بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / سامية زكى يوسف

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد

Fibro-scan Based Score and novel noninvasive serum marker, FGF-21, to assess Liver Fibrosis in Morbidly Obese Patients

Thesis

Submitted for partial fulfillment of Master's degree In gastroenterology and Internal medicine

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2022

النتيجة المعتمدة على المسح الليفي مع استخدام (FGF-21) كأحدث تحليل لتقييم التليف الكبدي في مرضى السمنة المفرطة المصابين بمرض الكبد الدهني

رسالة

توطئة للحصول علي درجة الماجستير في أمراض الجهاز الهضمي

مقدمة من

الطبيب / مصطفى عزب الديساوي

بكالوريوس الطب و الجراحة- جامعة

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Acknowledgement

First and foremost thanks to ALLAH, the Most Merciful.

I wish to express my deep appreciation and sincere gratitude to ***Prof. Dr. ESem biomy,*** *Professor of gastroenterology and Internal medicine, Ain Shams University, for his close supervision, valuable instructions, continuous help, patience, advices and guidance. He has generously devoted much of his time and effort for planning and supervision of this study. It was a great honor to me to work under his direct supervision.*

I wish to express my great thanks and gratitude to ***Dr Mohamed Magdy,*** *Assistant Professor of gastroenterology and Internal medicine, Ain Shams University, for his kind supervision, indispensable advice and great help in this work.*

Last and not least, I want to thank all my family, my colleagues, , for their valuable help and support.

Finally I would present all my appreciations to my patients without them, this work could not have been completed.

Contents

List of Abbreviations

Abb.	**Full term**
ALT	Alanine aminotransferase
APRI	AST-to-Platelet Ratio Index
AST	Aspartate aminotransferase
AUC	Area under the curve
cAMP	Cyclic adenosine monophosphate
CK-18	Cytokeratin 18
ECM	Extra ceullular matrix
ELF	Enhanced liver fibrosis
FGFRs	Fibroblast growth factor receptors
GGT	Gamma-glutamyl transferase
HA	Hyaluronic acid
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL	High density lipoproteins
HSCs	Hepatic stellate cells
IASL	International Association of the Study of the Liver
IL	Interleukin
IQR	Interquartile range
LDL	Low density lipoproteins
LFTs	Liver function tests
MASH	Metabolic associated steatohepatitis
MMPs	Matrix metalloproteinase
MRE	Magnetic resonance elastography
MRE	Magnetic resonance elastography
MS	Metabolic syndrome
NAFLD	Nonalcoholic fatty liver disease
NASH	Nonalcoholic steatohepatitis
OELF	Original ELF
PBC	Primary biliary cirrhosis
PCOS	Polycystic ovarian Syndrome
PKA	Protein kinase A
ROC	Receiving operating characteristic
TE	Transient elastography

✍List of Abbreviations

Abb.	**Full term**
TIMP	Tissue inhibitor of metalloproteinase
VLDL	Very-low-density lipoprotein

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INTRODUCTION

Finding a means to noninvasive diagnosis of non-alcoholic fatty liver disease (NAFLD) and its entities has been the aim of many research efforts since recently, and seems to remain a very much needed goal among many clinicians and researchers in the field of hepatology. Why is it that way? NAFLD is today considered to be the most common liver disease in adults. The prevalence of NAFLD in general population is very high, in the range of 15%-30% according to various studies, and is even increasing, due to the rising prevalence of diabetes and obesity**. *(Ratziu et al., 2009)***.

Spectrum of NAFLD includes two entities with very different natural course and prognosis: simple steatosis, which mostly has a benign non-progressive course and good prognosis, and non-alcoholic steatohepatitis (NASH), which demonstrates progression of fibrosis in about 30%-40% of patients and has a proven potential to eventually lead to cirrhosis an end-stage liver disease including hepatocellular carcinoma**. *(Ekstedt et al., 2006)*, *(Matteoni et al., 1999)*, *(Adams et al., 2005)***

NASH seems to be present in a surprisingly high proportion of NAFLD patients, including 40% to 75% of cases with elevated aminotransferase levels, those data coming from recent studies using current histological definitions and including substantial number of patients

(Ekstedt et al., 2006), (Söderberg. et al., 2010), (Fracanzani etal., 2008)

In studies of liver biopsy findings from apparently healthy living liver donor candidates, the proportion of NASH among patients with newly discovered NAFLD was about 30%**. *(Minervini et al., 2008)***

Even in patients with normal aminotransferase levels, proportion of NASH among NAFLD cases seems to be almost the same, and the whole spectrum of NAFLD including advanced fibrosis and cirrhosis has been observed in patients with completely normal laboratory findings**. *(Fracanzani et al., 2007), (Mofrad et al., 2002), (Sorrentino et al., 2005)***

Liver biopsy is still considered the gold standard in diagnosis and the only reliable tool for distinguishing NASH from simple steatosis and for grading and staging the disease, providing important information about severity of steatosis, lobular inflammation, hepatocellular ballooning, and degree of fibrosis**. *(Neuschwander-Tetri et al., 2019)***

Minimal histological criteria for NASH include steatosis, hepatocyte injury (in the form of ballooning or apoptosis) and lobular inflammation. Similarly to other chronic liver diseases, fibrosis is usually divided histologically in four stages: perisinusoidal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis

(F3) and cirrhosis (F4). Liver biopsy also has several negative aspects: it is invasive, unpleasant for patients, it usually includes hospitalization and a day or two lost at work, and the adequate interpretation of the specimen requires a pathologist with expertise in hepatopathology, which altogether makes it a costly and time-consuming procedure. Another significant drawback of liver biopsy, and in medical terms the most important one is its substantial sampling variability, which has been consistently proven for several chronic liver diseases including NAFLD. In a well-designed study by Ratziu et al**.** ***(Ratziu et al., 2005)***

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Aim of the work

This prospective cohort study aims to develop and validate noninvasive scoring system for assessment liver fibrosis in morbidly obese patients with NAFLD.