

COMPARISON OF DYNAMIC THREE PHASE COMPUTED TOMOGRAPHY VERSUS DELAYED PHASE IMAGING IN HEPATOCELLULAR CARCINOMA DIAGNOSED ON HISTOPATHOLOGY

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Background

Dynamic Computed Tomography uses a large bolus of injection of contrast material for the evaluation of hepatocellular carcinoma (HCC). In dynamic CT there are multiple phases which are without contrast, arterial, venous and delayed.

Objective

To compare the dynamic three phase computed tomography versus delayed phase imaging hepatocellular carcinoma diagnosed on histopathology.

Methods

All patients with histopathological proven HCCA, referred to radiology department for multiphase CT before treatment with abdominal pain, raised alpha-fetoprotein blood levels, hcv + from past 5-10 years, ultrasound finding suggestive of liver mass, weight loss, both genders, with age group is between 45 to 80 years.

Results

The study group consisted of 44 patients. There are 31 male and 13 females with an age range 45–80 years and the mean age is 61 years, with known history of hepatitis and the duration of hepatitis was divided into five groups; 5 years, 6 years, 8 years, 9 year, and 10 years. The number of patients who suffered hepatitis was 3 from five years, and 4 from six years, 6 from eight years, 1 from nine years and thirty from ten years, 32 patients were diagnosed malignant or suspicious lesion on ultrasound while 12 was not detected on ultrasound for any malignancy in liver. On arterial phase of contrast 41 numbers of lesions appeared as hyper-attenuated while 3 lesions were hypo-attenuated. On venous phase of contrast only 3 lesions appeared hyper attenuated while 41 was

hypo attenuated. On delayed phase of contrast only 3 lesions were hyper-attenuated, 37 was hypo-attenuated while 4 was Iso- attenuated. All lesions were iso-attenuated on without contrast and in arterial phase of contrast 93.2 % of the results were hyper-attenuation while in both of the measures i.e. venous or delayed had 3 results of hyper-attenuation marking 100% similarity. And hypo-attenuation among both procedures is 90% similar. In without contrast all lesions was iso-attenuated while in arterial phase hyper-attenuated in lesions was dominant. In venous phase hypo-attenuated in lesions was dominant. While the results of delayed phase of contrast was almost similar to the venous phase.

Conclusion

Arterial phase is considered as better than the without contrast, portal venous and delayed phase imaging for the evaluation of hepatocellular carcinoma because arterial phase shows more lesions with more hypervasucular involvement, than the portal venous and delayed phases images with more hyper attenuation appearance. While the venous phase and the delayed phase imaging is similar in the washout appearance of lesion.

Key Words

Hepatocellular carcinoma, Computed Tomography.

Introduction

Hepatocellular carcinoma is a primary liver malignancy with hepatocellular differentiation. It is the 5th most common type of malignancy and one of the leading causes of cancer caused deaths worldwide. In 2013 a total of 30640 primary liver cancers and 21670 deaths due to liver cancer were recorded. A male to female ratio for the occurrence of HCC is 2.4:1. Areas of higher incidence include Eastern and Southern Asia, Middle and Western Africa, Melanesia and Polynesia. Hepatocellular carcinoma is now the third leading cause of cancer deaths worldwide, with over 500,000 people affected. The incidence of hepatocellular carcinoma is highest in Asia and Africa, where the high prevalence of hepatitis B and hepatitis C strongly predisposes to the development of chronic liver disease and subsequent development of hepatocellular carcinoma. The presentation of hepatocellular carcinoma has evolved significantly over the past few decades. While, in the past, hepatocellular carcinoma generally presented at an advanced stage with right upper quadrant pain, weight loss, and signs of decompensate liver disease. Hepatocellular carcinoma is now increasingly recognized at a much earlier stage as a consequence of the routine screening of patients with known cirrhosis, using cross-sectional imaging studies and serum alpha-fetoprotein measurements. HCC most often occurs in patients suffering with chronic liver disease, cirrhosis, chronic viral hepatitis B or C and alcohol related liver disease.¹

The natural history of HCC is variable, but it is often an aggressive tumor associated with poor survival without treatment²

Epidemiologic features of HCC include many factors such as dynamic temporal trends; visible variations among geographic regions, racial and ethnological groups, a defined men and women

ratio; and the presence of many well-documented environmental potentially preventable risk factors. Alongside, a growing understanding of the mechanism happening on the molecular level that is responsible for inducing hepatocarcinogenesis which most likely never occurs in a healthy functioning liver, but the cancer risk increases sharply in response to chronic liver injury or presence of cirrhosis. Understanding these epidemiologic factors and molecular mechanisms associated with HCC can improve our current concepts for treatment of the disease³.

High prevalence of hepatitis B and hepatitis C are strong predisposing factors in developing chronic liver disease and ultimately developing hepatocellular carcinoma. HCC is currently the major cause of deaths in patients with compensated cirrhosis and the mortality rate of hepatocellular carcinoma with association to cirrhosis is rising whereas non-cancerous complications of cirrhosis are decreasing or somehow stable. Alongside cirrhosis hepatitis C virus infection is associated with the highest incidence hepatocellular carcinoma in patients with underlying cirrhosis. 25% of patients diagnosed with HCC do not have any medical history of cirrhosis or other factors responsible. Most of the patients diagnosed with HCC with cirrhosis are 60 or more years of age and of 20-40 years without cirrhosis. Aflatoxins, alcohol consumption, cigarette smoking, non-alcoholic fatty liver disease, hemochromatosis and chronic liver disease are some of the major risk factors inducing hepatocellular carcinoma. Approximately 90% of hepatocellular carcinomas are due to some known underlying aetiology, the most common ones are chronic viral hepatitis B and C, alcohol consumption and exposure to aflatoxins. The available modalities for HCC screening include both serologic markers and radiographic tests. The imaging tests most commonly used for the diagnosis of HCC include ultrasonography (US), multiphase computed tomography (CT), and magnetic resonance imaging (MRI) with contrast.⁸ CT triphasic scan is an acknowledged non-invasive imaging technique and can be used as first line imaging modality for differentiating focal liver lesions especially hepatocellular carcinoma. In triphasic computed tomography hepatocellular carcinoma enhances during the arterial phase because of its blood supply from abnormal hepatic arteries. Contrast medium in the surrounding liver parenchyma is diluted during this phase because the parenchyma blood supply arises mostly from the portal veins, which are not yet opacified. In the portal venous phase, the surrounding liver parenchyma becomes relatively hyper-attenuated and the lesion is perceived to be hypo-attenuated because of its lack of portal venous supply. The characteristic imaging appearance of hepatocellular carcinoma is its enhancement pattern in arterial phase hyper-enhancement and venous or delayed phase washout.⁹ LIRADS (Liver Image Reporting and Data System) supports the use of multiphase computed tomography and magnetic resonance imaging for diagnosis of HCC along with contrast enhance ultrasound. These have improved the diagnostic accuracy of the disease.

Methods

Arterial phase of contrast in Computed Tomography: This is the phase when the contrast is in the arteries and has not enhanced the organs and other soft tissues usually achieved at 15-20

sec of post contrast injection or immediately after bolus tracking⁴. Hepatic artery is the primary feeder to the HCC. It is important to optimize the protocol of imaging based upon the characteristic arterial phase enhancement of HCC with hyper enhancement or wash in phase³⁹.

Venous phase of contrast in Computed Tomography: In this phase the liver parenchyma enhances through blood supply by the portal vein and some enhancement of the hepatic veins usually achieved at 60-70 sec of post contrast injection with wash out .⁸

Delayed phase of contrast in Computed Tomography: There is wash out of contrast in all structures also known as except "equilibrium phase" usually achieved after 5-10 minutes of contrast injection with wash out¹⁰.

Results

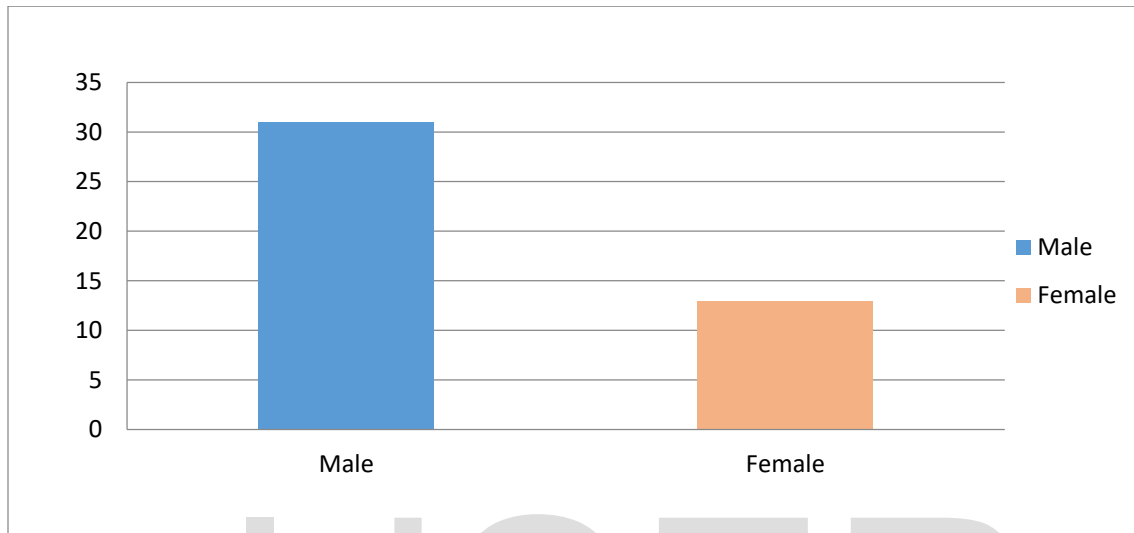
The age range of participants was minimum 45 years and maximum was 80 years with the mean age of 61.16 ± 9.57 (SD).

	Frequency	Percent	
Valid	Male	31	70.5
	Female	13	29.5
	Total	44	100.0

Table: 1. Age of participants

Out of 44 patients there were total 31 male (70.5 %) and 13 females (29.5%) patients.

Gender of participants



All 44 patients were suffering with history of hepatitis C + and the percentage of hepatitis c duration within five years was of 6.8 %, six year was of 9.1 %, 8 years was of 13.6%, 9 years was of 2.3 % and of ten years was 68.2 %.

. But in 19 cases (57.6) % shows less enhancement as compare to post contrast T2 FLAIR weighted images, in remaining 8 cases (24.2) % both sequences do not reveal any abnormality so considered as equal.

Duration (Years)	Frequency	Percent
5	3	6.8
6	4	9.1
8	6	13.6
9	1	2.3
10	30	68.2
Total	44	100.0

Table: 2. Duration of Hepatitis C

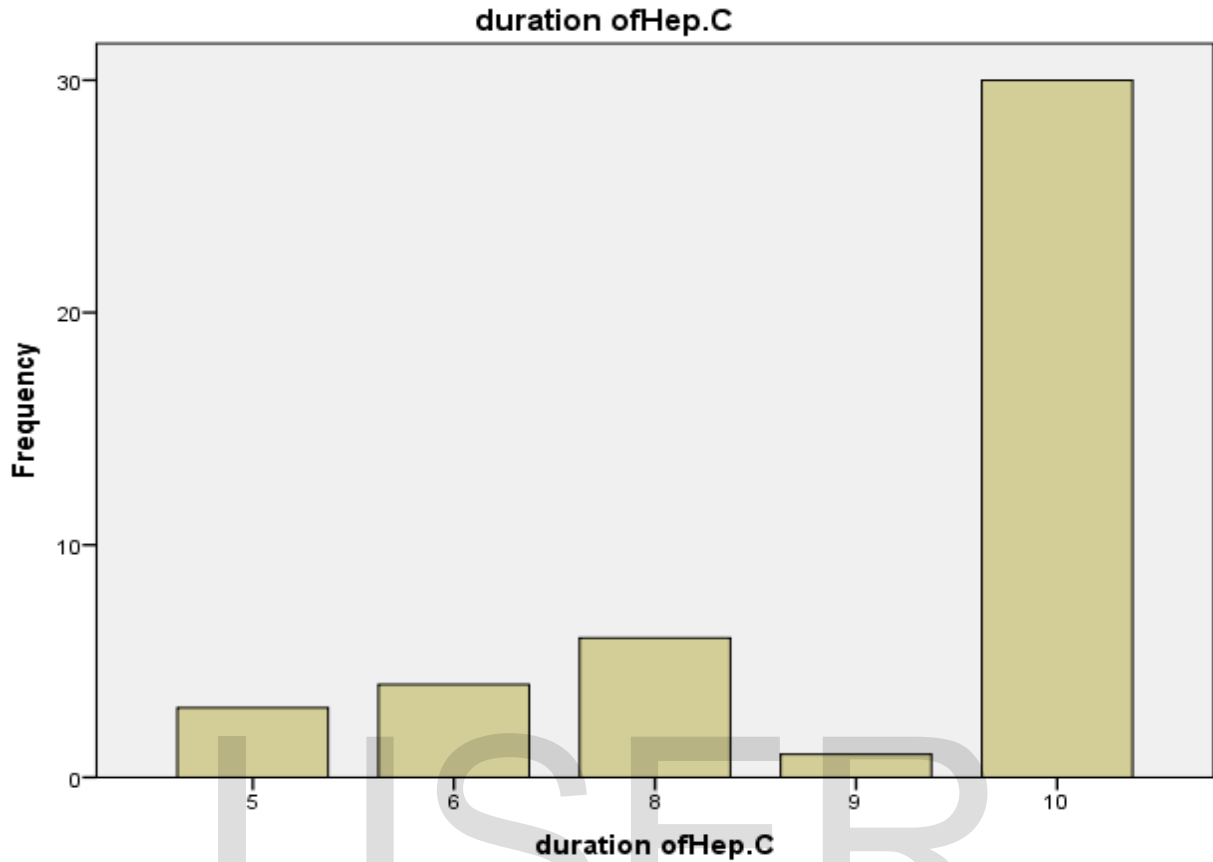


Chart: 2. Duration of Hepatitis C

Out of total 44 patients, 32 (72.7%) patients were diagnosed with mass on ultrasound while 12 patients (27.3%) were not diagnosed on ultrasound.

	Diagnosis	Frequency	Percent
Valid	-	12	27.3
	+	32	72.7
	Total	44	100.0

Table: 3. Ultrasound mass

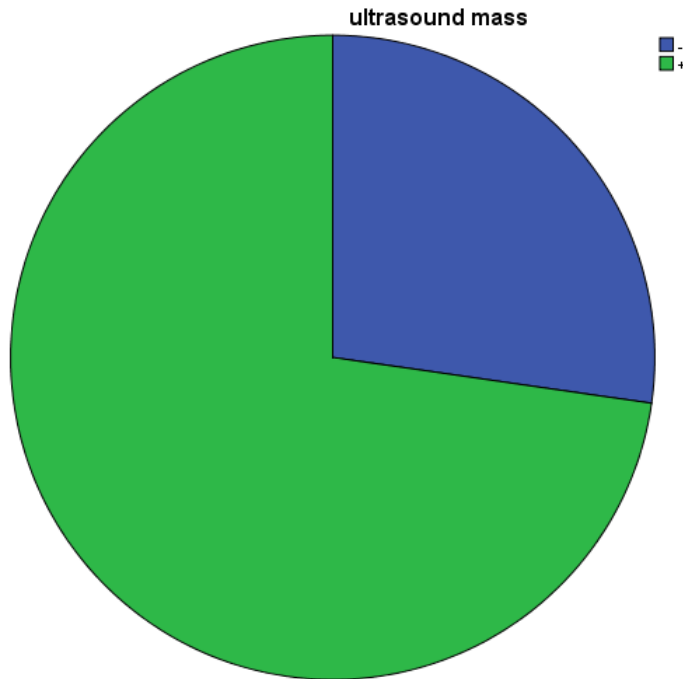


Chart: 3. Ultrasound mass

Out of 44 patients with known history of hepatitis c, 32 (72.7%) patients were reported to have mass in their ultrasound while 12(27.3) patients were negative on their ultrasound.

		ultrasound mass		Total
		-	+	
hepatitis c	+	12	32	44
Total		12	32	44

Table: 4. Hepatitis c * ultrasound mass Cross-tabulation

There were 25 (56.8%) multiple lesions while 19 (43.2%) single lesion.

Lesions		Frequency	Percent
Valid	multiple lesion	25	56.8
	single lesion	19	43.2
	Total	44	100.0

Table: 5. No. of lesion

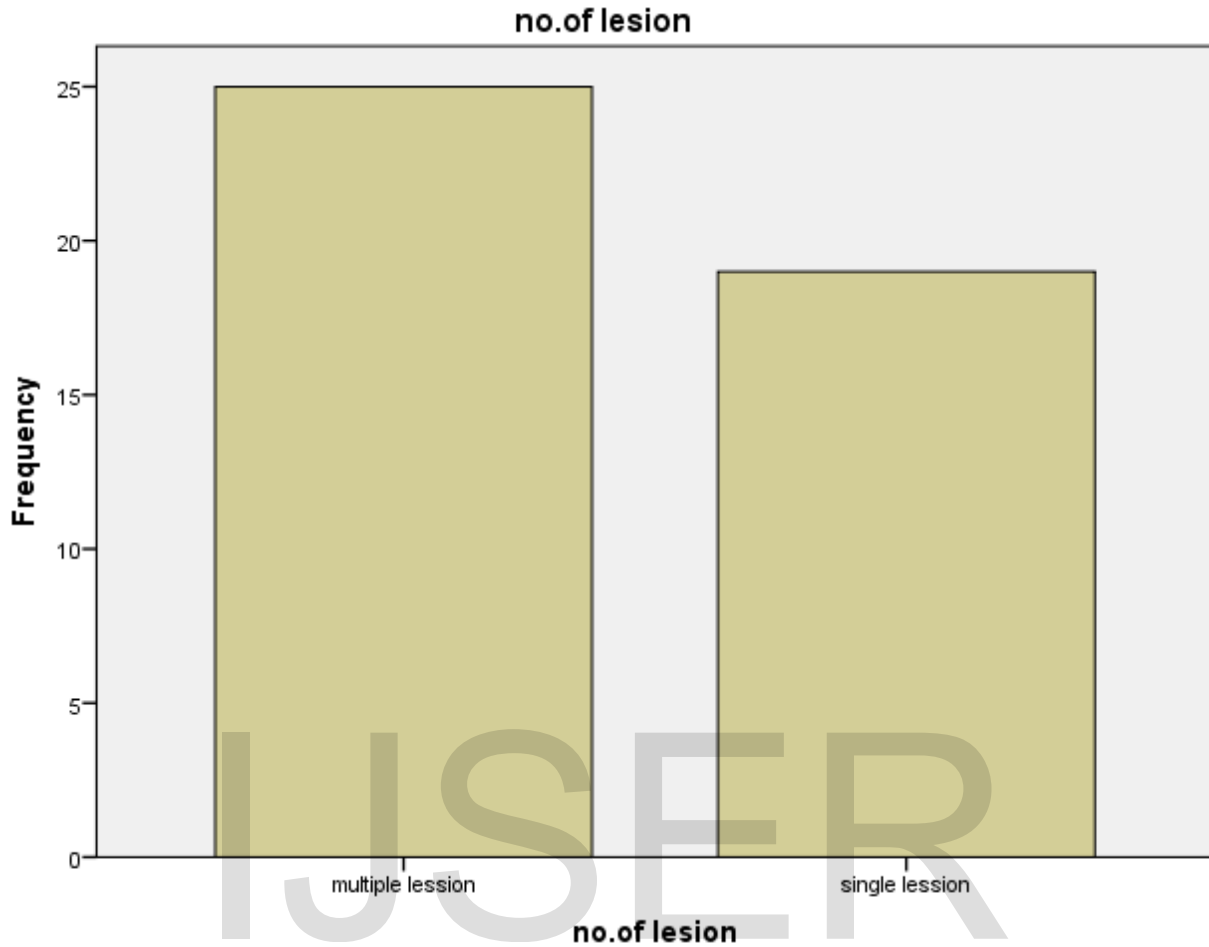


Chart: 4. No. of lesion

On arterial phase of contrast 41 (93.2%) number of lesions appeared as hyper-attenuated while 3 (6.8%) lesions was hypo-attenuated.

	Attenuation	Frequency	Percent
Valid	Hyperattenuated	41	93.2
	Hypoattenuated	3	6.8
	Total	44	100.0

Table: 6. Arterial Phase of CT.

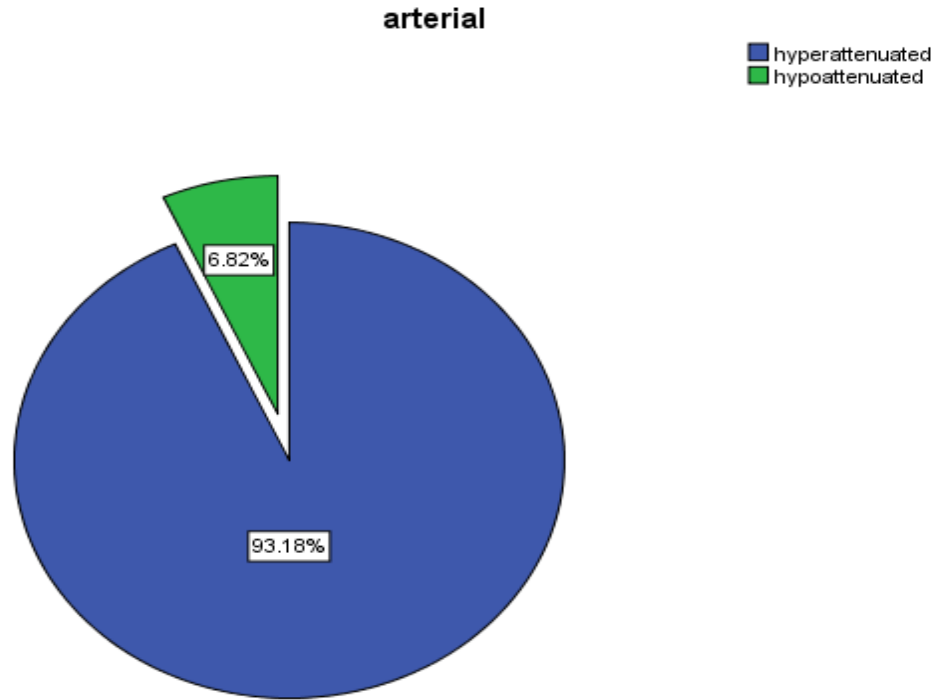


Chart: 5. Arterial Phase of CT.

On venous phase of contrast only 3 (6.8%) lesions appeared hyper attenuated while 41 (93.2%) was hypo attenuated.

	Attenuation	Frequency	Percent
Valid	Hyperattenuated	3	6.8
	Hypoattenuated	41	93.2
	Total	44	100.0

Table: 7. venous phase of CT.

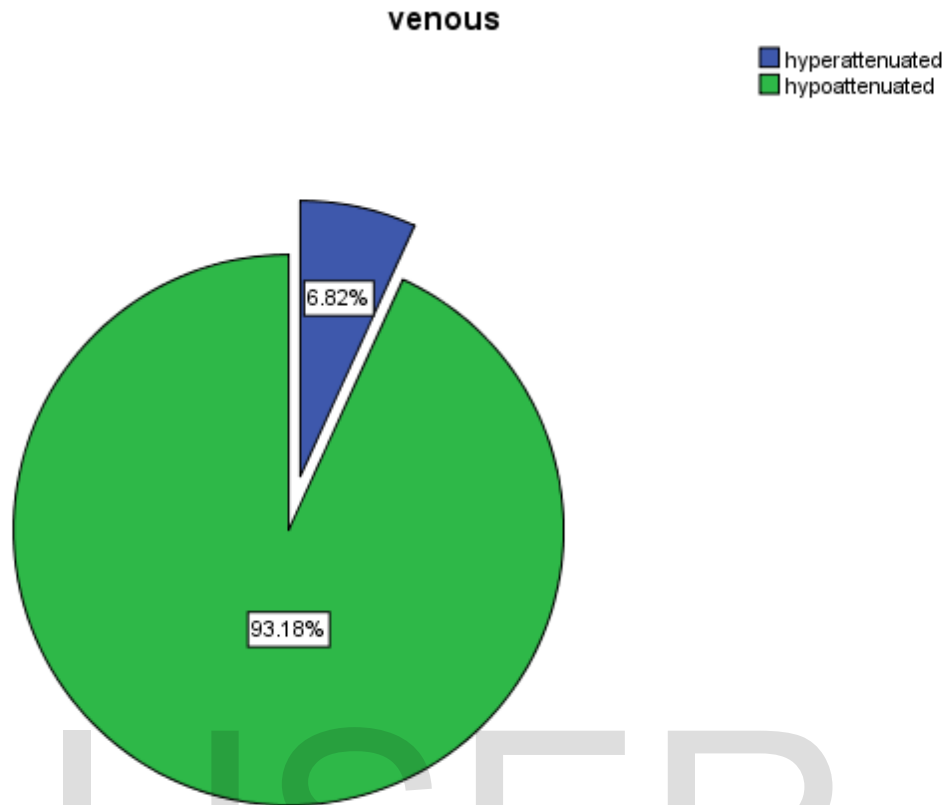


Chart: 6 venous phase of CT

On delayed phase of contrast only 3 (6.8%) lesions was hyper-attenuated, 37 (84.1%) was hypo-attenuated while 4 (9.1%) was iso- attenuated.

Attenuation		Frequency	%
Valid	hyperattenuated	3	6.8
	hypoattenuated	37	84.1
	isoattenuated	4	9.1
	Total	44	100.0

Table: 8. Delayed phase of CT.

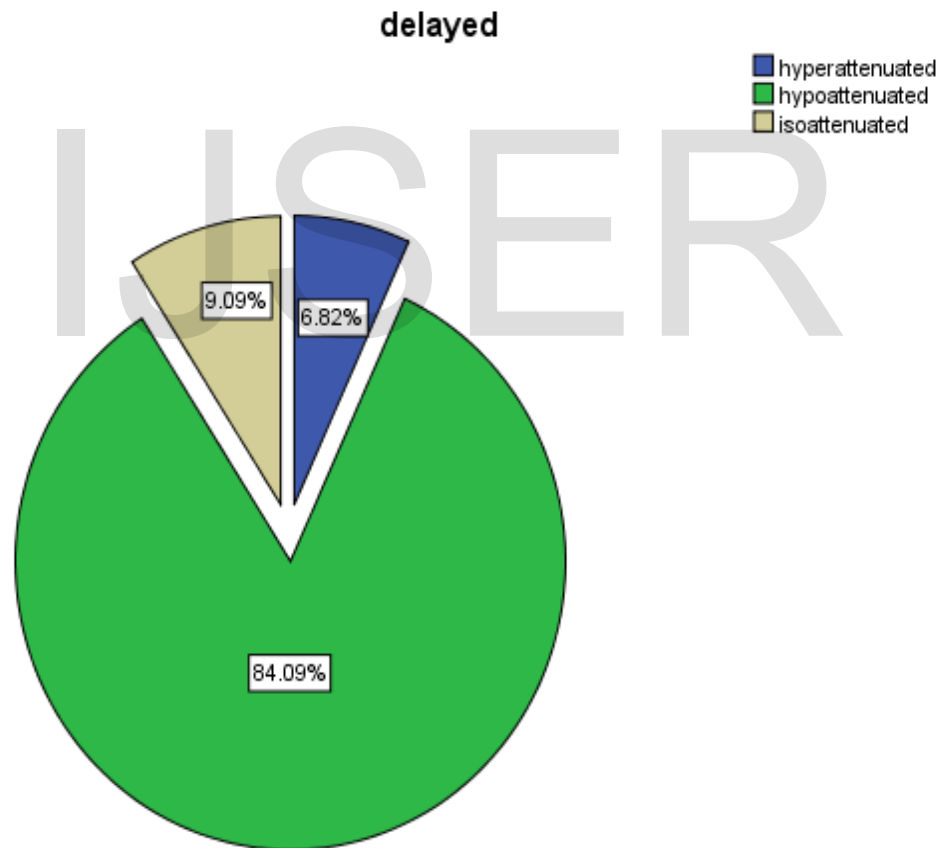


Chart: 7. Delayed phase of CT.

The graphs show that all lesions were iso-attenuated in without contrast and in arterial phase of contrast 93.2 % of the results were hyper-attenuation while in both of the measures i.e. venous or delayed had 3 results of hyper-attenuation marking 100% similarity. And hypo-attenuation among both procedures was 90% similar (41, 37).

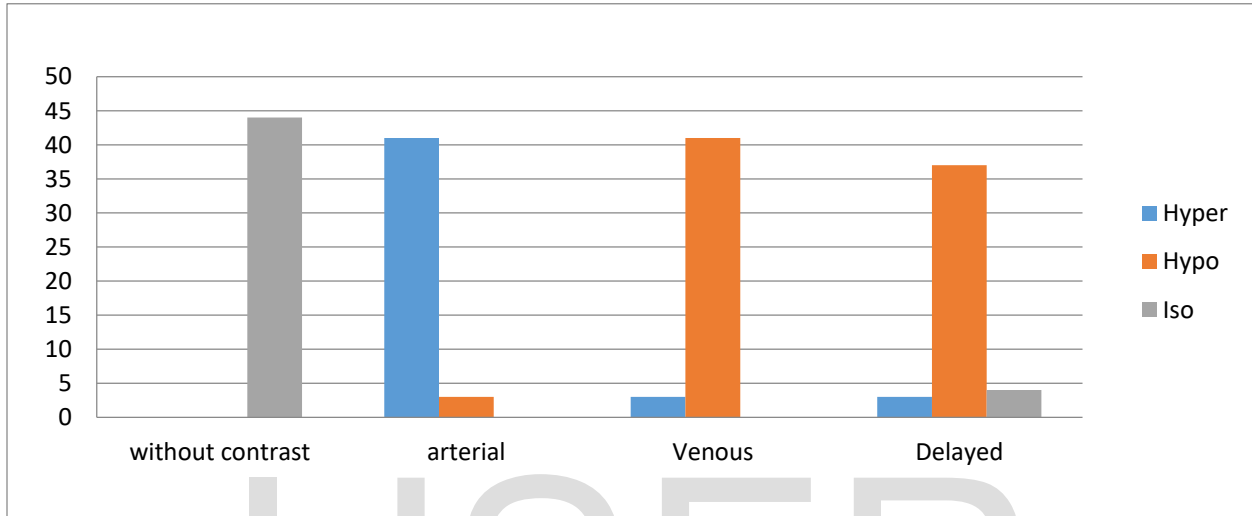


Chart: 8. Comparison of phases of dynamic CT & Delayed phase.

Summary of phases		
Arterial		
	Count	Percentage
hyper	41	93.2
hypo	3	6.8
iso	-	-
Venous		
	Count	Percentage
hyper	3	6.8
hypo	41	93.2
iso		
Delayed		
	Count	Percentage %
hyper	3	6.8
hypo	37	84.1
iso	4	9.1

Table: 9. Summary of Phases.

In arterial phase hyper-attenuated in lesions was dominant. There were 31(70.5%) males and 13 (29.5%) females.

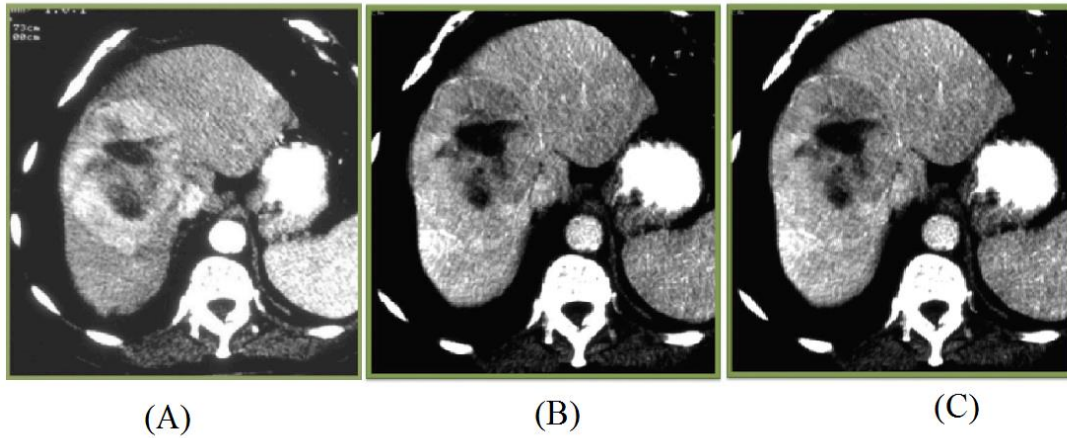


Figure 2:(A) Hepatocellular Carcinoma Displayed in the Arterial Phase Enhancement
(B)Hepatocellular Carcinoma Displayed in the Portal Phase Enhancement (C)Hepatocellular
Carcinoma Displayed in Late Phase Enhancement.¹⁶

Discussion

			gender of participants		Total
			Male	Female	
Arterial	Hyperattenuated	Count	30	11	41
		% within arterial	73.2%	26.8%	100.0%
	Hypoattenuated	Count	1	2	3
		% within arterial	33.3%	66.7%	100.0%
Total	Count	31	13	44	
	% within arterial	70.5%	29.5%	100.0%	

Table: 10. Arterial phase of CT * gender of participants Cross-tabulation

In venous phase hypo-attenuated in lesions was dominant. There were 31(70.5%) males and 13 (29.5%) females.

			gender of participants		Total
			Male	Female	
Venous	Hyperattenuated	Count	3	0	3
		% within venous	100.0%	.0%	100.0%
	Hypoattenuated	Count	28	13	41
		% within venous	68.3%	31.7%	100.0%
Total	Count	31	13	44	
	% within venous	70.5%	29.5%	100.0%	

Table: 11. Venous * gender of participants Cross-tabulation

Conclusion

Arterial phase is considered as better than the portal venous and delayed phase images in the detection of hepatocellular carcinoma because arterial phase shows more lesions than the portal venous and delayed phase images with more hyper attenuation appearance of lesions. Venous and delayed imaging shows similar results, so adding a delayed phase to dynamic CT is not much beneficial it just adds extra phase, radiation exposure with increase in time of imaging and cost of scan as well.

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References

1. Balogh J, Victor D, 3rd, Asham EH, Burroughs SG, Boktour M, Saharia A, et al. Hepatocellular carcinoma: a review. *Journal of hepatocellular carcinoma*. 2016;3:41-53.
2. Chou R, Cuevas C, Fu R, Devine B, Wasson N, Ginsburg A, et al. Imaging techniques for the diagnosis of hepatocellular carcinoma: a systematic review and meta-analysis. *Annals of Internal Medicine*. 2015;162(10):697-711.
3. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. *Gastroenterology*. 2007;132(7):2557-76.
4. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. *Gastroenterology*. 2004;127(5):S35-S50.
5. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *Journal of hepatology*. 2018;69(1):182-236. (peter R Galle, A. F.-I. (2018). EASL clinical guideline: Management of hepatocellular carcinoma. *journal of hepatology*, 182-236.
6. O'Connor S, Ward J, Watson M, Momin B, Richardson L. Hepatocellular Carcinoma-United States, 2001-2006. *Morbidity and Mortality Weekly Report*. 2010;59(17):517-20.
7. Fagrezos D, Lama N, Maniatis P, Triantopoulou C, Papailiou J, editors. Typical and atypical imaging of hepatocellular carcinoma 2016: European Congress of Radiology 2016.
8. Ibrahim AKA, Ayad CE. Triphasic Computed Tomography Hounsfield and Pattern in Differentiation of Focal Liver Lesions.
9. McEvoy SH, McCarthy CJ, Lavelle LP, Moran DE, Cantwell CP, Skehan SJ, et al. Hepatocellular carcinoma: illustrated guide to systematic radiologic diagnosis and staging according to guidelines of the American Association for the Study of Liver Diseases. *Radiographics*. 2013;33(6):1653-68.
10. Wald C, Russo MW, Heimbach JK, Hussain HK, Pomfret EA, Bruix J. New OPTN/UNOS policy for liver transplant allocation: standardization of liver imaging, diagnosis, classification, and reporting of hepatocellular carcinoma. *Radiological Society of North America, Inc.*; 2013.
11. Navin PJ, Venkatesh SK. Hepatocellular Carcinoma: State of the Art Imaging and Recent Advances. *Journal of clinical and translational hepatology*. 2019;7(1):72.
12. D, j. (2019, September 10). hepatocellular carcinoma-general. Retrieved september 18th, 2019, from [pathologyoutlines.com](http://www.pathologyoutlines.com/): <http://www.pathologyoutlines.com/topic/livertumorHCC.html>

13. Inayoshi J, Ichida T, Sugitani S, Tsuboi Y, Genda T, Honma N, et al. Gross appearance of hepatocellular carcinoma reflects E-cadherin expression and risk of early recurrence after surgical treatment. *Journal of gastroenterology and hepatology*. 2003;18(6):673-7.
14. McEvoy SH, McCarthy CJ, Lavelle LP, Moran DE, Cantwell CP, Skehan SJ, et al. Hepatocellular carcinoma: illustrated guide to systematic radiologic diagnosis and staging according to guidelines of the American Association for the Study of Liver Diseases. *Radiographics*. 2013;33(6):1653-68.
15. Karahan O, Yikilmaz A, Isin S, Orhan S. Characterization of hepatocellular carcinomas with triphasic CT and correlation with histopathologic findings. *Acta Radiologica*. 2003;44(6):566-71.
16. Fagrezos D, Lama N, Maniatis P, Triantopoulou C, Papailiou J, editors. Typical and atypical imaging of hepatocellular carcinoma 2016: European Congress of Radiology 2016.

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