

**Role of Transient Elastography in Prediction of
Esophageal Varices in Patients with HCV-
related Chronic Liver Disease**

Thesis

Submitted for partial fulfillment of M.D. degree
In Tropical Medicine

By

Noha Mamdouh EL Wakil

M.B., B.Ch, M.Sc.

Faculty of Medicine – Ain Shams University

Supervised by

Prof. Ali Ahmed Zaki Helmy

Prof. of Tropical Medicine

Faculty of Medicine – Ain Shams University

Prof. Waleed Abd EL Aaty Hamed

Prof. of Tropical Medicine

Faculty of Medicine – Ain Shams University

Assist Prof. Mohammed Omar khalifa

Assist Prof. of Tropical Medicine

Faculty of Medicine – Ain Shams University

Dr. Enas Hassan Allam

Lecturer of Tropical Medicine

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2015

**Role of Transient Elastography in Prediction of
Esophageal Varices in Patients with HCV-
related Chronic Liver Disease**

Thesis

Submitted for partial fulfillment of M.D. degree
In Tropical Medicine

By

Noha Mamdouh EL Wakil

M.B., B.Ch, M.Sc.

Faculty of Medicine – Ain Shams University

Supervised by

Prof. Ali Ahmed Zaki Helmy

Prof. of Tropical Medicine

Faculty of Medicine – Ain Shams University

Assist Prof. Waleed Abd EL Aaty Hamed

Assist Prof. of Tropical Medicine

Faculty of Medicine – Ain Shams University

Dr. Enas Hassan Allam

Lecturer of Tropical Medicine

Faculty of Medicine – Ain Shams University

Dr. Mohammed Omar khalifa

Lecturer of Tropical Medicine

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2013

Introduction

The development of portal hypertension is a common consequence of chronic liver disease leading to the formation of esophageal and gastric varices responsible for variceal bleeding, associated with a high mortality rate, as well as other severe complications such as portosystemic encephalopathy and sepsis (*Castera et al., 2012*).

Esophageal varices are the most important portosystemic collaterals because their rupture results in variceal hemorrhage, which is a catastrophic portal hypertension event. The average risk of bleeding in cirrhotic patients without previous hemorrhage is 30%, with a mortality rate of 50% in 6 weeks (*Wang et al., 2012*).

Pharmacological treatment and endoscopic band ligation are widely considered to be effective and safe in preventing hemorrhage from ruptured esophageal varices (*Villanueva and Balanzó, 2008*).

Upper GI endoscopy is the best way of assessing the presence of oesophageal varices, where its accuracy is much greater than that of radiology (including multidetector CT-angiography) (*De Franchis, 2009*). Endoscopy has the further advantage of allowing to detect indicators of increased bleeding

risk (the red color signs and wale marks) that cannot be detected accurately by other imaging techniques (*De Franchis, 2010*).

Based on the relatively silent process of cirrhosis, guidelines recommend that all cirrhotic patients should be screened for esophageal varices. From a recognized natural history, expert panels agreed that screening endoscopy should be conducted every 2–3 years for cirrhotic patients without esophageal varices, and annually for those with decompensated liver cirrhosis (*Garcia-Tsao et al., 2007*). The number of patients indicated for esophageal varices screening depends on the prevalence and selective criteria of liver cirrhosis. Screening for esophageal varices proposed by current guidelines has a considerable endoscopic burden and financial cost, particularly in developed countries. Additionally, even asymptomatic patients might be required to undergo an unpleasant endoscopy requiring sedation, thereby increasing the medical workload and resulting in limited compliance (*Wang et al., 2012*).

Transient elastography is a novel, non-invasive, ultrasound technique-based technology that allows measuring liver stiffness. Established evidence indicated that transient elastography had good sensitivity and specificity for fibrosis, significant fibrosis and cirrhosis, and has been popular over the past few years (*Tsochatzis et al., 2011*).

A good correlation between liver stiffness and portal hypertension as well as the presence of oesophageal varices has been reported, suggesting that it could be an interesting tool for the non-invasive evaluation of portal hypertension and the presence and the size of oesophageal varices (*Bureau et al., 2008*).

Aim of the work

Evaluate the role of liver stiffness measurement performed using transient elastography as a non-invasive tool for prediction of the presence and the size of esophageal varices in patients with HCV-related chronic liver disease.

Patients and Methods

The study will be conducted on 60 patients with HCV-related chronic liver disease.

Study Details

Study Design: Cross-sectional study.

Estimated Enrollment: 60 patients

Place of the study: Tropical Medicine Department, Ain Shams University Hospitals.

Type of patients: Both out- and in-patients.

Eligibility:

Ages Eligible for Study: 18 Years and older

Genders Eligible for Study: Both

Study Start Date: 1/1/2013

Inclusion Criteria:

1. Signed informed consent.

-
-
2. Adult patients with HCV-related chronic liver disease as confirmed by positive HCV Ab +/- positive HCV RNA by PCR assay and absence of other causes of liver diseases.
 3. Presence of Chronic liver disease as confirmed by clinical, biochemical and radiological investigations.

Exclusion criteria:

- Refusal to sign an informed consent.
- Chronic liver disease due to causes other than HCV.
- Presence of ascites (as it interferes with fibroscan images and gives invalid results).
- Presence of any hepatic focal lesion of any nature (haemangiomas, dysplastic nodules, HCC or metastatic lesions) as it will give variable or even invalid readings in fibroscan.

Methods:-

All participants in the study will be subjected to the following:

A. Informed consent: details of the study and its aim will be explained, and the patient will be asked to sign a written consent.

B. Full history taking and clinical assessment.

C. Laboratory investigations including:

- Complete blood count.
- Liver function tests: AST, ALT, serum Albumin, serum bilirubin (total and direct).
- HCV antibody
- Prothrombin time, concentration and INR.
- Renal function tests: Urea and Creatinine
- Screening for concomitant aetiology of chronic liver disease:
HBs Ag, anti HBc antibody, ANA .

D. Abdominal ultrasonography :

- Size and echogenicity of the liver and presence of focal lesions.
- Splenic size.
- The status of ascites (absent or present).

E. Esophago-gastro-duodenoscopy (EGD):

Upper GI endoscopy will be performed by a single experienced operator, unaware of the results of liver stiffness measurement.

E. Transient Elastography (Fibroscan):

Measurement of liver stiffness will be done usually within days following or preceding upper tract endoscopy (maximum

one week before or after OGD). Fibroscan will be performed by a single experienced operator, unaware of the results of OGD.

A fibroScan device (EchoSens, France) will be used in this study.

F. Platelets count / Spleen diameter ratio will be calculated .

Sample Size Justification

Sample size was calculated using STATA[®] version 11 program, setting the type-1 error (α) at 0.05 and the power ($1-\beta$) at 0.8. Results from a previous study by *Wang et. al. (2012)* revealed that minimal sample size of 35 patients.

Reference for program:

StataCorp. 2001. Statistical Software: Release 7.0. College Station, TX: Stata Corporation.

REFERENCES

- **Bureau, C.; Metivier, S.; Peron, J.M. et al. (2008):** Transient elastography accurately predicts presence of significant portal hypertension in patients with chronic liver disease. *Aliment Pharmacol Ther* 2008; 27: 1261–8.
- **Castera, L.; Pinzani, M. and Bosch, J. (2012):** Non invasive evaluation of portal hypertension using transient elastography. *Journal of Hepatology*. 2012; vol. 56 j 696–703.
- **De Franchis, R. (2009):** Cirrhosis: screening for esophageal varices. *Nat Rev Gastroenterol Hepatol*. 2009;6: 449–450.
- **De Franchis, R. (2010):** Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol*. 2010; 53:762–768.
- **Garcia-Tsao, G.; Sanyal, A.J.; Grace, N.D. et al. (2007):** Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology*. 2007; 46:922–38.

-
-
- **Tsochatzis, E.A.; Gurusamy, K.S.; Ntaoula, S. et al. (2011):** Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a meta-analysis of diagnostic accuracy. *J Hepatol.* 2011; 54: 650–9.
 - **Villanueva, C. and Balanzó, J. (2008):** Variceal bleeding: pharmacological treatment and prophylactic strategies. *Drugs* 2008; 68:2303–24.
 - **Wang, M.H.; LO, H.G.; Chen, C.W. et al. (2012):** Efficacy of transient elastography in screening for large esophageal varices in patients with suspicious or proven liver cirrhosis. *Journal of Digestive Diseases* 2012; 13; 430–438.

**دور قياس المرونة اللحظية للكبد في التنبؤ بوجود دوالي
المرئ في مرضى الكبد المزمن الناتج عن فيروس (س)**

رسالة

توطئة للحصول على درجة الدكتوراة في طب المناطق الحارة
مقدمة من الطيبة

نهى ممدوح الوكيل

تحت إشراف

الأستاذ الدكتور / على أحمد زكى حلمى

أستاذ طب المناطق الحارة

كلية الطب – جامعة عين شمس

الأستاذ الدكتور م / وليد عبد العاطى حامد

أستاذ مساعد طب المناطق الحارة

كلية الطب – جامعة عين شمس

الدكتورة / إيناس حسن علام

مدرس طب المناطق الحارة

كلية الطب – جامعة عين شمس

الدكتور / محمد عمر خليفه

مدرس طب المناطق الحارة

كلية الطب – جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٣

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ اَعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
وَرَسُولُهُ وَالْمُؤْمِنُونَ

صدق الله العظيم
سورة التوبة آية (105)



*First and foremost, thanks for Allah for guiding and helping
me to finish this work.*

*I would like to express my deepest thanks and sincere gratitude to **Prof. Ali Ahmed Zaki Helmy**, Professor of Tropical Medicine, Faculty of Medicine_ Ain Shams University, for his close supervision, continuous support, valuable instructions, and sincere advice. I am very much grateful for his noble characters and generous help.*

*I would like to express my gratitude and sincere thanks to **Prof. Waleed Abd EL Aaty Hamed**, Professor of Tropical Medicine, Faculty of Medicine – Ain Shams University, for his valuable supervision, constant support, and encouragement in the conduction of this work,*

*I wish to introduce my deep respect and thanks to **Assist. Prof. Mohamed Omar Khalifa**, Assistant Professor of Tropical Medicine, Faculty of Medicine -Ain Shams University, for his valuable supervision and sincere advice.*

*My deep thanks and appreciation to **Dr. Enas Hassan Allam**, Lecturer of Tropical Medicine, Faculty of Medicine – Ain Shams University, for her continuous supervision of this work. Thanks for her support and endless advices and help.*

List of contents

Subject	Page
Acknowledgment	-
List of Abbreviations	i
List of Tables	iii
List of Figures	v
Introduction and Aim of the Work	1
Review; chapter I: Esophageal Varices	4
Review; chapter II: Transient Elastography	34
Patients and Methods	55
Results	65
Discussion	86
Summary	100
Conclusions and Recommendations	103
References	105
Protocol	
Arabic summary	