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ORIGINAL ARTICLE

Diagnostic Accuracy of Quantitative Washout Calculated on Triphasic CT Scan for Diagnosis of Hepatocellular Carcinoma keeping Histopathology as Gold Standard

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ABSTRACT

Aim: To find out how accurate the quantitative washout is at diagnosing hepatocellular carcinoma on a triphasic CT scan compared to the histopathology, which is the gold standard. It can be used as a supplement to the subjective visual analysis of washout to help the radiologist diagnose hepatocellular carcinoma.
Methods: From the OPD and indoor database, 150 patients of both sexes were included who had abnormal lesions confirmed by ultrasound. In order to quantify washout during the delayed phase, CT scans were performed in three phases on all patients. On delayed phase, a region of interest between normal liver parenchyma and lesions was obtained. Those lesions having a percent attenuation ratio greater than 107 were identified as hepatocellular carcinoma.
Results: The ages of 150 patients who met the inclusion criteria ranged from 15 to 85. There were 93(62%) males and 57(38%) females, for a total gender ratio of 2:1. Of the 105 patients who tested positive for HCC on a CT scan, 96 actually had HCC. Among 45 patients who tested negative for HCC on a triphasic CT scan, 8 were erroneously labelled as negative. Quantitative washout on Triphasic CT scan has an overall sensitivity of 92.30%, a specificity of 80.40%, a positive predictive value of 82.20%, a negative predictive value of 88.66% and a diagnostic accuracy of 88.66% for identifying hepatocellular cancer.
Conclusion: Based on our findings, quantitative washout assessment for hepatocellular carcinoma is an easy, highly sensitive, and objective way that can be used as an adjunct to qualitative washout for hepatocellular carcinoma diagnosis.
Keywords: Hepatocellular carcinoma HCC, Percentage attenuation ratio, Washout, Delayed phase

INTRODUCTION

The most frequent kind of primary liver cancer is hepatocellular carcinoma. The fatality rate linked with this kind of tumour is the fourth highest in the world, and it is the sixth most often diagnosed tumour worldwide[1]. HCC is the fourth most frequent kind of liver illness in Pakistan[2]. A history of alcohol use, chronic hepatitis B or C infection, and nonalcoholic fatty liver disease (NAFLD) are all substantial risk factors for hepatocellular carcinoma (HCC).

Histopathology is without a doubt the most reliable investigation for the diagnosis of HCC; nonetheless, there may be significant inter-observer variability. A biopsy of the lesion is not always possible owing to the invasive nature of the method and the risk of complications in patients with considerable ascites and impaired coagulation[3,4].

Imaging methods are often employed to determine the nature of liver lesions. As a consequence of developments in imaging modalities over the past two decades, we are now better equipped to spot and diagnose the nature of liver lesions. According to the European Association for the Study of the Liver (EASL), hepatocellular carcinoma (HCC) can be diagnosed with a single investigation if the AFP levels are greater than 400ng/mL [5,] or if two imaging modalities [ultrasound, CT, or MRI] show a coincidental lesion with arterial hypervascularization in a cirrhotic liver, regardless of AFP levels. A second study to confirm the lesion is not required in the following scenarios, according to the American Association for the Study of Liver Diseases (AASLD): (1) the lesion is larger than 2cm in diameter[2]; the liver is cirrhotic; and (2) the lesion exhibits arterial hypervascularity and wash out during the portal venous (PV) or delayed phase[6].

On dynamic contrast CT imaging of the liver, typical HCC appears hyperdense in the late arterial phase compared to the surrounding liver, isodense or hypodense in the portal venous phase, and hypodense in the delayed phase. The hepatic artery is the primary source of blood supply for HCC; therefore, HCC shows maximum enhancement on the arterial phase. The portal vein is responsible for 75% of the blood reaching the normal liver, while the hepatic artery is only responsible for 25%, therefore best visualised during the portal venous phase[7,8]. During the portal venous phase, the liver will continue to enhance, but HCCs will face washout since there will be no blood flow via the portal veins. This enhancement of HCC during the arterial phase has been shown to increase tumour detection rates by up to 10%[9,10]. The hypodense appearance of HCCs in the portal venous and delayed phases might be caused by slow wash-in and wash-out of fibrotic tissue of the surrounding cirrhotic liver[11]. By utilising the criteria of hypervascularity in the arterial phase and washout in the delayed phase, it is feasible to obtain excellent sensitivity (64–89%), specificity (96%), and a positive predictive value for HCC diagnosis (93%). A variety of variables, including fatty metamorphosis, intralesional fibrous stranding, calcifications, necrosis, and so on, may explain the heterogeneous CT appearance of HCC[14,15].

Another way for evaluating washout is to calculate the percentage attenuation ratio of the lesion during the delayed phase. This ratio is calculated by multiplying the lesion's attenuation to that of the nearby normal liver by a factor of 100. If the lesion washout value is more than 107, HCC is most likely present. In terms of sensitivity, which is 100%, and specificity, which is 75.8%, quantitative washout outperforms radiologist interpretation for the identification of HCC[16].

We aim to develop a quantitative definition of washout as well as calculate the diagnostic accuracy of quantitative washout formulas, a correlation between these findings and radiologists' interpretation of washout in hypervascular liver lesions, and to see if it can successfully replace biopsy as the gold standard.

MATERIALANDMETHODS

It was a descriptive cross-sectional study**.** Department of Diagnostic Radiology, Bahawal Victoria Hospital, Bahawalpur. Department of Diagnostic Radiology, Bahawal Victoria Hospital, Bahawalpur, hosted this research from February 2022 to September 2022. This research project was approved (permit number 1069) by the ethical review committee of Bahawal Victoria Hospital, Bahawalpur. All patients gave their informed consent before their clinical data was analyzed. Patient's clinical records and data were de-identified and anonymised prior to analysis. This

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study was conducted over a period of six months, from February 2022 to September 2022. This study was carried out according to the non-probability purposive sampling technique. Our sample size was 150. Using a sensitivity and specificity calculator, we determined the sample size keeping 64% prevalence of HCC[13], the sensitivity of quantitative washout was 91.76%, the specificity was 80.8%, the margin of error was 5% and the confidence interval was 95%. Patient selection was done according to the following criteria:

Inclusion Criteria: This research comprised 150 individuals with a clinical suspicion of hepatocellular carcinoma. Patients between the ages of 15 and 85 were included, and they were of either sex, with or without a positive history of hepatitis B, hepatitis C, or cirrhosis, as determined by ultrasonography.

Exclusion Criteria: Patients who were known to be allergic to contrast medium, were pregnant, or who had abnormal renal function or extrahepatic malignancy were excluded.

Hepatocellular Carcinoma: Lesions labelled on triphasic CT scan to be hepatocellular carcinoma if the quantitative washout value was > 107.

Quantitative washout (QW): Quantitative washout = delayed phase liver attenuation (AAD)/delayed phase lesion attenuation **(**LAD) X100

True Positive: Triphasic CT scan and histopathology both validated the diagnosis of hepatocellular carcinoma.

True Negative: According to the results of the triphasic CT scan and the histopathology, the patient did not have HCC.

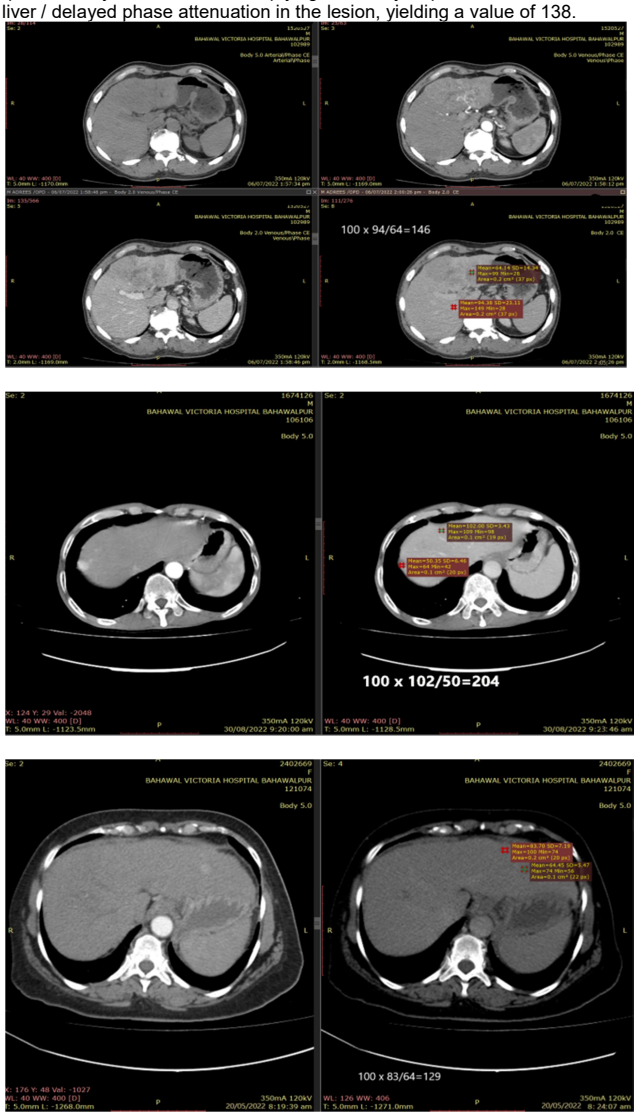
False Negative: Initially diagnosed as non-HCC using a triphasic CT scan, however histopathology confirmed the diagnosis as HCC.

False Positive: On the triphasic CT scan, the patient was diagnosed with HCC; however, histopathology revealed that the patient did not have HCC.

CT Triphasic technique: The Toshiba Aquillion, a 64-slice helical CT scanner, is used for all of the CT scan that were carried out. During imaging, we used a matrix size of 512 by 512, a voltage of 120 kV, a tube current ranging from 180 to 350mAs, and a reconstruction slice thickness of 5 mm. The plain CT scan had a slice thickness of 10 mm and a spacing of 20 mm between each slice. In each patient, a nonionic iodinated contrast agent (Ultravist/Omnipaque) containing 300mg of iodine per milliliter is administered at a injection rate of 3-4ml/sec with dose of 1-1.5 ml/kg. When bolus tracking, the arterial phase may be timed by situating the region of interest (ROI) over the aorta at the level of the celiac axis (threshold 100HU). This will allow for accurate timing of the arterial phase. After 25 seconds, a CT images of the early arterial phase were obtained while the patient held his breath for 30 seconds. The PV phase was acquired 45 seconds after the injection, whereas the delayed phase was obtained 5–6 minutes later on average. For the image volume reconstruction in axial, sagittal and coronal views, the default setting for displaying the liver and other soft tissues were used at interval of 5 millimeters.

Image analysis: All images for each patient were reviewed by a 3rd-year resident under the supervision of a single certified radiologist. Analysis of the attenuation of lesions on a CT scan, also known as quantitative washout, was made simpler by the use of region of interest (ROI) analysis. This feature is included in PACS (picture archival and communication systems). On the images that were obtained during the arterial phase, the portal venous phase, and the delayed phase, an area of interest (ROI) was drawn over the lesion and the surrounding liver, and Hounsfield units were measured. In order to avoid any miscalculation, artefacts, cysts, ducts, or blood vessels were avoided. To measure the amount of washout that occurred during the delayed phase, we used the percent attenuation ratio of liver to lesion. Quantifying washout may be done using a formula, i.e., attenuation of liver on delayed phase (AAD) divided by attenuation of lesion on delayed phase (LAD)x100. In order to make a diagnosis of HCC, a lesion's percent attenuation ratio needed to be more than 107. The results from histopathology were utilised for comparison.

Figure 1: CT scans recorded at 45 seconds and 5 minutes following the start of the procedure indicate early arterial enhancement and washout on the porto venous and delayed phase respectively. Calculating washout quantitatively involves 100 multiplying the delayed phase attenuation in the liver / delayed phase attenuation in the lesion, yielding a value of 138.



Statistical analysis: For the purpose of analyzing the data, SPSS 21 Statistics software was used. Descriptive statistics, percentage and frequency were calculated for qualitative data like gender, viral marker status and histopathology findings. Mean ± standard deviation for quantitative data like age were calculated. We determined the sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of CT scan for HCC by using a 2x2 table and using histopathology as the gold standard. We excluded potentially confounding variables by using stratification, such as the size of the lesion, the patient's age, and their gender. A p-value of 0.05 was chosen to serve as the threshold for significant differences.

RESULTS

One hundred fifty individuals took part in the study. The ages of the participants varied from 15 to 85 years old, with a mean age of 47.60 years and a standard deviation of 12.41 years. The age range of 56–65 years was the most prevalent, which made up 40.75% of the population. Among them, 57 were female patients

and 93 were male patients. The size of the lesion ranged from 2 cm to 20 cm, with a mean size of 3.6 ± 1.04 cm.

Quantitative washout on Triphasic CT validated the diagnosis of HCC in 105 (70%) of the patients and no HCC in 45 (30%) of the patients. Histopathology confirmed the presence of HCC in 104 (69.33%) of the patients; however, in 46 (30.66%) of the cases, no evidence of HCC was found.

The histopathology revealed that 96 of the patients who tested positive on the triphasic CT scan really did have HCC, whereas 9 of the patients tested negative. The findings of a triphasic CT scan were negative for 45 individuals, and table-I reveals that 8 of those patients had HCC (a false negative), whereas 37 of them patients did not have HCC (a true negative) (p = 0.0001). The current study found that quantitative washout calculated on a delayed phase CT scan had a sensitivity of 92.30%, specificity of 80.40%, positive predictive value of 91.40%, negative predictive value of 88.66%, and diagnostic accuracy of 86.66% when it was used to diagnose HCC. The study used histopathology as the reference standard. The pattern of liver lesions is shown in Table II.

Figure-2: The diagnostic accuracy of quantitative washout on triphasic CT for the detection of hepatocellular carcinoma

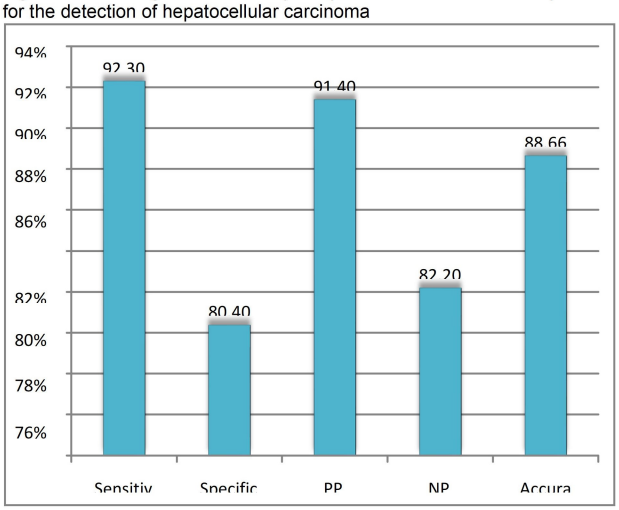


Figure 3:Frequencies of patient of Hepatocellular carcinoma indifferent age groups

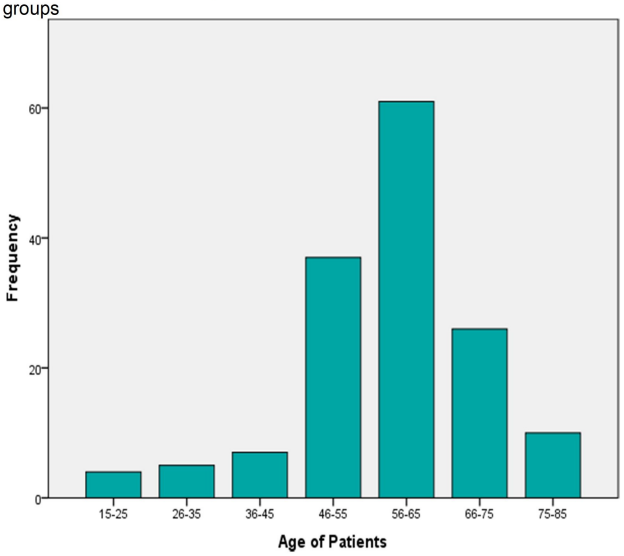


Table I: Triphasic CT and Histopathology findings (n=150)

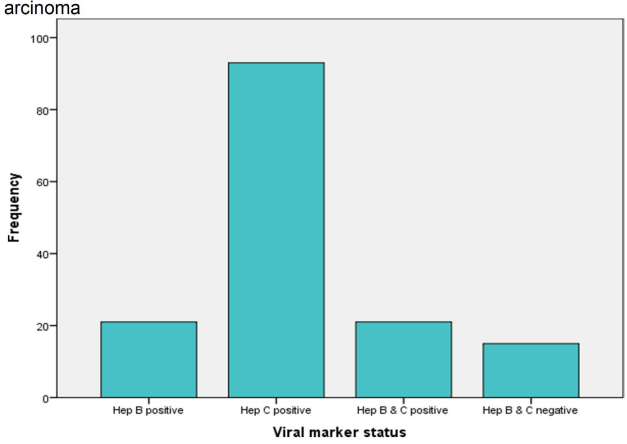
Nature of Lesion	Positiveon Triphasic CT	Negative on Triphasic CT
Positive on Histopathology	96(TP)	08(FP)
Negative on Histopathology	09(FN)	37(TN
Total	105	45

Table 2: Pattern of liver lesionson triphasic CT scan

Pattern of lesion	Ratio	Percentage
Solitarylesion	57	38%
Multifocallesions	71	47.3%
Illdefinedinfiltrativelesions	22	14.7%
Total	150	

P value 0.0001

Figure 4: Viral marker status of our patient with suspicion of hepatocellularc arcinoma



DISCUSSION

If HCC is detected at an earlier stage, patient survival over the long term may be improved, and the efficacy of therapy may be boosted to its full potential. It is usual for hepatocellular carcinoma to be hyperdense in the arterial phase in comparison to the non-tumerous liver parenchyma and to appear hypodense on the portovenous and delayed phases[15-17]. The most essential tumour differentiating trait for the non-invasive diagnosis of HCC is known as washout in the porto venous and delayed phase; therefore, it is a component of the liver Imaging Reporting and Data System[18]. This function is used for grading liver lesions in patients who have hepatic cirrhosis. As a consequence of this, the triphasic CT scan is considered to be the diagnostic test of choice for the purpose of evaluating liver lesions. Delayed phase images demonstrate high sensitivity for the washout interpretation[19-21].

In the delayed phase, CT attenuation of the lesions must decrease at a larger rate than that of the liver that surrounds them (Fig. 1). This is necessary for the washout to be visually noticeable for the radiologist. During the portovenous phase, the liver parenchyma shows further enhancement, which conceals enhancement of the lesion. In fact, the vast majority of lesions showing the most significant enhancement during the arterial phase become isodense or hypodense in relation to the normal liver tissue in the portovenous phase. Further, qualitative washout detection depends on the expertise of a radiologist and subjective visual assessment. It also depends upon window width and level settings that usually differ in different setups. It seems reasonable that an improved comprehension of what we mean when we say "washout" would be useful to the accuracy of HCC diagnosis.

The use of a quantitative definition has the potential to lessen the variation that occurs among the various observers. In addition to this, washout could be easier to comprehend for radiologists with less expertise or referring doctors. It's likely that in the not-too-distant future, computer algorithms driven by artificial intelligence may be able to automatically identify liver lesions. In

that case, having a definition of the term that can be quantified would be helpful[9,14,18,22].

In this research, we compared the role of quantitative analysis of washout using ROI analysis (area of interest) to the qualitative analysis of washout on a triphasic CT scan. By the results of this research, it is noted that calculating the percent attenuation ratio of lesion and normal background liver produces the best results to establish tumour wash-out. Based on our findings, a percent attenuation ratio of greater than 107 in the delayed phase is excellent for calculating lesion wash-out.Visual analysis alone would have missed HCC lesions in the same way that qualitative analysis of wash-out alone did in the research by[21]. That study found that wash-out was present in 72.4% of cases of HCC when visual wash-out alone was used as the sole criteria for assessment. We were able to identify 96 out of 104 (92.3%) of the lesions that were present in our sample by using quantitative washout analysis. In a second study, conducted by [22], in 94 patients with one lesion, attenuation of HCC was compared in the arterial and delayed phases. With a threshold of 10 HU for lesion attenuation (arterial-delayed), they achieved a sensitivity of 91.5% and a specificity of 80.9%.

In a study conducted, HCC lesions were shown to have a median percentage attenuation ratio of 121 (PAR; defined as the ratio of the attenuation of the nearby liver to that of the lesion during the delayed phase x 100) that was substantially higher than the PAR for non-HCC lesions, which was 101. The best possible diagnostic performance for HCC was attained using delayed phase imaging with a PAR of ≥107. This finding demonstrates a specificity of 74.8%, a sensitivity of 100%, a positive predictive value of 63.3%, and a negative predictive value of 100%[12].

Another study done and showed PAR (percentage attenuation ratio) measured in 132 patients in delayed phase on a triphasic CT scan had an accuracy of 87.8%, a sensitivity of 91.76%, a specificity of 80.85%, a positive predictive value of 89.66%, a negative predictive value of 84.4%, and a diagnostic accuracy value of 87.88% when applied to the process of diagnosing hepatocellular carcinoma[23].

The merits of our study include the utilisation of a large and consistent sample group, as well as the histopathological confirmation of our results. Both of these aspects validated the findings that we have obtained. In the past, a subjective judgement of the lesion density in comparison to normal liver tissue was required to identify HCC in a triphasic CT scan. An objective and accurate method that may be utilised to strengthen the diagnosis of hepatocellular carcinoma beyond visual evaluation is the direct quantitative measurement of the lesion attenuation ratio between the lesion and non-tumorous liver in the delayed phase. This is an objective and reliable method that can be used in addition to subjective visual assessment to improve the hepatocellular carcinoma diagnosis.

CONCLUSION

In conclusion, washout is an excellent indicator for the existence of HCC in individuals with potentially cancerous tumors. For quantitative washout, we have established a threshold value (percentage attenuation ratio ≥ 107), which correlates well with a biopsy-proven diagnosis of HCC. Quantitative washout, in addition to visual analysis on a triphasic CT scan, is a very sensitive diagnostic tool for hepatocellular cancer. It is a reliable alternative to histopathology for the non-invasive diagnosis of HCC.

Authorship and contribution declaration: Each author of this article fulfilled following Criteria of Authorship:

1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.

All authors agree to be responsible for all aspects of their research work.

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