# PREDICTING THE GRADES OF OESOPHAGEAL VARICES IN HCV CIRRHOTIC PATIENTS

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# **ABSTRACT**

**Introduction:** oesophageal varices is one of the most common and life threatening complications of liver cirrhosis. the need for use of non invasive modalities for its prediction rather than endoscopy is important to decrease burdens and increase patient compliance.

**Aim:** to predict oesophageal varices presence by fibroscan and possible grading by degree of liver stiffness in Hepatitis C Virus related cirrhotic patients.

**Methods:** the study was carried out on 150 patients with HCV related liver cirrhosis attending Ministry of Health outpatient clinics and hospitals after being writtenly consented that they agreed to participate in this study

All patients were subjected to full history taking & thorough clinical examination, full laboratory investigations include complete blood picture, liver profile tests, kidney function tests, abdominal ultrasound, liver stiffness measurement by fibroscan and upper GIT endoscopy.

The patients were divided according to upper GIT endoscopy results into three groups. Group 1: included 50 patients with liver cirrhosis and without oesophageal varices. Group 2: included 50 patients with liver cirrhosis and small oesophageal varices (Grade I&II). Group 3: included 50 patients with liver cirrhosis and large esophageal varices (Grade III & IV).

**Results:** there was a statistically significant increase in liver stiffness, INR, total bilirubin, ammonia level and spleen size among patients with ov than those without and among those with large varices than those with small varices, while there was a statistically significant decrease in the level of Hb

level, platelet count and serum albumin level among patients with varices than those without and among patients with large varices than those with small varices.

**Conclusion:** liver stiffness measurement by Transient Elastography could be used as a valuable non-invasive screening tool for the prediction of the presence and size of oesophageal varices in HCV cirrhotic patients.

Key words: Oesophageal varices; Fibroscan; Grading; Non-invasive methods

#### INTRODUCTION

Cirrhosis is a consequence of almost all progressive chronic liver diseases, approximately 10%-20% of patients with chronic hepatitis C virus infection have cirrhosis at first clinical presentation, and as many as 20%-30% of those who don't have cirrhosis will eventually develop this condition and its complications within one or more decades (Ikeda *et al.*, 1998).

Development of oesophageal varices is a major complication that may occur in up to 90% of cirrhotic patients (Jensen 2002). Esophageal varices may lead to variceal bleeding that is a life threatening event that has an incidence of 5% in patients with small oesophageal varices and up to 15% in those with large esophageal varices. Mortality per bleeding episode is around 10%- 20% (Carbonell *et al.*, 2004). Therefore, The current screening method is endoscopy at 2-3 years in patients without esophageal varices and at 1-2 years in those with small varices, this approach is invasive. That is why selection of patients with large esophageal varices at high risk for bleeding has become an issue of growing importance screening for esophageal varices in cirrhotic patients is a strong recommendation in all consensus statement (De Franchis 2005). In this respect, several clinical, biological, ultrasonographic and elastrographic (Transient Elastography-TE) methods

have been proposed (and some of them were validated) as non-invasive alternatives to endoscopy (De Franchis et al., 2008). This work was designed to study the validity of liver stiffness measurement by fibroscan to predict the presence of oesophageal varices in cirrhotic patients due to hepatitis C virus infection (Primary aim) and to determine the association between grades of esophageal varices and the degree of liver stiffness measured by fibroscan.

#### PATIENTS AND METHODS

This is a cross sectional study performed on 250 patients in the period from April 2015 to September 2018. Diagnosis of liver cirrhosis was based on history, clinical, laboratory and radiological data. Only 150 patients who met the inclusion criteria were recruited after being consented to participate in the study after fulfilling the following criteria:

Inclusion criteria: 1- Adult patients ≥ 18 years, 2-Hepatitis C virus infection, 3- Liver cirrhosis without moderate or massive ascites, mild pelvic ascites could be recruited, 4- no history of upper GIT bleeding or hepatocellular carcinoma and 5- BMI <35.

exclusion criteria for the recruited patients: 1- Patients age <18 years, Other causes of liver cirrhosis except HCV, 2- BMI > 35, 3- Liver cirrhosis with moderate or massive ascites, 4- History of upper GIT bleeding or hepatocellular carcinoma, 5-Patients with abdominal collaterals in abdominal ultrasound. Patients were classified into three Groups: Group 1: included patients with liver cirrhosis and without esophageal varices. Group 2: included patients with liver cirrhosis and small esophageal varices (Grade

I&II). Group 3: included patients with liver cirrhosis and large esophageal varices (Grade III & IV).

After getting a written consent from all patients, they were asked to undergo the following:

- I- Full history taking with special emphasis on previous history of Schistosomiasis, history of viral hepatitis or exposure to risk factors (such as anti-Schistosomiasis injections, blood transfusion or previous surgical operations), history of jaundice, disturbed conscious level, bleeding tendency, hematemesis or melena.
- II- Full clinical examination for stigmata of liver cell failure or signs of portal hypertension was obtained.

# III. Laboratory investigations included

Complete blood count, serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), total bilirubin, serum albumin, INR, Alphafeto protein and HCV Ab & Child-Paugh score.

In the 1960's Child-Pugh Score classification system was developed by Child and Turcotte to assess the likelihood of mortality in cirrhotic patients.

The score employs five clinical measures of liver disease. Each measure is scored 1–3, with 3 indicating most severe derangement (Cholongitas *et al.*, 2005).

Parameter	Score						
rarameter	1	2	3				
Ascites	None	Mild	Moderate or Severe				
Encephalopathy (grade)	None	1-2	3-4				
Bilirubin (mg/dL)	<2	2–3	>3				
Albumin (g/dL)	>3.5	2.8-3.5	<2.8				
INR	<1.7	1.8-2.3	>2.3				

### Interpretation of Child-Pugh score:

Child- Pugh grade	Child-Pugh Score		1 Year Survival	5 year Survival	10 year Survival
A	5-6	Indicates a well- functioning liver	84 %	44 %	27 %
В	7-9	Indicates significant functional compromise	62 %	20 %	10 %
С	10-15	Indicates decompensation of the liver	42 %	21 %	0 %

**IV. Abdominal ultrasonography:** Using real time scanning device Toshiba, Aplio MX with convex probe, 3-5uHz to detect the presence of liver cirrhosis(irregular surface, coarse texture, attenuated hepatic veins), Signs of portal hypertension (presence of abdominal collaterals, splenomegaly), ascites and to exclude hepatic focal lesion.

**V. upper Gastrointestinal endoscopy:** Using Olympus GIF 160-Q165 (EXERA II), to evaluate the presence and degree of varices in addition to any relevant upper GIT lesions.

Classification of oesophageal varices was done according to Thakeb classification (1988):

Grade I: Small straight cords of varices confined to the lower third of esophagus.

Grade II: Moderate sized clubbed varices, with well-defined areas of normal mucosa between them, forming several distinct variceal cords and confined to the lower half of the esophagus.

Grade III: Gross varices extending into the proximal half of the esophagus, normal mucosa might not be visible in between them unless the esophagus is fully distended with air

Grade IV: Varices like those of grade 3 but with dilated capillaries on top or in between them and encroaching on esophageal lumen.

- <u>VI. Liver Stiffness Measurement (LSM):</u> Using Fibroscan that was performed within days following or preceding upper GI tract endoscopy, the operators were not aware of the results of endoscopy.
- 1. Up to ten successful acquisitions were performed on each patient. Success rate was calculated as the ratio of the number of successful acquisitions over the total number of acquisitions.
- 2. The median value of successful measurements was kept as representative of the liver stiffness.
- 3. Only LSM obtained with 10 successful acquisitions and a success rate of at least 60% was considered reliable (Castera *et al.*, 2008).

The following shows the relation between Fibro scan reading in K Pascal and the stage of fibrosis (Vizzutti *et al.*, 2007).

F0	0 :2.9 KPa
F1	3 : 5.9KPa
F2	6 : 8.9KPa
F3	9:16.9KPa
F4	17: 75KPa

Pre-coded data was entered on the computer using "Microsoft Office Excel Software" 2010. Data was then transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analysed. Data was summarized using mean, standard deviation for quantitative variables and frequency, percentage for qualitative ones.

Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. Univariate and multivariate regression models were constructed to determine the significant independent predictors for the occurrence of OV, the grade of OV and occurrence of large OV. p values less than 0.05 was considered statistically significant.

# **RESULTS**

**Table (1):** comparison between patient with no varices group (1) and patients with small and large varices group (2) and (3) respectively:

Variabl		Group (1) no varices group	Group (2&3) Small and large ov			Sig.
, <b>41 14</b>		No. = 50	No. = 100			~- <b>8</b> ·
Δ	Mean±SD	$62.74 \pm 6.55$	$60.08 \pm 9.40$	1.704	0.075	NS
Age	Range	47 – 72	29 – 74	1./94	0.075	NS
Cov	Females	24 (48.0%)	50 (50.0%)	0.052	0.917	NS
Sex	Males	26 (52.0%)	50 (50.0%)	0.055	0.617	149
Creatinine	Mean±SD	$1.08 \pm 0.27$	$1.03 \pm 0.27$	1.010	0.210	NS
Creatinine	Range	0.5 - 1.44	0.5 - 1.44	1.019	0.310	IND
CI II D I	Child A	50 (100.0%)	41 (41.0%)			
Child Pugh	Child B	0 (0.0%)	41 (41.0%)	-1.780• 0.077 1.125• 0.262	HS	
score	Child C	0 (0.0%)	18 (18.0%)			
ACT	Mean±SD	$51.76 \pm 16.06$	$58.01 \pm 22.06$	1.700-	0.075 0.817 0.310 0.000 0.077 0.262 0.000 0.000 0.000 0.753 0.000 0.000 0.000	NS
AST	Range $32-92$ $22-112$ $-1.780^{\bullet}$ Mean±SD $41.56 \pm 18.50$ $38.06 \pm 17.68$ $1.125^{\bullet}$ Range $19-88$ $13-90$ $1.125^{\bullet}$ Mean±SD $1.26 \pm 0.20$ $2.04 \pm 0.54$ $-9.780^{\bullet}$	0.077	NS			
ALT	Mean±SD	$41.56 \pm 18.50$	$38.06 \pm 17.68$	1 125.	0.262	NS
ALI	Range	19 – 88	13 - 90	1.123•		110
INR	Mean±SD	$1.26 \pm 0.20$	$2.04 \pm 0.54$	0.790-	0.000	HS
IINK	Range	1 – 1.9	1.1 - 3.5	-9.780		115
Total	Mean±SD	$1.20 \pm 0.14$	$2.02 \pm 0.56$	10.212	0.000	HS
Bilirubin	Range	0.9 - 1.5	1.1 - 3.7	-10.212	0.000	113
Albumin	Mean±SD	$3.76 \pm 0.35$	$3.24 \pm 0.59$	-10.212•	0.000	HS
Albuillii	Range	3.1 – 4.8		3.743	0.000	пъ
Hemoglobin	Mean±SD	$11.66 \pm 0.87$	$10.35 \pm 1.27$	6.565•	0.000	HS
Tiemogroom	Range	9.3 – 13.2	7.8 - 13.2	- 1.794 0.0 - 0.053 0.8 - 1.019 0.3 - 48.626 0.0 - 1.780 0.0 - 1.125 0.2 - 9.780 0.0 - 10.212 0.0 - 5.745 0.0 - 0.315 0.7 - 9.020 0.0 - 11.005 0.0 - 0.024 0.9 - 10.609 0.0	0.000	110
TLC	Mean±SD	$4.47 \pm 1.07$	$4.41 \pm 1.15$	0.315•	0.817 0.310 0.000 0.077 0.262 0.000 0.000 0.000 0.753 0.000 0.981	NS
TLC	Range	2 – 6.5	1.8 - 6.5	- 0.053 - 1.019 - 48.626 -1.780• -1.125• -9.780• -10.212• 5.745• 6.565• 0.315• 9.020• -11.005• -0.024‡ -10.609•	0.755	110
Platelet count	Mean±SD	$137.84 \pm 21.67$	$96.83 \pm 28.24$	9.020•	0.000	HS
1 latelet count	Range	99 – 170	41 – 187	7.020	0.000	115
Ammonia	Mean±SD	$40.96 \pm 15.97$	$91.02 \pm 30.08$	-11 005•	0.000	HS
7 timinoma	Range	15 – 87	23 – 160	-11.005	0.000	пъ
AFP	Median(IQR)	4.10 (2.4 - 6)	4.00 (2.35 - 6.1)	-0.024*	0.981	NS
2 1 1	Range	1 – 10	1 – 10	0.0274	0.701	110
Spleen size	Mean±SD	$12.12 \pm 1.68$	$15.17 \pm 1.65$	-10 609•	0.000	HS
Spicen size	Range	8.7 – 15	12 - 20.1	10.007	0.000	110
Liver stiffness	Mean±SD	$26.62 \pm 6.05$	$52.82 \pm 13.80$	-12.801	0.000	HS
Liver summess	Range	17 – 39	33 – 75	12.001	0.000	115

NS: Non significant; S: Significant; HS: Highly significant

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, INR: International Normalised Ratio, TLC: total leucocytic count , AFP: Alphafetoprotein .

<sup>•:</sup> Independent t-test; ‡: Mann Whitney test

The previous table showed that there was no statistically significant difference between the different studied group as regard age , sex , creatinine level, AST,ALT,TLC and AFP . Child Pugh grade was statistically highly significant among patients with ov than patients without ov with p-value < 0.001. there was a high statistically significant increase in the level of INR, Total bilirubin , serum ammonia level , splenic size and fibro scan results among patients with small and large varices group (2) and (3) respectively than the patients with no varices in group (1)., while there was a high statistically decrease in the level of serum albumin , haemoglobin , and platelet count among patients of group (2) and (3) than among patients in group (1).

**Table (2):** Logistic regression analysis for predictors of presence of oesophageal varices

Predictors	P-value	Odda rotio (OD)	95% C.I.for OR			
Predictors	r-value	Odds ratio (OR)	Lower	Upper		
INR	0.000	12.093	11.163	14.341		
Total bilirubin	0.000	7.721	1.537	57.198		
Albumin	0.000	0.101	0.038	0.268		
Hemoglobin	0.000	0.367	0.252	0.535		
Platelet count	0.000	0.948	0.931	0.964		
Ammonia	0.000	1.082	1.056	1.108		
Fibro scan	0.000	2.052	1.411	2.984		
Spleen size	0.000	4.140	2.532	6.770		

INR: International Normalised Ratio

The previous table shows that all the previous studied parameters were found in a highly statistically significant association with presence of oesophageal varices.

**Table (3):** Receiver operating characteristic curve (ROC) for the diagnostic accuracy of oesophageal varices predictors

predictors	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
INR	>1.51	0.932	84.000	96.000	97.700	75.000
Total bilirubin	>1.32	0.960	93.000	88.000	93.900	86.300
Albumin	≤ 3.2	0.773	49.000	96.000	96.100	48.500
Hemoglobin	≤ 10.4	0.797	57.000	94.000	95.000	52.200
Platelet count	≤ 111	0.878	80.000	82.000	89.900	67.200
Ammonia	>60	0.918	86.000	90.000	94.500	76.300
Liver stiffness measurment	>35	0.986	90.910	96.000	97.800	84.200
Spleen size	>13.7	0.913	81.000	86.000	92.000	69.400

INR: international normalised ratio

The previous ROC curve shows the best cut off point for each independent predictor of the presence of oesophageal varices with its sensitivity, specificity, positive predictive value, negative predictive value and area under curve (AUC). The table shows that the fibroscan level was found the best predictor for presence of oesophageal varices with the higher AUC of 98.6% .

**Table (4):** Relation of oesophageal varices size with laboratory data of the studied patients

Variable		Oesophageal varices Groups						Post Hoc Analysis by LSD		
		No varices Group (1) No. = 50	Small varices Group (2) No. = 50	Large varices Group (3) No. = 50	Test value	P- value	Sig.	P1	P2	Р3
	Mean±SD			$60.22 \pm 22.74$						
I AST	Range	$31.70 \pm 10.00$ 32 - 92	22 - 107	24 - 112	2.182•	0.116	NS	0.320	0.038	0.277
	U	$41.56 \pm 18.50$								
I ALT	Range	19 – 88	15 – 90	13 – 87	3.200•	0.044	S	0.888	0.036	0.025
	Mean±SD	$1.26 \pm 0.20$	$1.84 \pm 0.42$	2.24± 0.58	C4 962- 0	0.000	***	0.000		0.000
INR	Range	1 – 1.9	1.1 - 2.9	1.1 - 3.5	64.863•	0.000	HS	0.000	0.000	0.000
Total	Mean±SD	$1.20 \pm 0.14$	$1.88 \pm 0.45$	$2.15\pm0.62$	50.224	0.000	0 110	0.000	0.000	0.003
bilirubin	Range	0.9 - 1.5	1.1 - 3	1.2 - 3.7	59.324•	0.000	HS	0.000	0.000	0.003
Albumin	Mean±SD	$3.76 \pm 0.35$	$3.38 \pm 0.52$	$3.09\pm0.62$	21.063• 0.0	0.000	.000 HS	0.000	0.000	0.006
Albuilliii	Range	3.1 - 4.8	2.3 - 4.8	1.8 - 4.1		0.000		0.000	0.000	0.006
Hemoglobin	Mean±SD	$11.66 \pm 0.87$	$11.02 \pm 1.11$	$9.68 \pm 1.04$	49.636• 0.0	0.000	HS	0.002	0.000	0.000
Ü	Range	9.3 - 13.2	8.6 - 13.2	7.8 - 13	49.030	0.000				
TLC	Mean±SD	$4.47 \pm 1.07$	$4.47 \pm 1.07$	$4.35 \pm 1.23$	0.197•	0.821	NIC	NS 1.000	0.587	0.587
TLC	Range	2 - 6.5	2 - 6.5	1.8 - 6.5	0.197	0.621	110			
Platelet count	Mean±SD	137.84 ± 21.67	109.82 ± 28.12	$83.84 \pm 21.83$	62.986•	.986• 0.000 I	000 HS	0.000	0.000	0.000
Count	Range	99 – 170	65 – 187	41 – 143						
Ammonia	Mean±SD	40.96 ± 15.97	$77.16 \pm 29.40$	104.88 ± 23.91	91.126•	0.000	HS	0.000	0.000	0.000
	Range	15 - 87	23 - 132	76 - 160						
AFP	Median(IQR )			4.00 (2.3- 6.2)	0.237‡	0.888	NS	0.806	0.839	0.615
	Range	1 - 10	1 - 10	1 – 9						
Spleen size	Mean±SD Range	$12.12 \pm 1.68$ 8.7 - 15	$14.78 \pm 1.52$ $12 - 20.1$	$15.56 \pm 1.70$ $12.5 - 20.1$	60.824•	0.000	HS	0.000	0.000	0.019
ll stiffness	Mean±SD Range	$26.62 \pm 6.05 \\ 17 - 39$	$41.67 \pm 5.91 \\ 33 - 50$	$64.20 \pm 9.56  44 - 75$	327.040	0.000	HS	0.000	0.000	0.000

NS: Non significant; S: Significant; HS: Highly significant

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, INR: International Normalised Ratio, TLC: total leucocytic count, AFP: Alpha-fetoprotein.

The previous table shows that there was highly statistically significant decrease in the level of ALT, albumin, hemoglobin and platelet count with the increase of oesophageal varices size and also highly statistically significant increase in the level of INR, total bilirubin, ammonia level, spleen

<sup>•:</sup> One Way ANOVA test; ‡: Kruskal Wallis test.

size and fibroscan levels with the increase of oesophageal varices size while no statistically significant relation found with AST, TLC and AFP.

**Table (5):** Logistic regression analysis for predictors of size of oesophageal varices:

Predictors	P-value	Odds ratio (OR)	95% C.I.for OR		
Fredictors	r-value	Odds ratio (OK)	Lower	Upper	
ALT	0.028	0.973	0.949	0.997	
INR	0.001	4.770	1.943	11.711	
Total bilirubin	0.019	2.545	1.167	5.551	
Albumin	0.019	0.416	0.199	0.868	
Hemoglobin	0.000	0.314	0.191	0.516	
Platelet count	0.000	0.956	0.935	0.977	
Ammonia	0.000	1.041	1.021	1.061	
Liver stiffness	0.002	1.695	1.205	2.384	
measurement	0.002	1.075	1.203	2.304	
Spleen size	0.023	1.360	1.044	1.772	

ALT: alanine aminotransferase, INR: international normalized ratio.

The previous table shows that there was highly statistically significant association found between all the studied parameters and the size of oesophageal varices of the studied patients.

Table (6): ROC curve analysis for predictors of size of oesophageal varicies

Predictors	<b>Cut off point</b>	AUC	Sensitivity	Specificity	+PV	-PV
ALT	≤50	0.623	92.00	30.00	56.8	78.9
INR	>2.2	0.698	44.00	86.00	75.9	60.6
Total bilirubin	>2.45	0.618	32.00	90.00	76.2	57.0
Albumin	≤3	0.613	48.00	72.00	63.2	58.1
Hemoglobin	≤10.2	0.804	78.00	72.00	73.6	76.6
Platelet count	≤88	0.755	52.00	84.00	76.5	63.6
Ammonia	>75	0.744	100.00	46.00	64.9	100.0
Fibro scan	>50	0.981	89.80	100.00	100.0	90.9
Spleen size	>14.7	0.645	70.00	58.00	62.5	65.9

ALT: alanine aminotransferase, INR: international normalized ratio.

The previous ROC curve showed the best cut off point for each independent predictors of the size of oesophageal varicies of the studied patients with its sensitivity, specificity, positive predictive value, negative predictive value and area under curve (AUC). The table showed that the fibroscan level was found the best predictor to differentiate between small and large oesophageal varicies with the higher AUC of 98.1%

#### **DISCUSSION**

Bleeding from oesophago-gastric varices is the most important complication of cirrhosis (D'Amico *et al* ., 2006). The first crucial step in prevention is to identify the patients at risk for bleeding by endoscopic screening, in order to select them for prophylactic treatment (Garcia-Tsao *et al* ., 2007). Since a variable proportion of patients will not have varices; thus, screening all cirrhotic patients with upper GI endoscopy implies a number of unnecessary endoscopies, which increase the workload of endoscopy units. In addition, compliance with endoscopic screening recommendations may be limited (Berzigotti *et al.*, 2008). Predicting the presence of esophageal varices by non -invasive means would permit to restrict the performance of endoscopy to those patients with a high probability of having varices (Bureau *et al.*, 2008). The aim of this study was to predict the presence of esophageal varices by measurement of liver stiffness by fibroscan in cirrhotic patients due to hepatitis C virus infection and to determine the grade of esophageal varices by the degree of liver stiffness.

In the present study Child Pugh score was statistically significant higher in patients with esophageal varices (Groups 2-3) than those without

esophageal varices (Group 1) and this is in agreement with Madhotra *et al.*, (2002) who found a significant relation between presence of varices and increased Child score. Thus, the more advanced liver disease the more likely the presence of varices.

In the present study, platelet count was significantly lower in patients with esophageal varices-Group 2 & 3 ( mean =  $96.83 \pm 28.24$ ), than in patients without oesophageal varices –group 1 (mean = $137.84\pm21.67$ ), p value = 0.000. Platelet count may decrease for several reasons in patients with chronic liver disease. Madthora *et al.*, (2002) reported that 32% of the studied cirrhotic patients had platelet count less than 68000/mm3 without detectable splenomegaly; this might be explained by the insufficient synthesis of thrombopoietin. Other potential explanations for this phenomenon are presence of antithrombocytic antibodies and thrombocyte associated immunoglobulin, which can be found in the sera of patients with liver diseases (Winkfeld *et al.*, 2003). Thus the use of platelet count alone as a non-invasive predictor of esophageal varices can be misleading and cannot be solely attributed to portal hypertension. Indeed, the use of the platelet count/spleen diameter ratio bypasses this possible drawback since it "normalizes" platelet count to splenic sequestration (Giannini *et al.*, 2003).

As regard spleen size, we found that it was statistically significantly higher in patients with esophageal varices-Group 2 & 3 (mean = $15.17\pm1.65$ ) than those without oesophageal varices –group 1 (mean =  $12.12\pm1.68$ ), p-value =0.000, so measurement of splenic size by ultrasonography is

considered a non-invasive predictor indicator of the development of gastro-esophageal varices in liver cirrhosis (Khadka *et al.*, 2017).

In this study liver stiffness measurement was significantly higher in patients with esophageal varices (Groups 2 & 3) mean =  $52.82\pm13.80$  KPa than those with no varices (Group 1) ) mean = $26.62\pm6.05$  KPa , p-value <0.001; at the best cut off value >35 KPa ,AUC of 98.6%, sensitivity was 90.9%, specificity was 96% , also it was significantly higher in patients with large varices (group 3) mean =  $64.20\pm9.56$  KPa than in patients with small varices (Group 2) mean =  $41.67\pm5.91$  KPa ; at the best cut off value > 50 KPa , AUC of 98.1%, sensitivity of 89.8% and specificity of 100% .

In agreement with our results Sporea *et al.*, (2011), they studied 1000 patients with transient elastography for liver stiffness measurement and showed more or less equivalent cut off values (For the presence of varices, the optimal Fibroscan cut-off was 31 kPa and for bleeding cut-off was 50.7 KPa), according to Lebrec *et al.*, (1980); the larger the size of varices the higher risk of bleeding and according to Sporea *et al.*, (2011), study cut off value for transient elastography to predict risk of bleeding could be considered as cut off value for prediction of large varices. Moreover, studies carried out by Vizzutti *et al.*, (2007), a cut- off value for prediction of varices was 17.6 kPa, these cut off values are smaller than the values reported in this study, but the different demographics and patients characteristics as well as the type of fibroscan machines could be the reason for these discrepancy. More over Castera *et al.*, (2009) showed that Transient elastography could be a valuable tool in diagnosis of cirrhosis but cannot replace endoscopy for variceal screening On multivariate analysis of other non-invasive parameters

for the detection of presence of varices in current results, the fibroscan has the highest significant value which confirm the previous study carried by Kazemi et al., (2006). Accordingly, liver stiffness measurement by fibroscan is suggested as a simple non-invasive physical parameter, allows Identifying patients with well-compensated cirrhosis a large Group ineligible for variceal screening as having a low probability of bearing varices and particularly large varices, limiting therefore the indications of endoscopic screening. The use of fibroscan in the prediction as well as grading of esophageal varices could be very helpful on planning for the management of cirrhotic patients to prevent the morbidity and mortality developing from bleeding varices.

#### **CONCLUSION**

Liver stiffness measurement by fibroscan is valuable in predicting the presence of esophageal varices in patients with liver cirrhosis and of higher diagnostic value than other non- invasive parameters in predicting the size of esophageal varices. It may help to select patients for endoscopic screening.

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# قياس درجة حلابة الكبد بالفيبروسكان للتنبؤ بوجود وحجو دوالى المرئ في مرخى التليف الكبدى الناتج عن الاحابة بفيروس سي [٣]

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# المستخلص

فيروس سى من أهم المشاكل الصحية فى مصر، ويقدر معدل انتشارة بين الفئات العمرية بين المدال المسح الصحى الديموجرافى الذى تم فى عام ٢٠٠٨ وبالتالى فإن معدل انتشاره فى مصر يعد الأعلى عالميا.

تليف الكبد هو المرحلة الاخيرة من تطور أى من أمراض الكبد المزمنة ويجعل المريض عرضه للعديد من المضاعفات بسبب زيادة ضغط الوريد البابي.

دوالى المرئ تعد من المضاعفات الكبرى التى تحدث فى حوالى ٩٠٪ من مرضى التليف الكبدى. يعد نزيف دوالى المريء حدث يهدد الحياة وبالتالى فإن الكشف عن دوالى المرئ فى مرضى تليف الكبد هو توصية قوية بالاجماع ولذلك تستخدم المناظير فى الكشف عن دوالى المرئ كل عامين إلى ثلاثة أعوام فى المرضى بدون دوالى المرئ وكل عام الى عامين فى المرضى ذوى دوالى المرئ الصغيرة. ولكن هذا النهج التداخلى يلقى قبولا سيئا لدى المرضى ويعتبر وسيلة مكلفة ماديا، بالتالى فإن الفحص الدورى لدوالى المرئ والعلاج الوقائى للدوالى عالية الخطورة موصى به لكل المرضى المصابين بتليف الكبد.

وبالرغم من أن المناظير تعد هي المعيار الذهبي لتشخيص دوالي المرئ إلا أن هذه الخدمة غير متوفرة بنطاق واسع في مراكز الرعاية الصحية.

فى هذا الصدد تم اقتراح العديد من الوسائل السريريه والبيولوجية والموجات فوق الصوتية وجهاز قياس صلابة الكبد كطرق غير تداخلية بديلة عن المناظير في تقييم دوالي المرئ.

الهدف من الدراسة: بحث إمكانية استخدام قياس درجة صلابة الكبد كبديل لاستخدام مناظير الجهاز الهضمى في التنبؤ بوجود وحجم دوالي المرئ في مرضى التليف الكبدى المصابين بفيروس سي الذين لم يسبق لهم النزف من دوالي المرئ من قبل.

خطوات العمل: هذه الدراسة المقطعية تمت على حوالى ١٥٠مريض من المترددين على العيادات الخاجية لوحدات الكبد والجهاز الهضمى بمستشفيات وزارة الصحة بعد الحصول على موافقة المرضى للمشاركة في هذه الدراسة.

جميع الاشخاص قيد الدراسة في هذا البحث تم اختيارهم من المرضى المصابين بتايف الكبد الناتج عن الاصابة بفيروس سى ولم يعانوا من قبل من نزيف الجهاز الهضمى الناتج عن نزيف دوالى المرئ وتم تشخيص اصابتهم بتليف الكبد الناتج عن فيروس سى بواسطة الحالة الاكلينكية، التاريخ المرضى، التحاليل المعملية، الموجات فوق الصوتية على البطن ولحوض وقياس صلابة الكبد بواسطة جهاز الفيروسكان.

وتم إجراء وظائف كبد وكلى وصورة دم كاملة ونسبة الامونيا بالدم وقياس زمن البروثرومبين وتم إجراء منظار مرئ ومعدة وأثنى عشر لجميع المشاركين في هذه الدراسة.

وشملت عينة البحث مرضى من الذكور والإناث، البالغين وأعمارهم أكبر من ١٨سنه والمصابين بتليف الكبد الناتج عن الإصابة بغيروس سى فقط ولا يعانون من استسقاء متوسط أو شديد بالبطن وسمح بمشاركة المرضى المصابين بإستسقاء بسيط وجميع المرضى تم اختيارهم بحيث يكون مؤشر كتلة الجسم لديهم أقل من ٣٥.

وتم استبعاد المرضى الذين عمرهم اقل من ١٨عاما والمرضى الرافضين المشاركة فى البحث وهؤلاء المصابين بتليف الكبد الناتج عن أمراض أخرى غير فيروس سى والمصابين بأورام سرطانية بالكبد والذين سبق إصابتهم بنزيف من دوالى المرئ.

نتيجة البحث: وجد أنه هناك زيادة ملحوظة في درجة صلابة الكبد ونسبة الصفراء ونسبة الامونيا وزمن البروثرومبين بين المرضى المصابين بتليف الكبد ويوجد لديهم دوالى بالمرئ بنسبة أكبر من المرضى الين لا يعانون من وجود دوالى بالمرئ كما وجد زيادة أيض بين المرضى المصابين بدوالى مرئ كبيرة الحجم مقارنة بالمرضى المصابين بدوالى صغيرة الحجم ووجد أن هناك نقص ملحوظ في نسب الزلال بالدم ونسب الهيموجلوبين والصفائح الدموية بين المرضى المصابين بتليف الكبد ويعانون من دوالى بالمرئ ووجد نقص ملحوظ في نسبهم بين المرضى المصابين بدوالى مرئ كبيرة الحجم مقارنة بالمرضى المصابين بدوالى مرئ كبيرة الحجم مقارنة بالمرضى المصابين بدوالى صغيرة الحجم.

الاستنتاج: قياس درجة صلابة الكبد بواسطة جهاز الفيبروسكان وجد أنه وسيلة جيدة كبديل لاستخدام مناظير الجهاز الهضمى فى التنبؤ بوجود وحجم دوالى المرئ فى مرضى التليف الكبدى الناتج عن الإصابة بفيروس سى.