Transient Elastography, Fib-4 score, Lok score and Fibrosis index score as Non Invasive Predictors of Oesphageal Varices, its Degree and Risk of Bleeding in Post Hepatitis C Virus Liver Cirrhosis

Thesis

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Abstracr

Background: Cirrhosis is the end result of chronic liver damage caused by chronic liver diseases. Common causes of chronic liver disease include Hepatitis C infection (long-term infection), Long-term alcohol abuse, Autoimmune inflammation of the liver, Disorders of the drainage system of the liver (the biliary system), such as primary biliary cirrhosis and primary sclerosing cholangitis, Hepatitis B (long-term infection), Medications, Metabolic disorders of iron and copper (hemochromatosis and Wilson's disease), Nonalcoholic Steatohepatitis (NASH). Egypt has the highest prevalence of hepatitis C virus (HCV) worldwide and a high morbidity and mortality from chronic liver disease. HCV is considered the most common aetiology of chronic liver disease in Egypt. Esophageal varices develop as a consequence of portal hypertension in patients with chronic liver disease and are present in approximately 50% of patients with cirrhosis of the liver.

Aims: To evaluate prescence of Oesphageal Varices and its degree and risk of bleeding in post HCV liver Cirrhosis using Transient Elastography, Fib-4 score, Lok score and Fibrosis index score as non-invasive procedures in comparison to upper endoscopy findings.

Methodology: This study was a cross sectional study that was conducted on 40 patients with post HCV liver cirrhosis to evaluate prescence of Oesphageal varices and its degree and risk of bleeding using Transient Elastography,Fib-4 score, Lok score and Fibrosis index score as non invasive procedures in comparison to upper endoscopy findings.patients were selected from Ain Shams University hospitals in the period from (June 2014) to (December 2015).

Results: Those 40 patients were divided into 2 groups: Group 1: 15 patients with liver cirrhosis (child A). Group 2: 25 Patients with advanced liver cirrhosis(child B,C).18 patients were child B and 7 patients were child C.

Conclusion: LSM and LOK score have significant correlation with EV risk of bleeding and can be used as non invasive markers to predict and follow up risky EVs which will need intervention by endoscopy. LSM and LOK score are sensitive and reliable tests in prediction of large and risky EVs.

Recommendations: Although Upper gastrointestinal endoscopy is the gold standard for diagnosis of esophageal varices size, grading and risk of bleeding in newly diagnosed patients with liver cirrhosis. LSM and LOK score can be used for prediction and follow up esophageal varices as regards risk of bleeding. We recommend to do upper endoscopy as soon as possible for patients with liver cirrhosis if LSM >46 kpa and Lok score > 0.86 as they mostly have large risky EVs which will need prophylactic intervention before bleeding occur.

Keywords: Transient Elastography, Fib-4 score, Lok score and Fibrosis index score, Oesphageal Varices, Hepatitis C Virus, Liver Cirrhosis

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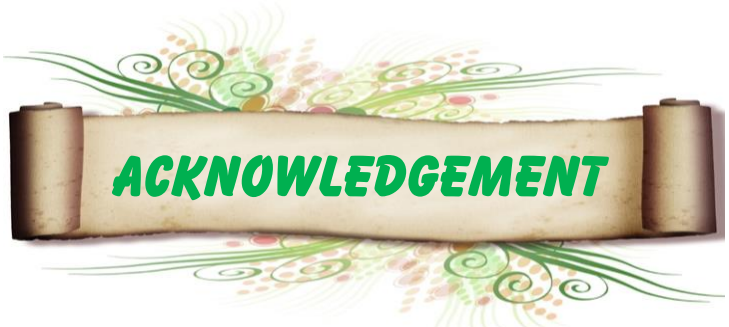

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Contents

List of Abbreviations

AASLD: American Association for the Study of Liver Diseases.

AFP: Alfa fetoprotein.

AIH: Auto immune hepatitis.

ALD: Alcoholic Liver disease.

ALF: Acute liver failure.

ALT: Alanine transaminase.

APRI: AST to Platelet ratio index.

AST: Aspartate transaminase.

BMI: Body mass index.

BP: Blood pressure.

bpm: Beat per minute.

BUN: Blood urea nitrogen.

CBC: Complete blood count.

CDC: Center for disease control.

CHB: Chronic hepatitis B.

CHC: Chronic hepatitis C.

CSPH: Clinically significant portal hypertension.

CTP: Child-Turcott-Pugh.

ECG: Electrocardiography.

EDHS: Egyptian Demographic Health Survey

EGD: Esophagogastroduodenoscopy.

EUS: Endoscopic ultrasound.

EVs: Esophageal varices.

FDA: Food and Drug administration.

FIS: Fibrosis index score.

HBV: Hepatitis B virus.

HCC: Hepatocellular carcinoma.

HCV: Hepatitis C virus.

HIV: Human immunodeficiency virus.

HR: Heart rate.

HTN: Hypertension.

HVPG: Hepatic venous pressure gradient.

IDSA: Infectious Diseases Society of America.

IDU: Intravenous drug use.

INR: International normalized ratio.

IRES: Internal ribosome entry site

ISMN: Isosorbide mononitrate.

IVC: Inferior vena cava.

LB: Liver biopsy.

LC: Liver cirrhosis.

LDL: Low density lipoprotein.

LEV: Large esophageal varices.

LSM: Liver stiffness measurement.

MELD: Model for end-stage liver disease.

NAFLD: Non alcoholic liver disease.

NASH: Non alcoholic steatohepatitis.

NPV: Negative predictive value.

NSBB: Non cardioselective beta blocker.

PAT: Parenteral-antischistosomal-therapy.

PBC: Primary Biliary Cirrhosis.

PCR: Polymerase chain reaction.

PEG-IFN: Pegylated interferon.

PHT: Portal hypertension.

PPG: Portal pressure gradient.

PPV: Positive predictive value.

PSC: Primary sclerosing cholangitis.

PT: Prothrombin time.

PTFE: Polytetra flouroethylene.

PTT: Partial thromboplastin time.

RCT: Randomised controlled trial.

SD: Standard deviation.

SE: Sensitivity.

SP: Specificity.

SVR: Sustained virological responses.

TE: Transient elastography.

TIPS: Transjugular intrahepatic portosystemic shunt.

UGIB: Upper Gastro Intestinal Bleeding.

WGO: World gastroenterology organization.

WHO: World health organization.

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Introduction

Cirrhosis is the end result of chronic liver damage caused by chronic liver diseases. Common causes of chronic liver disease include Hepatitis C infection (long-term infection), Long-term alcohol abuse, Autoimmune inflammation of the liver, Disorders of the drainage system of the liver (the biliary system), such as primary biliary cirrhosis and primary sclerosing cholangitis, Hepatitis B (long-term infection), Medications, Metabolic disorders of iron and copper (hemochromatosis and Wilson's disease), Nonalcoholic Steatohepatitis (NASH) ***(Schuppan and Afdhal., 2008).***

Chronic hepatitis C virus (HCV) infection is a major public health problem ***(Shaheen and Myers., 2007)***. It is estimated that 180 million people worldwide are chronically infected with HCV ***(Ghany et al., 2009)***. Chronic HCV infection is the major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma in developed countries ***(Sebastiani et al., 2008; Ghany et al., 2009)***. Cirrhosis from chronic HCV infection is also the most common indication for liver transplantation ***(Cheung et al., 2008)***.

Egypt has the highest prevalence of hepatitis C virus (HCV) worldwide and a high morbidity and mortality from chronic liver disease ***(Lavanchy and McMahon., 2000)***. HCV is considered the most common aetiology of chronic liver disease in Egypt. Esophageal varices develop as a consequence of portal hypertension in patients with chronic liver disease and are present in approximately 50% of patients with cirrhosis of the liver ***(Strickland et al., 2002)***.

Bleeding oesophageal varices is the gravest complication of liver cirrhosis, with a high mortality ***(D'Amico et al., 2006).*** Each variceal bleeding attack carries a mortality rate of 17%-57% ***(Merkel et al., 2004)***. Prevention of variceal bleeding vital, while non-selective beta blockers and prophylactic band ligation decrease the risk of bleeding by 50% ***(Imperiale and Chalasani., 2001).*** The grade of esophageal varices often correlates with the severity of liver disease. While approximately 85% of individuals with Child-Pugh C cirrhosis have varices, they are present in only 45% those with Child-Pugh A cirrhosis.

Upper gastrointestinal endoscopy is the best method for evaluating the presence of complication of portal hypertension including gastroesophageal varices and portal hyperten-sive gastropathy, and its routinely employed as a first-level approach to asses this syndrome ***(Grace et al., 1998)***. Indeed, esophageal varices are present in about 40%

of compensated cirrhotic patients and in 60% of those presenting with ascites at the initial diagnosis of cirrhosis ***(Schepis et al., 2001)***.

Moreover, upper gastrointestinal endoscopy discloses the characteristics of the varices (i.e. dimension and presence of red signs). Detection of these signs offers important predictive information for the occurrence of variceal bleeding ***(Merkel et al., 2000).*** Additionally, upper gastrointestinal endoscopy allows to assess the presence, extent, and severity of portal hypertension gastropathy.

The current guidelines recommend endoscopic screening to all cirrhotic patients. Those with decompensated cirrhosis should annually repeat endoscopy even if they have no varices, while those with compensated cirrhosis and don't have varices should repeat endoscopy every 2-3 years, and every 1-2 years for those with small varices ***(Grace et al., 1998).*** The annual incidence of variceal bleeding is 5% for small varices and 15–20% for large ones with portal pressure greater than 12 mm Hg, both with mortality rates ranging from 20 to 25% in the first week ***(Sharma and Aggarwal., 2007).*** The risk of death remains unchanged for up to 6 weeks after the bleeding and varies between 15 and 30% ***(De Franchis et al., 2008).***