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PhD Thesis

COMPARISON BETWEEN DIFFERENT ELASTOGRAPHY TECHNIQUES FOR THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS

SUMMARY

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INTRODUCTION

Liver fibrosis is part of the functional and structural changes that occur in most chronic liver diseases as a result of repetitive tissue injury leading to the accumulation of excess protein in the liver interstitial space. The ongoing injury in the absence of treatment may lead to the development of cirrhosis and liver-related complications in viral and non-viral chronic liver disease. Therefore, early diagnosis and accurate staging of liver fibrosis are of vital importance for clinical treatment.

Traditionally, liver biopsy has been the sole method available for liver fibrosis staging and it remains the gold standard for diagnosing and staging fibrosis, especially in complex liver diseases. Due to complications associated with performing a liver biopsy, efforts have been made to migrate towards noninvasive techniques for liver fibrosis assessment.

In recent years, the armamentarium of non-invasive methods available for liver fibrosis assessment has increased dramatically. Besides serum markers used either solitary or in complex mathematical formulations, imaging elastography techniques have been extensively used for this purpose.

Transient Elastography (TE) was the first non-invasive ultrasound elastography method developed to offer a quantitative assessment of hepatic fibrosis in patients with chronic liver disease by measuring liver stiffness and its clinical usefulness has been validated in a large number of studies globally. Since then extensive research has been conducted for the development of other ultrasound elastography techniques capable of overcoming the limitations of TE.

The present research aims to perform a comparative analysis between different shear-wave elastography techniques in terms of feasibility, accuracy, and diagnostic performance in staging liver fibrosis to identify the limitations of each technique and establish the optimal technique for liver stiffness assessment.

We evaluated the performance of Transient Elastography in comparison to Virtual Touch Quantification (VTQ) for the noninvasive assessment of liver fibrosis in a cohort of

patients infected with chronic HBV or chronic HCV to identify the strengths and limitations of each technique and make recommendations for their use in clinical practice.

Secondly, we evaluated the performance of a 2D-SWE technique in a cohort of patients with non-alcoholic fatty liver disease (NAFLD) using TE as the reference method to establish etiology-specific cut-off values for identifying advanced fibrosis and cirrhosis.

Lastly, we performed a comparative analysis of different SWE techniques using TE as the reference standard to identify the optimal method for the non-invasive assessment of liver fibrosis and make recommendations for their use in clinical practice. To achieve this we first analyzed a pSWE technique in comparison to a 2D-SWE technique in terms of feasibility, reliability, and diagnostic performance as well as establishing etiology-specific liver stiffness (LS) cut-off values for discriminating across fibrosis stages of different severity. Afterward, we performed a comprehensive analysis of two different two-dimensional shear wave elastography techniques to identify the advantages and limitations of each method as well as to establish etiology-specific LS cut-off values to be used in clinical practice in discriminating between different fibrosis stages.

GENERAL PART

LIVER FIBROSIS ASSESSMENT

The diagnosis and staging of hepatic fibrosis has become very important in clinical practice and can be carried out using invasive and noninvasive methods. Invasive methods consist of removing a small piece of liver tissue, so it can be examined under the microscope for signs of damage or disease, whereas noninvasive methods rely on two different approaches: a biological approach based on quantification of biomarkers in serum samples and a physical approach based on the measurement of LS. Accurate staging of liver fibrosis and appropriate treatment may reverse or prevent the progression to cirrhosis and its potential complications such as portal hypertension or hepatocellular carcinoma. Traditionally, the diagnosis and determination of fibrosis stage were carried out using liver biopsy which can provide valuable information about the etiology of CLD, in patients with unexplained elevated liver function tests. Although liver biopsy remains an important clinical tool in the hand of the hepatologist it is now infrequently used for the evaluation of liver fibrosis in patients with chronic HCV infection. Many noninvasive techniques are now

available and have become an important part of patient care as a safer, more accessible, and less costly strategy than liver biopsy for stratifying patients according to risk. These methods include ***indirect biomarkers, direct biomarkers,*** and ***imaging elastography***. In the current era, the optimal approach to fibrosis assessment is to use a combination of noninvasive serum markers/tests with Transient Elastography. Where Transient Elastography is not available, two different noninvasive serum markers/tests should be used.

According to the European Federation of Societies in Ultrasound in Medicine and Biology (EFSUMB) clinical practice guidelines, ***non-invasive ultrasound methods*** for the assessment of liver disease severity are classified into two categories:

- Displacement or strain imaging elastography techniques:
    - Quasi-static techniques: strain elastography (SE) and strain rate imaging (SRI)
    - Acoustic radiation force impulse (ARFI) imaging
- Shear wave elastography (SWE) techniques: Transient Elastography (TE), point Shear Wave Elastography (pSWE), also known as ARFI quantification, two dimensional and three dimensional Shear Wave Elastography (2D-SWE and 3D-SWE)

ULTRASOUND BASED ELASTOGRAPHY TECHNIQUES

Transient Elastography (TE)

TE was the first elastography technique to be commercialized and has had extensive validation and evaluation of its strengths and weakness in comparison with other methods. The primary role of TE is for the non-invasive diagnosis of liver fibrosis, intending to reduce the need for liver biopsy in the clinical management of CLD

TE is a reliable method for the diagnosis of cirrhosis in patients with CLD, with better performance in ruling out than ruling in cirrhosis (NPV 96% and PPV 74%). TE has better performance in accurately detecting cirrhosis than significant fibrosis (AUC values 0.80-0.99 for cirrhosis vs 0.65-0.97 for significant fibrosis and correct classification ranging from 80 to 98% for cirrhosis vs 57% to 90% for significant fibrosis). Several meta-analyses have confirmed the better diagnostic performance of TE for diagnosis of cirrhosis than

fibrosis, with reported AUC values of 0.84 and 0.94, respectively. Different cut-offs have been proposed for the diagnosis of cirrhosis according to etiologies ranging from 9.7 kPa in HBV to 22.7 kPa in alcoholic liver disease (ALD). However, one must consider that there is a wide array of threshold values for defining cirrhosis in these studies, partly since ROC curve analysis was used to define the cut-off values to maximize sensitivity and specificity and they have not been applied to a validation cohort. Another explanation could be related to the difference in cirrhosis prevalence in the studied populations (ranging from 8% to 54%), leading to spectrum bias. Based on a meta-analysis, some authors have proposed a cut-off of 13 kPa for the diagnosis of cirrhosis. Lastly, the cut-off choice must also consider the pre-test probability of cirrhosis in the target population, which varies considerably from the general population to tertiary referral centers.

Point Shear Wave Elastography (pSWE)

Point shear-wave elastography (pSWE) is a type of SWE in which tissue stimulation is performed at a certain depth by an acoustic radiation force impulse (ARFI) generated by the transducer, also known as ARFI quantification

pSWE, as opposed to TE, is feasible in patients with ascites. Moreover, several published studies have demonstrated that pSWE methods, both VTQ and ElastPQ have higher feasibility when compared to TE with reported values above 92%

Most studies evaluating the performance of pSWE methods, particularly for VTQ have been conducted in patients with mixed chronic liver disease with viral hepatitis being the predominant liver disease. These studies have demonstrated that VTQ more accurately detects cirrhosis (AUC values: 0.81-0.99) than significant fibrosis (AUC values: 0.77-0.94). Furthermore, several meta-analyses have confirmed the better diagnostic performance of VTQ for cirrhosis than for fibrosis. The cut-off values suggested in the two meta-analyses for the diagnosis of significant fibrosis were 1.34 m/s – 1.35 m/s and for the diagnosis of cirrhosis were 1.80-1.87 m/s.

Regarding ElastPQ, few data are available in patients with mixed chronic liver disease. In a study that compared ElastPQ with TE, which was considered as reference, the AUROC calculated for significant (F≥2), severe (F≥3) fibrosis and cirrhosis (F=4) were 0.94, 0.97, and 0.97 respectively. In another study where liver biopsy was used as a reference

method, ElastPQ had good diagnostic accuracy in identifying each liver fibrosis stage. For the diagnosis of cirrhosis, ElastPQ showed similar performance when compared to TE (AUC=0.834 and 0.879, respectively).

Two-dimensional Shear Wave Elastography (2D-SWE)

2D-SWE is a type of SWE where tissue interrogation is performed by placing the ARFI focus on multiple sequential locations generating patches of small SWS images that may be mosaicked to create a large ROI 2D-SWE image, which is displayed in grayscale or color

The most important advantage of 2D-SWE as compared to TE in characterizing diffuse liver disease is the possibility of performing LSM in patients with ascites, although an adequate B-mode ultrasound live image is necessary for reliable results

Several studies have shown good accuracy of 2D-SWE for predicting significant fibrosis and cirrhosis in patients with CLD of various etiology. In a study performed by Cassinotto et al. which enrolled 349 consecutive patients with CLD who underwent liver biopsy, 2D-SWE (SSI), pSWE (VTQ), and TE were compared. The AUC of 2D-SWE.SSI for the diagnosis of mild, significant, severe fibrosis and cirrhosis were 0.89, 0.88, 0.93, and 0.93, respectively. All methods correlated significantly with histological fibrosis scores. 2D-SWE.SSI had a higher accuracy than TE for the diagnosis of severe (F≥3) fibrosis (p=0.0016), and higher accuracy compared to VTQ for the diagnosis of significant (F≥2) fibrosis (p=0.0003).

A meta-analysis involving 1134 patients with liver diseases of mixed etiology published in 2018, analyzed the diagnostic performance of 2D-SWE.SSI for liver fibrosis assessment in comparison to liver biopsy. 2D-SWE.SSI showed good to excellent performance in LS assessment in patients with HCV, HBV, and NAFLD, for the diagnosis of significant (F≥2) fibrosis, and cirrhosis (F=4), with reported AUC of 86.3%, 91.6%, 85.9%, and 96.1%, 97.1%, 95.5%, respectively. The optimal cut-off for the diagnosis of significant fibrosis was 7.1 kPa.

SPECIAL PART

Having so many methods available for the evaluation of LS, the present research **aims** to compare different ultrasound-based elastographic techniques in terms of feasibility, accuracy, and diagnostic performance in staging liver fibrosis and make some recommendations regarding their use in clinical practice.

The main objectives of this thesis were:

1. To evaluate the reproducibility and feasibility of different ultrasound elastography techniques and to establish the optimal technique for liver fibrosis assessment in patients with various CLD and identify factors associated with failure or unreliable liver stiffness measurements using different ultrasound elastography techniques.
2. To compare the performance of an SWE technique to TE in the non-invasive assessment of liver fibrosis using liver biopsy as the reference standard
3. To compare the performance of a 2D-SWE technique to TE in the non-invasive assessment of liver fibrosis using TE as the reference standard
4. To compare the performance of a pSWE technique to a 2D-SWE technique in the non-invasive assessment of liver fibrosis using TE as the reference standard
5. To compare the performance of two different 2D-SWE techniques in the non-invasive assessment of liver fibrosis using TE as the reference standard

METHODS

ABDOMINAL ULTRASOUND

All the subjects included in the research underwent a complete abdominal ultrasound scan before liver biopsy or SWE elastography was performed with particular focus in the evaluation of liver structure and surface to look for signs of cirrhosis, to exclude focal liver lesions, to look for signs of biliary obstruction or portal vein thrombosis, to scan for ascites or signs of heart failure which could have an impact on LSM.

The ultrasound evaluation was carried out using several ultrasound systems from different manufacturers: Logiq E9 system (GE Healthcare, Wauwatosa, WI, USA) (version 2.0); Siemens Acuson S2000 system (Siemens AG, Erlangen, Germany), Phillips EPIQ 7

system (Phillips Healthcare, Bothell, WA, USA), Canon Aplio i800 system (Canon Medical Systems Corporation, Otawara, Tochigi, Japan) and Aixplorer® ultrasound system (Hologic SuperSonic Imagine S.A., Aix-en-Provence, France).

LIVER BIOPSY

The LB procedure was performed under ultrasound guidance with 1.4 and 1.6 mm Menghini type modified needles (Hepafix, B Braun, Melsungen AG, Germany) using the double-pass technique by an experienced operator with the patient under mild anesthesia using 2-5 mg midazolam intravenous with continuous oxygen saturation monitoring.

ELASTOGRAPHY EVALUATION

All elastography examinations were performed using several SWE elastography methods following the recommendations from the EFSUMB clinical practice guidelines. The examinations were performed with the patient lying in the supine or slight lateral left position with the right arm raised above the head using an intercostal approach, in fasting conditions for at least 4h.

Informed consent for liver biopsy and elastography measurements was obtained from all participants. The research was approved by the institutional review board and the Ethics committee of the Victor Babeș University of Medicine and Pharmacy Timișoara and Clinical Emergency County Hospital "Pius Brînzeu" Timișoara and was performed following the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh.

RESULTS

COMPARISON BETWEEN THE FEASIBILITY AND RELIABILITY OF SWE TECHNIQUES IN STAGING LIVER FIBROSIS

In the first study which included 169 patients with chronic HCV or HBV infection who also had LB performed, we found no significant difference in the technical success rate of TE (97.6% [165/169]) and VTQ (98.8% [167/169]) (p=0.41). Furthermore, there was no statistical difference between the reliable measurements of TE (98.2%) and VTQ (97.6% [165/169]) (p=0.70). These results are similar to other cross-validation studies which reported no significant differences between TE and VTQ in terms of reliability, intra or inter-observer reproducibility. However, we must take into consideration that the inclusion of only

non-obese subjects might have impacted the results of our study, since several studies have reported higher LSM failures in patients with obesity while using TE, even with the introduction of the XL probe.

In the study where the validity of LSM obtained using TE, pSWE and 2D-SWE was analyzed we found that the rate of valid LSM was similar using all three methods, TE, ElastPQ, and 2D-SWE.GE (95.4% vs. 92.6% vs. 93.1%, p=0.507). When analyzing factors leading to technical failure, we found that only higher BMI was associated with the impossibility to obtain valid LSMs using ElastPQ and 2D-SWE.GE, but interestingly not using TE, which could be explained by the availability of the XL probe.

In another study, we analyzed the feasibility of two 2D-SWE techniques implemented on different US systems and found no significant difference in terms of their reliability in LS assessment when compared to each other and TE (2D-SWE.GE vs. 2D-SWE.SSI vs TE: 95.6% vs. 92.7% vs. 94.7%, p=0.428).

PERFORMANCE OF TE AND VTQ IN STAGING LIVER FIBROSIS USING LIVER BIOPSY AS REFERENCE STANDARD

We performed a retrospective monocentric cross-sectional study on 245 patients diagnosed with chronic HCV or chronic HBV infection conducted in the Department of Gastroenterology and Hepatology, Timisoara County University Hospital between January 2010 and November 2018 who had liver biopsy performed to evaluate the diagnostic performance of TE and VTQ in staging liver fibrosis.

A significant, direct, and strong correlation between TE and VTQ liver stiffness measurements (rho Spearman's coefficient=0.826, with 95% confidence interval for rho (0.769, 0.870, p<0.001) was found.

The association between fibrosis stage classification by the two diagnostic methods is statistically significant (Chi-squared Test, p<0.001). The inter-rater agreement (kappa) was 0.545 (moderate agreement), with 95% CI for κ (0.449, 0.641), with an overall proportion of agreement of 51.59% (95% CI: 43.49, 65.71).

Of the 157 patients, 69 (43.9%) showed discordance between the TE and Metavir scores, while 72 (45.8%) showed discordance between the VTQ and Metavir scores. Several factors possibly associated with these discordances were analyzed, including age, gender,

BMI, ALT, AST, biopsy specimen length. Only biopsy specimen length was associated with the discordance between the TE and Metavir score (p=0.026), respectively VTQ and Metavir score (p=0.034).

These results indicate that both TE and VTQ have good diagnostic accuracy in the identification of patients with significant fibrosis and excellent diagnostic accuracy for advanced fibrosis and cirrhosis, results which are similar to the meta-analysis performed by Bota et al., where TE and VTQ were found to be equally accurate in diagnosing significant fibrosis and cirrhosis.

PERFORMANCE OF A 2D-SWE TECHNIQUE IN LIVER FIBROSIS ASSESSMENT USING TE AS REFERENCE STANDARD

The study cohort was composed of 112 consecutive adults with reliable LSM, 44 healthy subjects, and 68 subjects with chronic hepatopathies. This study aimed to evaluate the usefulness of a new 2D-SWE technique for the non-invasive assessment of liver fibrosis using TE as the reference standard.

Mean LS values assessed by 2D-SWE were similar to mean LS values assessed by TE (7.2±4.3 vs 7.47±8.13, p=0.66). For healthy volunteers, mean LS values by 2D-SWE were 5.15±2.61 kPa and by TE was 5.47±2.53 kPa, p=0.5.

A very strong positive correlation was found between the LS values obtained by TE and 2D-SWE: r=0.88, p<0.0001.

The results of our study are supported by another study performed by Cassinotto et al., which enrolled 294 patients with biopsy-proven NAFLD, and compared the performance of TE, VTQ, and 2D-SWE in the diagnosis of significant, severe fibrosis and cirrhosis. In this study, 2D-SWE had AUC values of 0.86, 0.89, and 0.88 for the diagnosis of significant fibrosis, severe fibrosis, and cirrhosis. This corresponds reasonably well with the results of our study where we reported AUC values of 0.89 and 0.94 for the diagnosis of significant fibrosis, and cirrhosis, respectively

COMPARISON BETWEEN THE PERFORMANCE OF A pSWE AND 2D-SWE TECHNIQUE FOR LIVER FIBROSIS ASSESSMENT

We performed a monocentric cross-sectional study conducted in a Department of Gastroenterology and Hepatology between January 2018 and January 2020 which included a total of 176 patients with chronic hepatitis C virus (HCV) infection.

The Kolmogorov-Smirnov test showed that ElastPQ and 2D-SWE.GE LSM were not normally distributed.

Regarding fibrosis distribution, we found significant differences between 2D-SWE.GE and ElastPQ LS values only in patients with liver cirrhosis (F4).

2D-SWE.GE LSM correlated better with TE than ElastPQ LSM ($r=0.88$, $p<0.0001$ vs. $r=0.74$, $p<0.0001$, z test $p=0.0001$). The correlation coefficient between ElastPQ LSM and 2D-SWE.GE LSM was $r=0.78$, $p<0.0001$.

Pairwise comparisons of AUROC curves between 2D-SWE.GE and ElastPQ have shown that there are no significant differences in their performance for staging $F\geq2$ fibrosis ($p=0.89$), $F\geq3$ fibrosis ($p=0.76$), and $F=4$ fibrosis ($p=0.86$).

The results of our study have shown that both methods, ElastPQ and 2D-SWE.GE has good performance in staging liver fibrosis when compared to TE, with similar LS cut-off values for predicting significant ($F\geq2$) fibrosis: 6.51 kPa vs. 6.5 kPa, for predicting advanced ($F\geq3$) fibrosis: 8.73 kPa vs. 8.17 kPa and for predicting cirrhosis ($F=4$): 11.1 kPa vs. 11.3 kPa.

COMPARISON BETWEEN THE PERFORMANCE OF TWO DIFFERENT 2D-SWE TECHNIQUES FOR LIVER FIBROSIS ASSESSMENT

We performed a monocentric cross-sectional prospective study conducted in the Department of Gastroenterology and Hepatology between January 2016 and November 2019 which included a total of 208 patients with chronic HCV infection who underwent LSM using TE, 2D-SWE.GE and 2D-SWE.SSI.

The two-sample t-test showed the mean LS values obtained by 2D-SWE.GE and 2D-SWE.SSI differs significantly between adjacent fibrosis stages.

2D-SWE.GE LSM correlated better with TE than 2D-SWE.SSI (r=0.75, p<0.0001 vs. r=0.57, p<0.0001, z test p=0.0012). Linear regression analysis showed a moderate correlation between LSM obtained by 2D-SWE.GE and 2D-SWE.SSI (r=0.63, R^2=0.4, P<0.0001), results which could be accountable to the narrow range of LS values in patients with low-grade fibrosis versus a wide range for significant fibrosis since most patients included in our study had advanced fibrosis or liver cirrhosis.

The Bland-Altman analysis revealed the mean difference in LSM between 2D-SWE.GE and 2D-SWE.SSI was 4.68±8.5 kPa.

The mean LS values were significantly higher for 2D-SWE.SSI than 2D-SWE.GE across all fibrosis stages (20.7 ± 11.5 kPa vs. 13.2 ± 2.8 kPa, p<0.0001).

GENERAL DISCUSSIONS

So far liver elastography proved to be a valuable tool for the noninvasive assessment of liver fibrosis regardless of which technique was used with good performance across all fibrosis stages. Moreover, we found no significant differences in terms of feasibility and technical failure when comparing different SWE techniques. Looking at the advantages and limitations of each technique we found obesity to be an important limiting factor across all SWE techniques analyzed, therefore research must be directed towards overcoming this limitation by developing better software or machines capable of acquiring reliable LSM.

In our research we found a moderate agreement between TE and histological fibrosis and between VTQ and histological fibrosis, indicating that both methods are good tools for the non-invasive assessment of liver fibrosis

Looking at the results of our research we found no significant difference across SWE techniques in terms of performance, therefore it is safe to recommend choosing the technique based on operator experience and clinical scenario considering the limitations as previously discussed. When choosing the elastography technique we need to consider that pSWE and 2D-SWE methods offer several advantages compared to TE providing direct visualization of the liver parenchyma, enabling simultaneous morphological and Doppler analysis of the liver, screening for focal liver lesions, and looking for signs of portal hypertension. Moreover, both methods allow the operator to position the ROI in the desired area of the liver, following the recommendations of the clinical practice guidelines.

Looking at the results of our research we found LS values obtained using different SWE techniques to be generally well correlated, although we found a wide array of values across different fibrosis stages, which is probably related to the different techniques used to generate and analyze SW data across manufacturers of US systems.

Currently, there is an ongoing need for the development of noninvasive surrogate markers in the screening of patients with cACLD, especially in the setting of NAFLD for patients who are at a high risk of NASH, where LB can reliably differentiate NAFLD from NASH. Several US systems manufacturers are developing machines capable of the quantification of not only liver elasticity as a marker of fibrosis but also inflammation and steatosis, offering a more comprehensive understanding of liver status by generating a multi-parametric report. Animal studies have shown that MPUS examinations have the potential to provide a comprehensive estimation of the main components of early-stage NAFLD

Furthermore, MPUS by combining the greyscale US with Doppler imaging and elastography with contrast-enhanced ultrasound is used to assess etiology, stage, complications, and prognosis of patients with CLD, as well as to characterize focal liver lesions (FLL)

Besides MPUS, Magnetic Resonance Imaging (MRI) and MRI-based elastography (MRE) are the most promising techniques in assessing liver disease. Recent developments in multi-parametric magnetic resonance imaging (MPMRI) have narrowed the gap between histological diagnosis and non-specific blood-based biomarkers, with important implications for the clinical care and treatment pathway in a variety of CLD.

Looking to the future, this armamentarium of techniques encompassing MPUS and MP-MRI could allow clinicians to increase their arsenals available to utilize on patients and direct appropriate treatments. By performing US examination followed by SWE to assess LS, steatosis, and inflammation, the clinician can accurately have an account of patients' disease severity. Moreover, if a mass is discovered in the liver during US examination, the clinician can immediately perform CEUS to provide a diagnosis with high probability.

"Point of care" Elastography (POCE) is one possible future direction for the development of US elastography. Lately, middle-class ultrasound machines from different vendors (Siemens, Philips, General Electric, Canon, or Samsung) have an inside module for

liver elastography (pSWE or 2D-SWE), which enables the clinician to perform an elastographic examination of the liver immediately after the conventional B-mode US examination. This strategy represents a real screening method in a population at risk of having cACLD (patients with risky alcohol behavior, NAFLD, type 2 diabetes mellitus, obesity, or metabolic syndrome), enabling prompt therapeutic intervention and steering of patients towards a specialist center for further disease severity evaluation.

After more than 15 years of active development and ongoing investigations, alternatives to liver biopsy for the staging of chronic liver diseases have revealed both their strengths and weaknesses. There is an ongoing need for developing novel strategies to move the field forward.

CONCLUSIONS

1. All elastography techniques evaluated in this research (TE, pSWE, and 2D-SWE) have good feasibility for the evaluation of LS.
2. The main causes that lead to failed or unreliable LSM regardless of the technique used were obesity, narrow intercostal spaces, poor compliance, and poor acoustic window.
3. There was no significant difference between the technical success rate of TE, pSWE, and 2D-SWE techniques evaluated in this research
4. A significant and strong correlation between TE and VTQ LSM and between TE and 2D-SWE LSM was found.
5. A better correlation was found between 2D-SWE.GE and TE LSM, then between ElastPQ and TE LSM or 2D-SWE.SSI and TE LSM.
6. A moderate correlation was found between LSM obtained by different 2D-SWE systems
7. Biopsy specimen length was the only factor associated with discordance between TE and Metavir, respectively pSWE and Metavir.
8. No significant difference was found between the performance of pSWE and TE when compared to LB across all fibrosis stages.
9. Pairwise comparisons of receiver operator characteristics (ROC) curves between 2D-SWE and pSWE have shown that there are no significant differences in their performance for staging F≥2 fibrosis (p=0.89), F≥3 fibrosis (p=0.76), and F=4 fibrosis (p=0.86).
10. Pairwise comparison of receiver operating characteristics curves (ROC) found no significant differences between two 2D-SWE techniques in identifying F≥2 fibrosis (0.97 vs. 0.96, P = 0.5650), F≥3 (0.97 vs. 0.95, P = 0.2935), or F=4 (0.97 vs. 0.96, p = 0.6914).
11. Provided sufficient training requirements are met any elastography techniques from those studied in this research can be used to accurately assess LS.