Reliability of Transient Elastography as a Non-Invasive Technique for Detection of Fibrosis in Budd Chiari syndrome Patients after Endovascular Intervention

Thesis

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List of Abbreviations

Abb.	Full term
AAR	The AST/ALT ratio
ACAs	Anticardiolipin Antibodies
ACL IgG	Anticardiolipin IgG
ACL IgM	Anticardiolipin IgM
AIH	Autoimmune hepatitis
ALB	Albumin
ALP	Alkaline phosphatase
ALT	Alanin amino-transferase
AMM	Agnogenic myeloid metaplasia
ANA	Anti nuclear antibody
Anti DNA	Anti double stranded DNA
Anti-beta-2GPI	Anti-beta 2 glycoprotein I
AP	The age/platelet index
APAs	Antiphospholipid antibodies
APC	Activated protein C
APCR	Activated protein C resistance
APLAS	Antiphospholipid antibody syndrome
APRI	The Aspartate Aminotransferase to Platelet Ratio Index
APS	Antiphospholipid syndrome
APTT	Activated partial thromboplastin time
ARFI	Acoustic Radiation Force Impulse Elastography
AST	Aspartate amino-transferase
AT III	Antithrombin III
BCS	Budd-Chiari syndrome
BD	Behcet Disease
BM	Bone marrow
BMI	Body mass index

List of Abbreviations Cont...

Abb.	Full term
BS	Bonacini's discriminant score
BUN	Blood urea nitrogen
CAP	Controlled attenuation parameter
CHB	Chronic hepatitis B
CHC	Chronic hepatitis C
CLD	Chronic liver disease
CML	Chronic Myeloid leukemia
CT	Computed Tomography
DIC	Disseminated intravascular coagulation
EASL	European Association for the Study of the Liver
ECM	extracellular matrix
EEC	endogenous erythroid colony
EFSUMB	European Federation of Societies for Ultrasound in Medicine and Biology
ELF	Enhanced liver fibrosis
ESR	Erythrocyte sedimentation rate
ET	Essential thrombocythemia
FAB	French-American-British
FDA	Federal Drug Administration
FISH	Fluorescent in-situ hybridization
FV	Factor V
FVa	Activated factor V
FVLM	Factor V Leiden mutation
HA	Hyaluronic acid
Hb	Hemoglobin
HCC	Hepatocellular carcinoma
HcT	Hematocrit
Hetero	Heterozygous

List of Abbreviations Cont...

Abb.	Full term
HH	Hyperhomocysteinemia
Homo	Homozygous
INR	International normalized ratio
IQR	interquartile range
IVC	Inferior vena cava
JAK_2	Janus tyrosine kinase-2
kPa	Kilopascal
LAC	Lupus Anticoagulant
LAP	Leukocyte alkaline phosphatase
LSM	liver stiffness measurements
LSN	liver surface nodularity
MF	Myelofibrosis
MMP/ TIMP	metallo-proteinase/ tissue inhibitor of metalloproteinase
MOVC	membranous obstruction of the IVC
MPDs	Myeloproliferative disorders
MRE	Magnetic resonance elastography
MRI	Magnetic resonance imaging
MTHFR	Methylenetetrahydro-folate reductase
NAD	No abnormality detected
NAFLD	Non alcoholic fatty liver disease
NASH	Non alcoholic steatohepatitis
OCPs	Oral Contraceptive Pills
OLT	orthotopic liver transplantation
PC	Protein C
PCR	Polymerase chain reaction
PGM	Prothrombin gene mutation
PICP	Procollagen type carboxy terminal peptide
PIIINP	Procollagen type III amino terminal peptide

List of Abbreviations Cont...

Abb.	Full term
PLT	Platelets
PNH	Paroxysmal nocturnal hemoglobinuria
PS	Protein S
PT	Prothrombin time
PTFE	Polytetrafluoroethylene
PTT	Partial thromboplastin time
PV	Polycythemia vera
PV	Portal vein
PVT	Portal vein thrombosis
SAAG	Serum-ascites albumin gradient
SD	Standard deviation
SLE	Systemic lupus erythematosus
SWE	Shear Wave Elastography
TB	Total bilirubin
TE	Transient Elastography
TGF- β	tumor growth factor β
TIPS	Transjugular Intrahepatic Portosystemic Shunt
WBCs	White blood cells
WHO	World Health Organization
β 2 GPI	β2-glycoproteine I

INTRODUCTION

Budd–Chiari (BCS) syndrome is a heterogeneous group of disorders characterized by hepatic venous outflow obstruction at the level of the hepatic venules, the large hepatic veins, the inferior vena cava till its junction with the right atrium ***(Valla, 2008).***

BCS is further classified as being primary or secondary, depending on the exact nature of the hepatic venous outflow obstruction. When flow is obstructed by compression or invasion of a lesion outside the hepatic venous outflow track, it is regarded as being secondary BCS; examples include malignant and cystic extrinsic obstruction. If flow is obstructed due to an end luminal aberration, then it is classified as being primary BCS ***(DeLeve et al., 2009).***

Hepatic venous outflow obstruction causes centrilobular congestion and hepatocyte necrosis, which if not treated can lead to hepatic lobulation and cirrhosis. The evolution and severity of these changes vary widely and depend upon the cause, degree and extent of obstruction. Thus, the clinical presentation of BCS has a wide spectrum and ranges from asymptomatic cases to fulminant hepatic failure ***(Darwish et al., 2009).***

The classic triad of abdominal pain, ascites, and hepatomegaly is observed in the vast majority of patients with

Budd-Chiari syndrome, but it is nonspecific. A high index of suspicion is needed to make the diagnosis. Patients with acute onset of obstruction typically present with acute right upper quadrant pain. Abdominal distention can also be a significant symptom, because of ascites. Jaundice is rarely observed ***(Goel et al., 2015).***

The goals of treatment are to prevent extension of thrombosis in the hepatic veins and to alleviate venous obstruction in order to decrease hepatic congestion. Few patients respond to medical treatment (anticoagulation with or without thrombolytic therapy, diuretics). However, most of patients need more invasive procedures to restore the hepatic blood flow including percutaneous angioplasty with or without stenting, transjugular intrahepatic portosystemic shunt (TIPS) or shunt surgery ***(Pieter and Frederik, 2015).***

Liver fibrosis is the single most important factor determining the prognosis in CLD. Detection of earlier stages of liver fibrosis may be helpful in prevention of its progression and may even result in complete regression if appropriate treatment is instituted ***(*Fowell and Iredale, *2006).***

Fibrosis is a dynamic process and many studies have suggested that liver fibrosis is actually reversible when the underlying condition is treated. In the early stages of fibrosis, it may be possible to achieve a total curative effect. Therefore,

the early diagnosis and prevention of liver fibrosis is of great importance in the clinical setting ***(Shin et al., 2016).***

Patients with advanced fibrosis and cirrhosis are generally recommended to undergo clinical surveillance for complications ***(Lok et al., 2009).*** Staging of liver fibrosis is therefore important in the management of CLD.

The presence and degree of hepatic fibrosis is crucial in order to make therapeutic decisions and predict clinical outcomes. Currently, the place of liver biopsy as the standard of reference for assessing liver fibrosis has been challenged by the increasing awareness of a number of drawbacks related to its use (invasiveness, sampling error, inter-/intraobserver variability). In parallel with this, noninvasive assessment of liver fibrosis has experienced explosive growth in recent years and a wide spectrum of noninvasive methods ranging from serum assays to imaging techniques have been developed. Some are validated methods, such as the Fibrotest and transient elastography, and are gaining a growing role in routine clinical practice, especially in chronic hepatitis C. Large-scale validation is awaited in the setting of other chronic liver diseases. However, noninvasive tests used to detect significant fibrosis and cirrhosis, the two major clinical endpoints, are not yet at a level of performance suitable for routine diagnostic tests, and there is still no perfect surrogate or method able to completely replace an optimal liver biopsy ***(Vasilios et al., 2012).***

Transient Elastography is a shear wave and ultrasound-based method, developed by Echosens® (France), initiated from the principles of Hooke's law, which characterizes a material's strain response to external stress ***(Arinc et al., 2018).***

The evaluation of the effectiveness of BCS treatment is generally based on symptoms, which inevitably introduces subjective factors and errors ***(Valla , 2009).*** Although Doppler ultrasound has unique advantages as a preferred test for BCS, it has certain technical limitations when used in follow-up examination. Doppler ultrasound may be affected by imaging depth and angle; it has less value in patients with porous and/or membranous lesions of the IVC, and is operator dependent***).*** Moreover, for lesions with less significant hemodynamic changes, Doppler ultrasound lacks sensitivity in evaluating short- and long-term outcomes after therapy ***(Boozari et al., 2008).***

Though unrelated to the degree of liver fibrosis, LSM is highly sensitive to the changes in hepatic venous pressure. Therefore, efficacy of treatment based on SWE can not only improve the outcome evaluation, but also reduce invasiveness ***(Wang et al., 2018).***

Liver stiffness (LS) measurements made with FibroScan Transient Elastography(TE) can be used as a noninvasive tool to assess hepatic congestion and there by indirectly provide insights into the technical outcome and the benefits of endo-