الدور التشخيصي لمؤشر تدهن الكبد و سمك جدار الشريان السباتى في مرض الكبد الدهنى الغير كحولي المشخص بالرنين المغناطيسي

رسالة توطئه للحصول علي درجة الدكتوراه في أمراض الباطنة

مقدمــــة

منار عماد الدين جبر

بكالوريوس الطب والجراحة ، ماجستير أمراض الباطنة جامعة عين شمس

تحت اشراف

ا.د/ أمسال شوقي محمد بكيسر

أستاذ أمر اض الباطنة والجهاز الهضمي والكبد كلية الطب جامعة عين شمس

ا.م.د/ نیقین إبراهیم موسی

أستاذ مساعد أمراض الباطنة والجهاز الهضمي والكبد كلية الطب جامعة عين شمس

أستاذ مساعد أمراض الباطنة والجهاز الهضمي والكبد كلية الطب جامعة عين شمس

کلیـــــــة الـطب جامـعة عین شمس ۲۰۱۷

الملخص العربي

يعد مرض الكبد الدهنى اللاكحولى المرض الاكثر شيوعا بين امراض الكبد المزمنه، و يشمل المرض العديد من الاشكال بداية من التراكم الدهني البسيط الي الالتهاب الكبدى اللاكحولى و نهاية بتشمع الكبد.

معظم مرضي الكبد الدهنى اللاكحولى لا يعانون من أي أعراض ويتم معرفة المرض عرضا اثناء الفحوصات الاكلينيكيه أو الموجات الصوتية علي البطن ،، ولكن الموجات الصوتية لا تستطيع الشعور بدهون الكبد القليلة التي يستلزم تشخيصها الفحص للتشخيص لما الهستولوجي لعينة من الكبد، والتي تعد وسيلة تداخلية لها مضاعفاتها التي منعتها من ان تبقي الطريقة المثلي لتشخيص هذا المرض.

أثبتت الدراسات حديثا أن تصلب الشرايين يلعب دورا هاما في المسار الطبيعي لمرض الكبد الدهني اللاكحولي و يمثل سمك جدار الشريان السباتي دلالة مبكرة لتصلب الشرايين. كما أثبتت الدراسات الحديثة قدرة أشعة الرنين المغناطيسي في تحديد كمية دهون الكبد بصوره أكثر دقه من العينة الكبدية. ونظرا لعدم إتاحة الرنين المغناطيسي كفحص روتيني علاوة علي تكلفته الباهظة وطول الفترة المستغرقة في تنفيذه أصبحت الحاجة لإيجاد طريقه أسهل واقل تكلفة في التشخيص.

نهدف من هذا العمل دراسة قدرة مؤشر تدهن الكبد وسمك جدار الشريان السباتي في استشعار تدهن الكبد اللاكحولي والتنبوء بدرجته.

اجريت هذه الدراسة علي ٣٠ شخص بالغ من المترددين علي عيادة الجهاز الهضمى والكبد بكل من مستشفى الباطنة جامعة عين شمس ومستشفى الشيخ زايد آل نهيان، و (١٥ شخص بصحة جيده من نفس المرحلة العمرية.

جميع الاشخاص خضعوا لأخذ تاريخ طبى مفصل مع استبعاد الاسباب الثانويه للكبد الدهنى ، كما خضعوا للفحص الاكلينيكى الكامل والفحوصات اللازمة لوظائف الكبد والكلي و مستوي الانسولين والدهون الثلاثيه بالدم بالاضافة للاشعة التليفزيونيه على البطن و الحوض والاشعة التلفزيونية على الشريان السباتى بالرقبه و اخيرا الرنين المغناطيسي على البطن.

وقد اظهرت الدراسة ان مؤشر تدهن الكبد وسمك الشريان السباتى لديهما القدره على التنبوء بمرض الكبد الدهنى اللاكحولى بكفاءه.



Arabic Summary

DIAGNOSTIC ROLE OF LIVER FAT SCORE AND CAROTID INTIMA-MEDIA THICKNESS IN MAGNETIC RESONANCE IMAGING PROVED NON ALCOHOLIC FATTY LIVER DISEASE

M.D Thesis Submitted for the partial fulfillment of requirements of M.D. Degree in Internal Medicine

By Manar Emad Eldin Gabr M.B.B.Ch, MSC Ain Shams University

Under supervision of

Professor. Amal Shawky Mohamed Bakir

Professor of Internal Medicine, Gastroenterology & Hepatology

Dr. Nevine Ibrahim Musa

Assistant Professor of Internal Medicine, Gastroenterology & Hepatology

Dr. Eslam Safwat Mohamed

Assistant Professor of Internal Medicine, Gastroenterology & Hepatology

> Faculty of Medicine Ain Shams University 2017



ACKNOW LEDGMENT

First of all, I wish to express my endless thanks to ALLAH for giving me the help to perform this work

I would like to express my deepest thanks and highest appreciation to **Professor. Amal Shawky Mohamed Bakir**, Professor of Internal medicine, Faculty of Medicine, Ain Shams University, for her valuable help, precious advice, continuous encouragement and constructive guidance that were the most driving forces for the initiation, progress and completion of this work.

I owe special thanks and gratitude to **Dr. Nevine**Ibrahim Musa, Assistant Professor of Internal Medicine,
Faculty of Medicine, Ain Shams University, and to **Dr.**Eslam Safwat Mohamed Assistant Professor of Internal
Medicine, Faculty of Medicinee, Ain Shams University, for
their precious help and fruitful guidance.

I owe special thanks to **Dr. Noha Mohamed Taha** Assistant Lecturer of Radiodiagnosis, Faculty of Medicine, Ain Shams University, for her precious help.

I owe special thanks to the Radiology department, Alsheikh Zayed AlNahyan Hospital, for their help in completion of this work

Also, I would like to convey my special thanks to my family for their constant support.

Manar Emad Eldin Gabr

List of Contents

	Title	Page
•	List of contents	i
•	List of Tables	ii
•	List of Figures	v
•	List of abbreviations	viii
Ir	ntroduction	1
A	im of the Work	4
R	eview of Literature	5
• (Chapter (1): Nonalcoholic Fatty Liver Disea	.s5
• (Chapter (2): Noninvasive diagnosis of hepatic s	teatosis50
Pa	atients and Methods	65
R	esults	79
D	iscussion	107
S	ummary	119
C	onclusion	122
R	ecommendations	123
R	eferences	124
A	rabic Summary	

List of Tables

Tab.	No.	Title P	age No.
Table	(1):	Life style recommendations for the successful management of NAFLD	
Table	(2):	Indications of liver biopsy in patients with NAFLD	
Table	(3):	Advantage and disadvantage of imagin techniques for evaluating hepatisteatosis	ic
Table	(4):	Studies on the association between no alcoholic fatty liver disease and carotic artery intima-media thickness in adult evaluation of the independent predictor for intima media thickness increase	id s: rs
Table	(5):	Ultrasound scoring of fatty liver	73
Table	(6):	Clinical and biochemical parameters of a sutied subjects	
Table	(7):	Characteristics of the studied subjects a regard Metabolic Syndrome	
Table	(8):	Characteristics of the studied subjects a regard diabetes mellitus	
Table	(9):	Classification of cases group according the hepatic steatosis score using U/S	
Table	(10):	Comparison between cases and controls a regards the gender	
Table	(11):	Comparison between cases and controls a regards age	

LIST OF TABLES (CONT...)

Tab. No.	Title	Page No.
Table (12): (Comparison between studied groups as regards Systolic blood pressure and Diastolic blood pressure	84
Table (13): (Comparison between cases and controls as regards Anthropometric measures	86
Table (14): (Comparison between cases and controls as regards fasting blood glucose, glycated heamoglobin, fasting Insulin levels, and Insulin resistance	86
Table (15): (Comparison between cases and controls as regards serum Iron, Ferritin, and blood hemoglobin	
Table (16): (Comparison between cases and controls as regards results of liver function tests	
Table (17): (Comparison between cases and controls as regards fasting lipid profile	90
Table (18): (Comparison between cases and controls as regards CIMT	
Table (19): (Comparison between cases and controls as regards NAFLD-LFS	
Table (20):	Comparison between cases with metabolic syndrome and cases without metabolic syndrome as regards Systolic blood pressure, triglycerides, and CIMT	93

LIST OF TABLES (CONT...)

Tab. No.	Title	Page No.
Table (21)	: Comparison between cases with metabolic syndrome and cases without metabolic syndrome as regards NAFLD-LFS	t S
Table (22):	Correlation berween NAFLD-LFS and clinical parameters	
Table (23):	Correlation between NAFLD-LFS and biochemical parameters	
Table (24):	Correlation between NAFLD-LFS and Radiological parameters	
Table (25):	Correlation between CIMT and Age	100
Table (26):	Correlation between CIMT and serum Triglycerides	
Table (27):	Correlation between CIMT and grade of hepatic steatosis	
Table (28):	Mutivarient analysis for predictors of NAFLD	
Table (29):	Cutoff value of NAFLD-LFS; sensitivity and specificity.	
Table (30):	Cutoff value of CIMT; sensitivity and specificity	
Table (31):	Cutoff value of combined NAFLD-LFS and CIMT; sensitivity and specificity.	

List of Figures

Fig. No.	Title	Page No.
Figure(1):Glo	obal prevalence of NAFLD	7
_	altiple hit hypothesis for devel	•
Figure(3):Cli	nical conditions associated with NA	FLD 32
Figure(4):Dia	agnostic flow-charts in NAFLD	34
Figure(5):Tos	shiba Nemio XG	74
Figure(6):Ima	age of hepatic steatosis scoring by U	/S74
Figure(7):Doj	ppler imaging of Carotid artery	75
Figure(8):MR	RI of liver with Inphase and outphase	e sequences 76
Figure(9):Gen	nder distribution among all studied s	ubjects 81
_	lassification of studied subjects acco	-
	lassification of studied subjects accordence of metabolic syndrome	
_	lassification of all studied subjects are presence of Diabetes Mellitus	_
•	haracteristics of cases group ltrasound degree of hepatic steatosis.	•
	omparison between the studied grou	-
	omparison between studied groups Body Mass index	_

List of Figures (cont...)

Fig. No.	Title	Page No.
Figure(16):	Comparison between studied groups waist circumference	
Figure (17):	Comparison between studied groups liver enzymes	
Figure (18):	Comparison between studied groups fasting lipid profile	
Figure(19):	Comparison between studied groups CIMT	
Figure(20):	Comparison between studied groups NAFLD-LFS	
Figure(21):	Comparison between cases with syndrome and cases without syndrome as regard CIMT	metabolic
Figure(22):	Comparison between cases with syndrome and cases without syndrome as regard NAFLD-LFS	metabolic
Figure (23):	Correlation between NAFLD-LFS a	
Figure(24):	Correlation between NAFLD-LFS and A	ALT 97
Figure(25):	Correlation between NAFLD-LFS a	
Figure (26):	Correlation between NAFLD-LFS a Triglycerides	
_	Correlation between NAFLD-LFS an	_

List of Figures (cont...)

Fig. No.	Title	Page No.
Figure(28):Co	orrelation between NAFLD-LFS and H	IOMA-IR 99
Figure(29): Co	orrelation between NAFLD-LFS and H	IbA1C 99
_	orrelation between NAFLD-LFS and nepatic steatosis.	-
Figure(31): C	Correlation between NAFLD-LFS and C	CIMT101
Figure(32): C	Correlation between CIMT and Age	101
Figure(33): Co	orrelation between CIMT and Triglycerides	
Figure (34):Co	orrelation between CIMT and grade of steatosis	-
Figure(35): R	OC cure analysis for diagnostic performance of NAFLD-LFS in discrimination of N	
Figure (36):R	OC cure analysis for diagnostic performance of CIMT in discrimination of NAFLD	
Figure(37): R	OC cure analysis for diagnostic performance of combined NAFLD-LFS and C discrimination of NAFLD	IMT in

List of Abbreviations

Abbreviation		Meaning
ApoA1	:	Apolipoprotein A-1
AUROC	:	Area under the receiver operating characteristic
A2M	:	A2-Macroglobulin
AMPK	:	AMP-activated protein kinase
ATP	:	Adenosine Triphosphate
BCAAs	:	Branched-chain amino acids
BCFAs	:	Branched-chain fatty acids
BMI	:	Body mass index
CAP	:	Controlled attenuation parameter
CHC	:	Chronic hepatitis C
ChREBP	:	Carbohydrate response element binding protein
CIMT	:	Carotid artery Intima Media Thickness
CK-18	:	Cytokeratin 18
CKD	:	Chronic Kidney disease
CRP	:	C-reactive protein
CT	:	Computed tomography
CVD	:	Cardiovascular disease
DBP	:	Diastolic blood pressure
DNL	:	De novo lipogenesis
DPPIV	:	Dipeptidyl-peptidase IV
ER	:	Endoplasmic reticulum
FFAs	:	Free fatty acids
Fiaf	:	Fasting induced adipocyte factor
FLI	:	Fatty Liver Index
FXR	:	farnesoid X receptor