

DIAGNOSTIC ACCURACY OF QUANTITATIVE WASHOUT IN DIAGNOSING HEPATOCELLULAR CARCINOMA

Original Research

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy and remains a leading cause of cancer-related deaths worldwide. The condition is often associated with chronic liver disease (CLD), particularly in high-prevalence regions like Pakistan. Timely and accurate diagnosis plays a crucial role in improving treatment outcomes. Quantitative washout on triphasic computed tomography (CT) has emerged as a promising non-invasive imaging biomarker for HCC, offering objective assessment of lesion behavior during contrast-enhanced phases.

Objective: To determine the diagnostic accuracy of quantitative washout on triphasic CT in diagnosing hepatocellular carcinoma, using histopathological findings as the gold standard.

Methods: A cross-sectional study was conducted at the Dow Institute of Radiology, Dow University of Health Sciences, from 11th October 2024 to 11th April 2025. A total of 192 patients aged 30–80 years with clinical suspicion of HCC underwent triphasic CT scans. Delayed phase attenuation values were measured to calculate quantitative washout. All patients subsequently underwent liver biopsy, and histopathology served as the reference standard. Data analysis was performed using SPSS version 22.0. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated using 2×2 contingency tables.

Results: The mean age of participants was 54.49 ± 10.88 years, with 124 (64.6%) males and 68 (35.4%) females. Mean quantitative washout was 141.99 ± 28.63 Hounsfield Units. Quantitative washout on CT identified HCC in 170 (88.5%) patients, while histopathology confirmed HCC in 162 (84.4%). The diagnostic parameters showed sensitivity of 100.00%, specificity of 73.33%, PPV of 95.29%, NPV of 100.00%, and diagnostic accuracy of 95.83%.

Conclusion: Quantitative washout on triphasic CT is a highly sensitive and accurate imaging technique for diagnosing hepatocellular carcinoma, supporting its integration into diagnostic protocols for CLD patients.

Keywords: Chronic Liver Disease, Computed Tomography, Diagnostic Accuracy, Hepatocellular Carcinoma, Histopathology, Imaging Biomarkers, Triphasic CT.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most prevalent primary malignant tumor of the liver and represents a significant global health concern due to its increasing incidence and high mortality rate (1,2). It ranks among the fastest-growing causes of cancer-related deaths worldwide, with a particularly alarming trend in regions with limited healthcare resources (3). Chronic liver disease (CLD), regardless of etiology, remains the most critical risk factor for the development of HCC (4). The most common underlying causes of CLD include chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV), excessive alcohol consumption, and the increasingly recognized non-alcoholic fatty liver disease (NAFLD) (4). International guidelines strongly advocate for routine surveillance in high-risk individuals, particularly those with cirrhosis, using ultrasound (US) with or without serum alpha-fetoprotein (AFP) levels to enable early detection of HCC (5,6). The burden of HCC is notably rising in Pakistan, where viral hepatitis—especially HCV and HBV—are the predominant etiological factors. Epidemiological data from the country show that HCV is responsible for approximately 66% of HCC cases, while HBV accounts for around 34% (7). These figures underscore the urgent need for enhanced diagnostic strategies tailored to the regional context. Although ultrasound is widely utilized as the first-line tool for HCC surveillance due to its accessibility, affordability, and absence of ionizing radiation, its effectiveness is limited by high operator dependency and moderate sensitivity. While non-contrast ultrasound has a sensitivity of 59.3%, contrast-enhanced ultrasound (CEUS) offers improved performance, with sensitivity reported at 84.4% (8). Despite these advancements, the diagnostic accuracy of ultrasound-based modalities remains suboptimal, particularly in detecting small or atypical lesions.

Cross-sectional imaging techniques, including triphasic computed tomography (CT) and magnetic resonance imaging (MRI), are considered the gold standards for definitive HCC diagnosis (9,10). However, each modality presents inherent limitations. MRI, although highly sensitive, is costly, time-consuming, and not universally accessible in resource-constrained settings. Triphasic CT, on the other hand, offers a faster and more widely available alternative, with a pooled sensitivity of approximately 73.6% for HCC detection (8). Recent studies have explored the use of quantitative imaging features to enhance diagnostic precision. One such parameter, quantitative washout on the delayed phase of triphasic CT, has demonstrated promise. This involves calculating the percent attenuation ratio, which reflects the degree of contrast washout from the lesion compared to the surrounding liver parenchyma. Quantitative washout has been shown to yield a sensitivity of 91.7% and a specificity of 80.8% in differentiating HCC from other hepatic lesions (11,12). Given the high prevalence of HCV in Pakistan and the rising incidence of HCC, the need for early, accurate, and accessible diagnostic tools is paramount. Early-stage identification of HCC allows for curative interventions such as hepatic resection or liver transplantation. Conversely, delayed diagnosis often precludes curative options, relegating patients to palliative care and significantly impacting survival outcomes (13). A prior local study investigating quantitative washout involved a limited sample size of 132 patients and warrants validation on a broader scale (12). The current study aims to address this gap by evaluating the diagnostic accuracy of quantitative washout in diagnosing HCC on triphasic CT using histopathological findings as the gold standard, thus contributing to the refinement of imaging-based diagnostic strategies in high-risk populations.

METHODS

This cross-sectional study was conducted at the Dow Institute of Radiology, Dow University of Health Sciences, Ojha Campus, Karachi, over a six-month period from 11th October 2024 to 11th April 2025. The objective was to determine the diagnostic accuracy of quantitative washout on triphasic CT for detecting hepatocellular carcinoma (HCC), using histopathological findings as the gold standard. The study followed a non-probability consecutive sampling technique. The calculated sample size was 192 patients, based on a previously reported sensitivity of 91.7% and specificity of 80.8% (12), with a 7% margin of error, a 34% prevalence of HCC in Pakistan (5), and a 95% confidence level. Ethical approval was obtained from the relevant Institutional Review Board (IRB), specifically the College of Physicians and Surgeons Pakistan. All participants provided written informed consent prior to enrolment. Male and female patients aged between 30 and 80 years who were clinically suspected of having HCC—based on symptomatology defined in the operational definitions—and referred for triphasic abdominal CT scans were included in the study. Patients were excluded if they had previously been treated for HCC, were known to have fatty liver disease, had a documented allergy to contrast agents, had undergone only a single-phase CT scan, or declined participation.

Patients meeting the inclusion criteria underwent triphasic CT imaging on a multislice CT scanner. The imaging protocol began with a non-contrast scan, followed by intravenous contrast administration using a power injector. The arterial phase was acquired 30–40 seconds post-injection, the portal venous phase at 65–70 seconds, and the delayed phase at approximately five minutes. A consultant radiologist with over three years of experience in CT reporting assessed all images on a dedicated workstation. Quantitative washout was calculated based on attenuation values recorded for both the liver parenchyma and the lesion in the delayed phase, and these were documented in a predesigned proforma. To establish a definitive diagnosis, all patients subsequently underwent ultrasound-guided liver biopsy performed by an interventional radiologist with more than three years of procedural experience. Two core biopsy samples were obtained and preserved in formalin for histopathological evaluation. Data were analyzed using SPSS version 22.0. Quantitative variables such as patient age, duration of symptoms, attenuation values, and calculated quantitative washout were expressed as means and standard deviations. Categorical variables, including gender and HCC diagnosis on imaging and histopathology, were presented as frequencies and percentages. Diagnostic performance metrics—sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy—were computed using 2×2 contingency tables, with histopathological findings considered the gold standard. Subgroup analyses were conducted to evaluate the effect of potential confounding factors such as gender, age, and symptom duration on diagnostic performance. Post-stratification, diagnostic parameters were recalculated to assess their stability across subgroups.

RESULTS

The study included 192 patients with a mean age of 54.49 ± 10.88 years. Among them, 38.5% were aged ≤ 50 years, while 61.5% were older than 50 years. The gender distribution comprised 124 males (64.6%) and 68 females (35.4%). The mean duration of symptoms was 20.36 ± 7.96 days, with 24.5% of patients experiencing symptoms for ≤ 14 days and 75.5% reporting symptoms lasting longer than 14 days. Regarding imaging parameters, the mean liver attenuation in the delayed phase of CT was 64.75 ± 16.64 Hounsfield Units (HU), with 45.3% of patients showing liver attenuation ≤ 60 HU and 54.7% showing >60 HU. The mean lesion attenuation was 46.80 ± 13.22 HU, and 72.9% of patients demonstrated lesion attenuation values ≤ 60 HU. The calculated mean quantitative washout was 141.99 ± 28.63 HU. Notably, 87.5% of patients exhibited quantitative washout values >110 HU, indicating a high likelihood of hepatocellular carcinoma. On imaging evaluation using quantitative washout, HCC was detected in 88.5% of patients, while histopathology confirmed HCC in 84.4% of the cases. When histopathology was taken as the gold standard, the diagnostic performance of quantitative washout on triphasic CT demonstrated a sensitivity of 100.00%, specificity of 73.33%, positive predictive value (PPV) of 95.29%, negative predictive value (NPV) of 100.00%, and overall diagnostic accuracy of 95.83%.

Subgroup analyses revealed age-related differences. Among patients aged ≤ 50 years, diagnostic accuracy was 97.30%, with 100.00% sensitivity and 83.33% specificity. For patients aged >50 years, the diagnostic accuracy was 94.92%, with 100.00% sensitivity and 66.67% specificity. Gender-based analysis showed an accuracy of 94.35% in males and 98.53% in females. Both genders had 100.00% sensitivity, while specificity was higher in females (88.89%) compared to males (66.67%). Symptom duration was also stratified. Patients with symptoms ≤ 14 days had a diagnostic accuracy of 97.87%, with 100.00% sensitivity and 88.89% specificity. Those with symptoms >14 days showed a slightly lower accuracy of 95.17%, maintaining 100.00% sensitivity but with a specificity of 66.67%.

Table 1: Descriptive Statistics of Patient Demographics and CT Imaging Parameters (n = 192)

Parameter	Mean \pm SD	Minimum	Maximum
Age (years)	54.49 ± 10.88	31	79
Duration of Symptoms (days)	20.36 ± 7.96	7	36
Liver Attenuation on Delayed Phase (HU)	64.75 ± 16.64	33	98
Lesion Attenuation on Delayed Phase (HU)	46.80 ± 13.22	29	79
Quantitative Washout (HU)	141.99 ± 28.63	88	210

Table 2: Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=192)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	162	8	170
No	0	22	22
Total	162	30	192

Table 3: Age ≤50 years and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=74)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	28	7	35
No	7	77	84
Total	35	84	119

Table 4: Age >50 years and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=118)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	100	6	106
No	0	12	12
Total	100	18	118

Table 5: Male gender and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=124)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	103	7	110
No	0	14	14
Total	103	21	124

Table 6: Female gender and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=68)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	59	1	60
No	0	8	8
Total	59	9	68

Table 7: ≤14 days duration of symptoms and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=47)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	38	1	39
No	0	8	8
Total	38	9	47

Table 8: >14 days duration of symptoms and Diagnostic accuracy of quantitative washout taking histopathology as gold standard (n=145)

HCC on quantitative washout	HCC on histopathology		Total
	Yes	No	
Yes	124	7	131
No	0	14	14
Total	124	21	145

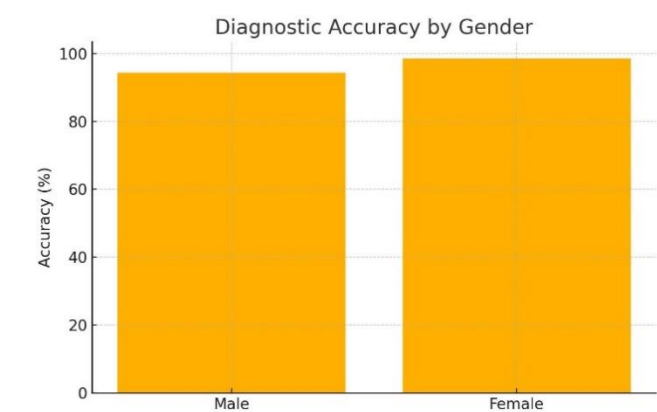


Figure 1 Diagnostic Accuracy by Gender

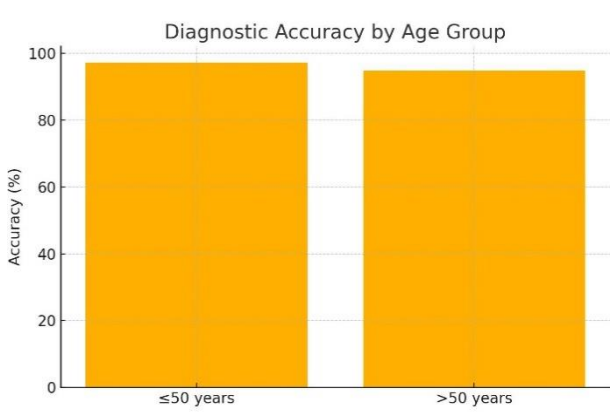


Figure 2 Diagnostic Accuracy by Age Group

DISCUSSION

The present study evaluated the diagnostic performance of quantitative washout in detecting hepatocellular carcinoma (HCC) on triphasic computed tomography, using histopathological findings as the reference standard. With a sample of 192 patients, the findings demonstrated an excellent diagnostic accuracy of 95.83%, supported by a sensitivity of 100.00%, specificity of 73.33%, positive predictive value of 95.29%, and negative predictive value of 100.00%. These results underscore the potential of quantitative washout as a non-invasive, highly sensitive imaging marker for HCC detection, particularly in settings where early diagnosis significantly impacts therapeutic options and patient outcomes (14,15). Quantitative washout on delayed phase imaging showed a particularly strong correlation with histologically confirmed HCC cases. These findings are consistent with earlier literature that emphasized the utility of attenuation-based washout values in differentiating malignant hepatic lesions. In one referenced study, the percentage attenuation ratio on delayed phase imaging provided a sensitivity of 100% and a specificity of 75.8% for diagnosing HCC when using a cut-off value of ≥ 107 (16). This mirrors the diagnostic performance observed in the current study and reinforces the reliability of CT attenuation metrics as objective, reproducible parameters. Another study that used receiver operating characteristic (ROC) analysis identified a cut-off of 10 Hounsfield Units between arterial and equilibrium phases, achieving 91.5% sensitivity and 80.9% specificity. That investigation also reported a substantial increase in lesion detection rates when combining region of interest (ROI) analysis with traditional visual interpretation, further supporting the complementary value of quantitative assessment (17,18).

Washout identification during the portal venous phase has also been explored as an adjunct to delayed phase imaging. It was noted that portal venous phase washout appeared in 60% of histologically proven HCCs and had substantial interobserver agreement, with larger lesion size and increased background liver attenuation serving as predictive factors (19,20). While these findings are notable, the present study reinforces that delayed phase imaging continues to offer superior sensitivity in identifying washout compared to portal or hepatic venous phases. In another investigation comparing venous and delayed phases, washout was more frequently and objectively detected in the delayed phase, supporting its diagnostic primacy in characterizing HCCs, especially in cirrhotic livers (21,22). The current study’s strength lies in its robust diagnostic methodology, the use of histopathology as the definitive standard, and the inclusion of stratified analyses across age, gender, and symptom duration subgroups. The sample size was larger than in previously conducted regional studies,

enhancing the reliability and generalizability of the findings within similar healthcare settings. Furthermore, quantitative parameters minimized subjective bias, addressing a common limitation of visual-only image interpretation.

Nonetheless, this study is not without limitations. Being a single-center study, the findings may be influenced by institutional practices, patient demographics, and radiological protocols, which may not be universally applicable. Another limitation is the exclusion of patients with non-alcoholic fatty liver disease, a group increasingly recognized as at-risk for HCC, potentially limiting the representativeness of the cohort. The study also did not stratify diagnostic performance based on lesion size, tumor stage, or background liver condition, which could have provided deeper insights into the utility of washout across varying clinical contexts. Future research should focus on multicentric trials with diverse patient populations and standardized imaging protocols. Additionally, integration of quantitative washout analysis with radiomics or artificial intelligence-based tools may further refine diagnostic precision. Stratification based on tumor morphology, etiology of liver disease, and hepatic function could also help tailor imaging strategies for different risk profiles. Overall, the findings of this study affirm the value of quantitative washout as a reliable, non-invasive diagnostic marker for HCC. Its incorporation into clinical practice, particularly in regions with high disease burden and limited access to MRI, can facilitate early diagnosis, improve treatment planning, and potentially enhance patient survival outcomes.

CONCLUSION

The study concluded that quantitative washout on computed tomography is a highly effective diagnostic tool for identifying hepatocellular carcinoma. Its strong diagnostic performance highlights its value as a reliable, non-invasive method that can support early and accurate detection of HCC. This is particularly important in clinical settings where timely diagnosis can significantly influence treatment decisions and improve patient outcomes. Incorporating quantitative washout into routine imaging protocols has the potential to enhance diagnostic confidence and aid in the management of high-risk liver disease populations.

AUTHOR CONTRIBUTION

Author	Contribution
Nighat Hasan*	Substantial Contribution to study design, analysis, acquisition of Data
	Manuscript Writing
	Has given Final Approval of the version to be published
Samita Asad	Substantial Contribution to study design, acquisition and interpretation of Data
	Critical Review and Manuscript Writing
	Has given Final Approval of the version to be published
Aniqa Qureshi	Substantial Contribution to acquisition and interpretation of Data
	Has given Final Approval of the version to be published
Anmol Fariha	Contributed to Data Collection and Analysis
	Has given Final Approval of the version to be published
Javeria Sattar	Contributed to Data Collection and Analysis
	Has given Final Approval of the version to be published
Sara	Substantial Contribution to study design and Data Analysis
	Has given Final Approval of the version to be published
Syed Hameed-Ul-Hassan Shah	Contributed to study concept and Data collection
	Has given Final Approval of the version to be published

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