

ROLE OF TRIPHASIC CT SCAN WITH LATE ARTERIAL PHASE IN THE EVALUATION OF HEPATOCELLULAR CARCINOMA (HCC)

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Abstract

Background: Hepatocellular carcinoma (HCC) is one of the most lethal cancers globally, making early, accurate detection a primary determinant of survival. Triphasic contrast-enhanced computed tomography (CT) serves as a cornerstone diagnostic technique, with technical refinements such as a dedicated late arterial phase showing promise in improving diagnostic confidence by optimizing tumor-to-parenchyma contrast. Objective: This study aimed to evaluate the diagnostic accuracy of triphasic CT scans featuring a dedicated late arterial phase for identifying HCC in patients with chronic liver disease (CLD), using histopathological confirmation as the diagnostic gold standard. Materials and Methods: A prospective cross-sectional diagnostic accuracy study was conducted over a 4-month period in the Radiology Department of Mayo Hospital. The study enrolled 85 consecutive patients (≥ 40 years old) presenting with chronic liver disease risk factors and focal liver lesions suspected of being HCC on screening ultrasound. Triphasic liver CT scanning protocols were standardized to include a late arterial phase (35–40 seconds), a portal venous phase (60–70 seconds), and a delayed phase (5 minutes) using multidetector CT equipment (≤ 5 mm slice thickness). Imaging findings were correlated with histopathological results and analyzed using SPSS software. Results: The study population was predominantly male (76.5%) with a mean age of 58.87 ± 10.10 years. The primary etiological factor was Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) co-infection (27.1%), followed by isolated HCV (22.4%) and isolated HBV (20.0%). The mean diameter of the index lesions was 6.06 ± 3.43 cm, with 87.1% measuring ≥ 2 cm. Positive late arterial phase hyperenhancement was observed in 74.1% of patients, while positive portal venous phase washout was identified in 64.7%. Chi-square analysis demonstrated a highly significant statistical association between late arterial enhancement and final histopathological diagnosis of HCC ($\chi^2(1)=40.012$, $p<.001$), as well as between portal venous washout and final HCC diagnosis ($\chi^2(1)=19.443$, $p<.001$).

Complementary findings across all dynamic phases occurred in 83.5% of cases. Conclusion: Triphasic CT with a dedicated late arterial phase demonstrates strong diagnostic correlation and exceptional clinical utility for evaluating HCC within a chronic liver disease framework. The combination of late arterial hyperenhancement and subsequent venous/delayed phase washout enables strong non-invasive diagnostic confidence.

Introduction: Hepatocellular carcinoma (HCC) stands as a prominent global health threat and ranks as one of the top three causes of cancer-related mortality worldwide. Hundreds of thousands of deaths occur annually, with global incidence projections approaching nearly one million cases per year in the near future [1]. Historically, the global burden of HCC has been concentrated heavily within regions of East Asia and sub-Saharan Africa due to the high endemic prevalence of chronic Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infections. However, contemporary epidemiological trends demonstrate a shifting paradigm [2]. While widespread viral vaccination and highly effective direct-acting antiviral therapies have caused a decline in virus-associated HCC in high-income nations, non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease are rapidly emerging as prominent etiologies within increasingly metabolic-unhealthy populations [3-4].

The pathogenesis of HCC typically follows a slow, stepwise process where chronic, long-standing necroinflammatory liver injury culminates in hepatic cirrhosis. This altered, fibrotic microenvironment provides the direct biological substrate for malignant transformation [5-6]. The principal risk factors driving this process include chronic viral hepatitis, heavy alcohol consumption, hereditary hemochromatosis, and metabolic dysfunction-associated fatty liver disease. Among patients with established cirrhosis, the five-year cumulative risk of developing HCC varies distinctly according to the underlying cause, ranging from approximately 4% in advanced biliary cirrhosis to as high as 30% in hepatitis C-related cirrhosis [7-8]. Demographically, older age and male sex are independent risk factors; males account for nearly two-thirds of cases globally due to both underlying biological variations and differential exposure to environmental hazards like viral hepatitis and alcohol. Crucially, more than 80% of the global

HCC burden remains concentrated in developing nations, reflecting prominent healthcare disparities and highlighting the urgent need for robust non-invasive diagnostic workflows in resource-constrained environments [9].

Early identification of HCC fundamentally shifts the therapeutic landscape from palliative management to curative interventions. Curative strategies—such as orthotopic liver transplantation, surgical resection, and local thermal ablation—offer five-year survival rates between 50% and 70%, but they remain strictly contingent upon identifying tumors at an early stage. Unfortunately, due to sub-optimal screening infrastructure and the asymptomatic nature of early disease, nearly 80% of patients globally are diagnosed at advanced stages [10-11]. At these advanced stages, the cumulative five-year survival drops precipitously below 10%. This dramatic divergence in survival underscores the crucial importance of advanced multi-phase imaging techniques to optimize early tumor detection within high-risk cohorts under routine surveillance [12-13].

Over the past two decades, advances in cross-sectional imaging have revolutionized the management of HCC, allowing imaging-based criteria to safely replace invasive tissue biopsy for many patients [14]. Computed tomography (CT) and magnetic resonance imaging (MRI) exploit the distinct alterations in tumor vascularity that take place during multistep hepatocarcinogenesis [15]. While healthy liver parenchyma receives the vast majority of its dual blood supply (75%) from the portal vein and only 25% from the hepatic artery, developing HCC lesions undergo intense neoangiogenesis, becoming almost exclusively supplied by the hepatic arterial system. This unique hemodynamic transformation results in the classic radiological hallmark of HCC: intense contrast enhancement during the hepatic arterial phase (hyperenhancement) followed by a relative reduction in enhancement compared to the

surrounding liver parenchyma during the portal venous and delayed phases (washout) [16-17].

Triphasic contrast-enhanced multidetector CT (MDCT) is a widely available and highly reliable modality for capturing these hemodynamic patterns. The conventional triphasic scanning approach comprises an arterial phase (approximately 30 seconds), a portal venous phase (60-70 seconds), and a delayed or equilibrium phase (5 minutes) following a rapid intravenous contrast bolus injection [18-19].

The introduction of a dedicated *late arterial phase* represents a specific technical refinement. By intentionally delaying acquisition to 35-40 seconds post-injection, the late arterial phase captures peak contrast concentrations within hypervascular tumors while avoiding early scanning artifacts and minimizing premature portal venous contamination [20]. This technical adaptation is particularly valuable for improving the conspicuity of small or well-differentiated tumors that exhibit delayed arterial inflow, and for distinguishing true malignancies from benign regenerative or dysplastic nodules in advanced cirrhotic livers [21-22].

To standardize diagnostic thresholds and reduce interobserver variability, frameworks such as the Liver Imaging Reporting and Data System (LI-RADS) have been established. LI-RADS defines strict criteria combining lesion size and major features (arterial hyperenhancement, washout, capsule enhancement, and threshold growth) to assign categories ranging from benignity (LR-1) to definite HCC (LR-5) [20]. Despite these frameworks, characterizing small lesions (≤ 2 cm) and differentiating them from benign mimics like hemangiomas, focal nodular hyperplasia, and hypervascular dysplastic nodules remains a key clinical challenge [23-24].

Research Objectives

- To assess the accuracy of triphasic CT scans using a dedicated late arterial phase to diagnose hepatocellular carcinoma via visual characterization of enhancement and washout patterns, correlated with histopathological validation.

- To evaluate the diagnostic correlation and performance of triphasic CT criteria relative to the established histopathological gold standard.

Materials and Methods

Study Design and Settings

This study was conducted as a prospective cross-sectional diagnostic accuracy study within the Radiology Department of Mayo Hospital. Imaging procedures were executed utilizing a high-performance 356-slice Siemens Somatom multidetector CT scanner. The active data collection and clinical evaluation period spanned a duration of 4 months.

Eligibility Criteria

Inclusion Criteria

- Patients aged 40 years or older.
- Patients presenting with a clinical history of chronic liver disease (CLD) or liver cirrhosis from any underlying etiology (including HBV, HCV, alcohol, and NAFLD).
- Presence of a suspected focal liver lesion or abnormal nodule identified on initial screening ultrasound.

Exclusion Criteria

- Patients who had undergone prior local or systemic treatment for HCC, including surgical resection, transcatheter arterial chemoembolization (TACE), or radiofrequency ablation (RFA).
- Absolute contraindications to iodinated contrast media administration, such as severe renal dysfunction (estimated glomerular filtration rate < 30 mL/min/1.73 m²) or a documented history of severe anaphylactoid reaction to contrast.
- Patients presenting with primary extrahepatic malignancies or other co-morbidities that precluded histopathological completion.

Imaging Protocol and Technical Specifications

All included patients underwent a standardized, highly structured triphasic contrast-enhanced abdominal CT protocol. Patients were scanned in a supine position during a single breath-hold to reduce respiratory motion artifacts. Non-ionic iodinated contrast material was delivered intravenously via an automated power injector through an intravenous cannula at a rapid flow rate [25-26].

Image acquisition was precisely synchronized to target specific vascular phases using automated bolus tracking technology:

1. **Late Arterial Phase:** Initiated at a delay of 35–40 seconds post-injection to capture maximum tumor hypervascularity.
2. **Portal Venous Phase:** Initiated at 60–70 seconds post-injection to capture optimal parenchymal enhancement and early lesion washout.
3. **Delayed Phase:** Initiated at 5 minutes post-injection to evaluate definitive washout and the presence of tumor capsules.

Technical acquisition parameters were optimized using a slice thickness of ≤ 5 mm to minimize partial volume averaging effects, ensuring robust spatial resolution for smaller hepatic nodules. Radiation exposure was managed dynamically according to the As Low As Reasonably Achievable (ALARA) framework [27].

Outcome Variables

- **Independent Variables:** The core radiologic findings from the triphasic CT protocol, specifically the qualitative presence or absence of late arterial phase hyperenhancement and subsequent portal venous or delayed phase contrast washout.

- **Dependent Variable:** The definitive confirmation of hepatocellular carcinoma status via histopathological evaluation of biopsy or surgical resection specimens, serving as the clinical gold standard.

Data Analysis

Table 1: *Descriptive baseline metrics of the study population.*

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
Age	85	35	79	58.87	10.103
Lesion_Size_cm	85	0.0	18.4	6.056	3.4339

Regarding the clinical background of chronic liver disease, the single most frequent category was combined HBV/HCV co-infection, present in 23 patients (27.1%). Isolated HCV infection followed closely at 22.4% (n=19), and isolated HBV infection was documented in 20.0% (n=17).

Table 2: *Etiological background distribution of chronic liver disease.*

Etiological History	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Alcohol-related liver disease	16	18.8	18.8	18.8
HBV	17	20.0	20.0	38.8
HBV/HCV	23	27.1	27.1	65.9

The collected demographic details, clinical symptoms, multi-phase CT enhancement characteristics, and histopathological outcomes were tabulated within a structured proforma. Statistical processing was carried out using the Statistical Package for the Social Sciences (SPSS) software. Continuous variables (age, lesion size) were summarized as means and standard deviations, while categorical variables were expressed as frequencies and percentages. Pearson's Chi-Square (χ^2) tests were used to determine statistical associations between cross-tabulated imaging descriptors and final histopathological diagnoses. Cohen's Kappa (κ) was computed to measure diagnostic agreement beyond chance. The threshold for statistical significance was pre-defined at a p-value < 0.05 .

Ethical Considerations

The institutional review board of Riphah International University, Faisalabad Campus, provided formal ethical approval for this research. All participating patients were informed about the study objectives and provided written informed consent prior to enrollment.

Results

Demographic and Clinical Baseline Profiles

The final study cohort comprised 85 patients suspected of having hepatocellular carcinoma. The age distribution showed a mean of 58.87 ± 10.10 years, spanning a minimum of 35 to a maximum of 79 years. A pronounced male predominance was observed, with 65 male participants (76.5%) and 20 female participants (23.5%).

Alcohol-related liver disease accounted for 18.8% (n=16), while NAFLD and hemochromatosis were found in 4.7% (n=4) and 3.5% (n=3) of the cohort, respectively. Only 3 patients (3.5%) lacked a documented history of chronic liver injury.

HCV	19	22.4	22.4	88.2
Hemochromatosis	3	3.5	3.5	91.8
NAFLD	4	4.7	4.7	96.5
None	3	3.5	3.5	100.0
Total	85	100.0	100.0	

The presenting symptom profiles varied across the cohort. Isolated localized abdominal pain was reported by 20 patients (23.5%), while an additional 15 patients (17.6%) presented with a combination of abdominal pain and systemic weight loss. Isolated weight loss occurred in 16 patients (18.8%), isolated clinically apparent jaundice in 9 patients (10.6%), and a combined presentation of weight loss and jaundice in 6 patients (7.1%). Notably, nearly a quarter of the cohort (22.4%, n=19) were asymptomatic at the time of assessment, with liver nodules discovered incidentally during routine screening.

Morphological and Parenchymal Characteristics

On structural CT evaluation, multi-focal or multiple discrete lesions were the most common manifestation, identified in 50 patients (58.8%). A single isolated hepatic nodule was seen in 27 patients (31.8%), while 8 patients (9.4%) presented with diffuse liver involvement or patterns where standard target lesions were not discretely measurable.

Categorized by maximum dimension, the vast majority of target lesions (87.1%, n=74) measured ≥ 2 cm in size. Only 3.5% (n=3) of target lesions fell within the smaller 1 to <2 cm sub-centimeter range, while 9.4% (n=8) lacked measurable nodular metrics. The underlying hepatic parenchyma showed an extensive burden of cirrhosis across the study cohort. Moderate structural cirrhosis was the most common grading, noted in 38 patients (44.7%), followed by severe advanced cirrhosis in 28 patients (32.9%), and mild early cirrhotic changes in 11 patients (12.9%). Only 8 individuals (9.4%) demonstrated a non-cirrhotic parenchymal background.

Internal enhancement patterns and lesion textures were highly variable. Heterogeneous enhancement was the most common presentation (27.1%, n=23), followed closely by uniform homogeneous enhancement (25.9%, n=22). A classic complex mosaic architecture was identified in 16 lesions (18.8%), while frank localized areas of internal tumor necrosis or hemorrhage were observed in 12 lesions (14.1%).

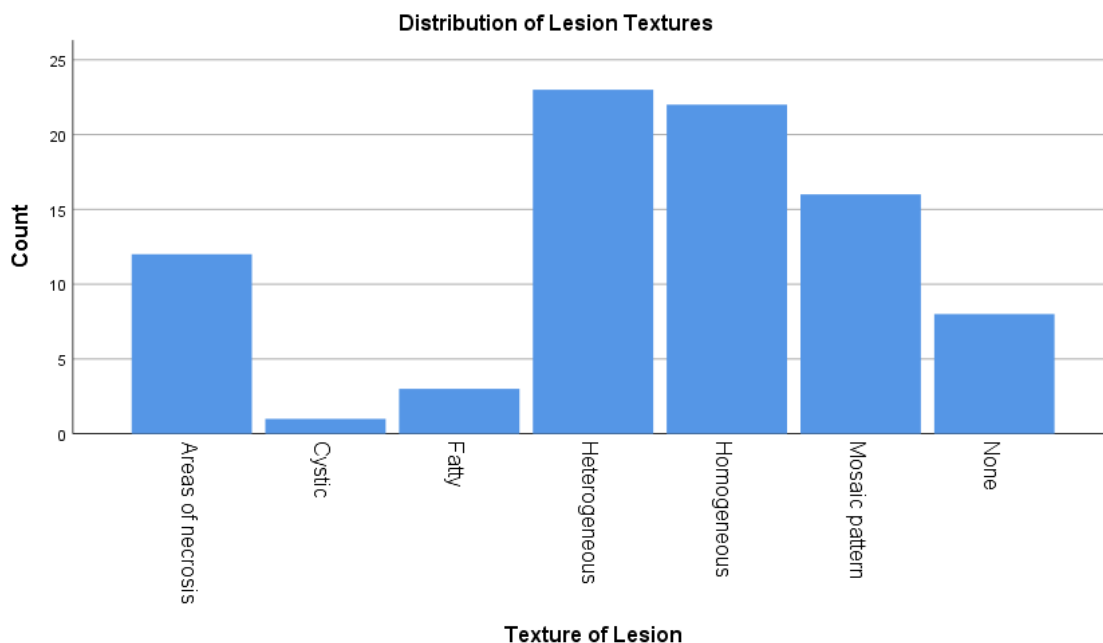


Figure 1: Internal lesion texture and enhancement homogeneity distribution.

Triphasic Enhancement and Phase Coordination

Dynamic phase assessments revealed that positive late arterial phase hyperenhancement occurred in 63 patients (74.1%), while 22 patients (25.9%) demonstrated negative, progressive, or completely iso-attenuating arterial dynamics. During the subsequent portal venous phase, a positive contrast washout signature was observed in 55 patients (64.7%), while 30 patients (35.3%) retained contrast or remained non-washed.

Importantly, multi-phase coordination analysis confirmed that the findings from the portal venous and delayed phases directly complemented or synchronized with the late arterial phase profiles in 71 cases (83.5%), reinforcing diagnostic clarity.

Diagnostic Correlation Against Gold Standard

Cross-tabulation of the dynamic late arterial hyperenhancement features against final histopathological findings demonstrated a strong correlation. Of the 63 patients displaying late

arterial hyperenhancement, all 63 received a confirmed diagnosis of HCC, yielding a positive predictive value of 100% within this cohort. Among the 22 patients with negative late arterial hyperenhancement, 12 were diagnosed with benign entities or had no confirmed tumor, while 10 patients had false-negative imaging profiles, representing histopathologically proven HCC that lacked typical arterial enhancement.

Similarly, cross-tabulating portal venous phase washout against histopathology revealed that of the 55 patients with a positive washout signature, 54 had confirmed HCC, while only 1 presented with a non-malignant mimic. Among the 30 patients with negative portal venous washout, 19 had histopathologically verified HCC, while 11 had benign findings. The association between portal venous phase washout dynamics and final diagnosis was highly significant ($\chi^2(1)=19.443$, $p<.001$).

Table 3 A: Chi-square test cross-tabulations for late arterial phase hyperenhancement versus histopathological diagnosis.

Late Arterial Phase Hyperenhancement	Histopathological Diagnosis (Gold Standard)	Total
	HCC n (%)	Benign/No Lesion n (%)
Positive	63 (100.0)	0 (0.0)
Negative	10 (45.5)	12 (54.5)
Total	73 (85.9)	12 (14.1)
		85 (100.0)

Table 3 B. Chi-square Test Results: Chi-square test cross-tabulations for late arterial phase hyperenhancement versus histopathological diagnosis.

Statistical Test	Value	df	p-value
Pearson Chi-square	40.012	1	<0.001
Continuity Correction (Yates)	35.640	1	<0.001
Likelihood Ratio	38.889	1	<0.001
Fisher's Exact Test	—	—	<0.001
Linear-by-Linear Association	39.542	1	<0.001

Pearson Chi-Square analysis confirmed a highly significant association between late arterial phase hyperenhancement and the final diagnosis of HCC ($\chi^2(1)=40.012$, $p<.001$).

Positive late arterial phase hyperenhancement showed a statistically significant association with histopathological diagnosis of hepatocellular carcinoma ($\chi^2 = 40.012$, $p < 0.001$). All participants with positive hyperenhancement were diagnosed with HCC, indicating that late arterial phase

hyperenhancement is a strong imaging predictor of HCC.

Discussion

This prospective cross-sectional study demonstrated that triphasic multidetector computed tomography (MDCT) with an optimized late arterial phase is a highly effective imaging modality for the diagnosis of hepatocellular carcinoma (HCC). A statistically significant association was observed between late arterial phase hyperenhancement and

histopathological diagnosis ($\chi^2 = 40.012$, $p < 0.001$), while portal venous phase washout also showed a strong correlation with HCC ($\chi^2 = 19.443$, $p < 0.001$). These findings confirm the diagnostic importance of combining arterial hyperenhancement with washout patterns for the non-invasive diagnosis of HCC.

The demographic characteristics of the study population were consistent with the established epidemiology of HCC. The mean patient age was 58.87 ± 10.10 years, indicating that HCC predominantly affects middle-aged and elderly individuals. A marked male predominance (76.5%) was observed, which agrees with previous studies reporting a higher incidence of HCC among men due to increased exposure to chronic viral hepatitis, alcohol use, and hormonal influences.

Chronic viral hepatitis remained the leading etiological factor in this cohort. HBV/HCV co-infection (27.1%), HCV infection (22.4%), and HBV infection (20.0%) together accounted for nearly 70% of all cases, emphasizing the continuing burden of viral hepatitis as a major risk factor for HCC in developing countries. These findings highlight the importance of surveillance programs for patients with chronic liver disease.

The mean lesion size was 6.06 ± 3.43 cm, and 87.1% of lesions measured ≥ 2 cm. Larger lesion size likely contributed to the high diagnostic performance of triphasic CT because classical imaging characteristics become more evident as tumor size increases. Nevertheless, the large average lesion size also suggests delayed clinical presentation, indicating the need for earlier screening among high-risk populations.

Late arterial phase hyperenhancement was detected in 74.1% of patients, and all positive cases were confirmed as HCC on histopathology, demonstrating excellent positive predictive value. Similarly, portal venous washout was observed in 64.7% of patients, with 54 of 55 positive cases confirmed as HCC, corresponding to a positive predictive value of 98.2%. Furthermore, portal venous and delayed phases complemented the arterial phase findings in 83.5% of patients, reinforcing the value of multiphasic imaging for improving diagnostic confidence [28].

Most participants had underlying cirrhosis, with moderate cirrhosis present in 44.7% and severe cirrhosis in 32.9% of cases. This reflects the well-established relationship between chronic liver cirrhosis and HCC development. Accurate differentiation of malignant lesions from regenerative or dysplastic nodules remains challenging in cirrhotic livers; however, the combination of arterial hyperenhancement and portal venous washout substantially improves diagnostic specificity [29].

Although contrast-enhanced MRI may provide greater sensitivity for detecting very small lesions, triphasic MDCT remains an excellent first-line imaging modality because of its wide availability, rapid acquisition, lower cost, and ability to evaluate tumor extent, vascular invasion, and extrahepatic disease. Overall, the findings of this study support the routine use of optimized triphasic CT protocols with late arterial phase imaging for the early detection and accurate diagnosis of HCC, particularly in regions where chronic viral hepatitis remains highly prevalent.

Conclusion

Triphasic computed tomography featuring a dedicated late arterial phase demonstrates strong diagnostic accuracy and clinical utility for evaluating hepatocellular carcinoma in patients with chronic liver disease. The technical optimization of the late arterial phase acquisition (35–40 seconds) captures characteristic tumor hypervascularity, while the subsequent portal venous and delayed phases provide reliable assessment of contrast washout.

In this study population, characterized by a high prevalence of viral hepatitis and advanced cirrhosis, the combination of late arterial hyperenhancement and subsequent washout correlated strongly with histopathological confirmation, supporting its use for confident, non-invasive diagnosis in accordance with current guidelines. Triphasic CT remains a highly practical, reproducible, and effective diagnostic modality to guide clinical decision-making and facilitate timely therapeutic intervention.

Limitations

The present study has the following limitations:

- The study was conducted at a single center with a relatively small sample size (N = 85), which may limit the generalizability of the findings to larger populations.
- Most lesions were relatively large (mean diameter 6.06 cm), which may have increased the diagnostic performance of triphasic CT compared with its performance in detecting lesions smaller than 2 cm.
- The study relied on qualitative visual assessment of enhancement and washout patterns without comparison with advanced imaging modalities such as contrast-enhanced MRI, which may have influenced diagnostic accuracy.

Conflict of Interest:

All the authors have no conflict of interest.

Recommendations

- Conduct large-scale, multi-center prospective studies to validate the diagnostic performance of optimized triphasic CT protocols in diverse patient populations.
- Evaluate the effectiveness of late arterial phase imaging for detecting small hepatic lesions (<2 cm), where early diagnosis of HCC remains challenging.
- Incorporate standardized quantitative assessment methods and compare triphasic CT with advanced imaging modalities, such as contrast-enhanced MRI, to further improve diagnostic accuracy and reproducibility.

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