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Possible use of 2D shear wave liver elastography in new-onset ascites evaluation

Andrej Hari^{1*} and Borut Štabuc²

Abstract

Background No data on the use of 2D shear wave elastography exists regarding the evaluation of the new-onset ascites causality.

Aims To determine whether 2D shear wave elastography can help in the non-invasive assessment of the new-onset ascites cause. To assess the applicability of liver stiffness measured by 2D shear wave elastography using Esaote MyLab Nine apparatus in patients with ascites.

Methods In 52 consecutive patients with new-onset ascites (January 2020 to October 2021), liver stiffness using 2D shear wave elastography was prospectively measured. The reliable measurements were used for further analysis. Relevant clinical and laboratory data was collected.

Results The calculated liver stiffness measurement cut-off value of 14.4 kPa held 94% accuracy, 100% sensitivity, and 83% specificity when determining ascites with serum ascites albumin gradient ≥ 11 g/L. Reliable 2D shear wave elastography success rate was 84%.

Conclusions 2D shear wave elastography may potentially be used to differentiate transudative from exudative ascites, especially in patients with portal hypertension and peritoneal carcinomatosis.

Keywords Ultrasound, Quality criteria, Cirrhosis, Carcinomatosis, Liver

Introduction

Ascites means the appearance of free fluid in the abdominal cavity. The most common processes involved in its occurrence are portal hypertension (PH) and peritoneal membrane disease. In the Western population, the most common cause of ascites is PH, which is due to cirrhosis in most cases [1–3]. The clinically relevant ascites division is based on the serum-ascites albumin gradient (SAAG) determination, which biochemically divides

ascites into exudate and transudate. While albumin-rich ascites (exudate) is due to inflammatory and/or neoplastic causes, ascites due to PH is a transudate characterized by SAAG values ≥ 11 g/L; this value has more than 97% accuracy in differentiating portal hypertensive causes from other causes [1–3]. However, several etiologies may be present simultaneously (mixed ascites), which complicates differential diagnosis [2, 4–6]. The most common causes of ascites are portal hypertension, neoplastic causes and inflammatory causes, or pancreatic ascites.

In particular, it is clinically very important to rapidly classify ascites into benign (mostly due to PH) and malignant (due to peritoneal carcinomatosis); more than 90% of new-onset ascites cases belong to one of these two etiologies [2, 6, 7]. In the presence of ascites, findings typical of cirrhosis such as morphological changes and PH-specific signs such as the presence of portosystemic

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collaterals (Table 2) can be used to postulate PH as the etiology [8, 9]. Imaging signs of cirrhosis and PH have high inclusion and low exclusion value.

Liver elastography is commonly used to further improve the cirrhosis and PH diagnosis [8, 9]. According to the Baveno VII consensus conference [10], the presence of clinically significant portal hypertension (CSPH) in patients with compensated advanced chronic liver disease (cACLD) can be reliably ruled out by liver elastography when the elastographic value is < 15 kPa and platelet count $> 150 \times 10^9$ per nanoliter of blood. The confirmatory threshold of elastography for CSPH in the most common cACLD etiologies is > 25 kPa, and from 15 kPa onward, the probability of CSPH presence slowly increases [10]. 2D shear wave elastography (2D-SWE) is a well validated method in this field [11–13]. In two studies performed in a subset of patients with cirrhosis with or without ascites, 2D-SWE showed a significantly positive correlation with invasively evaluated portal pressure [14, 15].

A study by Kolhaas et al. on a phantom model and using TE (XL probe) found that, in cases where the thickness of the perihepatic ascites layer did not exceed 20 mm, a non-hepatic cause of ascites could be reliably identified [16]. A clinical study performed by Bota et al. identified a good predictive value of point shear elastography (pSWE) to distinguish cirrhotic and non-cirrhotic etiology of ascites [17].

Given the wide availability of elastographic methods, we are interested in whether 2D-SWE can provide data allowing a non-invasive discrimination between PH-related causes and other causes in patients with new onset ascites. There is no study data in this area. Also, the applicability of 2D-SWE measurement using Esaote MyLab Nine apparatus in patients with ascites will be concurrently assessed.

Materials and methods

We obtained the approval of the regional General Hospital Celje Ethics Commission and performed a retrospective analysis of the prospectively collected data. Informed written consent was obtained from each patient included in the study. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and Istanbul.

Study population

Data collection, blood and ascites analysis, and ultrasound examination were performed between January 2020 and October 2021. Based on similarly designed studies, the size of our hospital center, and the statistical characteristics of the observed parameters, we conducted a study on a sample of 50 patients. The cohort was divided according to the SAAG value into Group 1

(SAAG ≥ 11 g/L) and Group 2 (SAAG < 11 g/L). Based on a preliminary statistical analysis, we decided to include at least 30 patients in Group 1 and 15 patients in Group 2. The cohort was completed when both conditions were met.

Our study included patients with new-onset ascites who were hospitalized in the internal medicine wards of the General Hospital Celje. The inclusion criteria were as follows: ultrasonographic confirmation of clinically relevant ascites (grade 2 or 3) and hemodynamically stable patients who did not require acute dialysis or vasopressor therapy. No previously known medical condition affecting the onset of ascites. Furthermore, for Group 1, there were as follows: the presence of liver cirrhosis (US or CT morphological signs, laboratory signs of impaired liver function according to the CHILD score) and only patients with sinusoidal PH. The exclusion criteria were as follows: extrahepatic cholestasis presence, portal venous thrombosis presence or thrombosis in any of the hepatic veins, the presence of cardiac cirrhosis, clinical signs of congestive right-sided heart failure, ultrasound-proven dilatation of the right hepatic vein > 10 mm at the characteristic site, the presence of cancer or infiltrative liver disease at the site of elastographic measurement, the presence of a mixed cause of ascites, serum bilirubin > 100 mmol/L and aminotransferase levels (AST, ALT) > 3 times the normal upper limit, and ascites due to bleeding or hollow organ perforation. Furthermore, for Group 1: the presence of spontaneous bacterial peritonitis, acute-on-chronic liver failure (ACLF), active varicose hemorrhage or hepatic encephalopathy Grade > 2 .

Sex, age, standard laboratory data on ascites and liver tests, mortality of patients, and data regarding the etiology of ascites were collected using our center's electronic case record system.

Blood and ascites analysis

Probatory ascites puncture and peripheral venous blood collection were performed on each patient on the same day. Ascites puncture was performed in all cases with an ultrasound-guided selection of the puncture site. Serum and ascites albumin values were obtained from concomitantly collected samples. The SAAG calculation was performed from the defined values. The performed biochemical analysis of ascites included standard parameters (albumin, leukocytes, and neutrophilic granulocytes values, amylase, creatinine, urea, glucose, etc.). At least 20 ml of ascites was used for a cytological cellular analysis. The analysis was repeated up to 3 times in case of unclear results.

2D-SWE and ultrasound examination

Each patient underwent 2D-SWE of the liver and an assessment of morphological cirrhosis signs by an investigator with >5 years of experience. The investigator was not aware of the ascites etiology. The subject fasted for at least 6 h and lay on their back during the examination. The 2D-SWE measurement was obtained during a deep exhalation or in a neutral breathing position. All measurements were performed using the Esaote MyLab Nine™ (Genoa, Italy) device with a monocrystalline high-frequency abdominal probe while following the manufacturer’s protocol for successful measurement. A one-shot image capture function was used during each

measurement (Fig. 1). The investigation was conducted in the ultrasound department of the Department of Gastroenterology, General Hospital Celje.

Elastography was performed with the lowest possible perihepatic amount of ascites, and paracentesis was performed before the examination if necessary (Table 1). Reliable elastographic measurement study protocol for Esaote MyLab Nine was defined according to established recommendations, study data [18–24], and manufacturer’s recommendations (Table 1).

Patients who did not have a reliable elastographic measurement were not included in further analyses. Data on the cause of failed or unreliable measurements

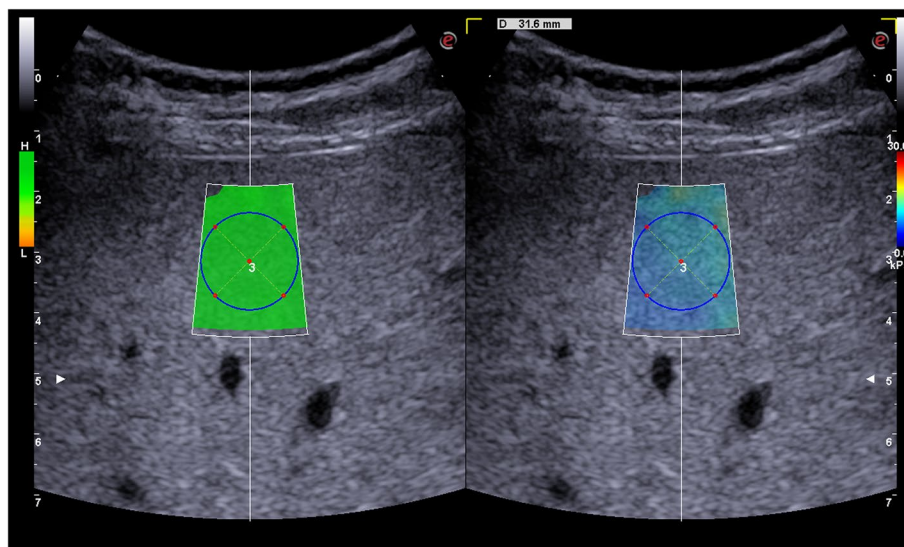


Fig. 1 Shear wave measurement example. Left screen: orange to green colour scale – low to high measurement’s quality according to the manufacturer. Right screen: blue to red colour scale – low to high liver stiffness

Table 1 Reliable liver stiffness measurement

Reliable liver stiffness measurement using Esaote 2D-SWE

- 6 successful measurements
- > 60% success of all the measurements taken
- IQR/LSM < 30%
- ROI > 10 mm in all measurements
- SD < 3x of LSM in all measurements
- Depth of the measurement < 50 mm
- Measurement > 1 cm below liver capsule and in a region without major vessels, bile ducts or masses
- Measurement in two different intercostal spaces
- Evenly distributed FOV colour
- Evenly spaced colour in ROI (no blue-red jumps)
- High quality measurement according to the manufacturer’s instructions^f
- Diameter of perihepatic fluid between probe and liver < 20 mm

^a IQR interquartile range, ^b LSM liver stiffness measurement, ^c ROI region of interest, ^d FOV field of vision, ^e SD standard deviation. ^f see Fig. 1

were recorded. The final elastographic result (liver stiffness measurement - LSM) was provided in kilopascals (kPa) along with the simultaneously recorded IQR/LSM value (%), region of interest (ROI) diameter (mm), and average measurement depth (mm). The value of the measurement was not limited upward.

The morphological signs of cirrhosis were as follows: Uneven surface and/or rounded liver edge assessed by a linear monocrystalline probe of the same apparatus; left hepatic lobe or caudate lobe hypertrophy, and signs of fibrously altered parenchyma. US portosystemic collaterals visualization and splenomegaly were used as confirmative PH signs (Table 2). These signs were used only as an inclusion criterion and never as an exclusion criterion. In unclear cases regarding the presence of liver cirrhosis or a sinusoidal form of PH, a transjugular liver biopsy (TJLB) with concomitant measurement of portal pressure (HVPG) was performed.

Statistical analysis

The value of the elastographic result was rounded to one decimal place, as was the IQR/LSM value. Internationally established units were used for laboratory data. Demographic and clinical population data, including laboratory data and 2D-SWE measurements, were recorded in an electronic database (SPSS Inc., Chicago, IL, USA) for statistical analysis. Descriptive summary statistics of the population were performed. Summary values were described as the average \pm standard deviation (SD) and/or as a median, range, and interquartile range when appropriate (according to the distribution of the processed data). Comparisons between Groups 1 and 2 were performed using Spearman's correlation method and using logistic regression (univariate and multivariate analyses). In order to evaluate the degree of LSM value separability, the probability of the LSM data in Groups 1 and 2 was evaluated using a receiver operating characteristic curve (ROC). The statistical

analysis was conducted with SPSS 26.0 (SPSS Inc., Chicago, IL, USA). The alpha value was set to 0.05. All the *p*-values were two-sided.

Results

The main characteristics of the study population are provided in Table 3.

Our study included 34 patients (65%) with new-onset ascites with SAAG \geq 11 g/L (Group 1). In these cases, cirrhosis and accompanying PH has been confirmed. Etiology of cirrhosis was due to harmful alcohol consumption (20 patients) and metabolically-induced steatohepatitis (8 patients) or a combination of both conditions. Cirrhosis was due to chronic HCV infection and primary biliary cholangitis in two patients.

Group 2 included 18 patients (35%) with new-onset ascites with SAAG < 11 g/L; ascites was due to cancer in 13 patients (25%) and in all cases with cytologically confirmed peritoneal carcinomatosis. Causes of peritoneal carcinomatosis included: upper and lower gastrointestinal cancer (four patients), ovarian cancer (three patients), pancreatic cancer (three patients), breast cancer (two patients), and primary peritoneal cancer (one patient). The remaining five patients (10%) had pancreatogenic ascites (two patients), tuberculosis (one patient), obscure cause (one patient), and immune-mediated ascites (one patient). To evaluate the presence of sinusoidal PH, three patients in Group 2 (5% of the total cohort) underwent an HVPG assessment. A total of 27 patients (52%) were deceased by the end of the study.

SAAG and 2D-SWE relationship

Spearman's analysis of the SAAG values correlation with the following variables was performed: LSM, depth of measurement, platelet count, ALT, and bilirubin. A positive association with LSM ($\rho=0.55$, 95% CI 0.31–0.72, $P<0.001$), a negative association with platelet counts ($\rho=-0.4$, 95% CI -0.6 –0.13, $P=0.005$) and a positive

Table 2 Ultrasound signs of cirrhosis and portal hypertension

Ultrasound signs of cirrhosis and portal hypertension

Nodular liver surface
Blunt liver edge
Coarse echopattern
Left lobe/right lobe ratio > 1.30
Caudate lobe/right lobe ratio \geq 0.65
Reduction of the median segment of the left hepatic lobe
Splenomegaly
Visualisation of portosystemic collaterals

Table 3 Main study population's characteristics

	Overall (N = 52)
SEX	
male	29 (56%)
female	23 (44%)
Etiology	
cirrhosis	34 (65%)
cancer	13 (25.0%)
other	5 (10%)
Patient's state	
Dead	27 (52%)
Alive	25 (48%)
SAAG > 11 g/L	
yes	34 (65%)
No	18 (35%)
Age (years)	
Median (SD)	63 (12)
Min-Max	38–91
ROI (mm)	
Median (SD)	14.5 (1.3)
Min-Max	10–15
Depth of the measurement (mm)	
Median (SD)	42 (6.1)
Min-Max	30–50
Trombocytes (per nL of blood)	
Median (SD)	223 (174)
Min-Max	31–904
ALT (IU/L)	
Median (SD)	53 (38)
Min-Max	8–170
Bilirubin (µmol/L)	
Median (SD)	34 (29)
Min-Max	4–100
INR	
Median (SD)	1.4 (0.35)
Min-Max	0.9–2.3
Serum albumin (g/L)	
Median (SD)	30 (5)
Min-Max	19–43
Ascites albumin (g/L)	
Median (SD)	14 (8)
Min-Max	3–31
SAAG	
Median (SD)	16.3 (7.6)
Min-Max	4–32

^a SAAG serum ascites albumin gradient, ^bSD standard deviation, ^cINR international normalized ratio, ^dmm millimeters, ^eROI region of interest, ^fnL nanoliter, ^gIU international units

association with bilirubin level ($\rho=0.52$, 95% CI 0.28–0.69, $P=P<0.001$) were demonstrated (Fig. 2).

SAAG ≥ 11 g/L showed a significant association with LSM (OR 1.15 (1.07–1.27); 95% confidence interval; $p=0.001$). The LSM distribution in Group 1 was significantly higher than in Group 2 ($p<0.001$, confirmed after adjustment for age and gender). Therefore, in the final analysis, we performed a ROC analysis predicting the LSM cut-off value when SAAG ≥ 11 g/L. The calculated cut-off value was 14.4 kPa (94% accuracy, 100% sensitivity, 83% specificity). In Group 1, the mentioned value defined all included patients (34 true positives, 0 false negatives). In Group 2, the mentioned value correctly defined 15 patients (15 true negatives, 3 false positives). The three false positive patients in Group 2 were patients who required invasive diagnostic evaluation (HVPB and transjugular liver biopsy) for a definitive diagnosis. The final diagnosis in these 3 cases were: extramedullary erythropoiesis in a patient with chronic myelogenous leukemia, porto-sinusoidal vascular disease (idiopathic PH) in 1 case, and ascites due to persistent leakage from the pancreatic duct injury in 1 case. The first two patients had SAAG < 11 g/L although we would expect it to be otherwise. The clear reason behind the lower than expected SAAG value could not be recognized.

Liver stiffness measurement by 2D-SWE

The distribution of liver stiffness measurement in the entire cohort in Groups 1 and 2 is provided in Table 4.

Measurement was attempted in 62 patients, and reliable elastographic measurement was performed in 52 patients (84% reliable measurement success rate). The main reasons for failed measurement were (ranked from most common to rare): obesity, depth of measurement, patients ability to hold their breath, insufficient liver volume, the influence of heart pulsatility on liver movement in ascites, insufficient ROI, and excessive end-result heterogeneity. The ultrasound machine's inability to perform the measurement was observed in $< 1\%$ of all measurements. The reasons for the latter were not clearly identified.

Discussion

The main finding of this study at a single secondary hospital center is that 2D-SWE of the liver can noninvasively discriminate between portal hypertension-related newly onset ascites. The proposed 14 kPa cut-off value is comparable to the values proposed for cirrhosis confirmation in the cACLD group [10, 18–20] and roughly comparable to the proposed values for noninvasive CSPH exclusion criteria in

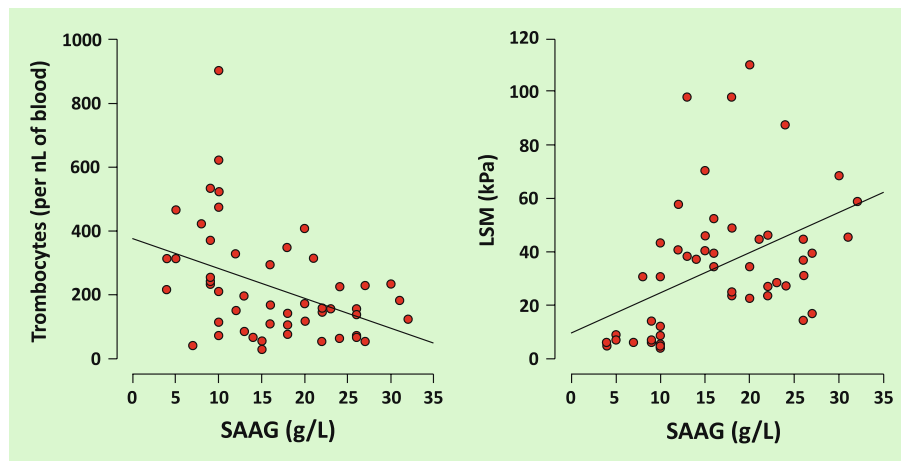


Fig. 2 Relationship between trombocytes, LSM and SAAG according to Spearman’s analysis. LSM – liver stiffness measurement. SAAG – serum ascites albumin gradient. kPa – kilopascals. nL – nanoliter

Table 4 Elastographic measurement parameters distribution

	Etiology		Overall (N = 52)
	Cirrhosis (N = 34)	Other (N = 18)	
LSM (kPa)			
Median (SD)	45.8 (23.6)	11.9 (11.2)	34.1 (25.8)
Min-Max	14.4–110	4.10–18.4	4.10–110
IQR (kPa)			
Median (SD)	9.62 (7.48)	1.83 (1.31)	6.93 (7.13)
Min-Max	1.20–35.0	0.400–5.60	0.400–35.0
IQR/LSM (%)			
Median (SD)	20.7 (7.66)	18.9 (5.95)	20.1 (7.11)
Min-Max	5.00–30.0	9.00–29.0	5.00–30.0

^a LSM liver stiffness measurement, ^bIQR interquartile range, ^cSD standard deviation, ^dkPa kilopascals

published studies and meta-analyses (cACLD populations) [6, 10–15, 24]. The result has important clinical value since our study defines liver elastography (noninvasive, bedside, widely available method), especially its 2D-SWE version, as the best investigative method for assessing CSPH in patients with newly formed ascites. This definition applies mainly to patients with dACLD in the stable disease phase and may be important for further study in patients with severe CSPH (HVPG > 16mmHg). According to our analysis, the close relationship between 2D-SWE and CSPH is also indirectly indicated by the characteristic association between SAAG, 2D-SWE, and platelet blood count. Thrombocytopenia is one of the characteristic CSPH consequences and is involved in most of the proposed noninvasive CSPH assessments guidelines [10].

Similar conclusions were reached by Bota et al. in a larger sample of patients where the liver fibrosis assessment was performed using pSWE [17]. Due to a different

design (strictly sequential patients inclusion), their study included significantly more patients with cirrhosis and a comparable number of patients in the exudative ascites group. The cut-off values of their study and ours differ (approximately 10kPa in Bota et al. versus 14kPa in our cohort). An important reason for this difference may be the used elastographic method, as 2D measurement performs liver stiffness analysis on a much larger liver parenchyma sample. Furthermore, the Bota et al. cohort does not clearly state whether the cut-off value analysis was performed under the SAAG < or ≥ 11 g/L condition. Furthermore, patients with cirrhosis and the rest of the group ratios are significantly different (approximately 3:1 in Bota et al. versus 2:1 in our study). The accuracy of the proposed cut-off value between their cohort and ours was otherwise comparable (95% accuracy versus 94%).

Our study’s calculated 14kPa cut-off value had an appropriate exclusion value for identifying patients with ascites not due to PH, especially in the patient group with peritoneal carcinomatosis resulting from metastatic cancer. Together with some other study data in this area [25–34] – elastography can provide additional non invasive diagnostic information.

Although the analysis was performed in a minimal number of patients, the 2D-SWE exclusion value determining the cause of ascites in groups other than liver cirrhosis or peritoneal carcinomatosis appears to be less accurate, especially in cases where etiologic differentiation was difficult and required extensive and invasive diagnostic work-up. A study by Bota et al. met similar findings [17]. Furthermore, 2D-SWE does not provide sufficient information on mixed ascites, where paracentesis is always required for a definitive determination.

The same applies to the cytological pattern analysis and inflammatory process evaluation in ascites [35–41].

Our study used SAAG, a commonly used sum in this field, to divide the ascites cause. A study on several patients by Li et al. used a serum ascites cholesterol gradient (SACG) to determine the cause of ascites. SACG proved to be comparable to SAAG in the PH ascites group and more sensitive in differentiating the cause in the mixed ascites and non-PH ascites group but was not evaluated in our study [42].

Regarding the 2D-SWE measurement using MyLab Nine and its clinical applicability, our study shows about an 85% success rate in performing reliable measurements. This percentage is significantly lower than those reported in studies that evaluated liver cACLD cohorts (typically >90 or even 95% applicability) [14–16, 24, 43, 44]. There are several reasons for this finding. In our study, the elastographic measurement was performed exclusively in patients with ascites. According to some studies, ascites should not significantly affect the elastographic result quality [14–16, 24, 44]. On the other hand, according to Zhang et al., it had a significant effect on both reliability and measurement quality, showing a similar effect on the end result as ROI size [45], with which the authors of our study agree.

It is also important to mention the lack of a protocol for reliable 2D-SWE [22]. The protocol in our study was a sum of study recommendations and past findings in this area [18–22]. The ultrasound machine type (MyLab Nine) also had a significant impact because there is no official validation yet compared with commonly available devices on the market (Supersonic Imagine, France) [20]. The results between different measurement systems can vary between 6 and 12% [19]. A recently published study provided head to head 2D-SWE comparison between MyLab Nine and Supersonic Imagine in a cACLD population in order to assess liver fibrosis staging thresholds with very good proven correlation [46]. To our knowledge, our study is the first one to evaluate the MyLab Nine 2D-SWE measurement in the dACLD group. The most important causes of unreliable measurement were comparable to those defined to date; however, the influence of the measurements' depth, especially with concomitant overweight, bilirubin level, patient participation, and the heart function's influence on liver movement during each measurement, is more pronounced in patients with significant ascites [15, 18, 19, 21, 47–50].

Our study has important limitations, which we must consider when interpreting the results. Our study was conducted in one hospital center with a relatively small group of patients and retrospective data analysis. Given these findings, 2D shear wave liver elastography has potential in evaluating new-onset ascites but needs further validation in a larger prospective study. Patients in our cohort had strictly defined inclusion and exclusion

criteria due to the potential impact on the SAAG and 2D-SWE results. In our estimation, this decision may have excluded up to 30% of the total patients with newly onset ascites. Elastographic measurement was also performed by a single investigator and on an US apparatus that is not study validated, meaning that we do not have data on inter-observer reproducibility and on head to head comparison with the validated US soft-ware. In the group of patients with transudation resulting from PH and cirrhosis, we did not precisely define the liver cirrhosis etiology influence on the ascites formation and elastographic measurement. Recent data suggest that, especially in the group with metabolically-induced liver cirrhosis, ascites in a small group of patients develop in parallel or before the proposed HVPG threshold values [50]. Also, it is important to note, that our study does not provide direct 2D-SWE comparison between dACLD and patients with normal liver stiffness which can explain why no false negatives were detected when performing ROC analysis in the Group 1. As such, it can not be fully translated to the populations with low PH-related ascites prevalence. The presence of free fluid is likely to make the accuracy of elastography suboptimal. Since there is no comparative clinical study and no gold standard to demonstrate the elastography accuracy in patients with ascites, we have to carefully interpret the results even in the most reliable measurements cases. Finally, paracentesis is still a required diagnostic procedure when evaluating new-onset ascites and can probably paradoxically enhance 2D-SWE quality as already mentioned.

Conclusions

The results of our study underline the feasibility, and good applicability of a simple and readily available ultrasound method to assess the PH-related cause of newly onset ascites at the bedside. Also, 2D-SWE held the accuracy necessary for differentiating between transudative ascites in patients with PH related to liver cirrhosis and exudative ascites in patients with underlying peritoneal carcinomatosis. In our view, the routine use of this method during ultrasound examinations of patients with newly onset ascites should be attempted to enable quick, noninvasive identification.

Abbreviations

PH	Portal hypertension
SAAG	Serum ascites albumin gradient
CSPH	Clinically significant portal hypertension
cACLD	compensated advanced chronic liver disease
TE	Transient elastography
2D-SWE	2D shear wave elastography
pSWE	Point shear wave elastography
US	Ultrasound
CT	Computed tomography
AST	Aspartate aminotransferase

ALT	Alanine aminotransferase
ACLF	Acute on chronic liver failure
LSM	Liver stiffness measurement
IQR	Interquartile range
ROI	Region of interest
TJLB	Transjugular liver biopsy
HVPG	Hepatic vein pressure gradient
SD	Standard deviation
ROC	Receiver operating characteristic
dACLD	Decompensated advanced chronic liver disease
MRI	Magnetic resonance imaging
CRP	C-reactive protein
TNF-alpha	Tumor necrosis factor alpha
CEA	Carcinoembryonic antigen
IGF	Insulin-like growth factor.
VEGF	Vascular endothelial growth factor
SACG	serum ascites cholesterol gradient

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Authors' contributions

Conceptualization, A.H.; Methodology, A.H.; Validation, A.H., B.Š.; Formal Analysis, A.H.; Investigation, A.H.; Resources, A.H., B.Š.; Data Curation, A.H.; Writing – Original Draft Preparation, A.H.; Writing – Review & Editing, B.Š.; Visualization, A.H.; Supervision, B.Š.; Project Administration, A.H., B.Š.; Funding Acquisition, not applicable.

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Availability of data and materials

Manuscript data and materials are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

We obtained the approval of the regional General Hospital Celje Ethics Commission and performed a retrospective analysis of the prospectively collected data. Informed written consent was obtained from each patient included in the study. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and Istanbul.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Tsochatzis TA, Bosch J, Burroughs AK. Liver cirrhosis. *Lancet*. 2014;383:1749–61.
2. Hou W, Sanyal AJ. Ascites: Diagnosis and Management. *Med Clin North Am*. 2009;93:801–17.
3. Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal

- Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;74:1014–48.
4. Gordon FD. Ascites. *Clin Liver Dis*. 2012;16:285–99.
5. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the Management of Ascites, Spontaneous Bacterial Peritonitis, and Hepatorenal Syndrome in Cirrhosis. *J Hepatol*. 2010;53:397–417.
6. Turco L, Garcia-Tsao G. Portal Hypertension. *Clin Liv Dis*. 2019;23:573–87.
7. Oey RC, van Buuren HR, de Man RA. The diagnostic work-up in patients with ascites: current guidelines and future prospects. *Neth J Med*. 2016;74:330–5.
8. Berzigotti A, Abraldes JG, Tandon P, et al. Ultrasonographic Evaluation of Liver Surface and Transient Elastography in Clinically Doubtful Cirrhosis. *J Hepatol*. 2010;52:846–53.
9. Berzigotti A, Ashkenazi E, Reverter E, et al. Non-invasive Diagnostic and Prognostic Evaluation of Liver Cirrhosis and Portal Hypertension. *Dis Markers*. 2011;31:129–38.
10. de Franchis R, Bosch J, Faculty BVII. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol*. 2022;76:959–74.
11. Thiele M, Hugger MB, Kim Y, et al. 2D shear wave liver elastography by Aixplorer to detect portal hypertension in cirrhosis: An individual patient data meta-analysis. *Liver Int*. 2020;40:1435–46.
12. Grgurevic I, Madir A, Trkulja V, et al. Assessment of clinically significant portal hypertension by two-dimensional shear wave elastography. *Eur J Clin Investig*. 2022;18:e13750.
13. Thiele M, Madsen BS, Procopet B, et al. Reliability Criteria for Liver Stiffness Measurements With Real-Time 2D Shear Wave Elastography in Different Clinical Scenarios of Chronic Liver Disease. *Ultraschall Med*. 2017;38:648–54.
14. Matos J, Paparo F, Bacigalupo L, et al. Noninvasive Liver Fibrosis Assessment in Chronic Viral Hepatitis C: Agreement Among 1D Transient Elastography, 2D Shear Wave Elastography, and Magnetic Resonance Elastography. *Abdom Radiol (NY)*. 2019;44:4011–21.
15. Lee SM, Lee JM, Kang HJ, et al. Liver Fibrosis Staging With a New 2D-shear Wave Elastography Using Comb-Push Technique: Applicability, Reproducibility, and Diagnostic Performance. *PLoS One*. 2017;12:e0177264.
16. Kohlhaas A, Durango E, Millonig G, et al. Transient elastography with the XL probe rapidly identifies patients with nonhepatic ascites. *Hepat Med*. 2012;4:11–8.
17. Bota S, Sporea I, Sirlu R, et al. Value of acoustic radiation force impulse elastography for the assessment of ascites syndrome. *World J Radiol*. 2012;28:205–9.
18. Ferraioli G, Wong VWS, Castera L, et al. Liver Ultrasound Elastography: An Update to the World Federation for Ultrasound in Medicine and Biology Guidelines and Recommendations. *Ultrasound Med Biol*. 2018;44:2419–40.
19. Dietrich CF, Bamber J, Berzigotti A, et al. EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Long Version). *Ultraschall Med*. 2017;38:e16–47.
20. Procopet B, Berzigotti A. Diagnosis of Cirrhosis and Portal Hypertension: Imaging, Non-Invasive Markers of Fibrosis and Liver Biopsy. *Gastroenterol Rep (Oxf)*. 2017;5:79–89.
21. Dubinsky TJ, Shah HU, Erpelding TN, et al. Propagation Imaging in the Demonstration of Common Shear Wave Artifacts. *J Ultrasound Med*. 2019;38:1611–6.
22. Procopet B, Berzigotti A, Abraldes JG, et al. Real-time shear-wave elastography: applicability, reliability and accuracy for clinically significant portal hypertension. *J Hepatol*. 2015;62:1068–75.
23. Kim DW, Suh CH, Kim KW, et al. Technical Performance of Two-Dimensional Shear Wave Elastography for Measuring Liver Stiffness: A Systematic Review and Meta-Analysis. *Korean J Radiol*. 2019;20:880–93.
24. Cho YS, Lim S, Kim Y, et al. Abdominal Wall Thickness Affects Liver Stiffness Measurements by 2-D Shear Wave Elastography in Patients with Chronic Liver Disease. *Ultrasound Med Biol*. 2019;45:2697–703.
25. Salman MA, Salman AA, Hamdy A, et al. Predictive value of omental thickness on ultrasonography for diagnosis of unexplained ascites, an Egyptian centre study. *Asian J Surg*. 2020;43:13–9.
26. Getnet W, Kebede T, Atinafu A, et al. The Value of Ultrasound in Characterizing and Determining the Etiology of Ascites. *Ethiop J Health Sci*. 2020;29:383–90.

27. Çekiç B, Erdem Toslak I, Şahintürk Y, et al. Differentiating Transudative From Exudative Ascites Using Quantitative B-Mode Gray-Scale Ultrasound Histogram. *Am J Roentgenol.* 2017;209:313–9.
28. Risson JR, Macovei I, Looock M, et al. Cirrhotic and malignant ascites: Differential CT diagnosis. *Diagn Interv Imaging.* 2012;93:365–70.
29. Zafar I, Majeed AI, Asad MW, et al. Diagnostic Accuracy of Different Computed Tomography Signs for Differentiating Between Malignant and Cirrhotic Ascites Keeping Ascitic Fluid Cytology as Gold Standard. *Cureus.* 2021;13(12):e20254.
30. Ştefan PA, Lebovici A, Csutak C, et al. Computed Tomography in the Diagnosis of Ascites: The Role of Fluid Attenuation Values. *Curr Med Imaging.* 2021;7:390–5.
31. Csutak C, Ştefan PA, Lupean RA, et al. Computed tomography in the diagnosis of intraperitoneal effusions: The role of texture analysis. *Bosn J Basic Med Sci.* 2021;1(21):488–94.
32. Ştefan PA, Csutak C, Lebovici A, et al. Diffusion-Weighted Magnetic Resonance Imaging as a Noninvasive Parameter for Differentiating Benign and Malignant Intraperitoneal Collection. *Medicina (Kaunas).* 2020;1(56):217.
33. Ştefan PA, Puscas ME, Csutak C, et al. The utility of texture-based classification of different types of ascites on magnetic resonance. *J BUON.* 2020;25:1237–44.
34. Bonatti M, Valletta R, Zamboni GA, et al. Ascites relative enhancement during hepatobiliary phase after Gd-BOPTA administration: a new promising tool for characterising abdominal free fluid of unknown origin. *Eur Radiol.* 2019;29:2830–6.
35. Werner B, Warton K, Ford CE. Transcending Blood-Opportunities for Alternate Liquid Biopsies in Oncology. *Cancers (Basel).* 2022;3(14):1309.
36. Abdel-Razik A, Eldars W, Elhelaly R, et al. C-reactive protein and insulin-like growth factor-1 in differential diagnosis of ascites. *J Gastroenterol Hepatol.* 2016;31:1868–73.
37. Abdel-Razik A, Mousa N, Elalfy H, et al. A Novel Combination of C-Reactive Protein and Vascular Endothelial Growth Factor in Differential Diagnosis of Ascites. *J Gastrointest Cancer.* 2017;48:50–7.
38. Han N, Sun X, Qin C, et al. Value of 18 F-FDG PET/CT Combined With Tumor Markers in the Evaluation of Ascites. *Am J Roentgenol.* 2018;210:1155–63.
39. Liu F, Kong X, Dou Q, et al. Evaluation of tumor markers for the differential diagnosis of benign and malignant ascites. *Ann Hepatol.* 2014;13:357–63.
40. Buyukberber M, Koruk M, Savas MC, et al. Leptin levels in the differential diagnosis between benign and malignant ascites. *World J Gastroenterol.* 2007;21(13):398–402.
41. Yuksel I, Karahmet F, Coskun Y, et al. Significance of serum and ascitic fluid C-reactive protein in differential diagnosis of benign and malignant ascites. *Dig Dis Sci.* 2014;59:2588–93.
42. Du L, Zhu S, Lu Z, et al. Ascitic cholesterol is superior to serum-ascites albumin gradient in the detection of non-portal hypertensive ascites and the diagnosis of mixed ascites. *Aliment Pharmacol Ther.* 2019;49:91–8.
43. Lee JH, Lee SM, Yoon JH, et al. Impact of respiratory motion on liver stiffness measurements according to different shear wave elastography techniques and region of interest methods: a phantom study. *Ultrasonography.* 2021;40:103–14.
44. Hirooka M, Koizumi Y, Hiasa Y, et al. Hepatic elasticity in patients with ascites: evaluation with real-time tissue elastography. *Am J Roentgenol.* 2011;196:W766–71.
45. Zhang XQ, Zeng J, Jin JY, et al. Shear-Wave Dispersion Slope of the Liver: Effect of Study Protocol and Ascites on the Measurement Applicability. *Ultrasound Med Biol.* 2022;48:59–67.
46. Garcovich M, Faccia M, Di Stasio E, et al. Correlation Between QElaXto Techniques and Supersonic Imagine for Liver Stiffness Quantification in Chronic Liver Disease. *J Ultrasound Med.* 2022;41:877–86.
47. Yoo J, Lee JM, Joo I, et al. Assessment of liver fibrosis using 2-dimensional shear wave elastography: a prospective study of intra- and inter-observer repeatability and comparison with point shear wave elastography. *Ultrasonography.* 2020;39:52–9.
48. Kim TY, Jeong WK, Sohn JH, et al. Evaluation of portal hypertension by real-time shear wave elastography in cirrhotic patients. *Liver Int.* 2015;35:2416–24.
49. Rodrigues SG, Montani M, Guixé-Muntet S, et al. Patients With Signs of Advanced Liver Disease and Clinically Significant Portal Hypertension Do Not Necessarily Have Cirrhosis. *Clin Gastroenterol Hepatol.* 2019;17:2101–2109.e1.
50. Mendoza YP, Rodrigues SG, Delgado MG, et al. Inflammatory activity affects the accuracy of liver stiffness measurement by transient elastography but not by two-dimensional shear wave elastography in non-alcoholic fatty liver disease. *Liver Int.* 2022;42:102–11.

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