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ASSESSMENT OF DIAGNOSTIC ACCURACY OF TRI-PHASIC COMPUTED TOMOGRAPHY IN DIFFERENTIATING BETWEEN CIRRHOSIS NODULES AND HEPTOCELLULAR CARCINOMA NODULES

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ABSTRACT

Hepatocellular carcinoma is basically a type of tumor originating from liver cells. In primary liver cancer, hepatocellular carcinoma is the most prevalent kind. The most frequent primary hepatic tumor, hepatocellular carcinoma ranks sixth globally interms of frequency of occurrence and can cause up to one million deaths yearly. Cirrhosis is a disease that leaves the liver permanently damaged and scarred. Cirrhosis is the term describing the histological development of regenerative nodules surrounded by fibrous bands as a result of chronic liver injury. The normal function of the liver is hampered by the replacement of healthy liver tissue with scar tissue. Computed Tomography (CT) scan is best for identifying and evaluating hepatic cancers. When contrast material is injected, multiphasic scanning with helical CT improves hepatocellular carcinoma detection and staging. The aim of this study was to assess the diagnostic accuracy of tri-phasic computed tomography in differentiating between cirrhotic nodules and hepatocellular carcinoma nodules. This was a cross -sectional study design. It was carried out in Arif Memorial Teaching Hospital. Non-probability convenient Sampling technique was used. Statistical analysis were conducted using SPSS version 26.0, with Receiver Operating Curve (ROC) and independent sample t- test was applied to assess the diagnostic accuracy of tri-phasic CT for differentiating both nodules.

Initial finding of Area under curve (AUC)for a ROC curve value of 0.4 and independent sample t- test shows a 0.01 p. value for cirrhotic nodules while for hepatocellular

carcinoma nodules Area under curve (AUC)for a ROC curve shows a value of 0.9 and independent sample t- test shows a value of 0.8.
According to my study results, AUC of a ROC curve analysis shows 0.4 value (less than 0.5) for cirrhotic nodules which means a true negative value while AUC for ROC curve analysis for HCC nodules shows a value of 0.9 which means a true positive results. In conclusion tri- phasic computed tomography has good diagnostic accuracy for hepatocellular carcinoma nodules as compared to cirrhotic nodules. This study improves the financial status of our country because CT is a costly modality. This study aligns with united nation sustainable development goal number 08 (decent work and economic growth).
Keywords: *Computed Tomography, Hepatocellular carcinoma, Cirrhotic Nodules.*

INTRODUCTION

The most frequent primary hepatic tumor, hepatocellular carcinoma (HCC) ranks sixth globally in terms of frequency of occurrence and can cause up to one million deaths yearly. The incidence of discovering HCC by computed tomography (CT) has grown from 1.4 to 2.4 per 100,000 over the past 20 years, and this has resulted in a 41% increase in the overall death rate (1). Cirrhotic liver is one of the trickier radiological cases. It is challenging to identify significant underlying problems because of the damaged and twisted liver architecture. The fact that these patients have a significantly higher risk of developing hepatocellular carcinoma exacerbates the issue. Not only are these tumors hard to find in cirrhosis patients, but the disease itself can produce lesions that resemble tumors. Owing largely to arterial phase enhancement's improved capacity to detect early, tiny lesions, contrast-enhanced helical CT has emerged as the most widely utilized screening modality for hepatocellular carcinoma in cirrhosis patients while it is well known that the sensitivity of helical CT and contrast-enhanced MR imaging to detect hepatocellular carcinoma in cirrhosis patients ranges from 50% to 70% (4).

CT technique is best for identifying and evaluating hepatic cancers. When contrast material is injected, multiphasic scanning with helical CT improves hepatocellular carcinoma detection and staging. However, because the gold standard for the diagnosis of hepatocellular carcinoma or other nodules is typically based on either the findings at partial hepatic resection or clinical and imaging studies with or without biopsy, it is impossible to ascertain the true sensitivity and specificity of multiphasic helical CT (4,5). It is commonly recognized that, regardless of the cause of liver illness, cirrhosis is the most powerful risk factor for the onset of hepatocellular carcinoma. The occurrence of HCC in different liver disorders, particularly liver cirrhosis, has not yet been precisely compared, though. Furthermore, it is currently unknown how much cirrhosis increases in a variety of liver illnesses. In this study, we conducted a meta-analysis to compare the incidence of HCC in LC in different liver illnesses. We also examined the ways in which the occurrence of developing HCC in the cirrhotic condition is rising in comparison to the non-cirrhotic state in different liver disorders. We also go over potential pathways for HCC formation in a variety of liver conditions (7).

Any liver lesion outside of the normal parenchyma, regardless of whether it results in structural or functional abnormalities of the hepato-biliary system, is called as a liver nodule. These lesions can be changed in size. Both benign and malignant tumors are possible. Regional and ethnic variations are evident in the prevalence of different liver pathologies. In Europe and the US, a liver nodule is more likely to be a metastatic deposit than a primary malignancy; however, with a prevalence of 8–10%, hepatocellular carcinoma ranks as the fourth most prevalent liver disease in Pakistan. When compared to data from the West, this prevalence rate is considerable (8).

Objective:

The objective of this study was to assess the diagnostic accuracy of tri-phasic computed tomography in differentiating between cirrhotic nodules and hepatocellular carcinoma nodules.

LITERATURE REVIEW

Tüysüz U et.al in 2024 suggested that Budd-Chiari syndrome (BCS), regenerative nodules may form from hepatic atrophy and increasing fibrosis due to decreased portal and venous outflow and hyper- arterialization. We used contrast-enhanced CT to assess the frequency and detection rate of hepatocellular carcinoma, as well as the imaging properties of regenerative hepatic nodules, their incidence rates in diagnosis and follow-up, and the yields of the CT scan technique validated by pathological examination. Thirty-three liver transplant recipients with primary chronic BCS were included in this two-center retrospective analysis. A multiphase procedure was employed to acquire images throughout the arterial, portal-venous, and delayed phases prior to and following the application of contrast. Images from three-dimensional tomography and CT angiography were acquired. The main conclusion was the balance between the pathological and CT imaging findings. Relationships between nodule incidence rate in BCS and nodule malignancy development rate, as well as between nodule and HCC development and blood type and disease duration, were secondary outcomes. Computed tomography demonstrated a sensitivity of 78.3%, a positive predictive value of 90.0%, a specificity of 80.0%, and a negative predictive value of 61.5% in identifying the nodules that were pathologically identified (35).

Sangiovanni A et.al in 2020 suggested that De novo HCC occurred in 48 patients (annual incidence 3.1/100 patient-years, 75% BCLC 0-A) and recurred in 40 patients (mean yearly incidence 29.9/100 patient-years, 83% BCLC 0-A) throughout a median study period of 17 months in group 1 and 16 months in group 2. In patients with UNMNs in group 1, the HCC immediate incidence peaked at 4.2 months, while in group 2, it peaked at 7.7 months. Multivariable Cox regression models showed that the incidence of de novo HCC was independently associated with UNMNs (hazard ratio [HR] 3.11; 95% CI 1.47–6.57: p = 0.003), ascites detected at any time prior to enrollment (HR 3.04; 95% CI 1.23–7.51; p = 0.02), and alpha-fetoprotein log-value (HR 1.90; 95% CI 1.05–3.44; p = 0.03), while alcohol abuse history (HR 2.10; 95% CI 1.08–4.09; p = 0.03) and history of HCC recurrence (HR 2.87; 95% CI 1.35–6.09; p = 0.006) were associated with HCC recurrence (25)

METHODOLOGY

1-Research design:

This study was a cross -sectional study design.

2-Clinical setting:

The study was carried out in Arif Memorial Teaching Hospital.

3- Sample size:

$$\textbf{Sample Size} = \frac{Z^2\text{-}1a/s\ P\ (1\text{-}P)}{d^2}$$

1-a = 95

P= 80

d=7%

Sample Size= 126

4-Sampling technique:

Non-probability convenient Sampling technique will be used.

5-Duration of study:

The duration of my study was 6 months.

6- Selection criteria:

1- Inclusion criteria:

1.a. We enrolled those patients in our study who were come in radiology department for CTscan with cirrhosis.

We also enrolled those patients in our study who were come in radiology department for CT scan with hepatocellular carcinoma

2- Exclusion criteria:

2.a. We excluded those patients in our study who were come in radiology department for CT scan other than cirrhotic and hepatocellular carcinoma disease (16).

2.b. We also excluded those patients in our study who were come in radiology department for CT scan for biliary track, portal vein and hepatic artery diseases.

2.c. **Ethical consideration:**

All participants in research must take part voluntarily, free from any concoction or undue influence, and their rights, dignity and autonomy should be respectful and appropriately protected. An autonomous person is capable of deliberation about personal goals and of acting under the direction of such deliberation.

7-**Data collection procedure:**

The data was collected through questionnaire and CT scans. After taking the consent form, they were enrolled in the study.

8- **Data analysis:**

The data were entered and analyzed by using the statistical package SPSS (version 26). Quantitative data were present as Mean and Standard deviation while a Receiver Operating Curve was draw through SPSS. Data were interpreted in the form of graphs and tables (17).

RESULTS

Table 1: shows that total of 63 patients were presented with cirrhotic nodules on CT. out of 63, 33 patients of cirrhotic nodules have density on CT while 30 patients show no density on CT. The positive actual state is present.

density of cirrhotic nodules on CT	Valid N
Positive	33
Negative	30
Missing	0
Total	63

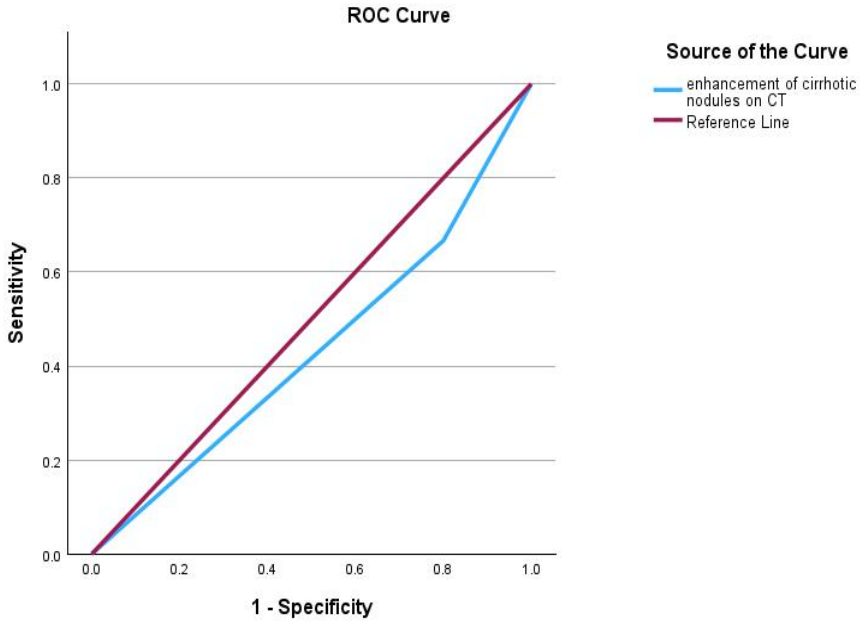

Figure1: A ROC curve is drawn to see the enhancement of cirrhotic nodules on CT. Blue line shows the enhancement of HCC nodules on CT while red line is reference line.

Table2: shows the area under the ROC curve of enhancement of cirrhotic nodules on CT. The area under the curve is 0.433.

Area Under the ROC Curve

enhancement of cirrhotic nodules on CT
Area
.433

Table3: Shows that total of 63 patients were presented with HCC nodules on CT.Out of 63, 42 patients of HCC nodules have density on CT while 21 patients show no density on CT. The positive actual state is present.

density of HCC nodules on CT	Valid N
Positive	42
Negative	21
Missing	0
Total	63

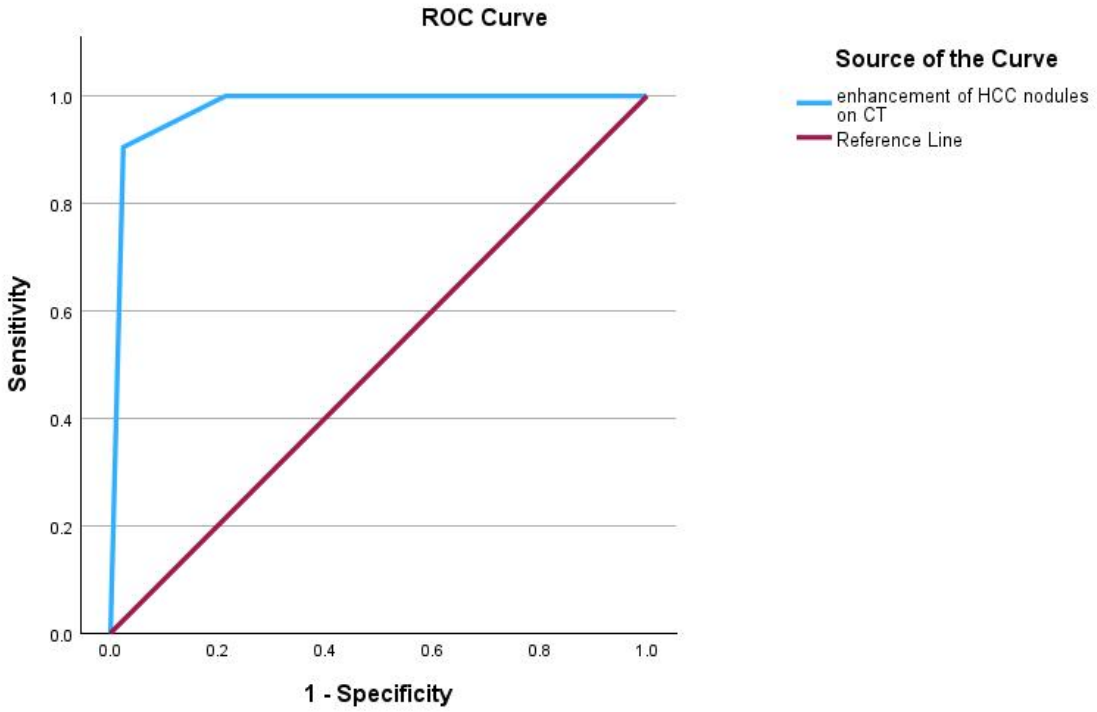

Figure2: A ROC curve is drawn to see the diagnostic accuracy of tri-phasic CT. Blue line shows the enhancement of HCC nodules on CT while red line is reference line.

Table4: shows the area under the ROC curve of enhancement of HCC nodules on CT. The area under the curve is 0.978.

Area Under the ROC Curve

enhancement of HCC nodules on CT
Area
.978

Table5: shows the independent samples t- test. Out of 63 patients 33 patients have density and enhancement of cirrhotic nodules on CT while 30 patients don't have density and enhancement. The Mean of 33 patients was 1.666 while Mean of 30 patients are 1.8000. Std. deviation of 33 is 0.478 while the other 30 patients have std. Deviation of 0.406.

	density of cirrhotic nodules on CT	N	Mean	Std. Deviation	Std. Error Mean
enhancement of cirrhotic nodules on CT	present	33	1.6667	.47871	.08333
	absent	30	1.8000	.40684	.07428

Table6: Levene test for equality of variance and t-test for equality of means. Lenene test shows the significance value of 0.019 and degree of freedom is 61. While the t-test for equality of means shows the significance value of 0.120 and 0.241.The confidence interval is 95% (0.05).

		Levene Test for Equality of Variances		t-test for Equality of Means						
						Significance		Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
		F	Sig.	t	df	One-Sided p	Two-Sided p			Lower	Upper
enhancement of cirrhotic nodules on CT	Equal variances assumed	5.838	.019	-1.185	61	.120	.241	-.1333	.1125	-.3583	.09164
	Equal variances not assumed			-1.194	60.74	.118	.237	-.1333	.1116	-.3565	.08991

Table7: shows the independent samples t- test. Out of 63 patients 54 patients have density and enhancement of hepatocellular carcinoma nodules on CT while 9 patients don't have density and enhancement. Mean and std. deviation of 54 samples are 2.9048 and 0.30079 respectively while the other 9 patients have mean and std. deviation of 2.111 and 0.33333 respectively.

	density of HCC nodules on CT	N	Mean	Std. Deviation	Std. Error Mean
enhancement of HCC nodules on CT	present	54	2.9048	.30079	.06564
	absent	9	2.1111	.33333	.11111

Table8: shows the independent samples t- test. Out of 63 patients 54 patients have density and enhancement of hepatocellular carcinoma nodules on CT while 9 patients don't have density and enhancement. Mean and std. deviation of 54 samples are 2.9048 and 0.30079 respectively while the other 9 patients have mean and std. Deviation of 2.111 and 0.33333 respectively.

		Levene's T for Equality Variances		t-test for Equality of Means							
						Significance		Mean	Std. Er	95% Confide Interval of Difference	
		F	Sig.	t	df	One-Sided p	Two-Sided p	Difference	Difference	Lower	Upper
enhancement of H nodules on CT	Equal varian assumed	.065	.80	6.417	28	<.001	<.001	.7936	.12368	.54030	1.04700
	Equal varian not assumed			6.150	13.882	<.001	<.001	.7936	.12905	.51664	1.07066

DISCUSSION

Based on this study, CT techniques is best for identifying and evaluating hepatic cancers. When contrast material is injected, multiphasic scanning with helical CT improves hepatocellular carcinoma detection and staging (4, 5). Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related deaths and the sixth most common type of cancer globally. HCC is the primary cause of death for patients with liver cirrhosis, which is complicated by HCC in over 90% of cases (23). According to a study it is widely known that liver cirrhosis of various etiologies is associated with an increased risk of developing HCC (10). Another study discovered that in patients with liver cirrhosis, hepatic- carcinogenesis is thought to be a primary cause of postoperative recurrence of de novo hepatocellular carcinoma (12).

In general Area under Curve (AUC) has value ranges from 0-1 for Receiver Operating Curve (ROC) curve. A value of 0.5 represents 50% of probability for correctly ranking random positive and negative examples. A value of 0.7 represents 70% of probability which means positive and negative with rank the positive is higher than the negative. A value of 0.8 and 0.9 represent excellent positive results.

According to my study results, AUC of a ROC curve analysis shows 0.4 value (less than 0.5) for cirrhotic nodules which means a true negative value while AUC for HCC nodules shows a value of 0.9 which means a true positive results.

In this study an Independent t- test is also applied. Out of 63 patients with cirrhotic nodules 33 patients have density and enhancement of cirrhotic nodules on CT while 30 patients don't have density and enhancement. Std. deviation of 33 is 0.478 while the other 30 patients have std. Deviation of 0.406 while out of 63 patients 54 patients have density and enhancement of hcc nodules on CT while 9 patients don't have density and enhancement. Mean and std.deviation of 21 samples are 2.9048 and 0.30079 respectively. While the other 9 patients have mean and std. Deviation of 2.111 and 0.33333 respectively.

A retrospectively study, assessed a contrast-enhanced CT dataset of 40 patients with three subject groups: healthy patient 14, cirrhosis 12 patients, and cirrhosis with HCC 14 patients. A unique approach was created and compared with the most advanced deep learning-based technology for the automatic 3D segmentation of liver utilizing modified region- growing segmentation technique. This study shows that CT is a good modality for picking up the HCC nodules (17).

According to my study AUC has value of 0.4 for Cirrhotic nodules and 0.9 value for HCC nodules which means cirrhotic nodules have true negative results while HCC nodules have true positive or excellent results on ROC curve. ROC curve represents that CT scan distinguished the HCC nodules better than the cirrhotic nodules.

In this study Lenene test shows the significance value of 0.019 and degree of freedom is 61.The t-test for equality of means shows the significance value of 0.120 and 0.241.The confidence interval is 95% (0.05) for

cirrhotic nodules while the significance value of 0.80 for HCC nodules and degree of freedom is 28. The t-test for equality of means shows the significance value of <0.001 and <0.001.The confidence interval is 95% (0.05). This study shows that the P. value is significance for HCC nodules while not significant for cirrhotic nodules.

CONCLUSION

Tri- phasic computed tomography has good diagnostic accuracy for hepatocellular carcinoma nodules as compared to cirrhotic nodules. This study improves the financial status of our country because CT is a costly modality. This study aligns with united nation sustainable development goal number 08 (decent work and economic growth).

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