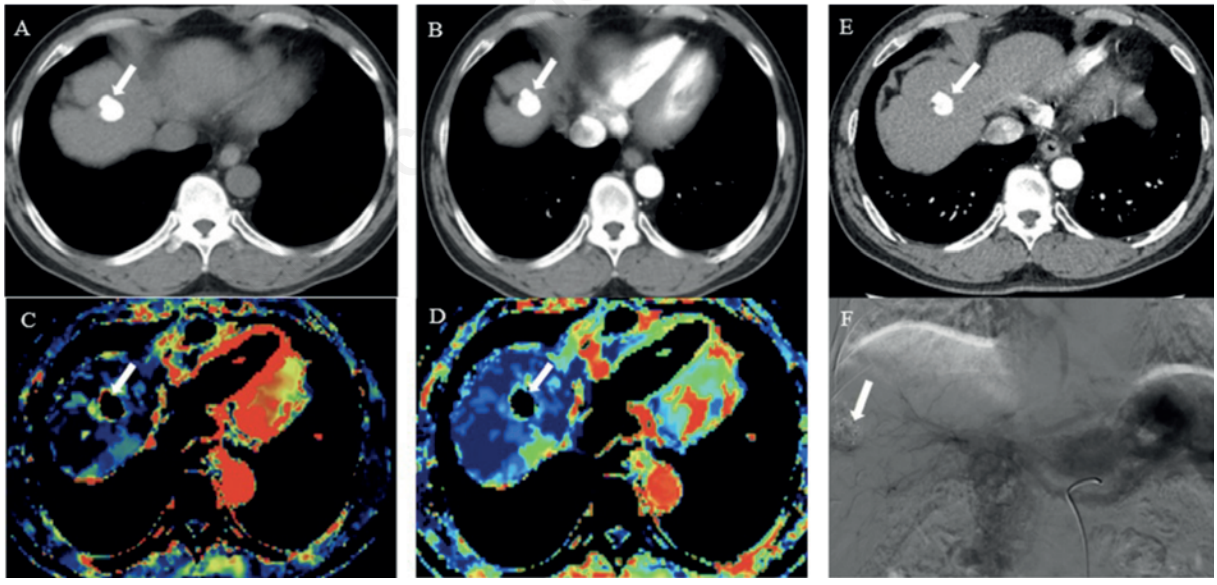


**Figure 3.** Complete response hepatocellular carcinoma in a 45-year-old male patient after transarterial chemoembolization, confirmed with contrast-enhanced computed tomography, computed tomography perfusion, and digital subtraction angiography. Hepatocellular carcinoma is filled with lipiodol after transarterial chemoembolization and shows no enhancement after injection (A and B). Perfusion maps show no signal for (C) hepatic arterial blood flow and (D) hepatic arterial fraction (indicated by arrow). (E) The arterial phase on contrast-enhanced computed tomography re-examined after two months shows no enhancement (indicated by arrow). (F) A 77-year-old male patient with hepatocellular carcinoma after transarterial chemoembolization without angiogenesis on contrast-enhanced computed tomography and computed tomography perfusion, confirmed with digital subtraction angiography (indicated by arrow).

negative predictive value of 83.3%. HAF (AUC=0.808) was also of high value for assessing the response of liver tumors after treatment. The HAF cutoff of ≥32.55% showed a sensitivity of 92.3%, specificity of 83.33%, positive predictive value of 92.3%, and negative predictive value of 83.33%. The combination of HABF+HAF had good predictive value for diagnosing liver tumor angiogenesis after TACE (AUC=0.782), with a sensitivity of 91.7%, specificity of 71.42%, positive predictive value of 84.6%, and negative predictive value of 83.3%. rTTP had no predictive value for diagnosing liver tumor angiogenesis after TACE (AUC=0.212) (Figure 4).

Of the 19 HCCs examined by DSA, 13 were found to be NR after TACE, while 6 were CR. CTP determined 13 of the 19 to be NR, while one was NR but no angiogenesis was observed after DSA. The concordance between the two methods in diagnosing liver tumor angiogenesis after chemotherapy for hepatic artery embolization is very high, with a kappa coefficient of 0.872 (Table 4). Of the 19 HCCs examined with DSA, seven were difficult to assess after TACE because of being completely or almost filled with lipiodol; of these, five HCCs were shown to have partially increased angiogenesis on DSA (Table 5).

## Discussion

The value of CTP is not only well recognized for diagnosis but also for HCC response evaluation. Promptly identifying HCC recurrence after locoregional therapies is crucial, but some institutions face obstacles in achieving efficient diagnoses and utilizing radiological modalities. However, CTP has revolutionized the early assessment of the HCC response to TACE or radiofrequency ablation. In Su *et al.*'s 2017 study,[15] of the HCC responses with high HABF

**Table 1.** Characteristics of the hepatocellular carcinoma perfusion parameters, hepatic arterial blood flow, hepatic arterial fraction, blood volume, blood flow, mean transit time, time to peak, and permeability surface, after transarterial chemoembolization (N=27).

| Perfusion parameter | Non-response | Complete response | P |
|---|---|---|---|
| HABF (ml/min/100g) | 78.30±40.41 | 33.67±38.74 | 0.028* |
| HAF (%) | 51.40±17.80 | 25.60±26.53 | 0.035* |
| BV (ml/100g) | 14.99±12.06 | 12.70±10.61 | 0.335* |
| BF (ml/min/100g) | 168.51±67.84 | 142.22±155.92 | 0.608* |
| MTT (s) | 8.73±5.76 | 14.62±12.68 | 0.219* |
| TTP (s) | 35.06±22.93 | 58.73±22.95 | 0.052* |
| PS (ml/min/100g) | 22.07±12.92 | 12.42±14.86 | 0.079* |

HABF, hepatic arterial blood flow; HAF, hepatic arterial fraction; BV, blood volume; BF, blood flow; MTT, mean transit time; TTP, time to peak; PS, permeability surface. *Mann-Whitney U test results.

**Table 2.** Characteristics of relative ratios of hepatocellular carcinoma perfusion parameters, hepatic arterial blood flow, hepatic arterial fraction, blood volume, blood flow, mean transit time, time to peak, and permeability surface, after transarterial chemoembolization (N=27).

| Relative ratio of perfusion parameter | Non-response | Complete response | P |
|---|---|---|---|
| rHAF | 310.63 | 2.85 | 0.161* |
| rHABF | 493.38 | 7.16 | 0.054* |
| rBV | 0.95 | 0.93 | 0.792* |
| rBF | 2.57 | 3.20 | 0.726* |
| rMTT | 0.58 | 0.99 | 0.661* |
| rTTP | 0.91 | 1.74 | 0.031* |
| rPS | 87.15 | 11.89 | 0.726* |

HAF, hepatic arterial fraction; HABF, hepatic arterial blood flow; BV, blood volume; BF, blood flow; MTT, mean transit time; TTP, time to peak; PS, permeability surface. r signifies the relative ratio of an HCC perfusion parameter after TACE/basal liver parenchyma. *Mann-Whitney U test.

**Table 3.** Diagnostic value of perfusion parameters in evaluating angiogenesis of hepatocellular carcinoma after transarterial chemoembolization (N=27).

| Perfusion parameter | Cutoff | AUC | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|---|
| HABF | 55.95 | 0.821 | 91.7 | 71.42 | 84.60 | 83.3 |
| HAF | 32.55 | 0.808 | 92.30 | 83.33 | 92.30 | 83.33 |
| HABF+HAF | - | 0.782 | 92.30 | 83.33 | 92.30 | 83.33 |
| rTTP | 0.90 | 0.212 | 46.2 | 33.3 | 46.2 | 16.7 |

AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; HABF, hepatic arterial blood flow; HAF, hepatic arterial fraction. r signifies the relative ratio of an HCC perfusion parameter after TACE/basal liver parenchyma.

and HAF compared to surrounding normal tissue yielded better outcomes.

On the other hand, we found that the NR group had significantly higher mean HABF and mean HAF than the CR group. These results are in line with the findings of several previous studies. Ippolito *et al.*,[7] concluded that recurrent HCC has higher HABF than the surrounding normal parenchyma (P<0.001) due to intratumoral hypervascularity; in their study, HABF and HAF of the NR group were 43.2±15.1 ml/min/100g and 61.7±7.5%, respectively, and of the CR group were 10.2±6.3 ml/min/100g and 9.9±9.2%, respectively. Enite and Rabee found HABF dominating in recurrent HCC compared to surrounding cirrhotic parenchyma.[16] In Salem *et al.*'s study,[8] HABF in recurrent HCC and surrounding cirrhotic parenchyma in the NR group was 124.68±19.69 and 37.12±8.99 ml/min/100g, respectively, and in the CR group, it was 52.5±11.9 and 29±16.51%, respectively (P<0.001). Osman *et al.*'s study assessing 70 post-treatment HCC found that post-TACE BV, MTT, and PS of CR HCC were significantly lower than those of recurrent HCC, an outcome with high sensitivity and specificity.[17] However, this result is in contrast to our findings, which did not support any significant differences between CR and NR groups after TACE. This may be due to the small number of samples in our study, which may not represent all ethnic groups.

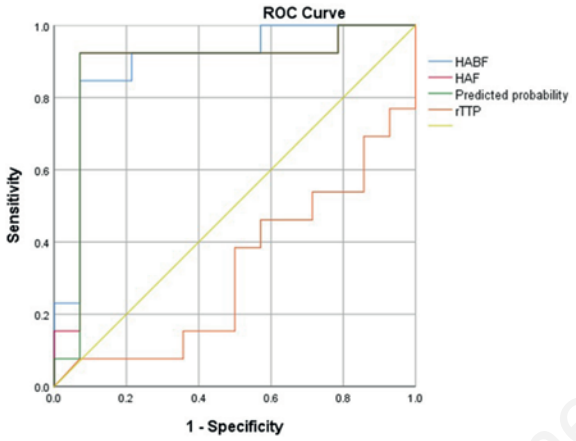


**Figure 4.** Receiver operating characteristic curve of perfusion parameters for diagnosing angiogenesis in hepatocellular carcinoma after transarterial chemoembolization. HABF, hepatic arterial blood flow; HAF, hepatic arterial fraction; rTTP, relative ratio of time to peak.

In our search of the medical literature, we did not find any studies focusing on evaluating the relative ratio of CTP parameters of HCC recurrent/normal surrounding parenchyma of the two patient groups (NR and CR). Our results suggest that rHABF, rHAF, rBV, rBF, rMTT, and rPS are not reliable for assessing the response of HCC to TACE. However, the lower rTTP of the NR group compared to the CR group had a sensitivity and specificity of 46.2% and 33.3%, respectively (Tables 2 and 3). We speculate that this may be associated with the TTP of HCC, which could be affected by several factors: unstable hemodynamics, hepatic perfusion disorder, and dysplastic nodules.

The NR group's ROC curve for HABF with the cutoff point of ≥55.95 ml/min/100g had a sensitivity, specificity, positive predictive value, and negative predictive value of 91.7%, 71.42%, 84.6%, and 83.3%, respectively. Similarly, at the cutoff point of HAF of ≥32.55%, the sensitivity, specificity, positive predictive value, and negative predictive value of the NR group were 92.3%, 83.33%, 92.3%, and 83.33%, respectively. In contrast, Salem *et al.*[8] found that recurrent HCC with a cutoff HABF of ≥85.85 ml/min/100g had a sensitivity and specificity of 100%; specificity was also 100% for the HAF cutoff of ≥51.4%.

We suggest that hypervascularity of recurrent HCC may explain the high HABF and HAF. This means that the blood supply to HCC mainly originates from the hepatic artery, which has a flow ratio higher than 20-25%.[18] In our study, a lower cutoff had lower sensitivity and specificity. Furthermore, the combination of HABF+HAF helped to evaluate the

**Table 4.** Diagnostic value of computed tomography perfusion for assessing angiogenesis in hepatocellular carcinoma after transarterial chemoembolization (N=19).

| DSA/CTP | Non-response | Complete response | Total |
|---|---|---|---|
| Non-response | 13 | 1 | 14 |
| Complete response | 0 | 5 | 5 |
| Total | 13 | 6 | 19 |
| Kappa | | 0.872, P=0.001* | |

DSA, digital subtraction angiography; CTP, computed tomography perfusion. *Fisher's exact test.

**Table 5.** Diagnostic value of contrast-enhanced computed tomography for assessing angiogenesis in hepatocellular carcinoma after transarterial chemoembolization (N=19).

| DSA/CECT | Complete response | Non-response | Total | P |
|---|---|---|---|---|
| Complete response | 4 | 0 | 4 | 0.001* |
| Difficult to determine | 2 | 5 | 7 | |
| Non-response | 0 | 8 | 8 | |
| Total | 6 | 13 | 19 | |

DSA, digital subtraction angiography; CECT, contrast-enhanced computed tomography *Fisher's exact test.

post-TACE neovascularity of HCC, with a sensitivity, specificity, positive predictive value, and negative predictive value of 91.7%, 71.42%, 84.6%, and 83.3%, respectively, values similar to those when the two parameters were considered separately. Computed tomography perfusion was valuable in assessing post-TACE neovascularity of HCC. The relationship between CTP and DSA was high, with $\kappa$=0.872. CECT had limited value for assessing the enhanced post-TACE features of HCC due to lipiodol, a disadvantage compared to CTP and DSA.

The present study has some limitations. First, the number of subjects in the study was small and may not be representative of all ethnic groups. Second, DSA was not indicated for all participants, which might have affected the HAF and HABF values. Therefore, there is room for further investigation of a larger patient sample, with consideration of DSA for all individuals.

## Conclusions

In summary, our study demonstrated higher HABF and HAF in the NR group than in the CR group, as well as differences in rTTP between the two groups. However, these findings were not statistically significant due to low sensitivity and specificity. Kappa values indicated that CTP was superior for assessing post-TACE neovascularity in HCC compared to CECT. We suggest that CTP should be considered a priority option in the list of non-invasive modalities due to its accuracy of tumor perfusion and residual HCC evaluation of post-TACE patients.

## References


1. Jelic S, Sotiropoulos GC. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21:v59-v64.
2. Yaghmai V, Besa C, Kim E, et al. Imaging assessment of hepatocellular carcinoma response to locoregional and systemic therapy. Am J Roentgenol 2013;201:80-96.
3. Popovic P, Leban A, Kregar K, et al. Computed tomographic perfusion imaging for the prediction of response and survival to transarterial chemoembolization of hepatocellular carcinoma. Radiol Oncol 2017;52:14-22.
4. Chen G, Ma DQ, He W, et al. Computed tomography perfusion in evaluating the therapeutic effect of transarterial chemoembolization for hepatocellular carcinoma. World J Gastroenterol 2008;14:5738-43.
5. Kim SH, Kamaya A, Willmann JK. CT Perfusion of the Liver: Principles and Applications in Oncology. Radiology 2014;272:322-44.
6. Ippolito D, Capraro C, Casiraghi A, et al. Quantitative assessment of tumour associated neovascularisation in patients with liver cirrhosis and hepatocellular carcinoma: role of dynamic-CT perfusion imaging. Eur Radiol 2012;22:803-11.
7. Ippolito D, Fior D, Bonaffini PA, et al. Quantitative evaluation of CT-perfusion map as indicator of tumor response to transarterial chemoembolization and radiofrequency ablation in HCC patients. Eur J Radiol 2014;83:1665-71.
8. Salem LN, Mohammed DM, Ziada DH, Elshafey MH. Dual input computed tomography perfusion in evaluating the therapeutic response of transarterial chemoembolization for hepatocellular carcinoma. Egypt J Radiol Nucl Med 2018;49:597-607.
9. Zhu Q, Zhang X, Li J, et al. Arterial blood supply of hepatocellular carcinoma is associated with efficacy of sorafenib therapy. Ann Transl Med 2015;3:285.
10. García-Figueiras R, Goh VJ, Padhani AR, et al. CT perfusion in oncologic imaging: a useful tool? Am J Roentgenol 2013;200:8-19.
11. Cheng HY, Shou Y, Wang X, et al. Adjustment of lipiodol dose according to tumor blood supply during transcatheter arterial chemoembolization for large hepatocellular carcinoma by multidetector helical CT. World J Gastroenterol 2004;10:2753-5.
12. Petralia G, Summers P, Viotti S, et al. Quantification of Variability in breath-hold perfusion ct of hepatocellular carcinoma: a step toward clinical use. Radiology 2012;265:448-56.
13. Hayano K, Lee SH, Yoshida H, et al. Fractal analysis of CT perfusion images for evaluation of antiangiogenic treatment and survival in hepatocellular carcinoma. Acad Radiol 2014;21:654-60.
14. Kim SH, Kamaya A, Willmann JK. CT perfusion of the liver: principles and applications in oncology. Radiology 2014;272:322-44.
15. Su TH, He W, Jin L, et al. Early response of hepatocellular carcinoma to chemoembolization: volume computed tomography liver perfusion imaging as a short-term response predictor. J Comput Assist Tomogr 2017;41:315-20.
16. Enite AM, Rabee H. Multi-detector CT perfusion as a diagnostic imaging modality to evaluate local therapy of hepatocellular carcinoma. Egypt J Radiol Nucl Med 2016;47:687-92.
17. Osman MF, Shawali IH, Metwally LIA, et al. CT perfusion for response evaluation after interventional ablation of hepatocellular carcinoma: a prospective study. Egypt J Radiol Nucl Med 2021;52:281.
18. Nakakuma K, Tashiro S, Hiraoka T, et al. Studies on anticancer treatment with an oily anticancer drug injected into the ligated feeding hepatic artery for liver cancer. Cancer 1983;52:2193-200.